EACS 2019 – Abstract Book

Women, pregnancy and children – pharmacokinetics, injectables, endocrinology

PS1/1

Outcomes for women in phase 3 trials of long-acting cabotegravir + rilpivirine: pooled ATLAS and FLAIR week 48 results

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Purpose: Women are under-represented in clinical trials. Monthly Long Acting (LA) CAB+RPV is non-inferior to current antiretroviral therapy (CAR) [1,2]. We describe the efficacy, safety and patient satisfaction in women participants.
Method: Pooled analysis was performed based on HIV-1 RNA≥50 c/mL at W48 (Snapshot; primary endpoint), HIV-1 RNA<50 c/mL, safety assessments and CAR treatment satisfaction (HIV-Treatment Satisfaction Questionnaire). Sub-group analysis by sex at birth was pre-planned.
Results: Across both studies, 162/591 (27.4%) and 168/591 (28.4%) women were randomized to LA and CAR arms, respectively. At baseline, 27.2% (44/162, LA) and 28.6% (48/168, CAR) of women had a BMI≥30 kg/m^2 compared to 13.0% of men. At W48, 5/162 (3.1%) and 1/168 (0.6%) of women in LA and CAR arms had HIV-1 RNA≥50 c/mL (difference in proportions [95% CI] 2.49 [−0.64, 6.54]), and 150/162 (92.6%) and 159/168 (94.6%) had HIV-1 RNA<50 c/mL (difference in proportions [95% CI] −2.05 [−7.87, 3.46]). These efficacy rates were similar to those observed in men. Seven (1.2%, LA) and seven (1.2%, CAR) confirmed virologic failures (CVFs) occurred in each arm, with 5/7 (LA) and 2/7 (CAR) arising in women. There were no significant differences observed between women and men in AEs, injection site pain or withdrawals. Of female responders at W44, 97% (96/99) in ATLAS and 100% (62/62) in FLAIR were "more satisfied" or "much more satisfied" to continue with LA (Question 10 HIVTSQs).
Conclusion: Monthly CAB+RPV LA was noninferior to daily oral three-drug regimens and demonstrated high efficacy rates in women. The regimen was generally well tolerated with high satisfaction rates, infrequent virologic non-response and low rates of AE/ISR-related treatment discontinuations. These results support the therapeutic potential of once-monthly CAB+RPV LA in women.

Table 1: Summary of Pooled ATLAS[1] and FLAIR[2] Data by Gender

	CAB + RPV LA N (%)			CAR N (%)		
	Women	Men	Total	Women	Men	Total
Sex at birth	162 (27.4)	429 (72.6)	591 (100)	168 (28.4)	423 (71.6)	591 (100)
BMI >30 (kg/m²)	44 (27.2)	56 (13.1)	100 (16.9)	48 (28.6)	55 (13.0)	103 (17.4)
HIV-1 RNA ≥50c/mL at W48	5 (3.1)	6 (1.4)	11 (1.9)	1 (0.6)	9 (2.1)	10 (1.7)
HIV-1 RNA <50c/mL at W48	150 (92.6)	400 (93.2)	550 (93.1)	159 (94.6)	399 (94.3)	558 (94.4)
Confirmed Virologic Failures	5 (3.1) [3]	2 (0.5)	7 (1.2)	2 (1.2)	5 (1.2)	7 (1.2)
Adverse Events (AE)						
Adverse Events	148 (91.4)	413 (96.2)	561 (94.9)	122 (72.6)	323 (76.4)	445 (75.3)
Severe Adverse Events	6 (3.7)	25 (5.8)	31 (5.2)	9 (5.4)	17 (4.0)	26 (4.4)
Drug-related Adverse Event	126 (77.8)	365 (85.1)	491 (83.1)	6 (3.6)	30 (7.1)	36 (6.1)
Injection Site Pain	107 (66.0)	351 (81.8)	458 (77.5)	NA	NA	NA
AE Leading to Withdrawal	4 (2.5)	18 (4.2)	22 (3.7)	4 (2.4)	5 (1.2)	9 (1.5)

1. Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1475;
2. Orkin C, et al. CROI 2019; Seattle, WA. Abstract 3947.
3. One participant in FLAIR had oral CAB/RPV dosing interrupted due to a false-positive pregnancy test and upon re-initiation of oral therapy, had suspected VF that was confirmed.

PS1/2

Dolutegravir (DTG) use during pregnancy and birth outcomes: data from the Antiretroviral Pregnancy Registry (APR)

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Purpose: To describe maternal demographics, pregnancy and neonatal outcomes among infants with prenatal exposure to DTG using data from the APR.
Method: The APR is a voluntary, international, prospective exposure-registration cohort study, monitoring for early warning signals of major teratogenic effects of ART and collecting data on pregnancy and neonatal outcomes. Descriptive analysis with frequency tabulation of pregnancy and neonatal outcomes is reported.
Results: Through 31 January 2019, 522 pregnancies with exposure to DTG were prospectively reported to APR with 281 periconception exposures, 62 later during 1st trimester, 117 during 2nd trimester and 62 during 3rd trimester. Median age at conception was 29 years and 80.8% were from the United States. At enrolment, 45.4% had CD4 count≥500 cells/μL, 32.6% had 200–499 cells/μL, 14.2% had<200 cells/μL and 7.9% unknown.
The 522 DTG exposed pregnancies resulted in 537 outcomes: 491 (91.4%) live births (15 twin births), 7 (1.3%) stillbirths, 15 (2.8%) induced abortions, and 24 (4.5%) spontaneous abortions. Among live births, 17 (3.5%) reported birth

Table 1. Birth Defect Outcomes of Pregnant Women Exposed to DTG Prospective Registry Cases with Follow-up Closed through 31 January 2019

	Total Outcomes N	Live Births	Defect Cases*	CNS Defect (1,2)	NTD Cases (1)	Encephalocele (2)
Any InSTI Exposure [3]	1487	1362	43	4	1	0
Periconception	834	725	21	3	1	0
Later First Trimester	135	129	2	0	0	0
Second/Third Trimester	516	506	20	1	0	0
Any Dolutegravir Exposure [3]	537	491	17	4	1	0
Periconception	289	248	9	2	1	0
Later First Trimester	62	59	2	1	0	0
Second/Third Trimester	186	184	6	1	0	0

Note: ART = antiretroviral therapy; CNS = central nervous system; NTD = neural tube defect. Note: Periconception is defined as any exposure 2 weeks prior to conception through 28 days gestational age; Later First Trimester is defined as any exposure in the first trimester that begins after 28 days gestational age. [1] NTD cases are a subset of CNS defects and are counted in both columns. [2] Encephalocele cases are a subset of CNS defects and are counted in both columns. [3] Includes cases with missing trimester of exposure. * Comparators for population expected rate of defects (2.72 - 4.17/ 100 live births from MACDP and TBDR respectively). MACDP =Metropolitan Atlanta Congenital Defects Program; TBDR=Texas Birth Defects Registry

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Table 2. Neonatal Outcomes (among Singleton, Live Births without Birth Defects)

Neonatal Outcomes	Overall DTG Exposed	Earliest exposure to DTG - Periconception	Earliest exposure to DTG - Later 1st Trimester	Earliest exposure to DTG - 2nd/3rd Trimester
Total Outcomes, N	447	226	57	164
Gestational Age* >= 37 weeks	398 (89.0%)	200 (88.5%)	48 (84.2%)	150 (91.5%)
Gestational Age* < 37 weeks (Preterm)	48 (10.7%)	26 (11.5%)	9 (15.8%)	13 (7.9%)
Gestational Age* Missing	1 (0.2%)	0	0	1 (0.6%)
Birth Weight* >= 2500 grams	382 (85.5%)	190 (84.1%)	49 (86.0%)	143 (87.2%)
Birth Weight* < 2500 grams (LBW)	54 (12.1%)	29 (12.8%)	8 (14.0%)	17 (10.4%)
Birth Weight* < 1500 grams (very LBW)	10 (2.2%)	5 (2.2%)	2 (3.5%)	3 (1.8%)
Birth Weight* Missing	11 (2.5%)	7 (3.1%)	0	4 (2.4%)

Note: DTG = Dolutegravir; LBW = Low Birth Weight. *Among singleton, live births without birth defects. Note: Periconception is defined as any exposure 2 weeks prior to conception through 28 days gestational age; Later First Trimester is defined as any exposure in the first trimester that begins after 28 days gestational age; Second Trimester begins at 14 weeks gestational age and Third Trimester begins at 28 weeks gestational age.

defects. For 1st trimester exposures, overall defect prevalence was 3.58% (11/307), 95% CI: 1.8–6.32. One neural tube defect (NTD) case of anencephaly with periconception DTG exposure was reported.
Among the 447 singleton, live births without birth defects, 48 (10.7%) were preterm (< 37 weeks of gestation); 54 (12.1%) had birth weight<2500 grams, and 10 (2.2%)<1500 grams.
Conclusion: APR data do not demonstrate an increased risk of overall birth defects with DTG use above the population expected rate of defects (2.72 - 4.17/ 100 live births from MACDP and TBDR respectively). The number of periconception outcomes is currently insufficient to refute or confirm an association of DTG with NTD. The Registry continues to closely monitor birth defects in pregnancies exposed to DTG and other integrase inhibitors, including NTDs with periconception exposure.

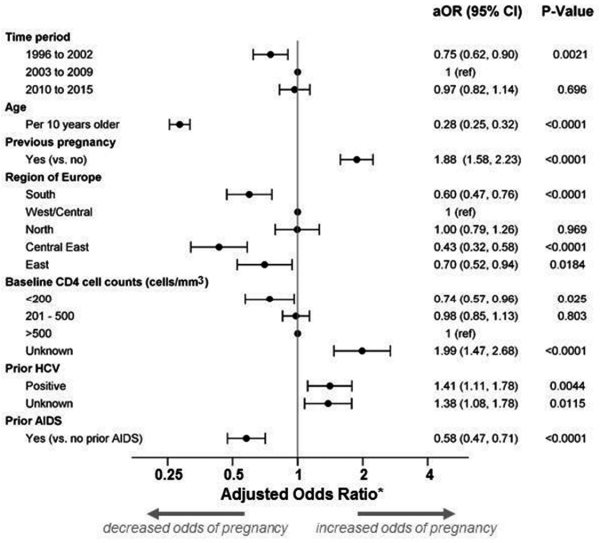
PS1/3

Prevalence and outcomes of pregnancies over a 20 year period: the EuroSIDA study

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Objectives: From a public health perspective it is important to evaluate time trends in prevalence and outcomes of pregnancies among HIV-positive women to ascertain equal access to care.
Methods: The EuroSIDA study collected pregnancy information 1996–2015 as annual cross-sectional audits of pregnancy and outcomes. Odds of pregnancy were modelled using logistic regression with generalized estimating equations accounting for repeated pregnancy information within women.
Results: Of 5535 women aged 16–50 years, 4217 (76.2%) had pregnancy information available. There were 1315 pregnancies reported in 912 women (21.6%). Of these, 319 (24.3%) occurred in 1996–2002, 576 (43.8%) in 2003–2009 and 420 (31.9%) in 2010–2015. The proportion of women with pregnancies were 28.1% (321/1143) in East Europe, 24.5% (146/596) in North, 19.8% (140/706) in West/Central, 19.3% (110/569) in Central Eastern and 16.2% (195/1203) in South. The proportion of women with a pregnancy decreased from 449(17.3%) in 2003–2009 to 341 (12.6%) in 2010–2015, consistently across all regions. After multivariable adjustment, the odds of pregnancy were lower in 1996–2002, in South, Central-East and East Europe compared to West/Central Europe, in older women, in those with low CD4 counts or previously diagnosed with an AIDS-defining condition, and higher in those with a previous pregnancy or who were HCV positive (Figure).



* Adjusted for all variables shown and additionally for ethnic group, smoking status, BMI, baseline viral load, time since HIV diagnosis, prior use of ART and HBV status

Adjusted odds of pregnancy

Pregnancy outcomes were reported for 999 pregnancies in 1996–2014, with 690 live births (69%), of which 342 (49.5%) were HIV-negative, 23 (3.3%) HIV-positive and 325 (47.1%) of unknown HIV status. There were 7 stillbirths, 103 spontaneous and 199 medical abortions.
Conclusions: Pregnancy was reported for one in five women in EuroSIDA with a significant increase after 2002 when more effective cART became available. Substantial differences were seen between regions with higher prevalence in Eastern Europe, mainly due to differences in age and CD4 counts. Further surveillance of rates and outcomes of pregnancies among HIV-positive women in Europe is warranted.

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PS1/4

Does menopause affect treatment response in HIV-infected women? A multicenter cohort in Spain

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Purpose: The aim of this study was to compare the immunovirological response at 48 and 96 weeks from antiretroviral therapy (ART) initiation among premenopausal and postmenopausal HIV-infected women aged 45–60 years from the cohort of the Spanish HIV/AIDS Research Network (CoRIS).
Method: Linear regression was used to assess mean differences in CD4 T-cell count and CD4% changes and logistic regression to estimate odds ratios (ORs) for CD4/CD8 ratio normalization (≥1.0), achievement of Multiple T-cell marker recovery (MTMR - CD4 count>500 + CD4%>=29% + CD4/CD8 ratio>=1) and virological suppression from ART initiation.
Results: Among 254 women included, 173 (68%) were premenopausal at ART initiation. Tenofovir disoproxil fumarate (TDF) + Emtricitabine (FTC) + Efavirenz (EFV) was the most frequent initial regimen, prescribed in 52 (30%) premenopausal and 23 (28%) postmenopausal women. Initial treatment regimens did not differ significantly between both groups.
At ART initiation, there were no significant differences between premenopausal and postmenopausal women in CD4 counts (208 vs 183 cell/mm^3; p=0.584), CD4 percentages (16.6% vs 15.0%; p=0.553) and CD4/CD8 ratio (0.30 vs 0.26; p=0.768), but premenopausal women had significantly lower viral loads than postmenopausal ones (4.7 vs 5.1 log copies/mL; p=0.021)
Compared to premenopausal women, a higher proportion of postmenopausal women achieved a CD4/CD8 ratio≥1 and MTMR at week 48; these differences lost statistical significance at week 96. There were no significant differences in CD4 count changes from ART initiation (absolute and percentage), nor viral load suppression, between both groups (table 1).
Conclusion: CD4/CD8 ratio≥1 recovery and MTMR were better among postmenopausal women at 48 weeks of follow-up, although these differences were not significant at week 96, probably due to a lower number of women. Menopause did not have a negative impact on CD4 change from ART initiation or viral suppression.

			Crude		Adjusted *	
CD4 count change		**N**	**Mean difference (95% CI)**	**p**	**Mean difference (95% CI)**	**p**
Week 48	Pre-meno	161	0	0.290	0	0.538
	Meno	77	29.64 (-21.35; 68.63)		13.27 (-30.40; 56.94)	
Week 96	Pre-meno	160	0	0.052	0	0.232
	Meno	73	55.77 (-0.40; 111.95)		35.43 (-23.91;94.78)	
CD4 percentage change			**Mean diff (95% IC)**	**p**	**Mean diff (95% IC)**	**p**
Week 48	Pre-meno	159	0	0.145	0	0.045
	Meno	75	-1.48 (-3.51; 0.54)		-2.29 (-4.41; -0.05)	
Week 96	Pre-meno	158	0	0.506	0	0.100
	Meno	72	-0.76 (-3.09; 1.56)		-2.04 (4.58; 0.42)	
CD4/CD8 ratio ≥1,0			**OR (95% IC)**	**p**	**OR (95% IC)**	**p**
Week 48	Pre-meno	94	1	0.039	1	<0.001
	Meno	55	1.92 (1.05; 3.53)		3.69 (1.91; 7.11)	
Week 96	Pre-meno	99	1	0.689	1	0.622
	Meno	51	0.80 (0.28; 2.32)		0.70 (0.17; 2.91)	
MTMR achievement			**OR (95% IC)**	**p**	**OR (95% IC)**	**p**
Week 48	Pre-meno	144	1	0.245	1	0.013
	Meno	73	1.65 (0.71; 3.83)		4.27 (1.35; 13.49)	
Week 96	Pre-meno	142	1	0.576	1	0.594
	Meno	65	1.34 (0.48; 3.70)		1.52 (0.33; 7.06)	
Viral Load suppression			**OR (95% IC)**	**p**	**OR (95% IC)**	**p**
Week 48	Pre-meno	165	1	0.967	1	0.642
	Meno	80	1.02 (0.38; 2.73)		0.75 (0.23; 2.47)	
Week 96	Pre-meno	159	1	0.125	1	0.914
	Meno	76	2.16 (0.81; 5.78)		1.76 (0.59; 5.26)	

*Adjusted for baseline (at ART initiation) CD4 count, baseline CD4%, baseline CD4/CD8, baseline viral load, calendar period of ART initiation

Immunological and virological response after ART initiation among pre-menopausal and menopausal women

PS1/5

Discontinuation of neonatal postexposure prophylaxis in infants born to HIV-infected mothers with suppressed plasma viral load: safety and implementation of the new Swiss recommendations

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Purpose: New recommendations for prevention of HIV mother-to-child transmission (MTCT) have been issued by the Swiss Federal Office of Public Health (FOPH) in January 2016. For the first time in a high-income country neonatal post-exposure prophylaxis (neoPEP) is no longer recommended in HIV exposed newborns if maternal HIV plasma viral load (pVL) is fully suppressed in the last trimester. We aimed to investigate the implementation and safety of the new national recommendations in Switzerland.
Method: We evaluated data from the Swiss Mother and Child HIV Cohort Study (MoCHiV) and the linked Swiss HIV Cohort Study (SHCS) database. Children born between 2010 and 2018 were included if information on maternal pVL in the last trimester was available. We compared the frequency of neoPEP in infants born before and after the introduction of the recommendations. HIV-status of the children was assessed by PCR at 6 months of Age.
Results: Maternal HIV pVL in the last trimester was <50 copies/mL in 363 of 383 (94.8%) children born during the study period. Of these, 264 of 267 (98.9%) children born before the guideline change in 2016 received neoPEP compared to 12 of 96 (12.5%) born afterwards (p-exact<0.001, see Figure 1). NeoPEP was administered to all 20 infants with detectable maternal HIV pVL in the last trimester, including 5 infants born 2016 onwards. None of the 87 children that didn't receive neoPEP was infected with HIV.
Conclusion: The new recommendations have been implemented rapidly in Switzerland. This indicates that treating physicians were well-informed and did accept the arguments provided. NeoPEP exposure was reduced by 86.4%, while no MTCT of HIV was observed. Our data suggests that neoPEP recommendations of other high-income countries should be reconsidered.

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Social and implementation science

PS2/1

Empowering home visiting nurses as leaders in the response to the HIV epidemic in Central Asia

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Purpose: In Central Asia, people living with HIV (PLHIV) on antiretroviral treatment (ART), face many obstacles to retention in care and treatment. These include stigma, discrimination, lack of support from relatives, and opioid and alcohol abuse. Considering the need to reach the 90–90–90 goals, home-based care has the potential to reduce many of these barriers.
Method: In January 2018, ICAP launched "SUPPORT4HEALTH," an enhanced nurse-led home-based intervention to improve adherence and retention of PLHIV in HIV care and treatment. Implemented in three countries (Kazakhstan, Kyrgyzstan, Tajikistan), the intervention focused on adult PLHIV who were newly initiated/restarted on ART and PLHIV on ART for six months or more with viral load >1000 copies/mL. The intervention includes eight home-visits and nine phone calls over a six months period and is provided in addition to the standard of care. During every visit nurse completes all information about performed activities into mobile application e-Nurse. ICAP uses this application for home visiting nurses' mentoring and monitoring.
Results: This structured and systematized 6-month intervention using nursing home visits is now implemented at 28 sites in three countries and includes 56 home visiting nurses. During the home visits, the nurses conduct clinical TB screening, drug and alcohol surveys, pill counts, adherence assessments, counseling of patients' partners and conversations with relatives to decrease stigma and discrimination. As of June 1, 2019, 3257 patients signed informed consent and were enrolled into the model. Among them, 1867 patients completed the model and 1530 (82%) achieved viral load suppression (<1000 copies/mL).
Conclusion: Empowering home visiting nurses as leaders in the response to the HIV epidemic contributes to establishing trusting relationships and specific support for patients with a variety of complex health needs to improve adherence among ART patients. Improved adherence is improving health care outcomes for patients and their communities.

PS2/2

Extension of HIV treatment coverage in Ukraine through advocating access of dolutegravir generics to market

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Purpose: High price of the antiretrovirals (ARV) of the first line is deemed to be among the main barriers to achieve the 90–90–90 global targets for the low-and middle-income countries. In its recent recommendations, the World Health Organization (WHO) recommended dolutegravir (DTG) as the main first-line and second-line treatment. Ensuring access of generic medicines to market leads to decrease of medicines price and, respectfully, secures increase in HIV treatment coverage.
Method: In 2016, price for the branded DTG for the Eastern European countries constituted more than 200 USD per monthly course. To decrease the price, All Ukrainian Network of People living with HIV (100 Percent Life) negotiated for extension of the license agreement for DTG for Ukraine. Upon receiving the license, 100 Percent Life facilitated the process of DTG inclusion into the procurement list of medicines. In 2017, 100 Percent Life held meetings with key stakeholders, which resulted in registration of the first generic DTG.
Results: In 2017, after the generic DTG entered the market the DTG price for monthly course decreased from more than 200 USD to 5 USD. Considering that 21 patients received ARV regimens with DTG in 2017 the state budget savings for annual course constituted 2730 USD. Decrease in prices enabled optimization of the ARV regimens in terms of scaling up towards DTG in accordance with WHO's recommendations. As of June, 2019 Ukraine procured DTG regimens for 15218 patients. Procurement of the generic DTG comparing with brands enabled savings of 1978340 USD.
Conclusion: The 100 Percent Life's project demonstrates possibility to extend HIV treatment coverage by advocating access of DTG generics to the market. Funds allocated as a result of budget savings were used for procurement of additional prophylaxis, support and care services for key-groups as envisaged within the transition plan from the donors funding.

PS2/3

Assisted partner notification services to improve HIV case identification and linkage to antiretroviral treatment for sexual contacts of male and female sex workers in low-resource setting: findings from a key population program in Kenya

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Purpose: Female and male sex workers (FSW and MSW) continue to report high prevalence of HIV and contribute significantly to new infections in Sub-Saharan Africa. Currently, 29.3% for FSW and 18.2% of MSM/MSW are positive compared to 5% general population. A 2009 modes of transmission study indicated that 14% of all new infections in Kenya are directly attributable to sex workers. Identifying sexual contacts of sex workers is key in improving overall HIV case identification and linkage to treatment. Assisted partner notification (aPNS) is effective for increasing HIV case identification among discordant couples but its effectiveness in identifying contacts of FSW and MSW is unknown.
Methods: FSW and MSW followed through a key population (KP) HIV prevention program in Mombasa, Kenya were tested at five specialized sex worker clinics (drop-in centers). FSW and MSW who tested positive were offered aPNS; those who agreed were requested to provide contacts of sexual partners in the recent six months. Clinical staff at drop-in centers contacted the partners on phone and offered HIV testing either at the drop-in centers or at other locations.
Results: Between April and June 2019, 587 HIV positive FSW and 166 MSW were identified. aPNS was offered to 250 FSW and 143 MSW. 98 FSW (39%) and 133 MSW (93%) index partners accepted aPNS and provided contacts for 162 partners for FSW and 227 for MSW. Among the contacts 36 were known HIV positive and 28 (14%) were newly identified positive.
Conclusion: aPNS holds potential to increase HIV testing for sexual contacts of sex workers who are at high risks of HIV in African settings. aPNS also provides a targeted approach with relatively high yields and is more cost-effective compared to mass testing, especially in low resource settings that experience occasional HIV test kit shortage.

Weight gain under integrase inhibitors: is this real?

PS3/1

Antiretroviral therapy and body weight in the START (Strategic Timing of Antiretroviral Treatment) trial

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Purpose: Obesity and HIV-infection are risk factors for cardiovascular disease making it important to understand how antiretroviral therapy (ART) affects body weight. Contrary to other ART naïve trials, START suggested that ART was associated with lower weight gain (JAHA 2017, doi:10.1161). We explore possible predisposing factors of weight changes in START.
Method: In START, HIV-positive adults with CD4 counts>500 cells/μL were randomly assigned to initiate ART immediately or defer (until CD4<350 cells/μL or progression to AIDS). Weight was measured at baseline and follow-up visits. The mean treatment difference (immediate-deferred) in percent change

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Figure 1
Mean Percent Change in Weight, by Baseline HIV RNA (copies/mL)

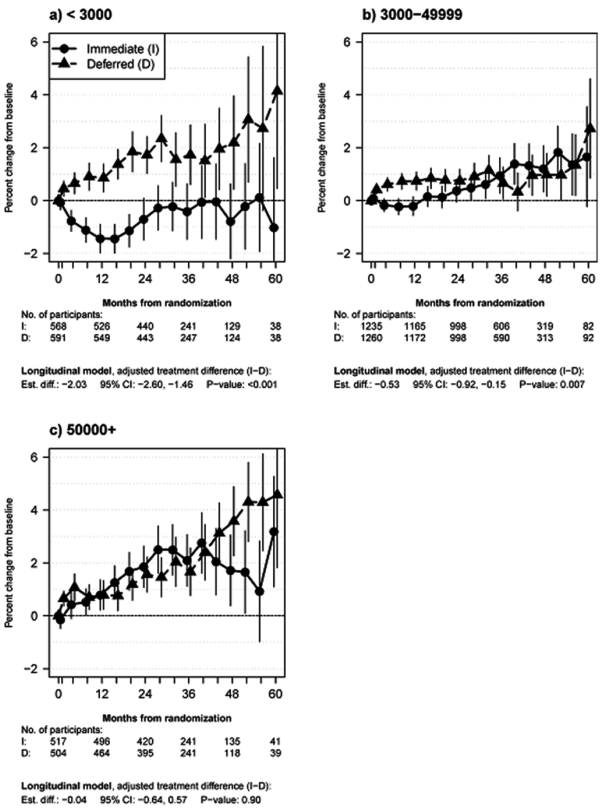


Figure 2
Difference Between Treatment Groups in Mean Percent Weight Change from Baseline, Within Subgroups

		Mean Percent Weight Change from Baseline (95% CI)*				
Baseline Subgroup	**N in Grp(%)**	**Immediate**	**Deferred**	**Immediate-Deferred Difference**	**P-value***	**Subgroup by Treatment Interaction P-value****
Age (years)						0.17
<30	1322 (28.2)	1.80 (1.33, 2.26)	2.93 (2.47, 3.39)	-1.13 (-1.67, -0.60)	<0.001	
30-49	2809 (60.0)	1.16 (0.80, 1.52)	1.79 (1.43, 2.15)	-0.63 (-1.00, -0.26)	<0.001	
50+	553 (11.8)	0.71 (0.07, 1.34)	1.37 (0.75, 2.00)	-0.67 (-1.49, 0.16)	0.11	
Gender						0.048
Male	3427 (73.2)	1.14 (0.84, 1.43)	1.76 (1.46, 2.05)	-0.62 (-0.95, -0.29)	<0.001	
Female	1257 (26.8)	1.17 (0.73, 1.61)	2.44 (2.01, 2.88)	-1.27 (-1.82, -0.72)	<0.001	
Geographic Region						0.019
High income (USA/Europe/Australis)	2155 (46.0)	1.73 (1.36, 2.10)	2.15 (1.78, 2.52)	-0.43 (-0.84, -0.01)	0.046	
Mid-low income (Asia/Africa/Latin America)	2529 (54.0)	0.87 (0.53, 1.20)	1.98 (1.64, 2.31)	-1.11 (-1.50, -0.72)	<0.001	
CD4 (cells/μL)						<0.001
<600	1474 (31.5)	1.51 (1.07, 1.94)	1.78 (1.34, 2.21)	-0.27 (-0.77, 0.24)	0.30	
600-800	2275 (48.6)	1.31 (0.93, 1.69)	1.98 (1.60, 2.36)	-0.67 (-1.08, -0.27)	0.001	
>800	935 (20.0)	0.83 (0.31, 1.36)	2.75 (2.23, 3.26)	-1.91 (-2.55, -1.28)	<0.001	
HIV RNA (copies/mL)						<0.001
<3000	1159 (24.8)	0.37 (-0.11, 0.85)	2.40 (1.93, 2.87)	-2.03 (-2.60, -1.46)	<0.001	
3000-49999	2495 (53.4)	1.29 (0.91, 1.66)	1.82 (1.45, 2.19)	-0.53 (-0.92, -0.15)	0.007	
50000+	1021 (21.8)	2.32 (1.81, 2.82)	2.36 (1.85, 2.86)	-0.04 (-0.64, 0.57)	0.90	
Pre-specified ART Class***						0.06
PI	815 (17.4)	2.00 (1.44, 2.55)	2.19 (1.65, 2.72)	-0.19 (-0.87, 0.49)	0.58	
NNRTI	3686 (78.7)	1.03 (0.69, 1.38)	1.99 (1.65, 2.34)	-0.96 (-1.28, -0.64)	<0.001	
INSTI	183 (3.9)	2.51 (1.47, 3.54)	2.38 (1.31, 3.44)	0.13 (-1.31, 1.57)	0.86	
Pre-specified NRTI						0.63
Tenofovir (TDF)	4163 (88.9)	1.28 (0.99, 1.57)	2.05 (1.76, 2.34)	-0.77 (-1.07, -0.47)	<0.001	
Other	521 (11.1)	0.82 (0.18, 1.47)	1.82 (1.20, 2.44)	-1.00 (-1.84, -0.15)	0.021	
Smoking status						0.42
Smoker	1499 (32.0)	1.23 (0.81, 1.65)	1.85 (1.44, 2.27)	-0.63 (-1.13, -0.12)	0.015	
Non-smoker	3185 (68.0)	1.22 (0.91, 1.53)	2.10 (1.79, 2.41)	-0.87 (-1.22, -0.53)	<0.001	

* Repeated measures longitudinal model adjusting for baseline weight, visit, treatment group, and each subgroup in separate models.
Models further adjusted for age, gender, region, CD4, and HIV RNA, as appropriate.
** Interaction p-value for age, CD4, and HIV RNA from model with the continuous variable.
*** Plus two background NRTIs.
CI: Confidence Interval; INSTI: integrase strand transcriptase inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; TDF: tenofovir disoproxil fumarate

in weight from baseline was estimated using repeated measures models for the full cohort and across 8 baseline-defined subgroups.
Results: START randomized 4684 participants; median baseline weight was 74 kg (25th, 75th-percentile: 64, 83), median follow-up was 3.0 years. Compared to baseline, weight increased by 1.13% (95% confidence interval [CI]:0.86, 1.48) in the immediate and 1.92% (95% CI: 1.65, 2.19) in the deferred groups. The mean treatment difference in percentage change in weight was −0.79% (95% CI: −1.08, −0.50; p<0.001). This difference was larger among participants with low baseline HIV-RNA (subgroup x treatment interaction p<0.001; fig. 1a, fig. 2). High CD4 counts, female gender and living in mid-low-income regions were associated with lower weight gain in the immediate ART group (subgroup x treatment interaction p<0.001, p=0.048, p=0.019, respectively). Participants taking NNRTIs seemed to have less weight gain compared to other ART classes, however, differences across ART classes were not significant.
Conclusions: ART initiation at CD4>500 cells/μL resulted in less weight gain than deferral. This effect was pronounced among participants with low baseline HIV-RNA levels suggesting that the impact of ART among those with high levels was countered by weight gain due to reduction in viral replication. The impact of integrase inhibitors could not be assessed due to minimal use in the trial.

PS3/2

Effect of doravirine on body weight and body mass index in treatment naïve adults with HIV-1

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Purpose: Studies suggest integrase strand-transfer inhibitors may cause more weight gain than protease inhibitors and non-nucleoside reverse transcriptase inhibitors in ART-naïve patients. Female sex, black race, and disease stage have been associated with weight gain in some studies. We compared the effects of doravirine (DOR) on body weight and BMI with those of ritonavir-boosted darunavir (DRV+r) and efavirenz (EFV) using data from the Phase 2 (P007) and Phase 3 trials (DRIVE-FORWARD and DRIVE-AHEAD) in treatment-naïve adults with HIV-1.
Method: Median change in weight was compared using the Wilcoxon rank-sum test, and proportions with≥5% weight gain were compared using the Miettinen-Nurminen method. The proportions whose BMI increased (change from underweight/normal to overweight/obese or from overweight to obese) were summarized, and the risk of BMI increase in each treatment group was estimated using a generalized linear model adjusting for region, gender, race, age, and baseline BMI, CD4 + T-cell count, and HIV-1 RNA.
Results: At 48 and 96 weeks, median weight change was statistically comparable between DOR and DRV+r but higher for DOR than EFV (table). The proportion with≥5% weight gain was comparable between DOR (26.5%) and DRV+r (23.1%) and higher for DOR than EFV (20.6%) at week 48 but was similar across all groups at week 96. The proportion with BMI increase was not significantly different for each comparison at both time points. Baseline CD4 + T-cell count and HIV-1 RNA predicted BMI increase at weeks 48 and 96, while race, age, and treatment group did not; sex predicted BMI increase at week 48 but not at week 96.
Conclusion: DOR and DRV+r had comparable effects on body weight and BMI. Median weight gain was statistically greater for DOR than EFV at both time points, while≥5% weight gain was greater at 48 weeks only. DOR and EFV had comparable effects on BMI.

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Effects on Body Weight and BMI by Treatment Group (DOR, DRV+r, EFV)

	Combined DOR Group		DRV+r Group		DOR vs DRV	Combined EFV Group		DOR vs EFV
Change in Body Weight (kg) from Baseline, Median (IQR)								
Week 48	N=751	1.00 (−1.20,3.90)	N=316	0.59 (−1.90,3.42)	p=0.117	N=402	0.00 (−2.60, 2.80)	p<0.001
Week 96	N=677	1.50 (−1.00,4.94)	N=268	0.70 (−1.85, 5.10)	p=0.147	N=362	1.00 (−2.20,4.60)	p=0.020
Proportion of Participants with≥5% Weight Gain (kg) from Baseline								
Week 48	N=751	26.5%	N=316	23.1%	p=0.245	N=402	20.6%	p=0.028
Week 96	N=677	31.8%	N=268	32.8%	p=0.749	N=362	32.0%	p=0.925
Proportion of Participants with Increased BMI								
Week 48	N=751	11.4%	N=315	11.1%	p=0.828	N=402	7.9%	p=0.062
Week 96	N=677	15.8%	N=267	15.3%	p=0.829	N=362	14.2%	p=0.474

PS3/3

The ADVANCE clinical trial: changes from baseline to week 96 in DXA-assessed body composition in TAF/FTC +DTG compared to TDF/FTC+DTG, and TDF/FTC/EFV

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Purpose: Following the increasing evidence-base to suggest integrase inhibitors lead to rises in body weight, there is a need to assess the impact on body composition among priority populations, such as black women. Dual-energy X-ray absorptiometry (DXA) can be used to assess body composition in patients to determine the type of weight gained. One aim of the ADVANCE study was to determine changes in body composition across treatment arms, using data from DXA scans.

Method: A sample of 1,053 treatment-naïve participants in South Africa were recruited and followed over a 96-week period. Participants were randomized to TAF/FTC+DTG, TDF/FTC+DTG, or TDF/FTC/EFV. DXA scans measured fat and lean mass at baseline, week 48, and week 96. Change from baseline across all DXA measurements, fat mass index (FMI) and treatment-emergent obesity were calculated.

Results: Changes in body composition are displayed in Table 1. The large increase in fat was evenly distributed between trunk and limb mass. Lean mass also increased to week 96. Treatment emergent obesity at week 96 was higher among women (30.5% TAF/FTC+DTG, 14% TDF/FTC+DTG, and 8% TDF/FTC/EFV) compared to men (4% TAF/FTC+DTG, 2% TDF/FTC+DTG, and 0% TDF/FTC/EFV), and statistically significant differences between TAF/FTC+DTG and the other groups (p<0.001). There were statistically significant differences between men and women across all DXA measurements, with women showing higher rises in fat, and weight more generally. Concomitant medications, appetite and nausea, and insomnia had no impact on these increases in weight, and quality of life was similar across all arms.

Table 1: Body composition change from baseline to week 96

Women	TAF/FTC+DTG (n=59)	TDF/FTC+DTG (n=52)	TDF/FTC/EFV (n=46)
Total weight (kg): mean (%change)	+9.3 (15.1%)	+5.0 (7.5%)	+2.9 (4.2%)
Trunk fat, mean(SD)	+3.4 (3.0)	+2.1 (2.2)	+1.2 (2.8)
Limb fat, mean(SD)	+3.1 (3.5)	+1.9 (2.3)	+1.2 (2.6)
Trunk lean, mean(SD)	+0.7 (1.3)	+0.3 (1.3)	-0.02 (1.4)
Limb lean, mean(SD)	+2.0 (1.4)	+1.1 (1.5)	+0.4 (1.6)
Men	**TAF/FTC+DTG (n=42)**	**TDF/FTC+DTG (n=42)**	**TDF/FTC/EFV (n=40)**
Total weight (kg): mean (%change)	+5.0 (7.4%)	+4.0 (6.2%)	0.0 (0.4%)
Trunk fat, mean(SD)	+1.7 (2.3)	+1.5 (2.0)	+0.4 (2.0)
Limb fat, mean(SD)	+1.3 (2.2)	+1.4 (1.7)	+0.3 (1.6)
Trunk lean, mean(SD)	+0.9 (1.6)	+0.2 (1.6)	-0.3 (1.4)
Limb lean, mean(SD)	+1.5 (1.8)	+1.2 (1.8)	+0.1 (1.3)

*Includes patients with paired weight and DEXA data at week 96. Excludes pregnant women

Conclusion: Our study demonstrates DTG used in combination with TAF is associated with large increases in weight, predominately fat. This increase is statistically significant and higher in women compared to men. Our results suggest these findings are not a return to health effect, with no clear plateau before week 96.

PS3/4

Integrase inhibitors dolutegravir and raltegravir exert proadipogenic and profibrotic effects and induce insulin resistance in adipose tissue and adipocytes

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Purpose: There is growing evidence that integrase inhibitors (INSTI) dolutegravir and raltegravir promote peripheral and central adipose tissue/weight gain in HIV-infected individuals, but the mechanisms involved remain unknown. We aimed to assess the effect of these molecules on adipose tissue morphology, function and metabolism.

Method: Morphology and function of subcutaneous (SCAT) and visceral adipose tissue (VAT) were studied in: -HIV-infected patients from the ObeVIH study, at the time of bariatric surgery (BMI 41.8 kg/m^2): 14 patients received INSTI (10 dolutegravir, 2 raltegravir, 2 elvitegravir) and 5 an INSTI-sparing regimen.
-Uninfected cynomolgus macaques treated or not 15 days with dolutegravir/tenofovir/emtricitabine.
Human Adipose Stem Cells (ASCs) were chronically treated with dolutegravir or raltegravir before or during adipogenesis. Adipogenic capacities, insulin response and extracellular matrix component expression were analyzed.

Results: SCAT from the ObeVIH patients presented peri-lobular and peri-adipocyte fibrosis in most samples. Conversely, VAT of INSTI-treated patient presented a higher level of peri-adipocyte fibrosis than that of non-INSTI-treated patients.
Dolutegravir-treated macaques presented a higher level of fibrosis and an increased adipocyte size in both SCAT and VAT, when compared to untreated macaques. Adipogenic marker expression was increased in SCAT and VAT, whereas adiponectin expression was decreased in SCAT, suggesting that, despite a pro-adipogenic effect, dolutegravir may favor insulin resistance.
In ASCs, INSTI-treatment increased collagen 1 and 6 and a-smooth-muscle-actin expression indicating a pro-fibrotic effect. In ASC-differentiated adipocytes, dolutegravir, and to a lesser extent raltegravir, increased lipid

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accumulation and adipogenic marker expression, decreased adiponectin expression and induced insulin resistance.
Conclusion: We demonstrate here for the first time, by using *in vivo* and in *vitro* complementary models, that INSTI exert a direct impact on adipose tissue adipogenesis, fibrosis and insulin resistance. These results, which reveal the adipose tissue toxicity of dolutegravir and raltegravir, are important to explain fat modifications reported in INSTI-treated HIV-infected patients.

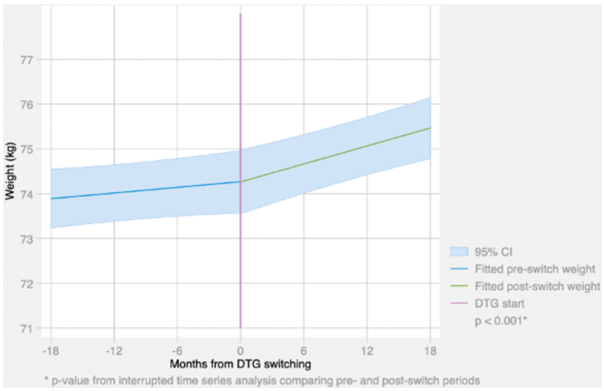
PS3/5

Changes in weight after switching to dolutegravir containing antiretroviral therapy in the Swiss HIV cohort study

C Mugglin[1], A Calmy[2], H Günthard[3], P Tarr[4], A Atkinson[1], A Scherrer[5], M Cavassini[6], C Marzolini[7], P Schmid[8], E Bernasconi[9], D Braun[5], G Wandeler[1], A Rauch[1] and Swiss HIV Cohort Study

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Purpose: We assessed changes in weight and BMI after switching to Dolutegravir (DTG) containing antiretroviral therapy (ART) among patients with suppressed HIV viremia in the Swiss HIV Cohort Study (SHCS).
Methods: Weight, other demographic and clinical characteristics were prospectively collected at 6-monthly follow-up visits. Switching was defined as changing to a DTG containing regimen after being at least 18 months on a triple-drug ART regimen. We excluded pregnant women and patients not virally suppressed 6 months before switching. We assessed weight change within a window of 18 months of DTG start by comparing pre- and post-switch changes using t-tests and interrupted time series analysis. Risk factors for disproportionate weight gain were identified using logistic regression comparing the top quartile of weight gainers to the rest.
Results: 2,215 patients met the inclusion criteria. Patients were predominantly white males (66%). At time of switch, median age was 51 (interquartile range (IQR) 44 - 56), median BMI 24.0 (IQR 21.7 - 26.8), and median time on ART 11 years (IQR 6 - 17). The Figure shows weight change before and after switching to DTG. Mean weight change over 18 months was 0.5 kg (95% confidence interval (CI) 0.3 - 0.7) before switching, and 1.0 kg (95% CI 0.8 - 1.2) after switching ($p<0.001$). BMI changed + 0.2 units (95% CI 0.1 to 0.2) before and + 0.3 units (95% CI 0.3 to 0.4) after switching ($p<0.001$). Risk factors for disproportionate weight gain included males (adjusted odds ratio (aOR) 1.5 95% CI 1.1 to 2.0) and people of African origin (aOR 1.5 95% CI 1.1 to 2.1).
Conclusion: Among patients on stable ART, switching to DTG was associated with a modest increase in weight compared to the time-period before switch. Weight gain was more prominent among participants of African origin and males.



Weight change 18 months before and after switching to a dolutegravir containing regimen (N=2,215)

PS3/6

Switching to an integrase inhibitor containing antiretroviral regimen is not associated with above-average weight gain in middle-aged people living with HIV on long-term suppressive antiretroviral therapy, the AGE$_h$IV cohort study

S Verboeket[1,2], A Boyd[3,4], F Wit[2,3], E Verheij[1,2], M Schim van der Loeff[2,4], N Kootstra[5], M van der Valk[2], P Reiss[1,2,3] and AGEhIV Cohort Study

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Purpose: Recently, several cohorts reported above-average weight gain in people with suppressed HIV-viremia after switching to an integrase inhibitor (INSTI) containing antiretroviral regimen. We evaluated similar changes in standardized bodyweight measurements from HIV-positive and HIV-negative AGEhIV cohort participants.
Methods: In 598 HIV-positive and 550 HIV-negative AGEhIV participants bodyweight was measured biennially. Virally-suppressed HIV-positive participants switching to an INSTI-containing antiretroviral regimen were matched 1:2:2 with (1) HIV-positive participants not changing antiretroviral regimen and (2) HIV-negative participants, using time-dependent propensity

Mean yearly change in body weight within each group, before and after real or hypothetical moment of switch to INSTI

		Before switch		After switch	
	N	kg/year	95% CI	kg/year	95% CI
INSTI switch	119	0.11	−0.11, 0.33	0.17	−0.22, 0.55
HIV-positive non-switchers	238	0.14	−0.06, 0.33	0.22	0.02, 0.42
HIV-negative	238	0.08	−0.12, 0.29	0.18	0.00, 0.36

Reported results were calculated from a linear mixed-effects model with bodyweight as the outcome, and the 3-way interaction-term study group*time*before/after switch as predictor variable.

Differences in mean yearly change in body weight

Difference in mean yearly change in body weight after vs. before real or hypothetical moment of switch to INSTI within each study group

	Δ kg/year	95% CI	P
INSTI switchers	0.06	−0.37, 0.48	0.8
HIV-positive non-switchers	0.08	−0.18, 0.34	0.5
HIV-negative	0.09	−0.16, 0.35	0.5

Difference in mean yearly change in body weight between study groups before and after real or hypothetical switch to INSTI

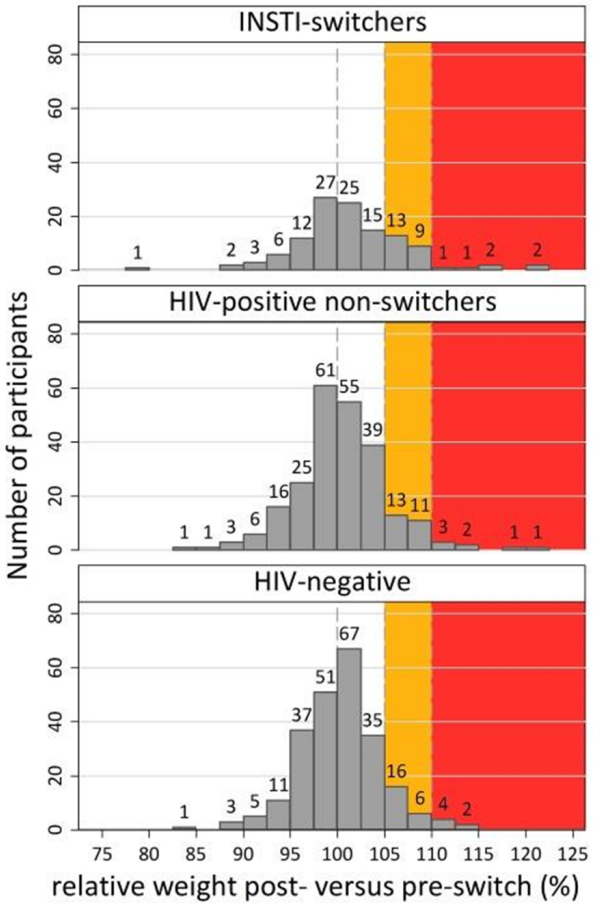
INSTI switchers vs. HIV-positive non-switchers	Before switch	−0.03	−0.32, 0.27	0.9
	After switch	−0.05	−0.49, 0.38	0.8
INSTI switchers vs. HIV-negative	Before switch	0.02	−0.28, 0.33	0.9
	After switch	−0.01	−0.44, 0.41	0.9

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scores based on gender, ethnicity, age and BMI. In all matched controls a hypothetical moment of switch was determined, at which matched controls most resembled propensity scores of the index-participant at INSTI-switch. Average yearly bodyweight changes before and after (hypothetical) switch within and between study groups were compared using linear mixed-effects models. The frequencies of>5% and>10% weight gain were compared using logistic regression.

Results: 119 HIV-positive participants switched to an INSTI-containing regimen (53% dolutegravir; 35% elvitegravir; 13% raltegravir) and had a bodyweight measured≥1 times before and after switch. In 49% the NRTI-backbone was simultaneously modified, the majority from tenofovir disoproxil/emtricitabine to tenofovir alafenamide/emtricitabine (18%) or abacavir/lamivudine (11%). There were no significant differences in yearly mean changes in bodyweight within and between the groups before and after (hypothetical) switch.

A>5% increase in bodyweight occurred in 28 (23.5%) HIV-positive participants after INSTI initiation, and in 31 (13%, p=0.013) non-switching HIV-positives, and in 28 (11.8%, p=0.005) HIV-negative controls, after their hypothetical moment of switch. A>10% increase in bodyweight occurred in 6 (5.0%), 7 (2.9%, p=0.3) and in 6 (2.5%, p=0.2) respectively.



Yellow and red fields indicate participants with a relative weight increase of >5% (yellow and red) and >10% (red), respectively. Numbers above the bars indicate absolute numbers of participants.

Frequency distributions of proportional weight changes; first post- vs. last pre-switch measurements

Conclusions: We found no evidence for above-average weight gain in virologically suppressed patients switching to an INSTI-containing regimen. However, clinically relevant weight gain upon switching to INSTI may be a relatively rare phenomenon deserving further investigation.

More than the sum of its parts? Multimorbidity in PLWH

PS4/1

AIDS defining and non-defining cancers in persons living with HIV in a single center cohort followed since 1986

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Purpose: To review AIDS-defining cancer (ADCs) and non-AIDS-defining cancer (NADCs) and temporal changes in the ADCs/NADCs ratio, in a large single center cohort.

Patients and methods: 5411 HIV-infected participants followed-up between 1986–2018. Data were collected from our clinical database. ADCs and NADCs were defined according to the CDC classification.

Results: We diagnosed 643 patients with at least one malignancy. Patients with NADCs were older and mostly male. (Table 1) HIV infection and cancer were simultaneously diagnosed in 21.3%, more frequently in the ADCs group 34.7% vs. 8.07% (p<0.001). Cancers were diagnosed as clinically advanced in 86 participants (13.4%), similarly distributed between groups, 10.9% ADCs vs 15.7% NADCs. The most frequent cancers were: cervix cancer (134, 20.8%), Kaposi sarcoma (132, 20.53%), non-Hodgkin lymphoma (52, 8.09%), Hodgkin lymphoma (43, 6.7%), hepatocellular carcinoma (32, 4.9%), anal cancer (30, 4.67%), head and neck tumor (27, 4.2%) and lung cancer (25, 3.9%).

NADCs increased over time resulting in a decrease in the ADCs/NADCs ratio with calendar year. (Figure 1) In the late ART period (>2006) NADCs were more frequent (65.6%) than ADCs, (p<0.001). (Table 2) In 2018, 25/30 (75%) were NADCs, being the most frequent hepatocellular carcinoma (5/25) and lung cancer (4/25). Overall, 430 (66.8%) cancers were related to oncogenic viruses: 166/430 human papillomavirus, 232/430 herpes virus 8 and EBV and 32/430 HBV and/or HCV.

Among 643 patients, 101 (15.9%) patients died due to cancer progression, with higher mortality in NADCs 25.3% vs ADCs 10.6% (p<0.001). Higher mortality was observed in pancreas (90%), lung (68%) and colon (60%) cancer.

Conclusions: NADCs increased over the time, being more frequent during the late ART period and with higher mortality. A malignancy was, in an important number of cases, the first manifestation of HIV infection. A significant proportion of cancers were related with oncogenic virus coinfection.

Table 1. Baseline characteristics

	ALL (n=643)	ADCs (n=320)	NADCs (n=323)	p-value
Sex, male, n (%)	422 (65.6)	169 (52.9)	253 (78.1)	<0.001
Age at cancer diagnosis (years), median (IQR)	44.2 (35.9–51.9)	38.5 (32.5–45.6)	49.6 (42.5–56.7)	<0.001
Caucasian Race, n (%)	<585 (91.7)	281 (88.6)	304 (94.7)	0.006
Route of HIV transmission, n (%)				
Sexual	381 (59.2)	217 (67.8)	164 (50.7)	<0.001
IDU	194 (30.2)	77 (24.1)	117 (36.2)	
Other/Unknown	68 (10.6)	26 (8.1)	42 (13.0)	
Chronic/previous Hepatitis coinfection, n (%)				
HBV *N=583/643	130 (22.3)	49 (16.9)	81 (27.5)	0.001
HCV *N=596/643	248 (41.6)	110 (37.3)	139 (45.7)	0.053
AIDS, n (%)	545 (84.7)	320 (100)	225 (69.7)	<0.001
Nadir CD4 (cells/mm^3), median (IQR) *N=507/643	135 (52–230)	133 (50–216)	140 (55–245)	0.48
Time of HIV infection at cancer diagnosis (years), median (IQR)	8.9 (1.9–17.7)	4.1 (0.1–10.9)	15.1 (6.6–21.7)	<0.001
Receiving ART at cancer diagnosis, n (%)	400 (62.1)	146 (45.7)	254 (78.4)	<0.001

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Table 2. Cancer distribution according to ART era at diagnosis

	Pre-ART (Before 1997)	Early ART (1996–2006)	Late ART (After 2006)
N Malignancies	50	191	403
ADCs, n (%)			
Non Hodgkin lymphoma	4 (8.0)	22(11.5)	26 (6.4)
Kaposi sarcoma	20 (40.0)	56 (29.3)	56 (13.9)
Cervix cancer	24 (48.0)	54 (28.2)	56 (13.9)
NADCs, n (%)			
Hodgkin lymphoma	0 (0)	21 (10.9)	22 (5.4)
Hepatocellular carcinoma	0 (0)	2 (1.05)	30 (7.4)
Anal cancer	1 (2.0)	7 (3.6)	22 (5.5)
Head/neck cancer	0 (0)	5 (2.62)	22 (5.5)
Lung carcinoma	0 (0)	2 (1.05)	23 (5.7)
Breast cancer	0 (0)	1 (0.52)	19 (4.7)
Prostate cancer	0 (0)	1 (0.52)	18 (4.5)
Colon cancer	0 (0)	0 (0)	10 (2.5)
Pancreas/Biliary duct	0 (0)	0 (0)	10 (2.5)

*Only shown more frequent cancer

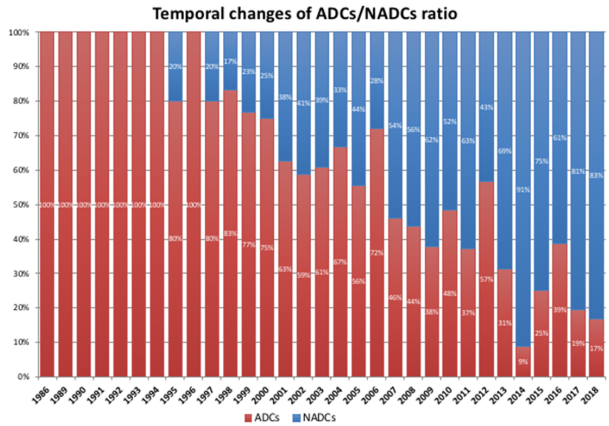


Figure 1. Temporal changes of ADCs/NADCs ratio

PS4/2

Incidence of CKD with TDF and non-TDF containing antiretroviral regimens by baseline D:A:D CKD risk in people living with HIV (PLWH)

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Purpose: Given recent evidence that the risk of renal toxicities with TDF may increase with coadministration of a pharmacoenhancer (Hill 2018), we assessed the risk of chronic kidney disease (CKD) associated with TDF and non-TDF containing regimens by D:A:D CKD risk and boosting.

Method: ART-naïve adults initiating treatment with eGFR≥60 mL/min/1.73 m^2 (last eGFR within 12 months pre-initiation) were identified in the OPERA cohort. CKD was defined as≥2 consecutive eGFR<60 mL/min/1.73 m^2, >90 days apart. The associations between TDF use, baseline D:A:D CKD risk, and incident CKD were assessed with unadjusted incidence rates (IR, Poisson regression) and adjusted survival analyses (pooled logistic regression). Secondary analysis evaluated the contribution of pharmacoenhancers.

Results: Of 9,802 PLWH included, 6,222 initiated TDF (76% low-risk D:A:D CKD score, 16% medium-risk, 8% high-risk) and 3,580 did not (79% low-risk, 13% medium-risk, 8% high-risk; Table 1); 40–47% initiated a boosted regimen (Table 2). Overall, 125 incident CKD events occurred over 24,382 person-years of follow-up. Within strata of D:A:D risk score, IRs were similar by TDF exposure, with high baseline CKD risk associated with highest incidence regardless of TDF use (Figure 1). Compared to the low-risk group without TDF, there was no statistical difference in odds of incident CKD in the medium-risk group without TDF (aOR: 2.32, 95% CI: 0.72, 7.52) or the low-risk group with TDF (aOR: 0.55, 95% CI: 0.19, 1.54; Figure 2). Odds of incident CKD did not differ by pharmacoenhancer exposure, with or without TDF.

Conclusion: In this large cohort of ART-naïve PLWH, incident CKD following ART initiation was relatively infrequent and was strongly associated with baseline CKD risk. TDF-containing regimens did not appear to increase the risk of CKD in those with a low baseline D:A:D CKD risk, the largest group of naïve PLWH, and may remain a viable treatment option.

Table 1. Baseline Demographic and Clinical Characteristics

	No TDF			TDF		
D:A:D CKD risk strata	Low-risk N=2,827	Medium-risk N=481	High-risk N=272	Low-risk N=4,743	Medium-risk N=994	High-risk N=485
Age, median (IQR)	29 (25, 35)	49 (41, 53)	52 (47, 57)	31 (26, 38)	48 (41, 53)	52 (46, 57)
Female, n (%)	254 (9.0)	97 (20.2)	79 (29.0)	566 (11.9)	174 (17.5)	146 (30.1)
eGFR, median (IQR)	117.8 (106.2, 128.2)	96.0 (85.3, 105.9)	77.4 (68.9, 85.6)	115.7 (104.8, 125.9)	95.8 (85.1, 106.8)	80.5 (73.1, 86.9)
Log10 HIV viral load (copies/mL), median (IQR)	4.7 (4.2, 5.1)	4.7 (4.1, 5.2)	4.8 (4.2, 5.3)	4.7 (4.2, 5.1)	4.8 (4.2, 5.2)	4.6 (4.1, 5.0)
Alcohol abuse, n (%)	51 (1.8)	16 (3.3)	6 (2.2)	109 (2.3)	42 (4.2)	10 (2.1)
HCV co-infection, n (%)	58 (2.1)	44 (9.1)	29 (10.7)	112 (2.4)	119 (12.0)	75 (15.5)
Diabetes, n (%)	34 (1.2)	49 (10.2)	40 (14.7)	34 (0.7)	70 (7.0)	42 (8.7)
Hypertension, n (%)	561 (19.8)	202 (42.0)	157 (57.7)	1074 (22.6)	383 (38.5)	252 (52.0)

Table 2. Initial ART and Other Medication Use at Baseline

	No TDF			TDF		
D:A:D CKD Risk Strata	Low-risk N=2,827	Medium-risk N=481	High-risk N=272	Low-risk N=4,743	Medium-risk N=994	High-risk N=485
Boosted regimen (PI or EVG), n (%)	1128 (39.9)	222 (46.2)	124 (45.6)	2231 (47.0)	457 (46.0)	207 (42.7)
Non-boosted INSTI, n (%)	1502 (53.1)	216 (44.9)	122 (44.9)	405 (8.5)	115 (11.6)	61 (12.6)
Non-boosted NNRTI, n (%)	197 (7.0)	43 (8.9)	26 (9.6)	2107 (44.4)	422 (42.5)	217 (44.7)
Concurrent nephrotoxic medication use, n (%)	292 (10.3)	78 (16.2)	46 (16.9)	798 (16.8)	233 (23.4)	123 (25.4)
Concurrent use of medication affecting proteinuria, n (%)	69 (2.4)	68 (14.1)	57 (21.0)	159 (3.4)	119 (12.0)	93 (19.2)

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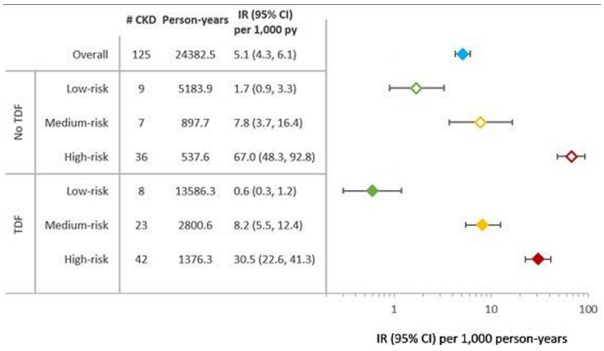
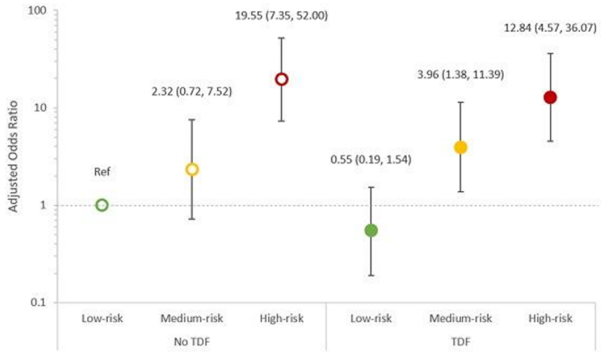


Figure 1. Unadjusted Incidence of CKD Over Follow-up



*After exclusion of 386 patients from the analysis due to missing race/ethnicity information. Pooled logistic regression estimated that with generalized estimating equations (autoregressive correlation structure), adjusted for baseline age (restricted cubic splines), sex, race/ethnicity, index calendar year (restricted cubic splines), and regimen, as well as time-updated alcohol abuse, HIV viral load ≥50 copies/mL, nephrotoxic medications, medications affecting proteinuria, HCV co-infection, diabetes and hypertension

Figure 2. Adjusted Association Between TDF Use, D:A:D CKD Risk Group and Incidence of CKD*

PS4/3

The ADVANCE trial: the impact of DXA-assessed bone mineral density of TDF/FTC/EFV and TDF/FTC+DTG versus TAF/FTC+DTG

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Purpose: In previous clinical trials and cohort studies, tenofovir disoproxil fumarate (TDF) has been associated with decreased bone mineral density (BMD) and renal function. One of the aims of the ADVANCE study was to determine whether BMD and renal changes over 96 weeks differed in HIV-infected persons taking TDF-containing regimens versus those taking tenofovir alafenamide fumarate (TAF)-containing regimens.
Method: We conducted a 96-week, open-label randomised trial in South Africa, comparing TAF/FTC+DTG, TDF/FTC+DTG and TDF/FTC/EFV. Inclusion criteria included age ³ 12 years, no prior ART>30 days, creatinine clearance>60 mL/min (>80 mL/min if <19 years), and HIV-1 RNA>500 copies/mL. Investigators were blinded to renal tubular markers and DXA scans unless patient safety concerns were an issue. Based on WHO classifications of BMD T-scores, treatment emergent osteopenia and osteoporosis was assessed across the three treatment arms.
Results: The TDF-containing arms had most impact on hip and spine DXA-assessed bone density and renal markers. Creatinine changes were minor (Table 1). Treatment emergent osteopenia for hip was lowest in the TAF/FTC+DTG arm (7%) versus 16% in the TDF/FTC+DTG and 18% in the TDG/FTC/EFV arms (p<0.001). Similarly, treatment emergent osteopenia for spine was lowest in the TAF/FTC+DTG arm (18%) versus 23% and 22% in the TDF/FTC+DTG and TDF/FTC/EFV arms respectively. However, there was no statistical difference seen between the arms. Grade 3–4 renal adverse events (AEs) and bone fractures were rare. None of the fractures were related to the study drugs. Tubular markers above the upper limit of normal (ULN) were higher in TDF-containing arms than in the TAF arm. (Table 1)
Conclusion: In the ADVANCE study, TAF/FTC+DTG had less impact on bone density and renal function than the TDF-containing regimens.

	Group 1 (TAF/FTC/DTG) (n=351)	Group 2 (TDF/FTC/DTG) (n=351)	Group 3 (TDF/FTC/EFV) (n=351)
Treatment-emergent osteopenia (n. %)			
Whole Body	5/287 (2)	6/302 (2)	2/275 (1)
Hip	15/227 (7)	38/234 (16)	40/225 (18)
Spine	37/203 (18)	50/220 (23)	45/202 (22)
Bone fractures* (n, %)			
Ankle fracture	0/351 (0)	2/351 (0)	1/351 (0)
Facial bone fracture	0/351 (0)	1/351 (0)	0/351 (0)
Lower limb fracture	0/351 (0)	1/351 (0)	0/351 (0)
Renal grade 3 or 4 AEs (n, %)	1/351 (0)	2/351 (1)	3/351 (1)
Grade 3 or 4 creatinine elevation (n, %)	0/351 (0)	0/351 (0)	1/351 (0)
Tubular markers above ULN (treatment emergent) (n, %)			
Beta 2 microglobulin	22/351 (6)	74/351 (21)	82/351 (23)
Retinol binding protein	10/351 (3)	26/351 (8)	38/351 (11)
Urine albumin to creatinine	57/351 (16)	81/351 (23)	83/351 (24)

AEs: Adverse Events, ULN: Upper Limit Normal
*All three fractures were a result of trauma. One patient fell off a wall, one patient was tasered and the third patient was in a car accident.

Changes in bone and renal markers

PS4/4

Pericardial adipose tissue volume is independently associated with HIV status

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Purpose: Larger pericardial adipose tissue (PAT) volume is associated with increased risk of cardiovascular disease (CVD). We aimed to assess PAT volume in persons living with HIV (PLWH) and uninfected controls and to determine if HIV status is independently associated with PAT volume. We furthermore investigated associations between PAT volume and CVD risk factors as well as HIV-specific factors.
Method: PLWH were recruited from the Copenhagen Comorbidity in HIV infection (COCOMO) study and matched 1:1 on age- and sex to uninfected controls from the Copenhagen General Population Study. PAT volume was measured by cardiac CT using identical protocols in PLWH and controls.
Results: A total of 587 PLWH and 587 controls were included (Table 1). Mean (SD) PAT volume was similar in PLWH and uninfected controls (192 (62) mL vs. 190 (66) mL, respectively, p=0.546). After adjusting for BMI, age, and sex, HIV status was associated with 15 mL [95% Confidence interval: 8, 21] larger PAT volume, p<0.001. Additional adjustment for CVD risk factors did not affect this association (Table 2). Among PLWH, larger PAT volume was associated with CD4 nadir<200 / cells/μL and prior use of thymidine analogous (TA)/didanosine (ddI). Among PLWH without TA/ddI exposure, combination antiretroviral therapy (cART) duration (per 5-year use) was associated with l6 mL [−6, −25] lower PAT volume, p=0.002. In TA/ddI exposed PLWH, cART duration was associated with 8 mL [−0.2, 15] larger PAT, p=0.058.
Conclusion: HIV status was independently associated with larger PAT volume after adjusting for BMI and common CVD risk factors. cART duration was associated with lower PAT volume in PLWH not exposed to TA/ddI. Further studies are needed to determine if PAT causes increased CVD risk in PLWH with TA/ddI exposure.

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Table 1. Characteristics of study population

Characteristic	Persons living with HIV	Controls
Age, years, median (IQR)	52 (47, 60)	52 (47, 60)
Sex, male, n (%)	518 (88)	518 (88)
Body mass index (BMI), kg/m^2, mean (SD)	24.8 (3.5)	26.6 (3.5)
Current smoker	157 (27)	82 (14)
Dyslipidemia, n (%)	128 (22)	191 (33)
Hypertension, n (%)	272 (46)	368 (63)
Use of antiretroviral treatment, n (%)	579 (98.6)	–
HIV RNA<50 (copies/mL), n (%)	560 (95.4)	–
Ever use of thymidine analogue or Didanosine, n (%):	336 (57)	–

Simple and multiple linear analyses of risk factors associated with pericardial adipose tissue volume in controls and PLWH.

	Unadjusted β [95% CI]	*P*	Adjusted* β [95% CI]	*P*
HIV, yes vs no	2.3 [-5.1, 9.6]	.546	16.7 [10.0, 23.4]	<.001
Sex, male vs. female	55.5 [44.5, 66.5]	<.001	44.5 [34.4, 54.6]	<.001
Age, per 10 years	21.5 [17.4, 25.5]	<.001	15.2 [11.3, 19.0]	<.001
BMI, per unit	6.8 [5.9, 7.7]	<.001	6.8 [5.8, 7.7]	<.001
Hypertension, yes vs. no	26.6[19.3, 33.9]	<.001	5.6 [-1.3, 12.4]	.113
Diabetes, yes vs. no	23.5 [2.2, 44.8]	.031	0.1 [-18.1, 18.2]	.994
Smoking status†				
Current smoker	13.4 [3.4, 23.3]	.008	13.1 [4.1, 22.1]	.005
Former smoker	21.3[13.1, 29.5]	<.001	13.2 [6.0, 20.4]	<.001
Dyslipidemia, yes vs. no	31.8[23.6, 40.0]	<.001	14.8 [7.6, 22.1]	<.001
Sedentary lifestyle‡	30.7[16.3, 45.1]	<.001	21.4 [8.8, 34.0]	<.001

*Adjusted for age, sex, BMI, hypertension, diabetes, dyslipidemia, smoking and physical activity
†Reference is 'Never smoker'
‡Reference is: Active lifestyle
Abbreviations: PLWH, people living with HIV; BMI, body mass index.

Linear analyses of risk factors associated with PAT volume (in mL)

PS4/5

Environmental exposures are associated with increased respiratory morbidity among persons living with HIV (PLWH)

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Purpose: Chronic respiratory disease has emerged as an important co-morbidity for PLWH. We aimed to a)determine the association between sources of indoor air pollution and respiratory morbidity, in a cohort of PLWH at risk for both pollutant exposure and lung disease, and b)describe how HIV modifies the impact of pollutants.
Method: We analyzed cross-sectional data from the Study of HIV Infection in the Etiology of Lung Disease(SHIELD) in Baltimore, Maryland, USA, consisting of both PLWH and HIV-uninfected participants. Participants complete lung function testing and questionnaires about environmental exposures; including secondhand smoke (SHS), NO_2 producing appliances(Gas Stoves), mold, and occupational exposures(dust, fumes). Respiratory symptoms included: chronic cough, wheeze, phlegm, and experiencing≥2 wheezing attacks/year. We utilized logistic regression to determine associations between sources of indoor air pollution and respiratory outcomes, adjusting for potential confounders(demographics, smoking status, injection drug use, lung function-FEV_1, household income, and HIV-status).
Results: Of 1997 participants, 1109(55.5%) were PLHW. Pollutant exposure was common, with 1490(74.6%) using NO_2 producing appliances, 646(34.2%) with significant occupational exposures, and 1373(68.3%) noting household SHS. A number of exposures were associated with chronic respiratory symptoms after adjusting lung function and traditional risk factors. Occupational exposures(OR 1.37; p=0.007), and mold(OR 1.79; p<0.001) were associated with higher odds of chronic phlegm and other symptoms. PLWH were notably more susceptible to the effects of SHS and NO_2 producing appliances. NO_2 exposure was linked to increased odds of chronic wheeze and wheezing attacks among PLWH (OR 1.41, p=0.023), but not in uninfected participants(OR 0.97; p=0.869) (p-interaction=0.040). Regular household SHS exposure was associated with greater risk for chronic phlegm (OR 1.43; p-value=0.015), even after accounting for personal smoking status, but only among PLWH(p-interaction=0.045).

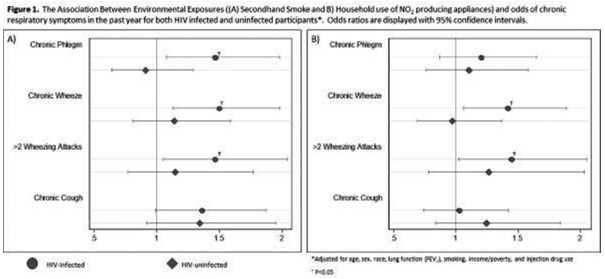


Figure 1. The Association Between Environmental Exposures ((A) Secondhand Smoke and B) Household use of NO_2 producing appliances) and odds of chronic respiratory symptoms in the past year for both HIV infected and uninfected participants*. Odds ratios are displayed with 95% confidence intervals.

The association between environmental exposures and respiratory symptoms for people living with HIV

Conclusion: We describe that indoor environmental exposures are common and associated with greater respiratory morbidity in a cohort of PLWH, with HIV increasing susceptibility to certain pollutants.

PS4/6

Comparing a risk score against physiological markers for predicting diabetes incidence in HIV+ individuals

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Purpose: To compare the performance of a clinical diabetes risk score with physiological markers for predicting diabetes incidence in HIV+ and HIV- individuals.
Method: We determined 10-year diabetes incidence (defined as self-reported diabetes medication use) in HIV+ and HIV- participants from the Women's Interagency HIV Study and the Multicenter AIDS Cohort Study. For each participant, we obtained baseline values for the Finnish Diabetes Risk Score (FINRISC), Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), HOMA for β-cell function (HOMA-β), and Triglycerides/HDL Cholesterol Ratio (TG/HDL). Discrimination of each model was assessed using the Harrell C-statistic. Calibration was assessed by comparing the observed versus the predicted cumulative probabilities of developing diabetes (determined from 1-Kaplan-Meier) in each tertile of the distribution.
Results: We included 2499 men (1285 HIV+ and 1214 HIV-, median age=44 years, 60% non-Hispanic white, 25% non-Hispanic black) and 2408 women (1812 HIV+ and 596 HIV-, median age=41, 12% non-Hispanic white, 62% non-Hispanic black). Over 10 years of follow-up, 10% of HIV+ men, 9% of HIV- men, 11% of HIV+ women, and 12% of HIV- women developed diabetes. FINRISC had the best discrimination, though it performed better in HIV- participants (men *c*=0.74 [95% CI 0.69, 0.78], women *c*=0.75 [0.70, 0.80]) than in HIV+ participants (men *c*=0.68 [0.62, 0.73]), women *c*=0.70 [0.66, 0.74]). HOMA-IR discrimination was similar by HIV status but better in men (HIV+ *c*=0.70 [0.65, 0.75]), HIV- *c*=0.72 [0.67, 0.77]) than in women (HIV+*c*=0.65 [0.61, 0.69], HIV- *c*=0.67 [0.60, 0.74]). TG/HDL and HOMA-β had poor discrimination (*c*<0.7 and<0.6, respectively). Regarding calibration, FINRISC underestimated risk among HIV- men in the highest risk tertile, while HOMA-IR and TG/HDL underestimated risk among all participants in the highest risk tertiles. HOMA-β was well-calibrated.
Conclusion: In HIV+ men, FINRISC predicted incident diabetes similarly to physiological markers. In HIV+ women, FINRISC was superior.

PS4/7

Development and validation of a comorbidity index for people living with HIV and its ability to predict frailty and mortality

D De Francesco[1], SO Verboeket[2], E Verheij[2], J Underwood[3], E Bagkeris[1], FW Wit[2], A Winston[4], P Reiss[2], CA Sabin[1] and POPPY Study and the AGEhIV Cohort Study
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Purpose: Despite the increasing prevalence of multi-morbidity in people living with HIV (PLWH), there is no tool designed specifically for PLWH to assess

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Association of the CBI, comorbidity count and VACS index with patient-reported physical and mental health, frailty, frailty development and mortality

Index	Physical health	Mental health	Frailty	Frailty development	Mortality
	rho (95% CI)	*rho* (95% CI)	C-statistic (95% CI)	C-statistic (95% CI)	C-statistic (95% CI)
	p vs. CBI	*p* vs. CBI	*p* vs. CBI	*p* vs. CBI	*p* vs. CBI
CBI	−0.34 (−0.41, −0.26)	−0.18 (−0.26, −0.10)	0.73 (0.66, 0.79)	0.62 (0.52, 0.72)	0.66 (0.56, 0.75)
Comorbidity count	−0.30 (−0.38, −0.22)	−0.15 (−0.23, −0.07)	0.71 (0.63, 0.78)	0.64 (0.54, 0.74)	0.71 (0.62, 0.79)
	p=0.08	p=0.16	p=0.27	p=0.55	p=0.12
VACS index	−0.07 (−0.15, 0.02)	0.10 (0.02, 0.19)	0.63 (0.56, 0.70)	0.55 (0.44, 0.66)	0.67 (0.56, 0.77)
	p<0.001	p<0.001	p=0.02	p=0.32	p=0.84

overall comorbidity burden. We developed and externally validated a comorbidity burden index (CBI), specific to PLWH, assessing its cross-sectional association with health status and ability to predict mortality and frailty.

Method: We developed the CBI using information on 65 comorbidities collected in PLWH enrolled in the POPPY (development) cohort and compared its performance against the comorbidity count and the VACS index in the AGE_hIV (validation) cohort. Spearman's correlation and the C-statistic assessed associations of indices with physical/mental health (SF-36), adapted Fried frailty phenotype prevalence and 4-year incidence, and 6-year all-cause mortality. These were compared across indices using the Steiger's and DeLong tests, as appropriate.

Results: The development and validation cohorts included 1073 [85% males, 16% black-Africans, median age 52 years] and 598 [88% males, 14% black-Africans, 53 years] PLWH, respectively. Of the three indices, the CBI demonstrated the strongest associations with physical and mental health (Table); these associations were significantly stronger than those of the VACS index (both p's< 0.001) but not of those of the comorbidity count (p=0.08, p=0.16). At baseline, 11.4% of PLWH were frail; frailty incidence and death rate were 19.5/1000 and 12.0/1000 person-years, respectively. Cross-sectionally, the CBI showed a stronger association with frailty than either the VACS index (p=0.02) or the comorbidity count (p=0.27). Whilst prospective associations with frailly development and mortality were strongest for the comorbidity count, the difference with associations of the CBI were not significant (p=0.55 and p=0.12, respectively).

Conclusion: The proposed CBI, specifically developed in PLWH showed strong associations with several health outcomes when externally validated. These findings justify the use of the CBI when adjustment for comorbidity is needed and when evaluating the effectiveness of interventions.

Basic and translational HIV biology

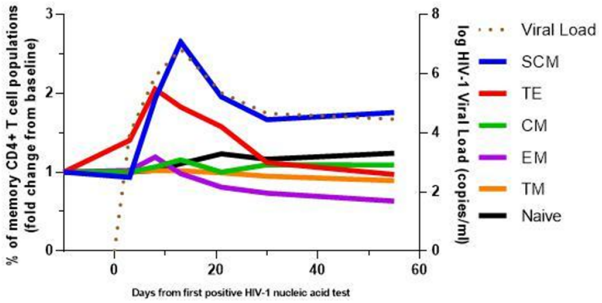
PS5/1

Stem-cell-like CD4$^+$ memory T cells expand during the acute HIV-1 infection accelerating disease progression

J Pušnik[1], MA Eller[2], B Tassaneetrithep[3], BT Schultz[1], LA Eller[2], S Nitayaphan[4], J Kosgei[5], L Maganga[6], H Kibuuka[7], G Alter[8], NL Michael[2], ML Robb[2], H Streeck[1] and RV217 Study Team

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Purpose: During acute HIV-1 infection a reservoir of latently infected cells is established, that represents an important road block for HIV cure through antiretroviral therapy. Maturational CD4 + T cell subsets play different roles in reservoir maintenance and differ in their susceptibility to HIV-1 infection.



Longitudinal changes in CD4 + T cell subset frequencies during the acute phase of HIV-1 infection

However, the dynamics and infectibility of these subsets during acute HIV-1 infection have not been sufficiently investigated.

Method: Using flow cytometry, we analyzed longitudinal changes in the frequency of memory CD4 + T cell subsets in peripheral blood of subjects from acute HIV-1 infection cohort RV217 (ECHO) and in HIV-1 infected cell cultures. We also performed flow cytometry-based proliferation assay, measurement of cytoplasmic p24 levels and qPCR-based measurement of HIV-1 integration in the cell cultures.

Results: We observed a profound expansion of stem-cell-like memory (SCM) CD4 + T cells (2.7-fold; p<0.0001) in parallel to viral load peak, which is believed to be a critical time for latent reservoir seeding. Since SCM were previously identified as an important long-lived latent reservoir, SCM expansion during acute HIV infection may be important contributor for HIV pathogenesis. Furthermore we found that the expansion of SCM is due to the upregulation of the Fas receptor on the surface of naive CD4 + T cells. Both, the extent of Fas upregulation and increase in SCM frequency were positively associated with the early set point viral load, a reliable predictor of the disease progression (rho=0.47, p=0.02, and rho=0.42, p=0.041 respectively). We also demonstrated that highly differentiated memory CD4 + T cell subsets show higher susceptibility to HIV-1 integration and replication, causing a decline in their frequencies towards the end of the acute phase.

Conclusion: Collectively, our findings revealed an expansion of SCM, known as the especially persistent reservoir component, during acute HIV-1 infection. The degree of this expansion was associated with rapid disease Progression.

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PS5/2

Correlation between cerebrospinal fluid (CSF) and plasma concentrations of neurofilament light protein (NFL) in treated HIV infection in the COmorBidity in Relation to AIDS (COBRA) study

J Alagaratnam[1,2], D De Francesco[3], H Zetterberg[4,5,6], A Heslegrave[7], J Toombs[7], N Kootstra[8], J Underwood[1,9,10], M Gisslén[11,12], P Reiss[13,14,15], C Sabin[3], A Winston[1,2] and COmorBidity in Relation to AIDS (COBRA) Collaboration

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Purpose: CSF NFL is an established biomarker of central nervous system neuro-axonal injury. A novel ultra-sensitive assay can determine plasma NFL. In untreated people with HIV (PWH), plasma and CSF NFL are strongly correlated. We assessed this correlation in antiretroviral therapy (ART)-treated PWH and lifestyle-similar HIV-negative controls, and determined factors associated with plasma and CSF NFL in PWH.
Method: Differences in paired plasma (Simoa digital immunoassay, Quanterix™) and CSF (sandwich ELISA, UmanDiagnostics) NFL between PWH and HIV-negative controls were tested for significance using Wilcoxon's test; associations between the values (after log-transformation) were assessed using Pearson's correlation. Log-transformed plasma and CSF NFL, standardised to Z-scores, were included as dependent variables in linear regression models to identify factors independently associated with values in PWH; factors significant ($p<0.05$) in univariable analyses for either outcome were included in the multivariable models.
Results: We included 132 PWH (median age 56 years, 94% male, 88% white, 100% HIV-1 RNA<50 copies/mL) and 79 HIV-negative controls (57 years, 92% male, 97% white). Neither CSF (570 vs 568 pg/mL, p=0.37) nor plasma (10.7 vs 9.9 pg/mL, p=0.15) NFL differed significantly between the two groups. Plasma and CSF NFL correlated moderately, with no significant difference by HIV status (PWH: r=0.52 (95% confidence interval 0.38–0.63); HIV-negative: r=0.47 (0.27–0.62), p (interaction)=0.63). In multivariable regression, older age and lower weight were each associated with higher plasma and CSF NFL Z-scores in PWH. Whereas lower plasma albumin and higher serum creatinine were associated with higher plasma NFL Z-scores, higher CSF protein was associated with higher CSF NFL Z-score.
Conclusion: In PWH on suppressive ART, the correlation between CSF and plasma NFL is weaker than previously described in untreated PWH but similar to that observed in lifestyle-similar controls. Consideration of renal function and body composition may be required when utilising plasma NFL.

Dependant variable	Independent variables (Additional variables included in the model were males, being on antihypertensive medication, duration diagnosed with HIV infection, duration on ART)	Parameter estimate (The associated impact (measured in standard deviations) of each independent variable on the dependent variable) (95% CI)	p-value
Log_{10} (plasma NFL) Z-score	Age (/10 years older)	0.60 (0.42, 0.79)	<0.001
	Weight (/5 kg higher)	−0.13 (−0.18, −0.08)	<0.001
	Serum creatinine (/10 µmol/L higher)	0.12 (0.04, 0.19)	0.002
	Plasma albumin (/10 g/L higher)	−0.39 (−0.69, −0.09)	0.012
Log_{10} (CSF NFL) Z-score	Age (/10 years older)	0.69 (0.50, 0.89)	<0.001
	Weight (/5 kg higher)	−0.07 (−0.12, −0.01)	0.021
	CSF protein (/1 g/L higher)	1.33 (0.50, 2.16)	0.002

PS5/3

TET2 genetic variation affects HIV viral load in ART-naïve persons

DD Murray[1], CR Macpherson[1], B Grund[2], C Ekenberg[1], A Zucco[1], J Reekie[1], D Fusco[3], J Gras[4], J Gerstoft[5], MN Polizzotto[6], JD Lundgren[1] and INSIGHT START study group and the FIRST study group

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Purpose: Ten-eleven methylcytosine dioxygenase 2 (TET2) and related genes (IDH1 & IDH2) in the TET2 pathway regulate de-methylation of human DNA. There is also a developing literature connecting the molecular function of the TET2 pathway to regulation of HIV and other retroviruses. We explored if genetic variability in the TET2 pathway explains variability in HIV viral load (VL) using data from two clinical trials (START and FIRST) that enrolled ART-naïve people with HIV.
Method: Participants from the START and FIRST clinical trials were genotyped using a custom content Affymetrix Axiom SNP array. Associations between genetic variation in genes of the TET2 pathway and log10(VL) at study entry were estimated using SKAT-O (gene-level) and linear regression models (SNP-level). START and FIRST were treated as separate cohorts and associations were assessed independently in each cohort. The leading four eigenvectors and sex were included as co-variates. To control for multiple testing at the SNP-level, the Benjamini-Hochberg procedure was used to limit the false discovery rate to<5% (q-value<0.05).
Results: Table 1 shows entry characteristics. Gene level variation in TET2 was significantly associated with VL in both START and FIRST (SKAT-O p-value<0.001). SNP-level analyses revealed 15 SNPs associated with VL in both START and FIRST (q<0.05) (Figure 1). Additionally, 13 and 8 SNPs were associated with VL in one of either START or FIRST, respectively (Figure 1). These SNPs were predominantly found in TET2 (35/36) and clustered in two linkage disequilibrium groups (Figure 2). Each TET2 SNP that associated with higher or lower VL in START associated with the same effect direction and a similar effect size in FIRST (Figure 2).
Conclusion: Genetic variation in TET2 is associated with HIV viral load, providing further evidence that TET2 is an important regulator of HIV-replication *in vivo*.

Baseline Characteristics for Participants of the START and FIRST trials

	START	FIRST
No. of Participants (genetic consent)	2546	544
Age (years) Median (IQR)	36 (29, 45)	38 (32, 44)
Female (%)	20.1	20.2
CD4 + count (cells/mm^3) Median (IQR)	651 (585, 759)	220 (43, 345)
(Log10 copies/mL) Median (IQR)	4.17 (3.54, 4.66)	5.09 (4.53, 5.54)
Region of residence - USA (%)	18	100
Region of residence - Europe/Australia/Israel (%)	49	0
Region of residence - South America/Mexico (%)	20	0
Region of residence - Africa (%)	13	0

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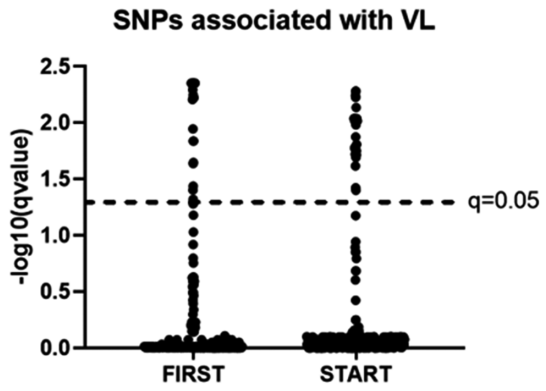


Figure 1 SNPs associated with VL. Q-values of individual SNPs were -log10 transformed and plotted on the y-axis. 36 SNPs were significantly associated with VL in one of either FIRST or START. 15 of these SNPs were significantly associated with VL in both cohorts. Whereas, 8 SNPs were significant only in FIRST and 13 were significant only in START.

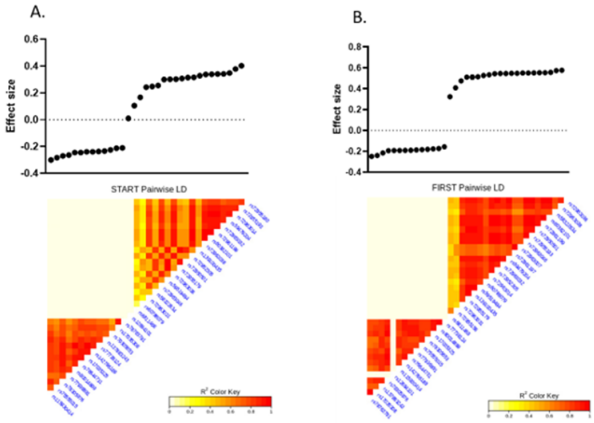


Figure 2 Pairwise Linkage Disequilibrium (LD) analysis of SNPs associated with VL in the START (A) and/or FIRST (B) cohorts. The LD shows two distinct clusters of SNPs in both studies, consisting of SNPs that are associated with lower VL (on the left), and those associated with higher VL (on the right). All TET2 SNPs that associated with higher VL in START associated with higher VL in FIRST. Likewise, TET2 SNPs that associated with a lower VL in START associated with a lower VL in FIRST. LD is measured using R^2 of each SNP pair; darker colour denotes higher associations.

Effect Size and LD of SNPs associated with VL

PS5/4

Temporal evolution of a unique N332 supersite directed bnAb lineage in slow progressing HIV-1 infection

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Purpose: Elicitation of broadly neutralizing antibodies (bnAbs) is considered as a prerequisite for a preventive HIV-1 vaccine but induction of bnAbs by immunization has so far not been successful. Unravelling pathways of bnAb development in natural infection thus provides a crucial basis to guide bnAb vaccine strategies. Here, we report on the evolution of ZPHI-12, a unique N332 supersite directed bnAb, which we isolated approximately five years post infection (p.i.) from a slow progressor with Subtype B infection enrolled in the Zurich Primary HIV Infection Cohort (ZPHI).
Method: To investigate the evolution of ZPHI-12 longitudinally we utilized a series of NGS strategies, which yielded 279 heavy and 44 light chain variants. Germline-reverted, representative intermediate and mature Ab variants were probed for neutralization activity against a multi-clade virus panel and binding properties on a panel of 61 different HIV-1 antigens.
Results: ZPHI-12 belongs to the V3 glycan class of bnAbs and binds the "GDIR" motif. Sequence analysis revealed an unusual stretch of seven tyrosines in the ZPHI-12 CDRH3 that has not been observed in other bnAbs. ZPHI-12 clonal relatives already appeared at week (wk) 46p.i. and showed superior breadth compared to the more mutated mature antibody. The most potent heavy chain variants were identified at wk89 and 115p.i. Phenotypic analysis of ZPHI-12 lineage Ab producing cells revealed large numbers of plasmablasts at wk89p.i., whereas the majority of ZPHI-12 lineage members at wk115p.i. was identified in memory B cells, suggesting that the peak of ZPHI-12 evolution had already passed.
Conclusion: Our study highlights the potential of differentiating plasmablast and memory B cell derived bnAb sequences longitudinally as this provides powerful means to improve time-based definition of bnAb evolution. The comprehensive knowledge of early ZPHI-12 lineage evolution we present elucidates the protracted development of bnAbs that are important for devising HIV-1 vaccination strategies.

PS5/5

Prevalence of InSTI resistance and effectiveness of InSTI-based regimens in HIV-infected patients: results from a European cohort study

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Purpose: The global dynamics of InSTI resistance remains to be investigated. This study aimed at analyzing InSTI resistance and effectiveness of InSTI-based regimens.
Method: INTEGRATE is a large European collaboration enrolling patients who started InSTI-based regimens from 1/1/2012. We investigated time to InSTI discontinuation (intra-class switch=discontinuation) and to virological failure (VF, defined as 1 viral load (VL)>1,000 copies/mL or 2 consecutive VL>50 copies/mL or 1 VL>50 copies/mL followed by treatment change).
Results: A total of 10,969 InSTI-based regimens were analysed of which 1,711 treatments from ART-naïve (group, G, 1), 2,975 from ART-experienced, InSTI-naïve, aviremic (G2a), 1,244 from ART-experienced,

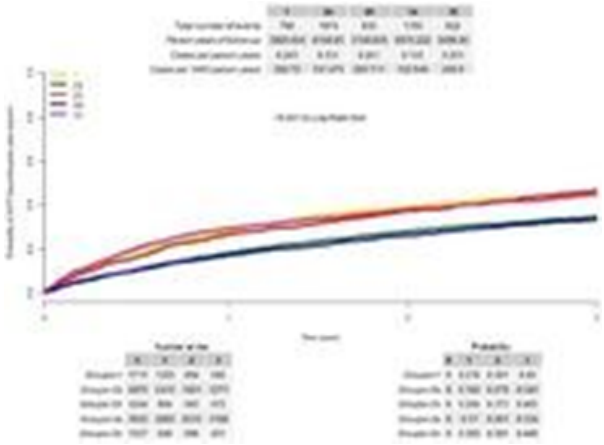


Figure 1. Estimated probability of InSTI discontinuation according to class exposure and baseline VL

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Table 1. Baseline characteristics of population

Variables	ART-naïve (n=1,711) Group 1	ART-experienced InSTI-naïve aviremic (n=2,975) Group 2a	ART-experienced InSTI-naïve viremic (n=1,244) Group 2b	ART-experienced InSTI-experienced aviremic (n=3,502) Group 3a	ART-experienced InSTI-experienced viremic (1,357) Group 3b
Baseline HIV-RNA Log10 (cps/mL), median (IQR)	4.9 (4.3–5.5)	1.4 (0–1.6)	3.4 (2.1–4.7)	1.4 (1.1–1.6)	2.6 (1.8–4.5)
Baseline CD4 cells count (cells/mm^3), median (IQR)	329 (139–510)	620 (440–815)	336 (170–560)	578 (381–807)	316 (145–551)
Raltegravir use, n (%)	401 (23.4%)	643 (21.6%)	474 (38.1%)	1191 (34.0%)	455 (33.5%)
Elvitegravir use, n (%)	421 (24.6%)	488 (16.4%)	173 (13.9%)	614 (17.5%)	176 (13.0%)
Dolutegravir use, n (%)	889 (52.0%)	1,845 (62.0%)	599 (48.2%)	1,750 (50.0%)	744 (54.8%)
Cumulative PI RAMs pre-baseline, n (%)	16 (0.9%)	96 (3.2%)	58 (4.7%)	331 (9.5%)	161 (11.9%)
Cumulative NRTI RAMs pre-baseline, n (%)	26 (1.5%)	262 (8.8%)	175 (14.1%)	641 (18.3%)	327 (24.1%)
Cumulative NNRTI pre-baseline, n (%)	10 (0.6%)	237 (8.0%)	184 (14.8%)	476 (13.6%)	274 (20.2%)
Cumulative INI RAMs pre-baseline, n (%)	1/520 (0.1%)	1/361 (0.3%)	3/355 (0.8%)	35/954 (3.6%)	61/805 (8.6%)

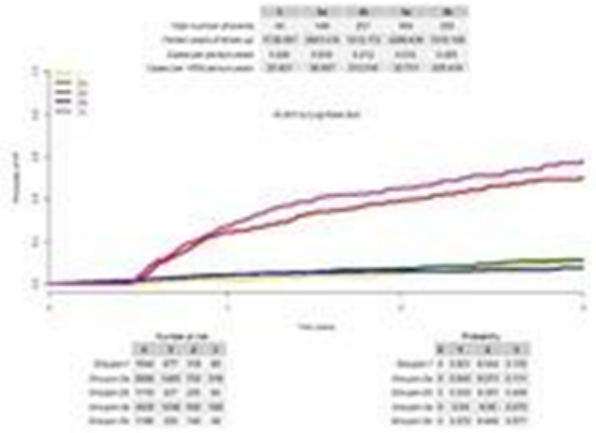


Figure 2. Estimated probability of VF according to InSTI exposure and baseline VL

InSTI-naïve, viremic (G2b), 3,502 from ART-experienced, InSTI-experienced, aviremic (G3a) and 1,537 from ART-experienced, InSTI-experienced, viremic (G3b) patients.

Transmitted InSTI major drug resistance mutations (DRMs) were detected in 1/520 (0.2%) patients from G1, 1/361 (0.3%) from G2a and 3/355 (0.8%) from G2b; however, InSTI-DRM were detected in 35/954 (3.6%) and 61/705 (8.6%) cases from G3a and G3b, respectively. The 1-year probability of InSTI discontinuation was 28% in G1, 18% in G2a, 26% in G2b, 17% in G3a and 29% in G3b and the 1-year estimated probabilities of VF were 2% in G1, 4% in G2a, 24% in G2b, 4% in G3a and 27% in G3b.

The Cox models showed that the use of first generation InSTIs was associated to a higher risk of InSTI discontinuation in all groups. A longer time of virosuppression predicted a lower risk of VF in G2a and G3a, while previous VF was associated to a higher risk of VF in all treatment-experienced patient groups (G2a-b, G3a-b).

Conclusions: InSTI resistance remains virtually non-existent without InSTI exposure and is detectable in a modest proportion of InSTI-experienced patients, making InSTI resistance testing mandatory after failure. Previous VF and duration of virosuppression before switch were independent predictors of VF.

PS5/6

In vitro analysis of doravirine activity on HIV-1 clones harboring multiple NNRTI resistance mutations

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Purpose: Doravirine is a NNRTI recently approved for HIV-1 therapy with improved efficacy, pharmacokinetics and safety profile compared to efavirenz and limited cross-resistance with rilpivirine and etravirine. This study aimed to evaluate the in vitro activity of doravirine in a panel of HIV-1 clones harboring combinations of major NNRTI resistance associated mutations (RAMs).

Method: Infectious clones with intermediate to high-level resistance to rilpivirine, etravirine, efavirenz and nevirapine were obtained from the AIDS Reagent Program. In vitro susceptibility to doravirine was measured by a TZM-bl cell-based assay and fold-change (FC) values were calculated with respect to the wild-type NL4–3 strain. FC values were compared with predicted doravirine activity by HIVdb and ANRS algorithms.

Results: Viruses harboring both doravirine and major NNRTI RAMs showed FC>100 in two cases (ID 12225 and 12237), while 12229, 12231, 12241 and 12243 showed a moderately decreased susceptibility (FC 4.0, 22.1, 3.1 and 6.2, respectively) (Figure 1). Two samples without doravirine RAMs but including 181C (12235 and 12239) showed a considerably reduced susceptibility to doravirine (FC 31.8 and 14.2, respectively), while the absence of doravirine

Virus ID	NNRTI Resistance Mutations	FC	Predicted susceptibility	
			HIVdb	ANRS
12227	K101P, K103N	0.4	PLL	S
12229	L100I, K103N, **H221Y**	4.0	I	R
12231	**K103N**, V179F, **Y181C**	22.1	LL	R
12233	K101E, Y181V	2.8	I	S
12235	A98G, K101E, Y181C, G190A	31.8	R	S
12237	V106I, Y181C, G190A, **H221Y**	>100	I	S
12239	A98G, K101E, E138K, Y181C	14.2	I	S
12241	K101E, E138G, **G190S**	3.1	I	R
12243	L100I, V179D, **M230L**	6.2	R	R
12225	E138G, **H221Y, F227L, M230L**	>100	R	R

DOR RAMs are in bold. FC: fold change; S: susceptible; PLL: potential low level resistance; LL: low level resistance; I: intermediate resistance; R: high level resistance

Figure 1. FC values and predicted susceptibility to DOR of viruses harboring NNRTI RAMs

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RAMs and Y181C (12227 and 12233) resulted in a minimal impact (FC of 0.4 and 2.8, respectively). HIVdb algorithm potentially underestimated doravirine activity in samples 12231, 12237 and 12239, predicted as low-level or intermediate resistance. Similarly, ANRS underestimated doravirine activity in samples 12235, 12237 and 12239, all considered as susceptible.
Conclusion: Doravirine susceptibility can be affected by NNRTI cross-resistance in samples harboring 181C plus one or more NNRTI mutations, even in the absence of specific doravirine RAMs. While doravirine remains active against most single major NNRTI mutants, doravirine resistance may thus result from the accumulation of multiple mutations, similarly to etravirine. In vivo studies are awaited to define the role of NNRTI resistance patterns on clinical doravirine activity.

Addressing the HIV and STI syndemics co-organised with the International AIDS Society (IAS)

PS6/1

The natural history of anal high grade squamous intraepithelial lesions in HIV positive and HIV negative gay and bisexual men

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Purpose: Gay and bisexual men (GBM), especially those living with HIV, are disproportionately affected by anal cancer. Prevention is hindered by incomplete understanding of the natural history of its precursor, anal high grade squamous intraepithelial lesions (HSIL). We aimed to describe the natural history of anal HSIL in GBM in Sydney, Australia, where anal HSIL is not routinely treated.
Method: The Study of the Prevention of Anal Cancer was a prospective, 3-year, cohort study conducted 2010–2018. HIV-positive and HIV-negative GBM aged≥35 years were recruited from community-based settings. HSIL was diagnosed on cytology and/or high-resolution-anoscopy-guided-biopsy at baseline and at 3 annual visits. Predictors of HSIL incidence and clearance were calculated using Cox regression.
Results: Among 617 men, 220 (35.7%) were HIV-positive, median age 49 years. There were 124 incident HSIL cases over 1097.3 person-years of follow-up (PYFU) (11.3 [95% CI 9.5–13.5] per 100PY). Univariate predictors of higher HSIL incidence included age<45 years (HR 1.64, 95% CI 1.11–2.41), HIV-positivity (HR 1.43, 95% CI 0.99–2.06), prior SIL diagnosis (p-trend<0.001) and HPV16 DNA detection (HR 3.39, 2.38–4.84). Over 695.3 PYFU, 153 HSIL cleared (clearance 22.0 [95% CI 18.8–25.8] per 100PY). Predictors of HSIL clearance were age<45 years (HR 1.52, 1.08–2.16), anal intraepithelial neoplasia (AIN)2 rather than AIN3 (HR 1.79, 1.29–2.49), smaller lesions (HR 1.62, 1.11–2.36) and lack of persistent HPV16 (HR 1.72, 1.23–2.41). There was one progression to cancer (incidence 0.224 [95% CI 0.006–1.25] per 100 PY).
Conclusion: Approximately one in ten men per year developed anal HSIL. Clearance was common, at about 20% per year after baseline HSIL. Progression to anal cancer was rare. These data strongly suggest that not all anal HSIL detected in screening requires treatment. Men with persistent HPV16 were less likely to clear HSIL and are more likely to benefit from effective HSIL treatments.

PS6/2

The role of E6/7 mRNA for anal cancer screening in HIV-infected men who have sex with men

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Purpose: To assess high-grade squamous intraepithelial lesions (HSIL) screening strategies that include E6/E7 oncogenes mRNA determination (E6/7-mRNA-test) and human papillomavirus (HPV) DNA detection biomarkers to triage candidates for High Resolution Anoscopy (HRA).
Method: HIV-infected men who have sex with men (MSM) from ELAVI-67 cohort (NCT03357991) underwent anal smear and HRA with biopsy of suspected dysplasia areas. Anal smear samples were tested by anal liquid-based cytology (aLBC), HPV DNA detection performed by both Linear Array (LA) (37 HPV genotypes) and Hybrid Capture®2 (HC2) (13 High-risk HPV (HR-HPV) genotypes), and E6/7-mRNA-test using Aptima® (14 HR-HPV genotypes). Two combined triage screening strategies were evaluated: 1) aLBC with a threshold of atypical squamous cells of undetermined significance (ASCUS) and/or positive biomarker; 2) aLBC ASCUS and low-grade SIL (LSIL) and positive biomarker (aLBC HSIL and ASCUS that cannot rule out HSIL (ASC-H) were considered direct HRA candidates).
Results: 280 participants, mean age 45.2, mean CD4 count 801 cells/mm^3, 96.4% undetectable viral load. aLBC results: 2.5% inadequate, 50% benign, 16.8% ASCUS, 16.1% LSIL, 3.2% ASC-H and 11.8% HSIL. HRA results: 60% benign, 21.8% LSIL and 18.2% HSIL. Positive biomarker results: 90% LA (44.6% considering 14 genotypes included in E6/7-mRNA-test), 35% HC2 and 46.4% E6/7-mRNA-test. aLBC with a threshold of ASCUS showed 78%

Sensitivity, specificity and Area Under the ROC Curve (AUC) for each biomarker alone and in two combined triage screening strategies

	Biomarker alone			First combined strategy: biomarker and/or aLBC			Second combined strategy: biomarker if aLBC ASCUS or LSIL		
	Sensitivity	Specificity	AUC	Sensitivity	Specificity	AUC	Sensitivity	Specificity	AUC
LA HPV DNA test (all 37 genotypes)	92.2%	10.6%	0.514	98%	8.4%	0.514	72.6%	59.7%	0.649
LA HPV DNA test (14 genotypes included in E6/7-mRNA test)	72.6%	61.7%	0.671	90.2%	41.9%	0.670	64.7%	72.2%	0.678
HC2 HPV DNA test	66.7%	72.1%	0.694	90.2%	43.2%	0.670	68.6%	78.9%	0.731
E6/7-mRNA test	80%	61.1%	0.705	90%	41.9%	0.657	70.6%	71.6%	0.706
p-value of AUC comparisons	<0.05 only LA HPV DNA test 37 genotypes vs other biomarkers			<0.05 only LA HPV DNA test 37 genotypes vs other biomarkers			>0.05 for all comparisons in this strategy		

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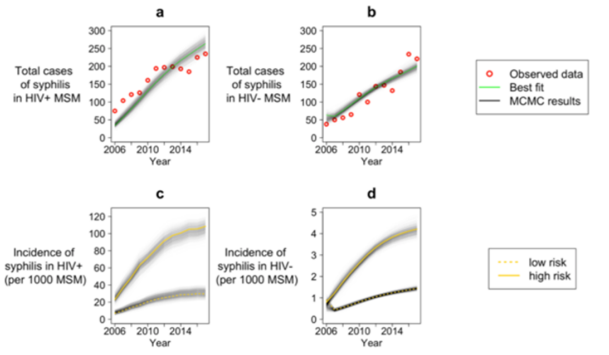
sensitivity and 56.1% specificity for biopsy-proven HSIL (AUC=0.68, p>0.05 compared with other biomarkers). Sensitivity and specificity of biomarkers are shown in the table.
Conclusion: E6/7-mRNA-test alone has high sensitivity and specificity, and could be considered for triage. LA has high sensitivity but low specificity due to the high HPV prevalence, not being useful for triage. First combined strategy increases sensitivity but decreases specificity and AUC are similar to aLBC alone, not providing triage advantages. Second combined strategy decreases sensitivity but increases specificity, with high AUC and the advantage of saving biomarker and HRA performance.

PS6/3

Modelling the syphilis epidemic among HIV-positive and negative MSM in Switzerland

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Background: Over the last decade, syphilis incidence among HIV-positive and negative men who have sex with men (MSM) has strongly increased in Switzerland. Here we use a mathematical model that considers factors such as changing sexual behaviour to reproduce the syphilis epidemic.
Methods: We set up a transmission model consisting of 36 coupled ordinary differential equations to model the syphilis epidemic in MSM in Switzerland between 2006 and 2017. We stratified the model by syphilis stage, cascade of care and sexual risk behaviour (MSM reporting occasional partners) to account for infectiousness, disease progression and exposure to transmission. Additional model layers include the episode of syphilis (first or recurrent) and HIV status. The model was parameterized and calibrated by fitting to the observed diagnosed cases from the Swiss HIV Cohort Study (SHCS) and the published data from the Federal Office of Public Health (FOPH), Switzerland.
Results: We assessed the information of 5560 HIV-positive MSM registered in the SHCS between 2006 and 2017. 1272 (22.8%) HIV-positive MSM had at least one episode of syphilis and 521 (41.0%) of them had recurrent episode(s) of syphilis. The overall diagnosed cases of syphilis among MSM in Switzerland have increased from 113 in 2006 to 456 cases in 2017. Our mathematical model reproduced the strong increase in syphilis diagnoses from a mean of 124 episodes in 2006–2008 up to a mean of 438 episodes in 2015–2017, with an estimated additional 35 episodes every year. The model also reproduced about three-fold higher syphilis incidence in MSM reporting occasional partners compared to MSM reporting no occasional partners.
Conclusions: Our model accurately reconstructs the syphilis epidemic among MSM in Switzerland by capturing changes in sexual risk behaviour and interactions between HIV-positive and negative MSM. Syphilis incidence increased markedly in both HIV-positive and negative MSM and correlated with sexual risk behaviour.



Model predictions and observed syphilis cases in HIV-infected and uninfected MSM

Antiretroviral therapy in special populations

PS7/1

RPV+DRV/cobi as 2DR option in HIV-infected subjects on virologic suppression

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Purpose: Rilpivirine plus cobi-boosted darunavir was compared to standard cART in virologically suppressed patients.
Method: Randomized, non-inferiority trial in chronically HIV-1 infected patients>18 years-old on a stable, effective
(>6 months) three-drug cART. The primary endpoint was non-inferiority of the virological response at 6 months between treatment groups, according to the FDA snapshot design.
Results: 160 patients received RPV+DRV/cobi or continued their ongoing triple-regimen (see figure 1). Patients were 73% males with a median age of 50 years and more than 10 years of cART history. NNRTIs were used in 70% of subjects, PIs in 38% and INIs in 22%. NRTIs included: TDF (49%); TAF (32%) and ABC (19%). Baseline median CD4 were 761 cells/mcL and median time below detection was 7.4 years.
RPV+DRV/cobi was non-inferior. At 6 months, 0% of patients with RPV+DRV/cobi presented a HIV-RNA level>50 copies/mL compared to 3.7% of controls (difference 3.75%, 95% CI −0.41 + 7.91). A HIV-RNA level <50 copies/mL was detected in 91.3% of patients on 2DR and in 93.8% of controls (difference −2.5%, 95% CI −10.65 + 5.65)(figure 2). CD4 medians slightly increased (20 cells/mcL) with RPV+DRV/cobi and decreased (77 cell/mcL) among controls. We observed a statistically significant increment of total cholesterol and LDL-cholesterol with RPV+DRV/cobi (17 and 12 mg/dl, respectively) and no change in HDL in either group. Bone mineral density was stable among switched patients and decreased among controls (+0.3 vs. −2.0 g/cm^2; p=0.025 within

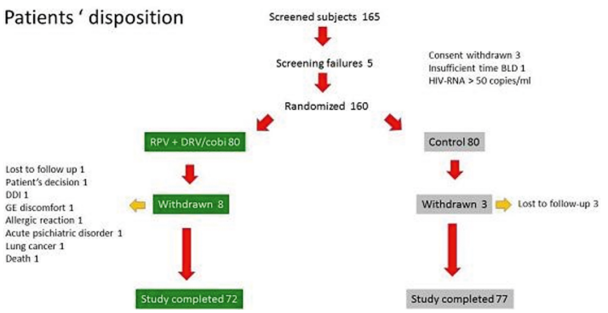


Figure 1. Patients' disposition

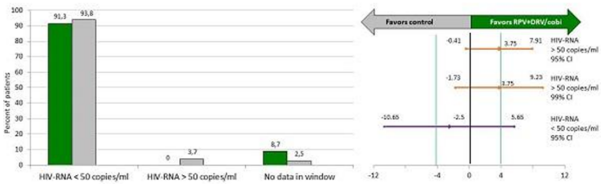


Figure 2. Snapshot analysis.

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controls). Five AEs (3 drug-related: psychosis; diarrhea; rash) in the RPV+DRV/cobi group lead to drug discontinuation/change. None among controls.
Conclusion: A RPV+DRV/cobi 2DR was non-inferior over 6 months to standard triple cART. The dual therapy was more friendly on bone metabolism.

PS7/2

Switching to DTG/3TC fixed dose combination (FDC) is non-inferior to continuing a TAF-based regimen (TBR) through 48 weeks: subgroup analyses from the TANGO study

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Purpose: The 2-drug regimen (2DR) of DTG/3TC reduces cumulative drug exposure in people treated for HIV-1 infection, when compared to traditional 3DRs. DTG/3TC 2-drug regimen (2DR) is non-inferior to DTG+TDF/FTC 3DR in HIV-1 infected ART-naïve adults (GEMINI) and in ART-experienced virologically suppressed participants switching from a TAF-based 3DR (TANGO). Here we present a key secondary endpoint from the TANGO study: Snapshot virologic success by baseline regimen third agent class, disease and demographic characteristics.
Method: TANGO is a randomized, open-label, multicenter, non-inferiority Phase III study evaluating the efficacy and safety of switching to DTG/3TC once daily in HIV-1 infected adults on TBR, with HIV-1 RNA<50 c/mL for>6 months, without prior virologic failure or historical NRTI or INSTI major resistance mutations. Participants were randomized 1:1 (stratified by baseline 3rd agent class: PI, NNRTI, INSTI) to switch to DTG/3TC or continue TBR through Week 148. The primary endpoint was the proportion of participants with plasma HIV-1 RNA^3 50 c/mL at Week 48 (FDA Snapshot algorithm, Intention To Treat-Exposed [ITT-E] population).
Results: 741 randomized/exposed participants (DTG/3TC: 369; TBR: 372) were included. Snapshot success rates across subgroups were generally consistent with the overall TANGO Week 48 study results and were similar between arms (Table 1). Zero participants on DTG/3TC and 1 participant (< 1%) on TBR met confirmed virologic withdrawal with no resistance mutations observed at failure.
Conclusion: Switching to DTG/3TC FDC was non-inferior to continuing a TAF-based 3DR in maintaining virologic suppression in HIV-1 infected ART-experienced adults through Week 48. Efficacy by subgroups was consistent with overall Week 48 study results, demonstrating that switching from TBR to DTG/3TC is effective at maintaining virologic suppression regardless of baseline regimen, patient or disease characteristics.

Table 1. Proportion of participants with plasma HIV-1 RNA < 50 c/mL at Week 48: Snapshot Analysis by subgroups – ITT-E population

		TANGO Study	
		DTG/3TC	TAF-Based Regimen
		n/N (%)	n/N (%)
Overall Population		344/369 (93.2)	346/372 (93.0)
Adjusted difference and 95% CI*		0.2 (-3.4, 3.9)	
Age (years)	< 35	118/130 (90.8)	109/119 (91.6)
	35- < 50	153/160 (95.6)	151/161 (93.8)
	≥ 50	73/79 (92.4)	86/92 (93.5)
Gender	Female	21/25 (84.0)	27/33 (81.8)
	Male	323/344 (93.9)	319/339 (94.1)
Race	White	278/296 (93.9)	272/289 (94.1)
	African Heritage	45/51 (88.2)	51/58 (87.9)
	Asian	12/13 (92.3)	12/13 (92.3)
	Other	9/9 (100)	11/12 (91.7)
Baseline Third Agent Class	INSTI	268/289 (92.7)	276/296 (93.2)
	NNRTI	49/51 (96.1)	42/48 (87.5)
	PI	27/29 (93.1)	28/28 (100)
Baseline CD4+ (cells/mm^3)	<350	31/35 (88.6)	29/30 (96.7)
	≥ 350	313/334 (93.7)	317/342 (92.7)

*: Adjusted difference for overall population (DTG/3TC – TBR) and 95% confidence intervals are based on a stratified analysis (adjusting for baseline third agent class) using Cochran-Mantel-Haenszel weights and an 8% non-inferiority margin.

Proportion of participants with plasma HIV-1 RNA<50 c/mL at Week 48: Snapshot Analysis by subgroup

PS7/3

Safety and efficacy of triple therapy with Dolutegravir plus 2 NRTIs, in treatment-naïve HIV-2 infected patients – 48 weeks results from a phase II study

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Objectives: Evaluate the efficacy, safety and tolerability of triple therapy with Dolutegravir (DTG) plus 2 nucleoside reverse transcriptase inhibitors in treatment-naïve HIV-2 infected patients.
Methods: A phase II open label study was conducted in Portugal (EudraCT: 2016-000346-61). DTG/abacavir/lamivudine or DTG+tenofovir (TDF)/emtricitabine was administered for 48 weeks. Inclusion criteria were CD4<500 cells/μL or plasma viral load (pVL)>40 copies/mL. Treatment efficacy was evaluated by the proportion of subjects achieving a pVL<40 copies/mL and/or by the change from baseline in CD4 cell count and in CD4/CD8 ratio at week 48 (W48).
Results: Thirty individuals were enrolled, 73% female and mean age of 54 years. At baseline 17 (56.7%) were viremic (mean pVL 403.3 (min-max: 56–1959) copies/mL), with median CD4 count 438 cells/μL (min-max: 86–1651) and CD4/CD8 ratio 0.81. Ninety percent of participants completed the study. At W24, all viremic participants at baseline, had a pVL<40 copies/mL. At W48, 27/30 participants had pVL<40 copies/mL (1 subject withdrawn, 1 discontinued due to adverse event and 1 was lost to follow-up). No virological failures were observed. Mean change from baseline of CD4 count and CD4/CD8 ratio at W48 were of + 95.6 (95% CI: 28.0–163.1) cells/μL and + 0.26 (95% CI: 0.17–0.43), respectively. The most common drug-related adverse events were headache (20.0%) and nausea (13.3%) and were grade 1–2. There were no serious adverse events. One subject discontinued due to drug-related insomnia, anxiety and memory disturbance. No AIDS associated clinical events were reported.
Conclusion: This is the first clinical trial assessing the use of DTG in HIV-2 infection. Our data suggest that DTG + 2NRTIs is a safe and effective first-line treatment, with CD4 cell recovery comparable to other regimens already tested in HIV-2 infection. There were no virological failures and no resistance mutations emerged, suggesting a higher genetic barrier of DTG in HIV-2 as observed in HIV-1.

PS7/4

HIV-1-RNA kinetics in blood plasma and in seminal plasma of men starting a dolutegravir-based regimen at the time of primary HIV-1 infection

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Purpose: The most advantageous first-line antiretroviral combination with regards to time course and magnitude of HIV-1-RNA decay in semen remains to be determined. Because primary HIV infection (PHI) harbors the highest risk of HIV-1 sexual transmission, we compared HIV-1-RNA (VL) kinetics in seminal

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Table: Evolution of immune-virological markers and ARV concentrations, median (Interquartile range (IQR)), n=19 participants

		Baseline	W2	W4	W8	W12	W24	W36	W48
HIV-1-RNA log10 copies/mL	SP	4.5 (3.6–5.0)	3.1 (2.6–3.7)	2.1 (1.3–2.9)	1.3 (1.3–1.9)	1.3 (1.3–1.9)	1.3 (1.3–2.0)	1.3 (1.3–1.9)	1.3 (1.3–1.3)
	BP	6.5 (5.6–7.9)	3.2 (2.9–4.1)	2.6 (2.2–3.0)	1.5 (1.4–2.2)	1.6 (1.3–2.1)	1.3 (1.3–1.6)	1.3 (1.3–1.4)	1.3 (1.3–1.4)
CD4 count (cells/mm^3)	BP	460 (332–561)		751 (552–861)		730 (572–942)	777 (589–970)		810 (578–950)
Total DTG concentration (ng/mL)	SP		147 (73–241)	126 (74–227)	145 (62–186)	119 (89–250)	135 (95–198)	105 (73–286)	136 (87–201)
	BP		2931 (1517–3401)	2226 (996–3292)	2430 (1277–3201)	2205 (1089–3068)	2140 (1340–3079)	1842 (1074–2739)	2226 (1720–3086)
	SP/BP		0.08 (0.03–0.09)	0.08 (0.05–0.13)	0.06 (0.03–0.09)	0.08 (0.06–0.09)	0.06 (0.05–0.10)	0.09 (0.06–0.11)	0.07 (0.03–0.08)
Free DTG concentration (ng/mL)	SP		63 (43–101)	54 (27–73)	63 (45–100)	77 (45–104)	74 (41–111)	72 (37–97)	61 (43–92)
	BP		6.3 (5.0–9.4)	5.3 (2.7–7.7)	7.4 (2.4–9.3)	5.1 (2.7–7.0)	5.1 (2.9–7.3)	5.2 (3.1–7.3)	5.2 (4.3–9.1)
	SP/BP		11.1 (5.6–21.2)	15.0 (11.5–17.0)	15.0 (6.4–18.6)	15.7 (14.4–20.7)	14.6 (5.7–21.8)	15.1 (10.3–24.1)	11.7 (7.4–16.7)

plasma (SP) and in blood plasma (BP) of men starting a dolutegravir-based regimen at the time of PHI.
Methods: Open, single-arm, prospective study enrolling men diagnosed at the time of PHI (≤3 months) and starting dolutegravir (DTG) plus TDF/FTC. Paired samples of BP and SP were collected at Baseline (BL), Week(W) W2, W4, W12, W24, W36 and W48, for VL quantification and measurement of TDF/FTC and total and free DTG concentrations (UPLC-MS/MS). The primary outcome was the achievement of a first VL below the lower limit of quantification (LOQ) in BP (20 cp/mL) and in SP (60 cp/mL), assessed with the Kaplan-Meier method.
Results: 19 men were enrolled, 4 at Fiebig stage II (F-II), 5 F-III, 1 F-IV, 4 F-V and 5 F-VI. Baseline markers and their evolution over time are shown in Table. At BL, median (IQR) VL was 6.5 (5.6–7.9) and 4.5 (3.5–5.0) $\log_{10}$cp/mL in BP and SP, respectively. Treatment was started a median of 7 days (3–12) after diagnosis. Between BL and W48, a significantly higher proportion of participants achieved a first VL below LOQ in SP (93.0%) than in BP (84.2%; p=0.008). Median time to reach a first VL below LOQ was 8 weeks in SP (95% CI: 5.6–10.4) and 24 weeks in BP (95% CI: 14.1–33.9). DTG concentrations in BP and SP were mainly expected, adequate and stable along the study period.
Conclusion: DTG-based regimen initiated at the time of PHI was able to rapidly achieve VL suppression in seminal plasma.

PS7/5

Dolutegravir and lamivudine for maintenance of HIV viral suppression in adults with and without historical resistance to lamivudine: 48-week results of a pilot clinical trial (ART-PRO)

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Purpose: To assess efficacy and safety of DTG + 3TC for maintenance of HIV-1 suppression in participants without M184V/I or K65R/E/N mutations in proviral DNA by population genotyping.
Method: Open, single-arm, 48-week pilot trial including HIV-1 infected adults, INSTI-naïve, CD4 count>350 cell/μL, VL<50 copies/mL for one year prior to study entry. Participants were excluded if baseline proviral DNA population genotyping detected M184V/I or K65R/E/N. Baseline proviral DNA Next Generation Sequencing (NGS) genotype was retrospectively performed to detect resistance minority variants. All participants were switched to DTG + 3TC. Primary efficacy endpoint was proportion of participants with VL<50 copies/mL at W48 (FDA snapshot, ITT-e). Safety and tolerability outcomes were incidence of AEs and treatment discontinuation.
Results: 41 participants switched to DTG + 3TC: 21 participants had M184V/I or K65R/E/N in historical plasma genotyping and 20 had not.(Table 1) Baseline NGS detected>5% 3TC mutations (combined M184V/I and K65R/E/N) in 15/21 (71.4%) of participants with and 3/20 (15%) of participants without prior history of 3TC resistance.
At week 48, 92.7% of participants (38/41) remained with VL<50 copies/mL. Of the 20 participants without historical 3TC resistance none met virological failure. Of the 21 participants with historical 3TC resistance, none met virological failure: 3 prematurely discontinued with suppressed viremia [2 protocol violations, one AE (insomnia, W8)]. (Table 2)(Figure 1)
One participant with historical M184I rebounded to 1120 copies/mL at W36 and resuppressed on DTG + 3TC, without M184I detection or integrase resistance in plasma by Sanger sequencing.(Figure 2) There were 10 blips, 4 in the group with historical resistance. There were 29 related AE, 4/29 were severe and only 1/29 led to discontinuation.
Conclusion: In this pilot trial, DTG + 3TC was effective maintaining virologic control despite history of lamivudine resistance and presence of archived 3TC mutations detected by NGS. Fully powered studies are needed to confirm our results. 144-week study extension of our trial is ongoing. (NCT03539224)

Table 1. Baseline characteristics

	All participants (n=41)	Historical resistance to 3TC (n=21)	No historical resistance to 3TC (n=20)	p value
Male sex, n (%)	32 (78.0)	16 (76.2)	16 (80)	0.768
Age (years), median (IQR)	52.3 (45.3–56.8)	53.3 (47–57.5)	50.7 (42.8–55.2)	0.636
Time since HIV diagnosis (years), median (IQR)	20.5 (14.8–25.0)	21.4 (17.4–23.4)	16.8 (11.9–27.3)	0.342
CD4 count (cells/mm^3), median (IQR)				
Nadir	196 (93–290)	160 (99–216)	259 (70–314)	0.161
Baseline	661 (532–886)	821 (574–952)	608 (484–813)	0.272
ART duration (years), median (IQR)	17.9 (13.0–21.3)	18.7 (17.1–20.9)	13.0 (7.8–21.5)	0.085
Duration of suppressed plasma HIV RNA (years), median (IQR)	7.7 (3.9–12.2)	9.7 (4.3–12.5)	7.4 (3.5–11.6)	0.636
Number of previous ART regimens, median (IQR)	6 (4–10)	7 (5–12)	4 (2–10)	0.272
Type of ART regimen at baseline, n (%)				
Including 3TC or FTC	28 (68.3)	9 (42.9)	19 (95.0)	<0.001
2 NRTIs + NNRTI or bPI	17 (41.4)	9 (42.9)	8 (40.0)	
bPI + NRTI	19 (46.3)	8 (38.1)	11 (55.0)	0.296
bPI monotherapy	5 (41.2)	4 (19.0)	1 (5.0)	
M184V/I detected by NGS in proviral DNA, n (%)				
>20%	7 (17.1)	6 (28.6)	1 (5.0)	0.090
>5%	17 (47.5)	14 (66.7)	3 (15.0)	0.003
>1%	27 (65.9)	20 (95.2)	7 (35.0)	<0.001
K65R/E/N detected by NGS in proviral DNA, n (%)				
>20%	1 (2.4)	1 (4.8)	0 (0)	0.367
>5%	2 (4.9)	2 (9.5)	0 (0)	0.226
>1%	3 (7.3)	3 (14.3)	0 (0)	0.135

*1 patient not amplify

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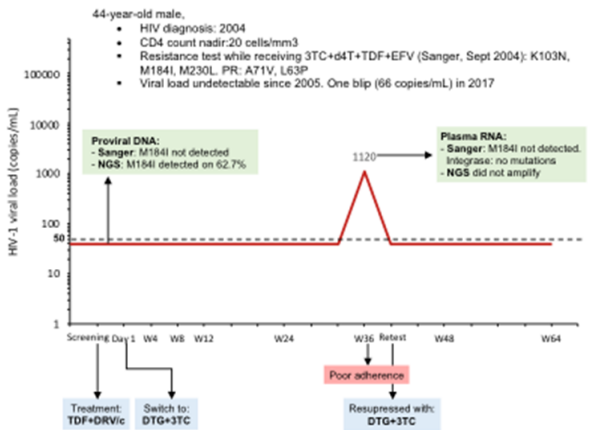
Table 2. Snapshot at W48, Intention to treat-exposed (ITT-e) analysis population.

	All participants (n=41)	Historical resistance to 3TC (n=21)	No historical resistance to 3TC (n=20)
HIV-1 RNA≤50 copies/mL	38 (92.7)	18 (85.7)	20 (100)
HIV-1 RNA≥50 copies/mL	0 (0)	0 (0)	0 (0)
HIV-1 RNA≥50 copies/mL in W48 window	0 (0)	0 (0)	0 (0)
Discontinuation Study Drug due to Lack of Efficacy	0 (0)	0 (0)	0 (0)
Discontinuation Study Drug due to other reasons and Last available HIV-1 RNA≥50 copies/mL	0 (0)	0 (0)	0 (0)
No virologic data at W48	3 (7.3)	3 (14.3)	0 (0)
Discontinuation Study Drug Due to AE	1 (2.4)	1 (4.8)	0 (0)
Discontinuation Study Drug due to other reasons and Last available HIV-1 RNA<50 copies/mL	2 (4.9)	2 (9.5)	0 (0)

Figure 1. Proportion of patients with virological suppression at W48 in Intention-to-treat-exposed (ITT-e) and Per-protocol (PP) analysis. ITT-e population is defined as all participants who received at least one dose of study treatment; PP population is defined as all participants who received at least one dose of study treatment and had no deviation to the eligibility criteria. Virological suppression was defined as an HIV RNA viral load of <50 copies/mL.



Figure 2. Viral load evolution of the patient presenting over 1000 copies/mL at W36.



PS7/6

Efficacy and safety of bictegravir/emtricitabine/tenofovir alafenamide vs comparators in cis-women and girls (living with HIV): an analysis of 5 clinical trials

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Purpose: Globally, the majority of people living with HIV are cis-women. Cis-women bear the brunt of HIV epidemic but remain significantly under-represented in clinical trials. Coformulated bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a once-daily, single-tablet regimen with demonstrated efficacy and safety in clinical trials of treatment-naïve and virologically suppressed adults, adolescents and children living with HIV. Efficacy and safety of B/F/TAF versus comparators in cis-women and girls across five phase 2/3 B/F/TAF clinical trials through 48 weeks were assessed.
Method: Analysis included cis-women and girls from five clinical trials: virologically suppressed adults (studies 1961, 4449), and adolescents and children (study 1474), and treatment-naïve adults (studies 1489, 1490). Participants were grouped by age: children (6–11), adolescents (12–17), adults (18–49) and older adults (≥50). Comparators included dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) (1489), DTG+F/TAF (study 1490), elvitegravir/cobicistat/F/(TAF or tenofovir disoproxil fumarate[TDF]) (study 1961) or atazanavir+ritonavir+F/TDF (study 1961). We assessed efficacy using FDA Snapshot for HIV-1 RNA<50 c/mL, safety, and tolerability at Week 48.
Results: 679 cis-women and girls were analyzed (table); age range was 6–74 years; 44% Black, 28% White, 17% Asian and 12% other. High and similar rates of virologic suppression were observed across age groups (B/F/TAF 87%-100%; comparators 86%-95%). No treatment-emergent resistance was detected with B/F/TAF versus 1 participant on comparator regimen developed resistance. Drug-related adverse events (AEs) occurred in similar proportions of participants taking B/F/TAF versus comparators. Overall rates of grade 3/4 AEs were low. No women and 1 girl discontinued due to any AE in B/F/TAF group vs 2 women in comparators.
Conclusion: B/F/TAF is an effective, safe and well tolerated HIV treatment in this large analysis of cis-women and girls living with HIV spanning ages 6–74 years. High rates of virologic suppression and low incidence of AEs, observed among diverse participants, make B/F/TAF an important treatment option for cis-women and girls.

	Virologically suppressed girls and women							Treatment-naïve women					
	6 to 11 years	12 to 17 years	18 to 49 years		≥50 years			18 to 49 years			≥50 years		
	Study 1474*		Study 1961				Study 4449*	Studies 1489-1490					
	B/F/TAF (n=27)	B/F/TAF (n=32)	B/F/TAF (n=191)	Comparators† (n=196)	B/F/TAF (n=43)	Comparators† (n=40)	B/F/TAF (n=11)	B/F/TAF (Pooled) (n=54)	DTG/ABC/3TC (1489) (n=22)	DTG+ FTC/TAF (1490) (n=29)	B/F/TAF (Pooled) (n=15)	DTG/ABC/3TC (1489) (n=11)	DTG+ FTC/TAF (1490) (n=8)
Baseline Characteristics													
Age, years (min, max)	6, 11	12, 17	21, 49	20, 49	50, 63	50, 63	65, 74	20, 49	20, 49	19, 49	50, 64	53, 68	51, 62
Black	24 (89%)	21 (68%)	72 (38%)	70 (36%)	19 (44%)	13 (33%)	1 (9%)	26 (48%)	17 (77%)	18 (62%)	7 (47%)	6 (55%)	6 (75%)
White	1 (4%)	1 (3%)	56 (29%)	52 (27%)	10 (23%)	15 (38%)	10 (91%)	19 (35%)	5 (23%)	6 (21%)	6 (40%)	5 (45%)	1 (13%)
Asian	2 (7%)	8 (26%)	43 (23%)	46 (23%)	5 (12%)	8 (20%)	0	0	0	1 (3%)	0	0	0
Other	0	2 (6%)	20 (10%)	28 (14%)	9 (21%)	4 (10%)	0	9 (17%)	0	4 (14%)	2 (13%)	0	1 (13%)
Outcomes at Week 48													
HIV-1 RNA <50 c/mL	26 (96%)	31 (97%)	181 (95%)	187 (95%)	43 (100%)	38 (95%)		47 (87%)	20 (91%)	25 (86%)	14 (93%)	10 (91%)	7 (88%)
Treatment-emergent resistance	0	0	0	1	0	0		0	0	0	0	0	0
Drug-related AE, all grades	7 (26%)	1 (3%)	17 (9%)	11 (6%)	3 (7%)	2 (5%)	Data will be presented at conference	10 (19%)	10 (45%)	6 (21%)	1 (7%)	4 (36%)	2 (25%)
Grade 3/4 AE	0	1 (3%)	10 (5%)	11 (6%)	1 (2%)	3 (8%)		7 (13%)	2 (9%)	5 (17%)	0	1 (9%)	2 (25%)
Discontinuations due to AE	1 (4%)	0	0	0	0	0		0	1 (5%)	0	0	0	1 (13%)
Grade 3/4 laboratory abnormalities	7 (26%)	13 (41%)	36 (19%)	42 (21%)	5 (12%)	6 (15%)		9 (17%)	5 (23%)	2 (7%)	3 (21%)	3 (27%)	3 (38%)

*Studies 1474 and 4449 are conducted as open-label , single-arm studies
†Comparator regimen included EJC/F/(TAF or TDF), or ATV+RTV+F/TDF
ATV, atazanavir; E/C/F/(TAF or TDF), elvitegravir/cobicistat/emtricitabine/(tenofovir alafenamide or tenofovir disoproxil fumarate); RTV, ritonavir

Data Table

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Antiretroviral therapy: today and in the future

PS8/1

Adherence and clinical outcomes in asymptomatic patients starting ART: the Swiss HIV Cohort Study

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Purpose: Since the advent of universal test and treat approach, a higher share of individuals initiating ART are asymptomatic with a preserved immune system. We explored the association between adherence and clinical outcomes in asymptomatic patients starting ART.
Method: ART-naive patients registered in the SHCS between 2003 and 2018. Asymptomatic was defined as CDC-stage A within 30 days of starting ART. Non-adherence was defined as any self-reported missed doses. Viral failure was defined as viral load>50 copies/mL on two consecutive measurements after>24 weeks on ART. Logistic regression models were used to measure the association between demographic variables and asymptomatic status. Cox proportional hazard models were used to assess the association between symptom status and viral rebound.
Results: Of 7131 individuals, 76% started ART when asymptomatic and this increased over time (62% in 2003 to 83% in 2017; p<0.001. In multivariable logistic regression models, asymptomatic individuals were more likely to be younger, MSM, more educated, having unsafe sex, have a stable HIV-positive partner, lower viral load, and have started ART in later calendar years. Adherence to ART was significantly better in asymptomatic with non-adherence reported in 48% versus 55% in symptomatic individuals (p<0.001). 1478 individuals (22%) experienced viral failure a median of 1.9 years (IQR: 1.1–4.2) after starting ART. In multivariable Cox models, asymptomatic individuals were at a decreased risk of viral rebound (HR 0.85, 95% CI: 0.74–0.98, p=0.02). After starting ART, 1025 individuals were tested for acquired resistances of which 185 (18%) were detected. Asymptomatic individuals were less likely to develop resistance (14% versus 27%, p<0.001) even in the subset starting ART after 2009 (12% versus 24%, p=0.02).
Conclusion: Despite concerns regarding lack of readiness in those starting ART when asymptomatic or shortly after diagnosis, there is consistent evidence of improved clinical outcomes in these individuals.

PS8/2

Assessments of very low level HIV replication for dolutegravir+lamivudine (DTG + 3TC) vs dolutegravir+tenofovir disoproxil/emtricitabine (DTG+TDF/FTC) in the GEMINI 1&2 studies through week 96

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Purpose: The GEMINI-1&2 studies in treatment-naïve adults showed DTG + 3TC was non-inferior to DTG+TDF/FTC at Week 96 by FDA snapshot algorithm<50 c/mL. Abbott's RealTime HIV-1 assay measures HIV-1 RNA (viral load, VL) from 40 c/mL to 10,000,000 c/mL, and provides qualitative target detected (TD) or target not detected (TND) for VL<40 c/mL. We assessed participants with TND over time and by baseline (BL) VL and CD4.
Method: The proportion of participants with VL<40 c/mL and TND status at Week 96 was analysed using a Cochran-Mantel-Haenszel test stratified by VL (≤100,000 vs>100,000 c/mL) and CD4 + cell count (≤200 vs>200 cells/mm^3) at BL. Participant subgroups were assessed using three approaches: Snapshot, Observed Analysis (only participants with VL<50 c/mL at Week 96 by Snapshot analysed), and Last Observation Carried Forward (LOCF). Times to TND Status were estimated using non-parametric Kaplan-Meier method.
Results: At Week 96 similar proportions of participants in each arm had TND overall, regardless of BL VL and for CD4>200 (Table 1). The % TND was lower in DTG + 3TC arm for CD4<200 (Table 2), however numbers in this subgroup were small limiting ability to make conclusions. Proportions with TND were similar between arms at all visits (Figure 1). Median time to TND (all participants or Observed Analysis populations) was 8 weeks in DTG + 3TC and DTG+TDF/FTC arms for overall population and in BL VL≤100,000 c/mL subgroup, and 16 vs 24 weeks in BL VL>100,000 c/mL subgroup.
Conclusion: Proportions of participants with TND were similar in the DTG + 3TC and DTG+TDF/FTC arms, regardless of BL VL. Median time to TND was similar overall and in BL VL≤100,000 c/mL subgroup, and shorter for DTG + 3TC vs DTG+TDF/FTC if VL>100,000 c/mL at BL. These data, utilizing a more stringent VL measure, continue to demonstrate the potency and a durable efficacy of DTG + 3TC in treatment-naïve subjects.

Table 1. Proportion of Participants with Plasma HIV-1 RNA <40 c/mL and TND at Week 96 Overall and by Baseline Plasma HIV-1 RNA Levels

Analysis[a]	Subgroup[b]	DTG+3TC n/N(%)[c]	DTG+TDF/FTC n/N(%)[c]	Treatment diff. (95% CI)[d]
Snapshot	Overall	474/716 (66)	484/717 (68)	-1.5 (-6.3, 3.2)
	≤100,000	400/576 (69)	405/564 (72)	-2.4 (-7.6, 2.9)
	>100,000	74/140 (53)	79/153 (52)	1.2 (-10.2, 12.7)
Observed	Overall	474/616 (77)	484/642 (75)	1.2 (-3.4, 5.8)
	≤100,000	400/499 (80)	405/510 (79)	0.7 (-4.2, 5.7)
	>100,000	74/117 (63)	79/132 (60)	3.4 (-8.7, 15.5)
LOCF	Overall	530/712 (74)	517/710 (73)	1.2 (-3.3, 5.7)
	≤100,000	560/573 (98)	547/557 (98)	-0.5 (-2.1,1.2)
	>100,000	131/139 (94)	148/153 (97)	-2.5 (-7.3,2.3)

a – Participants were included in assessment via: 1. FDA Snapshot algorithm; 2. Having HIV-1 RNA VL <50 c/mL at Week 96 (Observed Analysis); 3. Using Last observation carried forward (LOCF). Subjects without any post baseline HIV-1 RNA are not included. b – BL VL Subgroup in c/mL. c - Number Responded/Number Assessed (%); d – Used Adjusted for Overall, and Unadjusted as proportion of DTG+3TC - proportion of DTG+TDF/FTC for subgroups.

Table 2. Proportion of Participants with Plasma HIV-1 RNA<40 c/mL and TND at Week 96 by Baseline CD4 + cell count

Analysis[a]	Subgroup[b]	DTG + 3TC n/N (%)[c]	DTG+TDF/FTC n/N (%)[c]	Treatment diff. (95% CI)[d]
Snapshot	CD4≤200	27/ 63 (43)	32/ 55 (58)	-15.3 (−33.2, 2.5)
	CD4>200	447/653 (68)	452/662 (68)	0.2 (−4.9, 5.2)
Observed	CD4≤200	27/ 43 (63)	32/ 48 (67)	-3.9 (−23.5, 15.8)
	CD4>200	447/573 (78)	452/594 (76)	1.9 (−2.9, 6.7)
LOCF	CD4≤200	55/ 62 (89)	53/ 55 (96)	-7.7 (−17.0,1.6)
	CD4>200	636/650 (98)	642/655 (98)	-0.2 (−1.7,1.4)

a - Participants were included in assessment via: 1. FDA Snapshot algorithm; 2. Having HIV-1 RNA VL<50 c/mL at Week 96 (Observed Analysis); 3. Using Last observation carried forward (LOCF). Subjects without any post baseline HIV-1 RNA are not included. b - BL CD4 Subgroup in cells/mm^3. c - Number Responded/Number Assessed (%); d - Unadjusted proportion of DTG + 3TC - proportion of DTG+TDF/FTC.

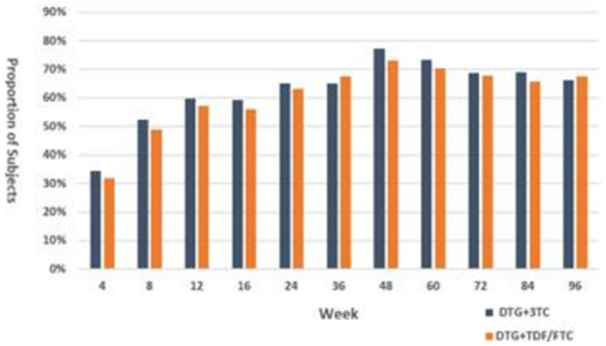


Figure 1. Proportion of Participants with TNDa by Visit: Snapshot analysis

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PS8/3

Dolutegravir/emtricitabine dual therapy is non-inferior to standard combination antiretroviral therapy in maintaining HIV suppression throughout 48 weeks (SIMPL'HIV study)

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Purpose: Dolutegravir (DTG)-based dual therapy is becoming a new paradigm for both the initiation and maintenance of HIV treatment. The SIMPL'HIV study investigated the outcomes of virologically suppressed patients on standard combination antiretroviral therapy (cART) switching to DTG + emtricitabine (FTC) in Switzerland. We present the 48-week efficacy and safety data on DTG+FTC vs cART.
Method: SIMPL'HIV is a multicentre, factorial, open-label, non-inferiority randomized trial among HIV-1 infected adults on cART with HIV-RNA<50 copies/mL for at least 24 weeks (no CD4 or pre-treatment HIV-RNA restriction). Participants were randomized 1:1:1:1 to switching to DTG+FTC or to continuing cART, and to patient-centred surveillance defined as reduced biological monitoring and individualized follow-up vs continuation of 3-monthly monitoring. The primary endpoint was the proportion of patients maintaining HIV-RNA<100 copies/mL throughout 48 weeks. Secondary endpoints included the proportion of patients with HIV-RNA<50 copies/mL at week 48 (FDA Snapshot).
Results: Ninety-three participants were randomized to DTG+FTC and 94 to cART. Mean nadir CD4 count was 259 cells/mm^3 (SD: 187); 17% were female. In the intention-to-treat analysis, the proportion of patients with HIV-RNA<100 copies/mL throughout 48 weeks was 93.5% (87/93) in the DTG+FTC group and 94.7% (89/94) in the cART group (difference: −1.2%, 95% CI: −7.8%; +5.6%; non-inferiority margin: −12.0%). In the week 48 window, FDA snapshot virological success was 90.3% vs 91.5% (difference: −1.1% 95% CI: −9.3%; +7.1%) (table 1). Protocol-defined virological failure (two consecutive HIV-RNA>100 copies/mL) was observed in one participant in the cART group and none in the DTG+FTC group, with no acquired drug resistance mutations. Overall rates of adverse events, including weight gain, were similar in both groups
Conclusion: Switching to DTG+FTC was non-inferior to cART in maintaining HIV suppression throughout 48 weeks and appears to be a safe maintenance therapy strategy.

FDA Snapshot analysis

Week 48 study outcome by FDA Snapshot analysis	DTG+FTC (N=93)	cART (N=94)
HIV-RNA<50 copies/mL*	84 (90.3%)	86 (91.5%)
HIV-RNA>50 copies/mL or change of therapy or discontinuation of therapy due to lack of efficacy**	2 (2.1%)	1 (1.1%)
Discontinuation of therapy due to adverse events	1 (1.1%)	1 (1.1%)
Discontinuation of therapy due to consent withdrawal or loss to follow-up	3 (3.2%)	3 (3.2%)
Included patients with missed data in the Snapshot time window	3 (3.2%)	3 (3.2%)

*Risk difference (95% CI): −1.1% [−9.3%; +7.1%] **According to FDA snapshot, failure is defined by HIV-RNA>50 copies/mL or change of therapy or discontinuation of therapy due to lack of efficacy; by contrast, the protocol-defined virological failure refers to two consecutive HIV-RNA>100 copies/mL.

PS8/4

Risk of failure in dual therapy versus triple therapy in naïve HIV-patients: a meta-analysis

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Purpose: Dual therapy is today an option in naïve HIV patients. The objective of this meta-analysis is to evaluate the relative risk of failure of two-drug compared to three-drug therapies in HIV-naïve patients.
Method: A systematic review and meta-analysis conducted using MEDLINE, Google Scholar and the Cochrane Library. All studies included had to fulfill the following inclusion criteria: present original data from randomized or non-randomized trials; investigate in naïve HIV subjects the efficacy of a triple (control group) versus a dual ARV (experimental group); report the primary outcomes at 48 and 96 weeks clearly defined as regimen failure, identified as patients that stopped therapy for any reason, and/or virological failure, at snapshot analysis, and/or incidence of adverse drug reaction leading to discontinuation of regimen; report data allowing the odds ratio estimates of relative risk (RR) to be calculated for the different outcomes of therapy; be published as full paper from January 2007 up to January 2019.
Results: From a total of 4,743 studies, 15 meet inclusion criteria allowing a meta-analysis on 5,606 patients. At 48 weeks no difference between experimental and control group was observed in RR of regimen (TF) and virological failures (VF) and adverse drug reaction leading to discontinuation of regimen (ADR) (Table 1). Likewise, at week 96 revealed no statistical difference in RR of TF, VF and ADR (Table 2). In figure 1 and figure 2 are presented the data regarding TF and VF at 48 weeks excluding the study maraviroc based. Regarding the RR of TF by dual-therapy at 48 weeks, in study INI-based was 1.07 (95% CI: 0.80–1.44), with PI-based was 0.70 (95% CI: 0.45–1.08) and with INI+PI was 1.52 (95% CI: 1.00–2.33) (fig. 1).
Conclusion: Dual-therapy is as effective as those with three drugs, showing no difference according different dual therapy.

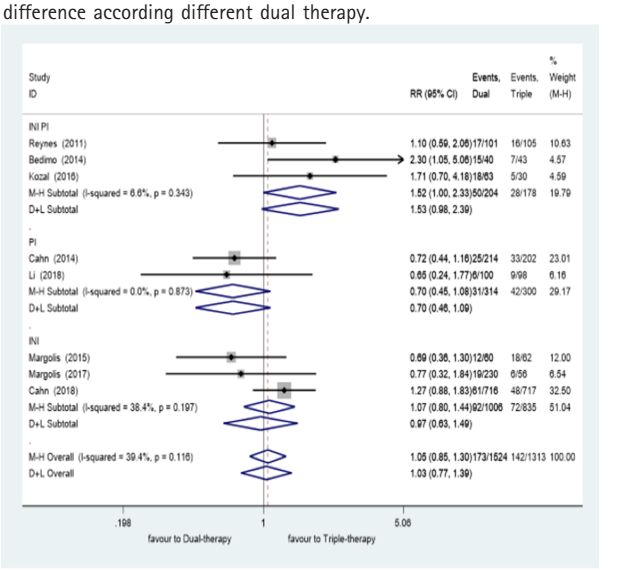


Figure 1. Treatment Failure at 48 weeks in study without Maraviroc

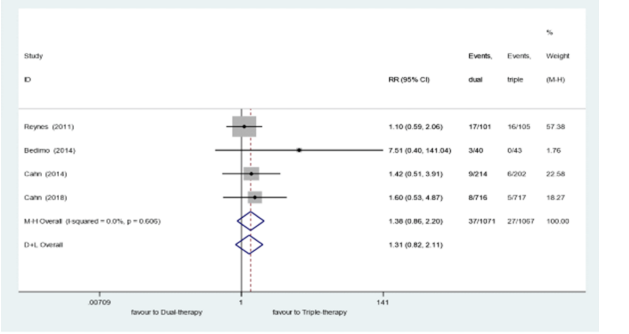


Figure 2. Virological failure at 48 weeks in study without Maraviroc

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Table 1. Meta-analysis of study presenting data at 48 weeks

Analysis	No. of studies	No. of patients Dual/triple	No. of events in analysis dual/ triple	RR Dual vs triple	95% CI	Heterogeneity test (I2%;p)
Treatment failure (TF)	12	2038/1865	285/223	1.10	0.84–1.44	51.7;0.019
TF in patients with less than 100000 copies of HIV RNA	7	1200/1198	161/106	1.52	1.21–1.92	16.4;0.304
TF in patients with equal or more than 100000 copies of HIV RNA	7	358/397	66/74	1.03	0.77–1.38	16.5;0.304
TF in patients with less than 100000 copies of HIV RNA in study without Maraviroc	4	808/790	83/58	1.40	1.01–1.93	31.3;0.225
TF in patients with equal or more than 100000 copies of HIV RNA in study without Maraviroc	4	263/277	35/46	0.82	0.56–1.21	18.2;0.299
Virological failure	8	1578/1612	86/52	1.63	0.93–2.85	49.1;0.056
Adverse drug reaction leading to discontinuation of regimen	9	1986/2023	72/88	0.83	0.62–1.12	5.1;0.391
Adverse drug reaction leading to discontinuation of regimen in study without Maraviroc	5	1472/1471	44/59	0.75	0.51–1.09	42.0;0.159

Table 2. Meta-analysis of study presenting data at 96 weeks and mutations

Analysis	No. of studies	No. of patients Dual/ Triple	No. of events in analysis Dual/Triple	RR Dual vs triple	95% CI	Heterogeneity test (I2%;p)
Treatment failure (TF)	4	941/1025	212/315	0.84	0.58–1.22	74.2;0.009
TF in patients with less than 100000 copies of HIV RNA	4	941/1025	153/216	1.07	0.89–1.29	0.0;0.53
TF in patients with equal or more than 100000 copies of HIV RNA	2	308/329	35/46	0.80	0.54–1.19	34.0;0.218
Virological failure	3	153/137	57/38	1.34	0.95–1.87	0.0;0.622
Adverse drug reaction leading to discontinuation of regimen	3	540/621	30/45	0.91	0.57–1.45	53.5;0.117
Mutation	9	149/120	54/41	1.13	0.85–1.52	0.0;0.450

PS8/5

Shorter time to treatment failure in PLHIV switched to dolutegravir plus either rilpivirine or lamivudine compared to integrase inhibitor–based triple therapy in a large Spanish cohort – VACH

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Objective: Randomized controlled clinical trials have demonstrated non-inferiority of two-drug combinations (2DC) of dolutegravir (DTG) plus either rilpivirine (RPV) or lamivudine (3TC) compared to triple-therapy (TT). Data on real-world effectiveness of 2DC strategies are limited. This study compared time to discontinuation due to treatment failure (TF) and adverse events (AEs) of DTG-based 2DC versus integrase inhibitor (INSTI)-based TT in a real-world setting.

Methods: A retrospective analysis was performed using data from the VACH cohort (prospective, multicenter, Spanish cohort of adult HIV patients). All patients switching to INSTI-based TT or to a 2DC consisting of DTG+RPV or DTG + 3TC between 02/05/2016–15/05/2019 were included. Unit of analysis was patient-regimen. Relevant endpoints were time to discontinuation due to TF (defined as clinician report of virological failure (VF), immunologic failure or disease progression), VF and AEs. Patients were censored at loss-to-follow-up, death or end of observation period (20/06/2019). Kaplan-Meier curves and Cox proportional hazard models (controlling for demographics, viral load, CD4, number of previous regimens/VFs, and years on antiretroviral therapy) were conducted.

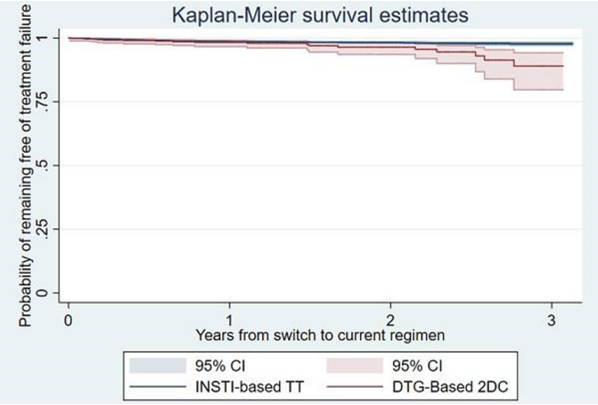
Results: 5,047 TT and 617 2DC patient-regimens were analyzed. Baseline patient-regimen characteristics differed between groups (Table); 2DC were older and more experienced but a higher proportion was virologically suppressed at switch. Time to TF was significantly shorter for 2DC (Figure, p<0.0001). The hazard ratio (HR) for discontinuation due to TF on 2DC vs TT was 2.334 (p=0.003). No difference was observed for discontinuation due to AEs (HR=0.797, p=0.488). Results were maintained when looking at discontinuations due to VF (HR=2.236, p=0.024) and when restricting to patients with viral load<50 copies/mL at regimen initiation.

Conclusion: In a real-world setting, the risk of discontinuation due to TF and VF were more than two-times higher in patients switching to DTG-based 2DC compared to INSTI-based TT, with no difference in discontinuation due to AEs.

Baseline Characteristics by Group

	INSTI-based triple therapy	DTG+3TC or DTG+RPV	p-value
Age (years), Mean (SD)	48.1 (10.7)	52.0 (10.3)	<0.0001
Gender, % Female	23.4	28.7	0.0020
AIDS diagnosis, % Yes	23.2	26.7	0.0264
CD4 count, % >350 cells/μL	81.8	82.9	0.4527
Viral Load, % <50 copies/mL	81.0	90.2	<0.0001
Duration of ART regimens (years), Mean (SD)	12.0 (8.4)	14.9 (8.1)	<0.0001
Number of previous ART regimens, Mean (SD)	5.3 (3.6)	7.4 (4.6)	<0.0001
Number of previous virologic failures, Mean (SD)	1.1 (2.4)	1.5 (2.9)	<0.0001
HCV, % Yes	32.6	35.4	0.1323

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PS8/6

Five-year follow-up of patients enrolled in NEAT001/ANRS 143 randomized clinical trial (NEAT001 LONG TERM (NLT) study)

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Background: Few long-term data are available on patients having initiated ART with a NRTI-sparing regimen. We assessed the 5-year outcome of patients enrolled in NEAT001/ANRS143 RCT (comparing DRV/r+RAL vs DRV/r+TDF/FTC).
Methods: Retrospective data collection, through anonymized eCRF, of patient outcomes up to 5 years post-enrolment. Of the 78 sites from 15 countries taking part in NEAT001, NLT was conducted in 39 sites in 8 countries. Data were analyzed without imputation. Chi2 (or Fisher's Exact) or Student's tests were used for comparisons.
Results: Last NEAT001 visit (W96) was conducted in 745/805 randomized patients (363/401 RAL+DRV/r and 382/404 TVD+DRV/r). Of these, 430 were enrolled in NLT (201 RAL, 229 TVD), with a median follow-up of 44.5 months (Table 1). The proportion of AIDS, non-AIDS events, virologic rebound and serious adverse events (AE) did not differ between groups (Table 1). During the entire follow-up, participants discontinuing ART for virologic failure and for AE in RAL vs TVD groups were 6.8% vs 5.9% (p=0.90) and 10.2% vs 15.8% (p=0.15); discontinuations for VF were more frequent in patients with baseline CD4<200/mm^3 (11.9% vs 5.3%; p=0.077) (Table 2). To date, >40% of participants in both groups were receiving boosted DRV, few participants were on RAL, mainly in initial RAL group (Table 2); proportions of total participants on boosted DRV±XTC were 8.5% vs 7.9% in RAL vs TVD group. Mean weight gain between baseline and last follow-up was 3.15 ± 7.79 vs 4.08 ± 6.49 kg in patients exposed>50% of follow-up to INI vs never exposed to INI (p=0.38). TDF exposure (>50% of follow-up vs never exposed) was associated with higher creatinine increase (p=0.036).
Conclusion: After a median of 5.7 years, patients initiating ART with DRV/r+RAL or DRV/r+TVD experienced few serious clinical events. A quarter of patients were still receiving their initial regimen, most discontinuations being for reasons unrelated to AE or virologic failure.

Table 1 NEAT001 LONG TERM (NLT) main outcomes according to initial randomization group

	W96-Year 4 DRV/r + RAL	DRV/r + TVD	Year 4-Year 5 DRV/r + RAL	DRV/r + TVD
Available data	182/201 (90.5%)	208/229 (90.8%)	177/201 (88.1%)	203/229 (88.6%)
Median follow-up, months	32.3	32.6	11.9	11.6
Unchanged ART since enrolment into NEAT001	27.5%	40.4%	22.2%	29.7%
AIDS event	N=0	N=1	N=1	N=1
Non-AIDS event	3.9%	5.9%	3.5%	7.0%
HIV RNA>50 c/mL	3.3%	2.9%	5.1%	4.4%
Serious adverse event	4.5%	4.4%	4.9%	4.6%

Table 2 End of follow-up (Year 5) discontinuations and ARV regimen

	DRV/r + RAL	DRV/r + TVD
Discontinuation for virologic failure since enrolment into NEAT001	6.3%	
- baseline CD4>200/mm^3	5.3%	
- baseline CD4≤200/mm^3	11.9%	
Discontinuation for adverse event since enrolment into NEAT001	10.2%	15.8%
On RAL-containing regimen at end of follow-up	25.0%	1.5%
On boosted DRV-containing regimen at end of follow-up	48.3%	41.1%

PS8/7

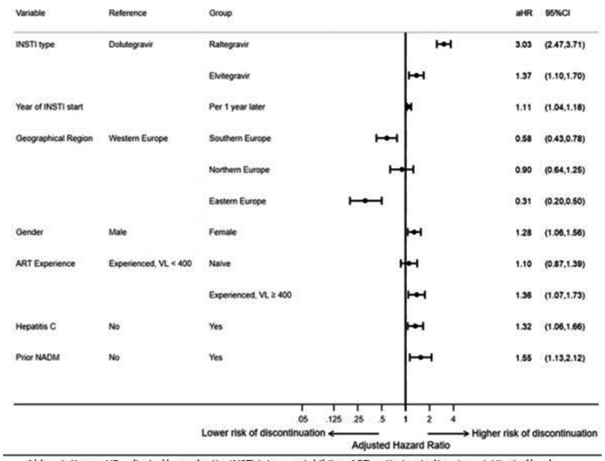
Uptake and discontinuation of Integrase Inhibitors (INSTIs) in a large cohort setting

L Greenberg[1] and on behalf of RESPOND – The International Cohort Consortium of Infectious Diseases

[1]UCL, London, UK

Objectives: To compare characteristics of those initiating INSTIs in real-world settings across Europe and Australia, and describe reasons for and factors associated with discontinuation of first INSTI-based regimen.
Methods: RESPOND participants first starting dolutegravir (DTG), elvitegravir (EVG) or raltegravir (RAL) after 1/1/2012 were compared using multinomial logistic regression. Kaplan Meier and Cox proportional hazards models describe time to and factors associated with discontinuation.
Results: Overall, 9702 persons started INSTIs; 5051 (52.1%) DTG, 1933 (19.9%) EVG, 2718 (28.0%) RAL. The likelihood of starting RAL or EVG versus DTG decreased over time (adjusted risk ratio 0.25 per year increase [95% CI 0.23–0.26] RAL, 0.81 [0.77–0.85] EVG; p<0.001) but was higher in Eastern (6.82 [5.07–9.19] RAL, 1.36 [1.02–1.81] EVG) and Southern Europe (3.00 [2.36–3.81] RAL, 1.23 [0.99–1.52] EVG) compared to Western Europe (p<0.001).
During follow-up, 2105 (21.7%) persons discontinued an INSTI; at 6 months after INSTI initiation 8.9% [8.3%-9.5%] had discontinued (6.4% DTG, 7.4% EVG, 14.0% RAL). Of discontinuations by 6 months, the main reason was toxicity (44.2% DTG, 42.5% EVG, 17.3% RAL). Nervous system toxicity accounted for a higher proportion of toxicity discontinuations on DTG (31.8% DTG, 23.4% EVG, 6.6% RAL). Treatment simplification accounted for more discontinuations on RAL (2.7% DTG, 1.6% EVG, 19.8% RAL).
By 6 months (Figure), those on RAL or EVG were more likely to discontinue than DTG. Other factors associated with discontinuation include year of INSTI initiation, gender, hepatitis C coinfection, prior non-AIDS defining malignancies, and region. Similar results were seen for discontinuations after 6 months and for treatment-naïve and experienced persons (p=0.79; interaction test).
Conclusions: Uptake of DTG versus EVG or RAL has increased over time. Discontinuation was highest on RAL, mainly due to treatment simplification. Albeit relatively low, the main reason for discontinuation within 6 months was toxicity; nervous system toxicity was highest on DTG.

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Abbreviations: aHR-adjusted hazard ratio; INSTI-integrase inhibitor; ART-antiretroviral treatment; VL-viral load; NADM-non-AIDS defining malignancies.
Significant results (p<0.05) from a Cox proportional hazards model, additionally adjusted for age, ethnicity, HIV risk group, CD4 nadir, CD4 at INSTI start, smoking status, hepatitis B, hypertension, diabetes, prior AIDS, end stage liver disease, cardiovascular disease, fracture, chronic kidney disease and all other factors in the figure. Baseline is defined as date of INSTI start.
Missing data for hepatitis C and prior NADM were fitted using unknown categories (data not shown)

Factors associated with INSTI discontinuation in the first 6 months after INSTI start

Emerging issues in public health and epidemiology of HIV in Europe

PS9/1

Current trends in HIV/AIDS epidemic in Russia

N Ladnaya[1], V Pokrovsky[1] and E Sokolova[1]
[1]*Central Research Institute of Epidemiology, Russian Federal AIDS Centre, Moscow, Russian Federation*

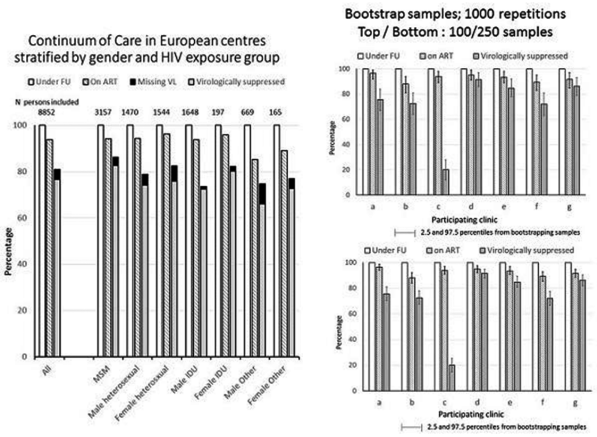
Purpose: Early diagnostic plays a crucial role in reaching the 90–90–90 targets, along with the timely provision of patients with an efficient HIV treatment.
Method: Analysis of data coming from the personalised accounting system, along with the data collected in the federal statistic surveillance forms containing the findings of HIV antibody tests and the federal Rospotrebnadzor forms for monitoring HIV response.
Results: Annually a significant proportion of Russia's population is tested for HIV. In 2016 more than 31 million of Russian citizens were tested (21 tests for each 100 Russian citizens), along with 2.1 million of foreign citizens. The number of tested Russians increased in 2016 by 57% from 1996, and by 24% from 2011. The number of newly diagnosed HIV cases by 2016 increased to 102 179 (69.7 HIV diagnoses per 100 000 population), which is 63.5% more than in 2011 and 65 times more than in 1996. Proportion of late diagnosis (CD4 cell count<350 per mm^3) was low: among the newly diagnosed patients in 2016, 33.7% had immunodeficiency. The number of people receiving ART increased threefold by 2016 compared to 2011 and 18 times compared to 2006. However, until 2016, only a third of the number of registered patients received ART (32.8%), which was is largely due to low adherence to medical care and treatment among drug users. The main reported modes of HIV transmission in 2016 became heterosexual contacts (50.0%)
Conclusion: There has been an increase in the number of new HIV cases associated with the continuation of the HIV epidemic among IDUs and the active transmission of infection among the heterosexual population in Russia. This trend can also be attributed both to low ART coverage among PLHIV, along with the continuing increase in the number of people tested for HIV in the country.

PS9/2

A simple tool to evaluate the effectiveness of HIV care for settings with gaps in data availability

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Purpose: Many HIV clinics do not have the IT infrastructure or resources to routinely report information on people on treatment and virologically suppressed. We investigated the minimal data required to make it feasible for clinics to estimate the "right-side" of the HIV continuum of care with the purpose of developing a simple, accessible, online tool to aid estimation.
Method: Data were collected on all people living with HIV seen at least once during 2017 at seven RESPOND clinics. The percentage on antiretroviral therapy (ART) and virologically suppressed (VS; VL<200 copies/mL [< 500 copies/mL in Belarus]) was calculated using the number in care as the denominator. Bootstrapping techniques using 1000 repetitions identified 2.5 and 97.5 percentiles for the percentage on ART/VS.
Results: Data from 8852 persons were included; Georgia (N=3839), Albania (N=542), Macedonia (N=202), Montenegro (N=150), Serbia (N=521), Belarus (N=133) and Poland (N=3465). Median age was 40 (IQR 34–48) and median CD4 count was 548 (IQR 360–753/mm^3). Overall, 93.8% were on ART (95% CI 93.3–94.2) and 76.7% were VS (95% CI 75.8–77.6%), where persons without a viral load measurement were assumed not to be VS. There were considerable differences in ART and VS and in the percentage with missing data across HIV exposure groups and gender (Figure). Continuums based on a random sample of 100 individuals produced a reliable estimate, while increasing the random sample to 250 decreased uncertainly around the estimate (Figure).
Conclusion: We provide proof of concept that collecting data from a small random sample of a clinic produces a reliable estimate of the 'right-side' of the HIV continuum. This methodology will be further developed into an online tool enabling clinics to estimate these figures for reporting and for a self-applied auditing tool, strengthening monitoring of the effectiveness of care in different population subgroups.



Figure

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PS9/3

HIV continuum of care: bridging cross-sectional and longitudinal analyses

G Touloumi[1], C Thomadakis[1], N Pantazis[1], G Vourli[1], V Papastamopoulos[2], V Paparizos[3], S Metallidis[4], G Adamis[5], M Psichogiou[6], G Chrysos[7], H Sambatakou[8], E Barbunakis[9], N Sipsas[10], M Chini[11], C Gogos[12], P Panagopoulos[13], O Katsarou[14], A Antoniadou[15] and Athens Multicenter AIDS Cohort Study (AMACS)

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Purpose: The established 90–90–90 target to end the HIV epidemic follows a cross-sectional continuum of care (CoC) analysis, without considering early diagnosis, rapid treatment initiation and durable suppression. We propose a new CoC analysis combining cross-sectional and longitudinal elements, i.e. time spent between and within stages of the CoC.

Method: Based on the cross-sectional CoC, we: a) divided the percentages of diagnosed by years since infection, estimating corresponding times by the method proposed by Pantazis et al (SMMR, 2017); b) divided percentages of those who ever initiated ART and those with viral suppression by current status (on ART, on follow-up-but-off ART, lost-to-follow-up (LTFU) and missing, unsuppressed and suppressed); c) add the cumulative incidence of ART initiation and viral suppression, treating LTFU as competing event. Viral suppression definition: VL<500 copies/mL. We applied the proposed method to people living with HIV (PLHIV) in Greece at the end of 2016, who participated in AMACS, the Greek multicenter HIV cohort study.

Results: According to Hellenic CDC, 81% of PLHIV were diagnosed in 2016. Among 7407 eligible AMACS participants, median time from infection to diagnosis was 3.3 years (IQR: 1.1–6.7). Among diagnosed, 86.6% were ever treated, of whom 86% remained on ART. Cumulative incidence of ART initiation and LTFU before ART initiation were 79.6% and 6.7% at 5 years, respectively (Figure 1). Among treated, 86.2% achieved viral suppression, of whom 85.2% were currently virally suppressed. LTFU was strongly dependent on CD4 count at diagnosis; the probability of LTFU after ART initiation at 5/10 years was 12.1/19.5% and 8.1/12.3% for those with<200 and>350 CD4/μL, respectively.

Conclusion: The new proposed analysis highlights time gaps in CoC not evident by the standard cross-sectional approach. Analysis by CD4 count highlights the need for early diagnosis and late presenters as key population for interventions that could decrease cascade shortcomings.

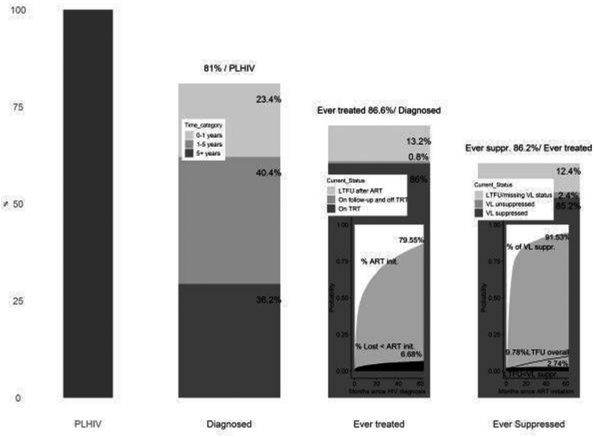


Figure 1. Greek HIV Continuum of Care at the end of 2016 applying the proposed method

Greek HIV CoC at the end of 2016 applying the proposed method, by CD4 count at HIV diagnosis

CD4 counts/μl	<200 (N=1864)	200–350 (N=1534)	>350 (N=3643)	Total (N=7407)	CD4 counts/μl	<200 (N=1864)	200–350 (N=1534)	>350 (N=3643)
ART status, (among diagnosed)	p<0.001				VL status, (among treated)	p<0.001		
Never treated	22 (1.2%)	26 (1.7%)	276 (7.6%)	376 (5.1%)	Never VL suppressed	153 (8.7%)	116 (8.1%)	382 (12.7%)
Lost before ART initiation	77 (4.1%)	83 (5.4%)	368 (10.1%)	614 (8.3%)	Lost before VL suppression	60 (3.4%)	31 (2.2%)	53 (1.8%)
Ever treated	1765 (94.7%)	1425 (92.9%)	2999 (82.3%)	6417 (86.6%)	Ever VL suppressed	1552 (87.9%)	1278 (89.7%)	2564 (85.5%)
ART current status, (among treated)	p<0.001				VL current status, (among ever VL suppressed)	p<0.001		
Off ART	23 (1.3%)	8 (0.6%)	21 (0.7%)	52 (0.8%)	VL unsuppressed	45 (2.9%)	21 (1.6%)	69 (2.7%)
Lost after ART initiation	328 (18.6%)	175 (12.3%)	299 (10.0%)	844 (13.2%)	Lost or missing VL status	276 (17.8%)	147 (11.5%)	251 (9.8%)
On ART	1414 (80.1%)	1242 (87.2%)	2679 (89.3%)	5521 (86.0%)	VL suppressed	1231 (79.3%)	1110 (86.9%)	2244 (87.5%)

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PS9/4

Reaching the second and third UNAIDS 90–90–90 targets is accompanied by a dramatic reduction in primary HIV infection and in recent HIV infections in a large French nationwide HIV cohort

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In late 2013, France was one of the first countries to recommend initiating combination antiretroviral therapy (cART) irrespective of CD4 cell count. To assess the impact on HIV incidence of achieving the second and third UNAIDS 90–90–90 targets (i.e. 90% of diagnosed people on sustained cART, and of those, 90% virologically controlled), we conducted a longitudinal study to describe the epidemiology of primary HIV infection (PHI) and/or recent HIV infection (patients with CD4 cell count≥500/mm^3 at HIV diagnosis) (PRHI) between 2007 and 2017 in a large French multicentre cohort. To identify changes in trends in PHI and PRHI, we used single breakpoint linear segmented regression analysis.

Results: During the study period, a total of 61,822 patients were followed in the Dat'AIDS cohort; 20,263 of these were new patients. Among them, 2,027 (10.0%) had PHI and 7,314 (36.1%) had PRHI. The second and third targets were reached in 2014 and 2013, respectively. The median delay between HIV diagnosis and cART initiation decreased from 9.07 (IQR: 1.39–33.47) months in 2007 to 0.77 (IQR: 0.37–1.60) months in 2017. A decrease in PHI (−35.1%) and PRHI (−25.4%) was observed since 2013. The break-points for PHI and PRHI were 2012.6 (95% CI 2010.8- 2014.4) and 2013.1 (95% CI 2011.3-2014.8), respectively.

Conclusion: Our findings show that the achievements of two public health targets in France and the early initiation of cART were accompanied by a reduction of about one third in PHI and PRHI between 2013 and 2017.

PS9/5

Similar but different: Using combined phylogenies of Austria and Switzerland reveals differences in transmission patterns of the local HIV-1 epidemics

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Objectives: Using combined phylogenies of two or more countries allows to detect differences in transmission dynamics of HIV-1 beyond differences in demographic characteristics. Austria and Switzerland, two neighboring countries of similar size and comparable numbers of new HIV-1 diagnoses per year, serve as an ideal show case for this type of analysis.

Methods: A maximum-likelihood phylogenetic tree was built using pol-sequences of the Swiss HIV Cohort Study (SHCS) and the Austrian HIV Cohort Study (AHIVCOS), with Los Alamos background sequences. Phylogenetic clusters of size 2 and cophenetic distance smaller than 0.03, with both patients being in the SHCS or AHIVCOS, called SHCS-cherries and AHIVCOS-cherries, respectively, were extracted from the tree. Demographic characteristics of SHCS and AHIVCOS patients were compared across the tree and cherries using Fisher exact tests. By varying the distance threshold for inclusion of the cherries (range: 0.015–0.045) and down-sampling SHCS sequences (range: 20%–100%), we assessed the robustness of the results.

Results: Overall, 554/2'219 (25.0%) AHIVCOS patients were in AHIVCOS-cherries and 4530/12'776 (35.5%) SHCS patients were in SHCS-cherries. The fraction of patients belonging to the group of intravenous drug users (IDU) was similar in both cohorts (p=0.29) (Figure 1A), but there were significantly (p<0.001) less AHIVCOS-cherries with one patient being IDU and the other patient non-IDU (20/277 (7.2%)) compared to SHCS-cherries (322/2265 (14.2%)) (green, Figure 1B). These differences were robust for varying cophenetic distances and down-sampling SHCS sequences with 6.8%-9.6% IDU-nonIDU-AHIVCOS-cherries and 10.4%-17.5% IDU-nonIDU-SHCS-cherries.

Conclusion: A combined phylogeny of Austrian and Swiss HIV-1 sequences revealed differences in transmission patterns in the respective local epidemics, which could not be detected by comparing cohort characteristics: Despite the same fraction of IDU, transmission events between IDU and other risk groups were more frequent in the SHCS as compared to the AHIVCOS.

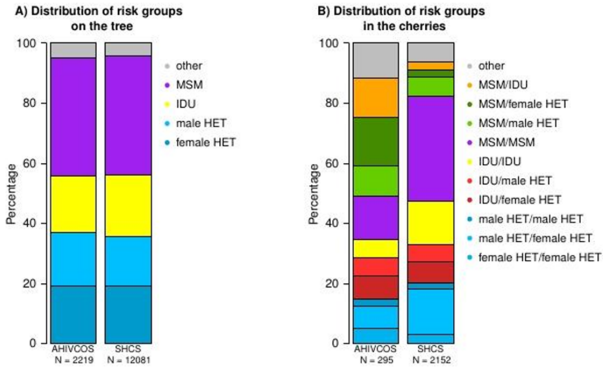


Figure: A) The distribution of risk groups on the tree for patients in the Austrian HIV Cohort Study (AHIVCOS) and the Swiss HIV Cohort Study (SHCS). B) The distribution of risk groups in the cherries with both patients being participants of the AHIVCOS or the SHCS. MSM: men who have sex with men; IDU: intravenous drug users, HET: heterosexual.

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PS9/6

'Chems4EU' a study describing chemsex use across 4 European countries in MSM attending HIV services

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Purpose: Our study aims to describe the rates of self-reported recreational drug use among MSM attending HIV services across centres in the UK, Spain, Greece and Italy, as well as rates of other sexual risk behaviours, STIs and ill-health.
Method: A cross-sectional multi-centre study, using a self-reported questionnaire was undertaken, focusing on chemsex drug use (sexualised use of methamphetamine, mephedrone, GHB/GBL, cocaine and ketamine), harms and whether support services were accessed.
Results: 1700 questionnaires were included in the primary analysis. The median age was 39 years (IQR 32–47). There were high rates of recreational drug use overall (51%) and chemsex use in the past 12 months was high (23%); ranging from 32% in UK to 12% in Italy, with Spain and Greece 22% and 19% respectively. Slamsex use (sexualised use of injecting the same group of drugs) was 13% UK, 2.8% Spain, 4.9% Greece and 0.6% Italy. (Table 1). There were high rates of harms across the countries; unwanted side effects in 41%, 22% reporting symptoms of drug withdrawal and a concerning percentage reporting overdose (7.3%) and non-consensual sex (7.1%). Over 25% reported negative impacts on work, friends / family and relationships. Only 16% overall accessed professional support services, with variability between the countries (UK 20%; Spain 16%; Greece 8.3% and Italy 4.8%) and>60% found these services met their needs. (Table 2).
Conclusion: This is a large study across 4 European countries which shows high rates of chemsex use amongst MSM attending for HIV care. There are high rates of harms overall, particularly unwanted side effects (41%) and symptoms of withdrawal (22%) and a concerning number reporting non-consensual sex (7.1%) and overdose (7.3%). Strikingly there are significant negative impacts on work, family/friends and relationships, but few accessing services.

Rates of Drug Use in HIV+MSM

	UK	Spain	Greece	Italy	Total
Number	544	534	449	173	1700
Age (years) (Median, IQR)	40 (32–49)	40 (34–47)	36 (32–42)	40 (32–47)	39 (32–47)
Recreational drug use, 12 m (n,%)	278 (51%)	239 (45%)	167 (37%)	57 (33%)	741 (44%)
Chemsex, 12 m (n,%)	174 (32%)	117 (22%)	84 (19%)	21 (12%)	396 (23%)
Slamsex, 12 m (n,%)	69 (13%)	15 (2.8%)	22 (4.9%)	1 (0.6%)	107 (6.3%)

Harms in HIV+MSM using Chemsex

	UK	Spain	Greece	Italy	Total
Number using Chemsex	174	117	84	21	396
Unwanted side effects (n, %)	70 (40%)	51 (44%)	35 (42%)	6 (29%)	162 (41%)
Drug withdrawal (n, %)	49 (28%)	31 (26%)	6 (7.1%)	0 (0%)	86 (22%)
Overdose (n, %)	11 (6.3%)	8 (6.8%)	9 (11%)	1 (4.8%)	29 (7.3%)
	16 (9.2%)	5 (4.3%)	5 (6.0%)	2 (9.5%)	28 (7.1%)

Table Continued.

	UK	Spain	Greece	Italy	Total
Non-consensual sex (n, %)					
Negative effect on work (n, %)	58 (33%)	31 (26%)	11 (13%)	5 (24%)	105 (27%)
Negative effect on friends/family (n, %)	50 (29%)	34 (29%)	13 (15%)	4 (19%)	101 (26%)
Negative effect on relationships (n, %)	53 (30%)	41 (35%)	16 (19%)	6 (29%)	116 (29%)
Accessed professional services (n, %)	35 (20%)	19 (16%)	7 (8.3%)	1 (4.8%)	62 (16%)

Severe infections co-organised with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID)

PS10/1

Frequency, presentation and predictors of strongyloidiasis in HIV-infected migrants at the Institute of Tropical Medicine Antwerp (ITM), Belgium

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Purpose: To determine the frequency of strongyloidiasis, defined as a positive S. stercoralis serology, in a cohort of HIV-positive migrants. Secondary objectives are to describe the clinical and laboratory presentation of Strongyloides-HIV coinfection and to identify epidemiological, clinical and laboratory predictors of coinfection.
Method: Retrospective study based on serological testing for *S. stercoralis* in all HIV-infected migrants followed at ITM. If untested, serology was performed on stored samples at first HIV viral load determination. The epidemiological, clinical and laboratory features of patients with and without strongyloidiasis were retrieved from the electronic medical files.
Results: Of the 2846 HIV patients in active follow-up, 732 (26%) had a migration background. Thirty-six patients (4.9%) were diagnosed with Strongyloides co-infection, including 29 during their medical evaluation and 7 retrospectively. Patients had a median age of 35.3 years (IQR 30.35–44.4), 78% originated from Sub-Saharan Africa and median time in Belgium was 3.5 years (IQR 0.8–5.7). Symptoms compatible with strongyloidiasis were present in 17 (47%) patients, of which two were diagnosed retrospectively. Eosinophilia (eosinophil cell count>450/μL) was observed in 19 (53%) participants. Median CD4 level was 386 /μL (IQR 299–520) at diagnosis of coinfection. Of note, 8 (22%) patients with strongyloidiasis had no reported symptoms nor eosinophilia. None of the patients developed hyperinfection syndrome or disseminated strongyloidiasis. There were no differences in age, gender, geographic origin, clinical presentation, CD4 level or viral load between patients with and without strongyloidiasis. Only eosinophilia was strongly correlated with the presence of Strongyloides infection in multivariate analysis [OR 10.74 (95% CI 5.19–22,251), p<0.001].
Conclusion: Strongyloidiasis was diagnosed in about 5% of HIV-infected migrants and was only predicted by the presence of eosinophilia. However, a sizeable proportion (22%) of coinfected individuals were asymptomatic and had normal eosinophil count, supporting universal screening of all HIV-positive patients native from tropical countries.

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PS10/2

Diagnosing tuberculosis in people living with HIV in a rural district of Mozambique: yield of TB-LAM, digital chest X ray and Xpert® Ultra

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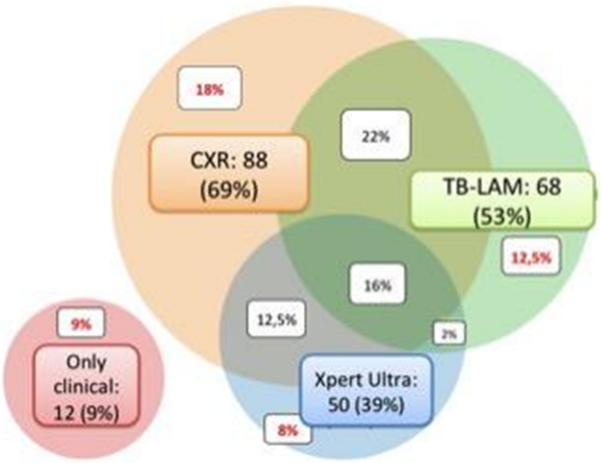
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Purpose: The implementation of new tuberculosis (TB) diagnostic tools among people living with HIV (PLHIV) in sub-Saharan Africa should be tested in real-life conditions among ambulatory and hospitalized patients.

Method: During a TB active-case finding strategy in Manhiça District, Mozambique, sputum induction and Xpert® Ultra were made available to officials of all district health centres and district hospital. All notified TB cases were HIV-tested. Those ART-naïve or poorly ART-adherent PLHIV were visited and offered counselling, clinical evaluation, digital chest-X-ray (CXR), CD4 cell counting, urine TB-LAM (if CD4<200 cells/mm^3 or seriously-ill) and timely ART initiation.

Results: Between June-December 2018, the ART status of 373 TB/HIV cases and 315 of their contacts who were HIV+ was assessed. 124/373 (33%) TB cases and 31/315 (9.8%) contacts were ART-naïve or poorly ART-adherent. Of those, 5/31 (16%) contacts had TB, giving a TB study population of 128, including 64/128 (50%) outpatients and 64/128 (50%) inpatients; the median CD4 counts were 214 (interquartile range [IQR] 74.5–357.0) and 72 (IQR 24.7–122.5) cells/mm^3 respectively; a sputum sample was obtained from 57/64 (89%) outpatients and 39/64 (61%) inpatients, and Xpert®Ultra was positive in 34/57 (60%) and 16/39 (41%) respectively; a CXR was done in 57/64 (89%) and 56/64 (88%), being TB-suggestive in 47/57 (82%) and 41/56 (73%) respectively. TB-LAM was positive in 65% (22/34) outpatients and 74% (46/62) inpatients. Overall, 116/128 (91%) cases had ³1 positive tests. Xpert Ultra® and TB-LAM were the only positive TB test in 33% and 14% outpatients and in 8% and 55% inpatients, respectively. ART was initiated in 94% (77/82) of ART-naïve cases. Six-month mortality was 21% (27/128) overall and 25% (17/68) among TB-LAM positive patients.

Conclusion: TB-LAM increased TB diagnosis confirmation by 14% and 55% in ambulatory and hospitalized HIV patients respectively. The test should become standard of care in HIV/TB high-burden settings.



Number and % of TB diagnosis yielded by each test and combination of tests of the 128 TB diagnosis

Number and proportion of TB diagnosis yielded by Xpert Ultra and TB-LAM.

Combined yield of TB tests		OUTPATIENTS (n: 64)	INPATIENTS (n: 64)
Xp ULTRA result	TB-LAM result	Yield of TB diagnosis	Yield of TB diagnosis
Positive	Positive	12 (19%)	11 (17%)
Positive	Negative	21 (33%)	5 (8%)
Negative	Positive	9 (14%)	35 (55%)
Negative	Negative	22 (34%)	13 (20%)

PS10/3

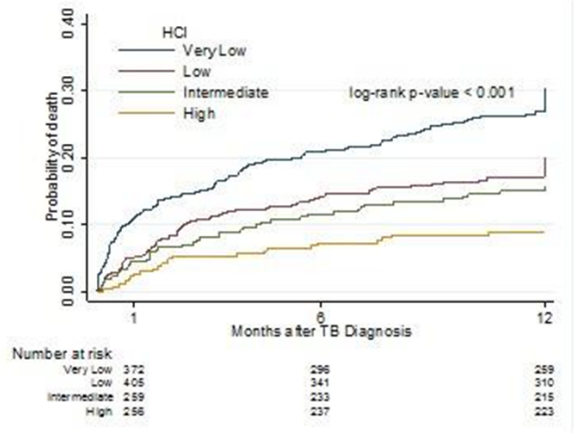
A New Health Care Index independently predicts 12-month mortality among HIV positive individuals diagnosed with tuberculosis

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Purpose: Based on data from 2004–7, we previously generated a health care index (HCI) for TB-HIV co-infected individuals which indicated that drug

Figure: Kaplan Meier estimates for probability of death after TB diagnosis according to HCI quartile using the TB:HIV dataset.



Final (bolded) and potential (un-bolded) coefficients used in making the HCI with their associated scores. HCI ranged from -1 to 22 with higher scores indicative of better utilisation of health care. HCI utilization quartiles were -1 to 5 =very low, 6 to 10 =low, 11 to 14 =intermediate, and 15 to 22 =high.

1. **Inclusion of RHZ in the initial TB treatment regimen (score contribution = 5)**
2. **Performance of DST for TB within one month of TB diagnosis & total number of known active drugs < 3 (score contribution = -1)**
3. **Performance of DST for TB within one month of TB diagnosis & number of known active drugs ≥ 3 (score contribution = 8)**
4. **HIV-RNA measurement obtained between six months before and one month after TB diagnosis (score contribution = 5)**
5. **Initiation of cART before or within one month of TB diagnosis (score contribution = 4)**
6. World Health Organization (WHO) definite diagnosis of TB
7. At least one CD4 cell count measurement obtained between six months before and one month after TB diagnosis
8. Use of co-trimoxazole prophylaxis before, or up to one month after TB diagnosis
9. Total number of drugs prescribed within the initial TB treatment regimen

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susceptibility testing (DST), initial TB regimens containing rifamycin, isoniazid and pyrazinamide (RHZ), and timely combination antiretroviral treatment (cART) predict 12-month mortality. To take account of improvements in diagnostic and management practices, we re-evaluated the HCI based on newer data.

Method: Using data from the TB:HIV Study (2011–4), we evaluated nine aspects of health care in Cox Proportional hazards models on time from TB diagnosis to death. We created a HCI using the significant covariates. Kaplan-Meier methods were used to estimate the probability of death within 12-months by HCI quartile. Harrell's C-statistic was used to assess model fit and improvement from the previous HCI.

Results: Of 1396 eligible individuals (72% male, 59% from Eastern Europe, 70% known HIV positive>3 months before TB diagnosis and 64% cART naïve at TB diagnosis), 269 died within 12-months of commencing TB treatment. We found RHZ (adjusted HR=0.67; 95% CI (0.50,0.89) vs. no RHZ), DST and active TB drugs (DST & < 3 known active TB drugs (1.09 (0.80,1.48)), DST & ≥3 known active TB drugs (0.49 (0.35,0.70) compared with no DST), a recent HIV-RNA measurement (0.64 (0.50,0.82), vs. no recent HIV-RNA) and timely cART initiation (0.72 (0.53,0.97) vs. no cART) to be associated with 12-month mortality, and these factors were used to create the updated HCI. A lower HCI was associated with an increased probability of death at 12-months; 30% (26,35) vs, 9% (6,13) in the lowest vs. highest quartile, Figure.

Conclusion: We found five main potentially modifiable health care components that were associated with 12-month mortality among TB/HIV positive individuals and created an index using these components. Validation of our HCI in a modern TB cohort could enhance our findings.

PS10/4

Comparison of TB drug susceptibility, treatment regimens and outcome among TB/HIV-patients in a setting with high prevalence of resistant TB: results from a national and supranational reference laboratories

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Purpose: Treatment of MDR-TB should be based on detailed information on resistance patterns of Mycobacterium tuberculosis (Mtb), and is a special challenge in areas with high prevalence of multi-drug resistant TB (MDR-TB). We aimed to compare results of conventional drug susceptibility testing (DST) performed in Minsk, Belarus (high MDR-TB burden country) with extensive geno- and phenotypic analyses performed at the WHO TB Supranational Reference Laboratory (SRL) in Denmark, and relate DST results to treatment patterns and outcomes for TB/HIV patients.

Type of TB in 30 TB/HIV patients from Minsk, Belarus according to the drug susceptibility testing performed in Belarus and at SRL in Denmark, and number of active drugs in the initial and consecutive TB-treatment regimens

Type of TB	N (%) Minsk	N (%) SRL	P-value	N Active drugs initially, median (IQR)		N Active drugs after 1st change, median (IQR)	
				Minsk	SSI	Minsk	SSI
Drug Sensitive TB	10 (33,3)	12 (40,0)	0,79	4 (4-4)	4 (4-4)	2 (2-2)	2 (2-2)
H-resistant TB	2 (6,7)	2 (6,6)	1,00	4 (3-4)	4 (3-4)	5 (5-5)	5 (5-5)
MDR-TB	8 (26,7)	3 (10,0)	0,18	0 (0-0)	0 (0-0)	5 (5-5)	4 (3-5)
Pre-XDR-TB	5 (16,7)	9 (30,0)	0,36	1 (0-1)	1 (0-1)	4 (3-4)	3 (2-4)
XDR-TB	5 (16,7)	4 (13,3)	1,00	0 (0-0)	0 (0-0)	3 (3-3)	3 (2-3)

TB - Tuberculosis
SRL – World Health Organization TB Supranational Reference Laboratory in Copenhagen, Denmark
H – Isoniazid
H-resistant TB – resistance to isoniazid only
MDR-TB: multidrug resistant TB - resistance to at least **both** isoniazid and rifampicin.
Pre-XDR TB: pre- extensive drug resistant TB - resistance to **either** any fluoroquinolone **or** to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance
XDR-TB: Extensive drug resistant TB - resistance to any fluoroquinolone **and** to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multidrug resistance

Type of TB and TB treatment regimens

Methods: 30 HIV-patients from Minsk with TB-diagnosis between 2011–2013, and with Mtb-culture samples were included. Descriptive statistics applied to compare DST results and analyze treatment regimens and outcome.

Results: Twenty-two (73%) patients were males; median age 37,2 years (IQR 30,4–41,0); 19 (63,3%) had a history of injecting drug use. There was a good agreement in DSTs for Rifampicin (R) and Isoniazid (H) –93%. For 2nd-line TB-drugs, discrepancies were more pronounced: 14 (46,7%) had disagreement for at least one 2nd-line TB-drug, and more patients were classified as having pre-XDR-TB according to SRL results (Table).

All patients started TB-treatment based on RH and pyrazinamide, which was an active regimen for 40% of patients only. Patients with at least MDR-TB changed to 2nd-line drugs after median of 1,5 months (IQR 1–2) to a median of 4 susceptible drugs (IQR 3–5). (Table) Median treatment duration after regimen change was 8 months (IQR 2–11). Only 4 (22%) patients received treatment for≥18 months, and 16 (53%) patients died within 24 months of follow-up.

Conclusions: Despite good quality local DSTs, patients were treated insufficiently. A delay in initiating adequate regimens, suboptimal number of active drugs and too short treatment duration were observed. Better accessibility to rapid molecular DSTs and 2nd-line TB-drugs should potentially allow constructing potent regimens, and initiating timely targeted DST-tailored treatment, ultimately improving outcome.

PS10/5

Influence of vitamin D deficiency on development of opportunistic infection in people living with HIV/AIDS (PWHA)

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Purpose: The association between vitamin D deficiency and development of chronic infections such as tuberculosis has been reported. However, there is few studies concerning the association between vitamin D deficiency and opportunistic infection (OI) in people living with HIV/AIDS (PWHA).

Method: To identify the association between vitamin D deficiency and OI, a retrospective observational study was conducted at a tertiary care hospital. PWHAs who had vitamin D (25-OH vitamin D) test results from 2012 to 2017 were enrolled. All enrolled PWHAs were divided into vitamin D deficiency group and non-deficiency group according to the vitamin D cutoff set by ROC curve analysis. The rates of OIs were compared between two groups.

Results: Among 440 PWHAs with≥1 vitamin D tests, 394 (89.5%) were male, 59 were more than 60 year old (13.4%), 237 (53.9%) were ART-naïve, 107 (24.3%) had CD4 + T cell<200/uL and 278 (63.2%) were vitamin D deficient according to general cutoffs (< 20 ng/mL).Seventy-five cases of OIs occurred in 63 PWHAs (14.3%); Most common OI was tuberculosis (27, 6.1%) following pneumocystis pneumonia (25, 5.7%) and CMV diseases (10, 2.3%). In ROC curve analysis, AUC was 0.700 (95% CI 0.62- 0.78, P<0.001) and vitamin D concentration of 15 ng/mL was proper cut-off to predict OIs.

Overall OI development significantly more prevalent in vitamin D deficiency group (aOR 3.603, 95% CI 1.740–7.461); tuberculosis (aOR 2.973, 95% CI 1.215–7.276) and CMV disease (aOR 9.218, 95% CI 1.103–77.026) significantly associated with vitamin D deficiency and pneumocystis pneumonia was not (aOR 1.459, 95% CI 0.551–3.864).

Conclusion: Vitamin D deficiency was associated with development of OIs, particularly with intracellular infections such as tuberculosis or CMV infections and stringent cutoffs of vitamin D deficiency (< 15 ng/mL) was well correlated with development of OIs in PWHAs.

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Where do we stand with HIV prevention today?

PS11/1

PrEP persistence and associated factors: an analysis from the ANRS Prevenir study

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Purpose: Pre-exposure prophylaxis (PrEP) has become an important component of HIV prevention, but little is known on PrEP persistence and factors associated with PrEP discontinuation. Our objective was to study both within the ANRS Prevenir study conducted since May 2017 in Paris area.
Method: The analysis was restricted to MSM participants enrolled in the Prevenir study (99% of participants) with at least one follow-up visit, whether already on PrEP at enrolment or not. PrEP discontinuation was defined as stopping PrEP, or being lost to follow-up. The rate of PrEP discontinuation was estimated using Kaplan-Meier estimate from date of PrEP initiation and analyses of factors associated with discontinuation used Cox model, both accounting for staggered entries in the study, using multiple imputation for missing characteristics.
Results: Out of 3057 participants in Prevenir, 2699 fulfilled inclusion criteria with a median age of 36 years (IQR: 29–43), 84% born French, 73% with>2-year university degree, 50% already on PrEP at baseline (median: 9.1 months), 51% using on demand PrEP. Overall 358 participants discontinued PrEP, including 258 being lost of follow-up and 100 stopping PrEP, mainly for no longer feeling at risk (76) and 4 for adverse events (one HCV infection, one grade 3: vomiting, two grade 1: diarrhea, and nausea/headache/dizziness). The 30-month discontinuation rate was estimated as 32% (95% CI: 29–35), including 11% (95% CI: 8–13) corresponding to stopping PrEP. Among the tested factors (see table), younger age was associated with a higher risk of discontinuing PrEP, while being already on PrEP at baseline and a higher educational level were associated with a lower risk of discontinuing PrEP.
Conclusion: Young MSM starting PrEP without a high educational level are at higher risk of PrEP discontinuation. More research is needed to understand the reasons and to design targeted interventions aiming at increasing PrEP persistence.

				Univariable				Multivariable		
		Total N	Nb evts	P-value	HR	IC -	IC+	HR	IC -	IC+
Age(years)	18 - 25[	227	49	<.0001	2.636	1.865	3.743	2.468	1.722	3.513
	25 - 30[	512	90		1.571	1.062	2.322	1.561	1.057	2.308
	30 - 40[	853	136		1.398	1.076	1.816	1.395	1.061	1.833
	>=40	1007	93		1			1		
Country of birth	France	2277	284		1			1		
	Other	422	74	0.0203	1.355	1.048	1.751	1.225	0.944	1.591
Regular sexual partner	no	1488	257		1			1		
	yes	1211	151	0.0726	0.825	0.669	1.018	0.868	0.710	1.060
Psychoactives drugs at the last sexual intercourse	no	2318	289		1					
	yes	381	69	0.3705	1.136	0.859	1.502			
Condom use at the last sexual intercourse	no	1706	211		1					
	yes	993	147	0.2793	1.125	0.909	1.393			
STIs in the last 12 months	no	1330	183		1					
	yes	1369	175	0.4044	0.91465	074162	1.12886			
Prior use of PeP	no	1634	289		1					
	yes	1065	149	0.4169	1.091	0864	1.347			
Prior psychiatric condition	no	2344	364		1					
	yes	355	54	0.6803	1.061	0801	1.404			
Already PrEP user at baseline	no	1352	258		1			1		
	yes	1347	130	<.0001	0.516	0399	0.667	0542	0417	0.705
Baseline use of PrEP	Daily PrEP	1325	166		1					
	On demand PrEP	1374	192	0.6889	1.043	0847	1.285			
Counselling (either peer or education by care givers)	Not offered	158	17	0.1217	1.327	0814	2.163	1.468	0891	2.395
	Offered but not accepted	351	30		0.731	0502	1.065	0815	0558	1.191
	Offered and accepted	2190	311		1			1		
Education	<High school	132	25	0.1514	1			1		
	High school to 2-year university degree	897	74		0.447	0401	1.843	0.567	0349	0.923
	>2-year university degree	1979	259		0.673	0433	1.048	0.662	0.378	0.959
Perceived financial situation	Confortable	772	66	0.1189	1			1		
	Adequate	1120	151		1.166	0864	1.573	1.039	0764	1.455
	Borderline	384	91		1.427	1.049	1.945	1.153	0838	1.595
	Difficult	213	30		1.256	0792	1.991	1.017	0629	1.646
Number of sexuals patners in the last 3 months		2699	358	0.3398	0.997	0990	1.003			
Number of unprotected anal sexual intercourse		2699	358	0.063	0.993	0983	1.002	0.992	0973	1.011

Factors associated with PrEP discontinuation in the Prevenir study

PS11/2

Monitoring PrEP implementation in Belgium: national surveillance results, 2017–2018

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Purpose: Since 01/06/2017, Pre-exposure Prophylaxis (PrEP) is reimbursed in Belgium for individuals at increased risk of HIV acquisition. PrEP is delivered in the HIV Reference Centres (HRCs). An authorization for reimbursement is valid for 12 months. First surveillance data are presented.
Method: Aggregated data on number and profile of the starters, regimen chosen at start, new STI diagnoses during follow-up, reported chemsex (GBL/GHB, Crystal Methamphetamine, Mephedrone or mixed use) and number of PrEP interruptions (>12 months without visit record) for the period 1/06/2017 until 31/12/2018 were collected from the 12 HRCs. Data were combined into a unique data set and analysed for distribution of those factors.
Results: Of the 2845 starters (Table 1), 99.3% were male, 98.8% men having sex with men (MSM), 81.5% Belgians, 51.7% were 25–39 years. At initiation, 53.8% and 46.2% opted respectively for a daily versus for non-daily regimen. At least one new STI was diagnosed in 22.6% of the users with proportions by HRC ranging from 11.9% to 44.5%; gonorrhoea and Chlamydia diagnoses were the most common (Table 2). There was one HIV seroconversion due to inconsistent PrEP adherence. Chemsex was reported by 22.9% of the users; 5.3% interrupted PrEP care.
Conclusion: In line with other countries, the uptake of PrEP in Belgium has been almost entirely limited to MSM, mainly Belgians. Heterosexuals from Sub-Saharan African origin - the other key-population affected by HIV in Belgium - are less represented among PrEP users. The variation of reported STIs may be partly explained by differences in testing practices across HRCs. STIs diagnosed outside HRCs are not captured by this data collection. This highlights the need to gather robust data to develop a tailored STI screening and treatment strategy for PrEP users. The frequent reporting of chemsex calls for offering pathways to support for those in need.

Profile of PrEP starters in Belgium, June 2017–December 2018

		Number	%
Gender (N=2844)	Men	2824	99.3
	Women	11	0.4
	Transgender	9	0.3
Age group (N=2840)	18–39	1654	58.2
	40+	1186	41.8
Nationality (N=2232)	Belgian	1820	81.5
	Sub-Saharan African	26	1.2
Risk group (N=2687)	MSM	2655	98.8
	Hetero	26	1.0

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Frequency and distribution of new STI diagnoses among PrEP users, June 2017–December 2018

	Number	%
At least one STI (N=2764)	625	22.6
Gonorrhoea (N=2764)	309	11.2
Chlamydia (N=2764)	260	9.4
Syphilis (N=2001)	128	6.4
HCV (N=2764)	10	0.4
HAV (N=2001)	4	0.2
HBV (N=2001)	0	0.0

PS11/3

Awareness gaps on pre-exposure prophylaxis among late adolescents and young adults in the region characterised by high HIV prevalence and sexual violence

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Purpose: The vulnerability of young women in South Africa to HIV transmission is well documented. In South Africa, over 270 000 people were newly infected with HIV in 2017, and the vast majority of them were young adults. This study examines the level of awareness of PrEP among young adults in Eastern Cape, South Africa.
Method: This cross-sectional study was conducted between June and November 2018 among 834 young adults (aged 16–24 years) selected using stratified random sampling with probability proportional to the size of each stratum. An electronic self-administered questionnaire was used to elicit demographic information, HIV testing, disclosure of HIV status to partners, discussion of HIV with partners and awareness of PrEP. Adjusted and unadjusted logistic regression model analysis were used to examine the predictors of PrEP awareness.
Results: The mean age of study participants was 21.09 years (SD: 1.70). Only 19.0% of the participants were aware of PrEP with no sex disparity (male 16.5% vs female 20.5%). Ever fewer proportion of the respondents knew where to obtained the drugs (14.5%), how much it cost (4.7%), have seen it (7.5%) and have used it (2.6%). There was no significant difference in the level of awareness of PrEP by sociodemographic and lifestyle behavioural characteristics. In the adjusted regression analysis, only discussion of HIV/STI with sexual partners [AOR: 1.76; CI: 1.10–2.81] and ever tested for HIV [AOR: 1.68; CI: 1.02–2.76] were associated with a higher likelihood of awareness of PrEP.
Conclusion: Awareness of PrEP is low among young adults who may need to use. Considering that PrEP is available in South Africa, awareness campaigns are needed to empower young adults, especially women in the country.

PS11/4

Risk factors for inadequate HIV and STI testing among German PrEP users

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Purpose: Safe use of HIV pre-exposure prophylaxis (PrEP) requires regular testing for HIV and sexually transmitted infections (STI). The objective was to identify risk factors for inadequate testing frequency among current PrEP users in Germany.
Method: From 24th July to 1st November 2018, we recruited PrEP users on geolocation dating apps for MSM, community-based HIV testing sites and a community website in Germany for an anonymous online survey. The outcome was inadequate testing interval, defined as>3 months for HIV and>6 months for STI. Risk factors were assessed with univariate logistic regression.
Results: We recruited 2118 current PrEP users; 52.3% used PrEP for>6 months. The median age was 38 years (IQR 31–45) and 80.83% identified as cisgender male and 0.76% as not cisgender-male (missing 18.41%). Testing frequencies were reported by 1821 participants for HIV and 1808 for STI. Of those, 27.07% and 40.93% reported inadequate testing frequencies for HIV and STI, respectively.
Common factors associated with inadequate testing frequency were on-demand or intermittent PrEP use (HIV: OR=5.63, 95% CI 4.15–7.64; STI: OR=2.55, 95% CI 1.83–3.55), no tests prior to PrEP start (HIV: OR=14.64, 95% CI=4.62–46.41, STI: OR=7.89, 95% CI 2.83–22.04), and≤10 anal sex partners within the last 6 months (HIV: OR=2.23, 95% CI 1.66–3.0, STI: OR=1.94, 95% CI 1.4–2.68). Use of PrEP from informal sources (OR=3.29, 95% CI=2.33–4.64) was associated only with inadequate HIV testing, while self-payment for tests was associated with inadequate STI testing (OR=1.55, 95% CI=1.11–2.17).
Conclusion: Inadequate testing frequency was common in German PrEP users. Coverage of costs for PrEP and medical testing should reduce some barriers for inadequate testing and could improve safe PrEP use. Future changes in testing behavior will be monitored.

PS11/5

Changes in bone mineral density over 2 years in men who have sex with men on tenofovir disoproxil fumarate-based HIV pre-exposure prophylaxis: longitudinal cohort data

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Purpose: Tenofovir disoproxil fumarate (TDF)-based HIV pre-exposure prophylaxis (PrEP) can reduce bone mineral density (BMD) by 1–2% or more over 12 months. Minimal longer-term data are available.
Method: Men who have sex with men (MSM) initiating daily TDF-emtricitabine (FTC) PrEP through a PrEP demonstration project were offered BMD assessment by dual-energy x-ray absorptiometry (DXA) using a single scanner at baseline and after completing 1 and 2 years of PrEP. Hip data are the mean of left and right hip results. We excluded participants who ceased PrEP or who received antiresorptive therapy. Mean changes were assessed using paired t-tests.
Results: Of 185 men with baseline scans, 118 (64%) and 51 (43%) men were assessed at a median (IQR) of 420 (391–449) and 824 (776–885) days on PrEP. The mean (SD) ages and body mass index (BMI) of those men that had baseline BMD assessment compared to the 282 that did not was 35 (10) and 32 (9) years ($p<0.05$) and 25 (4) and 25 (4) kg/m^2, respectively ($p>0.05$). Changes in BMD are shown in Table 1. No participant experienced a low trauma fracture during the study.

Table 1. BMD Changes

BMD assessments	Baseline to Year 1 (n=118)	p value	Year 1 to Year 2 (n=51)	p value
Change (%) median (IQR) g/cm^2				
L1–L4	−0.86% (−2.6–1.5)	0.045	−0.78% (−2.7–2.5)	0.499
Femoral neck (total)	−1.1% (−3.3–0.54)	0.0001	−0.42% (−2.7–1.9)	0.502
Total hip	−0.87% (−2.3–0.87)	0.004	0.49% (−0.82–1.5)	0.147
>3% BMD loss (%)				
L1–L4	23%		14%	
Femoral neck (total)	27%		22%	
Total hip	16%		6%	

Conclusion: Over 12 months, a substantial proportion of MSM on daily HIV TDF-FTC PrEP lose≥3% BMD at all measured sites over 24 months. There may be a plateau in loss after 12 months. Long-term studies of TDF-based PrEP in MSM are warranted.

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PS11/6

Can HIV epidemics be eliminated using PrEP?

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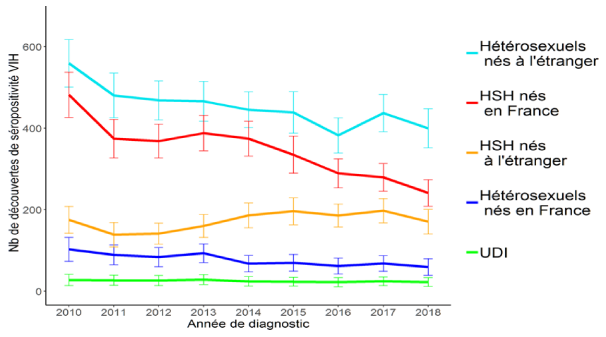
Purpose: Pre-exposure prophylaxis (PrEP) is highly effective in preventing HIV infection. Modeling studies concluded that PrEP could eliminate HIV epidemic, once certain PrEP coverage levels are achieved. However, whether and how such coverage levels can be reached remains unknown. Here we address this issue.
Method: We propose an innovative approach combining a compartmental model of HIV transmission at the population level, and a game-theoretic model for decision-making about PrEP at the individual level. Individuals at high-risk of HIV infection choose to use PrEP, or not to use PrEP, and undergo antiretroviral treatment (ART) if they acquire HIV, depending on the perceived risk of infection and relative cost of using PrEP, which includes price and access model of PrEP, consequences of being infected and lifelong ART, etc. We determine the conditions under which the voluntary use of PrEP could eliminate HIV among men who have sex with men (MSM) in the Parisian region of France.
Results: We found that if PrEP offers high protection at low relative cost, HIV can be eliminated. For instance if PrEP effectiveness is 86%, as in the IPERGAY trial, PrEP coverage among high-risk MSM can reach 63% (IQR: 57%-67%), the minimum required for elimination, if individuals have a fair risk perception and the relative cost of using PrEP versus ART is sufficiently low. Drop of condom use among PrEP users does not play a major role against elimination while the risk perception does. Moreover, we found that epidemic elimination is only temporary.
Conclusion: To reach PrEP coverage levels necessary to eliminate HIV, urgent efforts are needed to lower the cost of using PrEP. Furthermore, maintaining low cost for PrEP once the HIV epidemic is eliminated will be essential to sustain PrEP coverage levels and elimination in the long run.

PS11/7

Drop in HIV diagnoses among MSM in Paris: combined effect of PrEP, testing and political support to the communities

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Objectives: In 2016, the City of Paris launched its Fast-Track strategy to end HIV transmission by 2030, in the context of PrEP roll-out, universal treatment and new testing recommendations.
Methods: Paris Fast-Track Blueprint is based on research and epidemiological surveillance, political support for community engagement and resource mobilization, the implementation of combined prevention in an inclusive approach to sexual health. It was designed to tackle persistent long delays to diagnosis and high level of undiagnosed HIV prevalence among key affected populations (MSM and Sub-Saharan African migrants). A special emphasis was put on PrEP roll out.
Results: Between 2015 and 2018, HIV diagnoses have fallen by 16% overall in Paris, with a steep decrease of 28% among France-born MSM (Fig 1), as a result of an increase in PrEP coverage and screening frequencies. The number of HIV tests has gone up by 10%, along with increased investment in self-tests, outreach testing and daily communication focused on the trivialization of routine HIV testing.
ERAS survey among MSM shows a significant improvement in testing (between 2017 and 2019 among non-HIV-positive respondents: +10% reported a HIV test within the previous 12 months) and PrEP protection increased (2019 vs. 2017, aOR [95%CI]=2.7 [2.1–3.5]).
PrEP uptake in Paris has been boosted by the ANRS Prevenir study as well as the political support given to PrEP early adopters by City officials and public campaigns.
Conclusion: To date, the implementation of all the tools of combined prevention together with additional funding and a strong political will allow a true decline in new HIV diagnoses. However, those results call for additional efforts especially towards both migrant MSM and women. Free HIV tests in medical labs without prescription, incentives for GPs to offer sexual health check-ups and PrEP roll-out strategies among women and migrants are the next steps.



Viral co-infection and liver disease

PS12/1

"Giving HepC a place and letting it go again": response to a sexual risk reduction intervention in HIV/HCV co-infected men who have sex with men

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Purpose: Within the Swiss HCVree trial, HIV/HCV co-infected men who have sex with men received HCV treatment and a sexual risk reduction intervention to reduce HCV re-infection. This evaluation explored the response to intervention perceived by participants' to better understand intervention mechanisms and acceptance.
Method: Qualitative thematic analysis with a constructivist orientation was used. With a purposive sampling approach, 21 of 51 intervention participants were asked to participate in single semi-structured interviews 6 to 12 months' post-intervention. Seventeen respondents participated.
Results: The main theme "Giving HepC a place and letting it go again" describes how participants position themselves to the program and their sense-making work after having been exposed. The two sub-themes "Realizing it's about me and not risks" and "Strengthening awareness of what I do" provide insights into the process of the intervention.
Three constructed typologies illustrate individual differences within themes. "Modifiers" (n=5) perceived HCV as a serious problem. The intervention empowered them to move on with life-style changes aiming to eliminate HCV for lifetime. "Keepers" (n=4) perceived HCV as unproblematic and treatable. Through the intervention, they perceived their chosen risk reduction strategy (fewer sexual encounters) as unsuccessful, while medical treatment seemed easy. They imagined living with HCV or repeating treatment when re-infected. "Traders" (n=8) perceived HCV as a "disease of others" but manageable once

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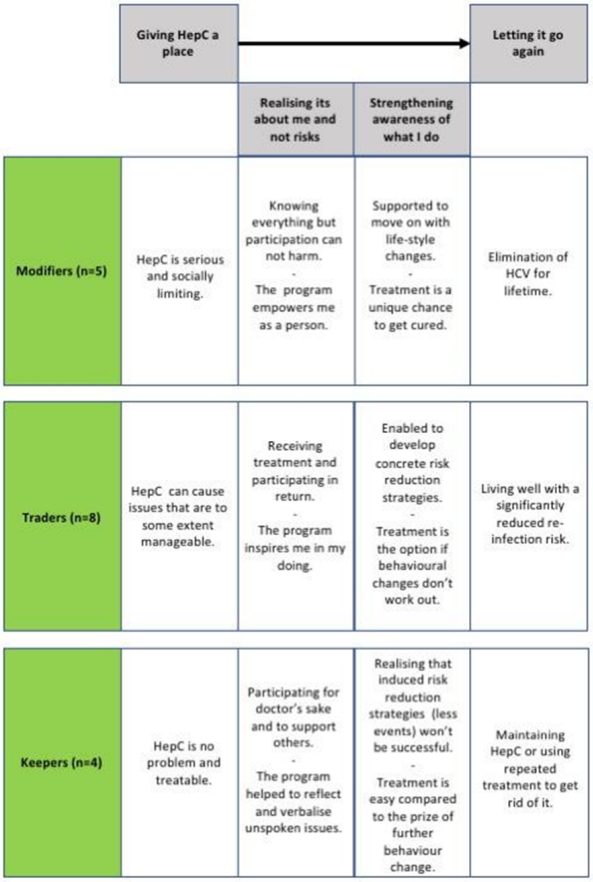


Figure 1. Main themes and three typologies of participants

affected. The intervention inspired them to develop concrete behavioral risk reduction strategies aiming to live with a minimized re-infection risk, with the option of medical treatment if behavioral changes failed.
Conclusion: Differences between groups in accepting the intervention and in subsequent sense-making work provide evidence for intervention tailoring to enhance effectiveness. These first insights show also that medical treatment has an impact on individuals' motivation for risk reduction, which varies between groups..

PS12/2

Impairment of CD8 T cell memory in DAA treated HCV/HIV co-infected patients

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Purpose: In comparison to spontaneous viral clearance, treatment of chronic hepatitis C infection (HCV) does not generate a memory T cell response conferring protection to re-infection. This study investigates the phenotypic changes of the T cell response to cognate antigen re-challenges in HIV-HCV co-infected individuals on suppressive antiretroviral therapy (cART) after successful direct acting antiviral (DAA) HCV-treatment.
Method: Peripheral Blood Mononuclear Cells (PBMCs) from HCV (genotype 1) co-infected patients of the Swiss HIV Cohort Study (n=11) were prospectively collected before and after successful DAA treatment. A comparator group that had spontaneously cleared HCV infection (n=6) was used to investigate T cell phenotype by fluorescent activated cell sorting (FACS) after ex vivo re-challenge for 10 days in comparison to direct ex vivo Stimulation (6 hours) with cognate HCV (NS3) and HIV (Gag) antigens.
Results: Ex vivo re-stimulation with NS3 for 10 days as proxy for HCV re-infection resulted in an increase of programmed cell death 1 (PD-1) positive effector memory (CD45RA-CCR7-) and decrease of terminal effector (TEMRA; CD45RA+CCR7-) CD8 T cells in persons after successful DAA treatment ($p=0.07$ and <0.05, respectively; Wilcoxon Rank Test). The same pattern was observed with Gag re-stimulation (both $p<0.05$). In contrast, no change in PD-1 expressing effector memory or TEMRA was observed in spontaneous HCV clearers after NS3 re-stimulation (p=ns). PD-1 expression changes were not limited to interferon-γ positive CD8 T cell populations.
Conclusion: HCV treated HIV positive individuals exhibit an impaired PD-1 positive CD8 T cell memory pool in contrast to spontaneous HCV clearers after antigen re-challenge. Our results offer a possible explanation for the lack of immune protection for HCV re-infections after a successful DAA treatment. Further analyses are needed to investigate the epigenetic imprinting of potentially dysfunctional memory T cells.

PS12/3

Evolution of non-invasive markers of liver fibrosis in HIV-hepatitis C virus (HCV) co-infection before and after sustained virologic response (SVR): results from the Canadian co-infection cohort

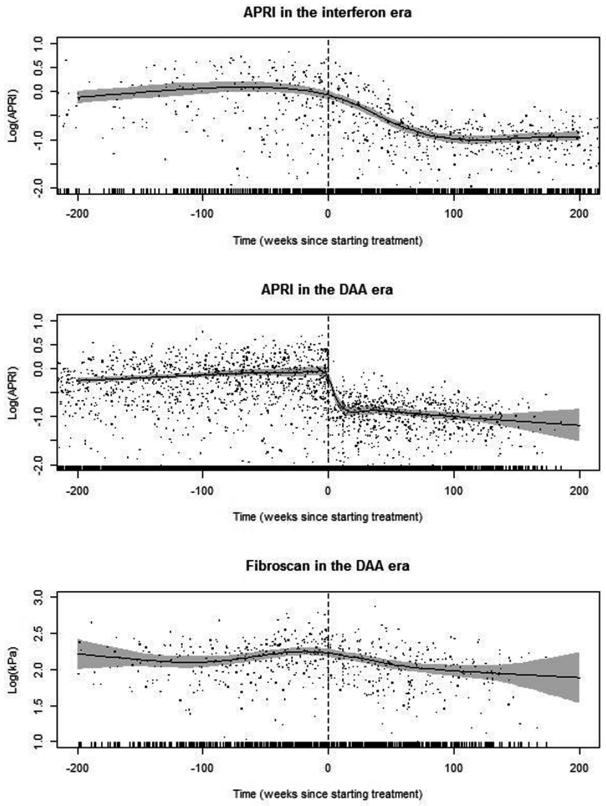
MB Klein[1], N Kronfli[1], S Wang[2], S Walmsley[3], M Hull[4], C Cooper[5], D Rouleau[6], J Gill[7], J Cox[1], J Young[8] and Canadian Co-infection Cohort

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Purpose: Noninvasive markers of liver fibrosis such as APRI and transient elastography (Fibroscan) have largely replaced liver biopsy for staging HCV. There is little longitudinal data on how these measures evolve after SVR. To inform monitoring of liver fibrosis after cure, we compared changes in these markers before and after SVR in coinfected patients.
Method: We selected patients from a prospective longitudinal cohort study who achieved SVR after a first treatment with either interferon/ribavirin or all oral direct acting antivirals (DAA), with at least one pre-treatment and one post-treatment fibrosis measure and without chronic hepatitis B. Changes in APRI or Fibroscan (in the DAA era only) were modelled using a generalised additive mixed model, assuming a gamma distribution and adjusting for sex, age at HCV acquisition, duration of HCV infection, and time varying BMI, hazardous alcohol use and detectable HIV RNA. We used our models to predict rates of change in fibrosis markers over time (Figure).
Results: Of 1842 patients enrolled, 144 achieved SVR with interferon and 400 with DAAs. Of these, 88 and 252 met inclusion criteria, respectively (Table).
Characteristics included patients at start of HCV treatment by treatment era

Characteristic at start of treatment	DAA Era (n=252)	Interferon Era (n=88)
Age (median years, IQR)	52 (8)	46 (12)
Male sex (n, %)	187 (74%)	74 (84%)
History of IDU (n, %)	187 (74%)	65 (74%)
Hazardous drinking (n, %)	94 (37%)	22 (25%)
Duration of HCV infection (median years, IQR)	25 (17)	16 (15)

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Predicted change in fibrosis markers before and after successful HCV treatment

Table Continued.

Characteristic at start of treatment	DAA Era (n=252)	Interferon Era (n=88)
HIV RNA<50 copies/mL (n, %)	213 (85%)	56 (64%)
BMI (median, IQR)	25 (5)	25 (5)
APRI (median, IQR)	0.82 (1.30)	0.91 (1.10)
Fibroscan (median KPa, IQR)	7.4 (8.7)	NA

In the DAA era, APRI increased (0.04 units/year; 95% CI, −0.09, 0.18) before, dropped dramatically during, and then declined minimally (−0.04 units/year; 95% CI, −0.10, 0.02) after, treatment. Fibroscan values, however, increased (1.02 KPa/year; 95% CI, 0.27, 2.10) before treatment, changed little by the end of treatment, and then declined (−1.15 KPa/year; 95% CI, −2.28, −0.42) after SVR.
Conclusions: APRI drops immediately after treatment initiation, more slowly with interferon than with DAAs, likely reflecting a reduction in hepatic inflammation associated with HCV RNA suppression. APRI therefore does not appear to be a good marker to follow changes in liver fibrosis. In contrast, Fibroscan appears to be a more valuable tool both to stage fibrosis and monitor its regression after cure.

PS12/4

HIV/HBV coinfection in Spain: prevalence and clinical characteristics

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Purpose: We assessed the prevalence of HIV/HBV coinfection in Spain in 2018 and compared the results with similar 5 similar studies performed since 2002.
Method: The study was nested in a survey designed to assess the prevalence of HCV infection in 43 centers during October-November 2018. Patients were selected using simple random sampling. We evaluated the presence of HBsAg, HBV-DNA, HDV antibodies (Ab), anti-HBV therapy, and liver fibrosis. Cirrhosis was defined by liver biopsy, transient elastography (>12.5 kPa), and clinical/biological findings.
Results: The reference population was 40,650 patients living with HIV (PLWH), and the sample size was 1,733. HBsAg serostatus was known in 1,673 patients (96.5%) and 54 (3.2%) were HBsAg-positive, 7 (13.0%) of whom had cirrhosis. No significant differences were found in the prevalence of HCV-Ab between HBsAg positives and negatives (40.7% vs. 32.7%, p=0.445), but spontaneous HCV clearance was more frequent among HBsAg positives in comparison with HBsAg negatives (54.5% vs. 17.0%, p<0.001). Of the HIV/HBV-coinfected patients, 38 (70.4%) had known serostatus for HVD, 10 of whom (26.3%) had HDV-Ab. All HIV/HBV coinfected patients were receiving anti-HBV therapy, and 33 (61.1%) had HBV DNA determined in the previous 12 months, 32 of whom (97.0%) had HBV DNA<80 IU mL. Main findings in the five national cross-sectional studies are shown in the table.
Conclusion: The prevalence of HIV/HBV coinfection in Spain in 2018 was 3.2%, a figure that remained stable since 2002. Most HIV/HBV-coinfected patients had complete suppression of HBV DNA, but HDV-coinfection and cirrhosis are common problems in this population group. Chronic HBV infection is soon to be the most prevalent chronic viral hepatitis among PLWH in Spain.

Trends in HIV/HBV coinfection in Spain

	2002	2009	2015	2016	2017	2018
Centers	39	43	41	43	43	43
Reference population	31,800	29,559	35,791	38,904	40,322	40,650
Sample size	1,260	1,458	1,867	1,588	1,690	1,733
Tested for HBsAg	92.7%	97.7%	97.1%	97.5%	96.2%	96.5%
HBsAg (+) among those tested	4.9%	3.4%	3.0%	3.9%	3.0%	3.2%

PS12/5

Outcomes after switching from TDF to TAF in HIV/HBV-coinfected individuals with renal impairment: a nationwide cohort study

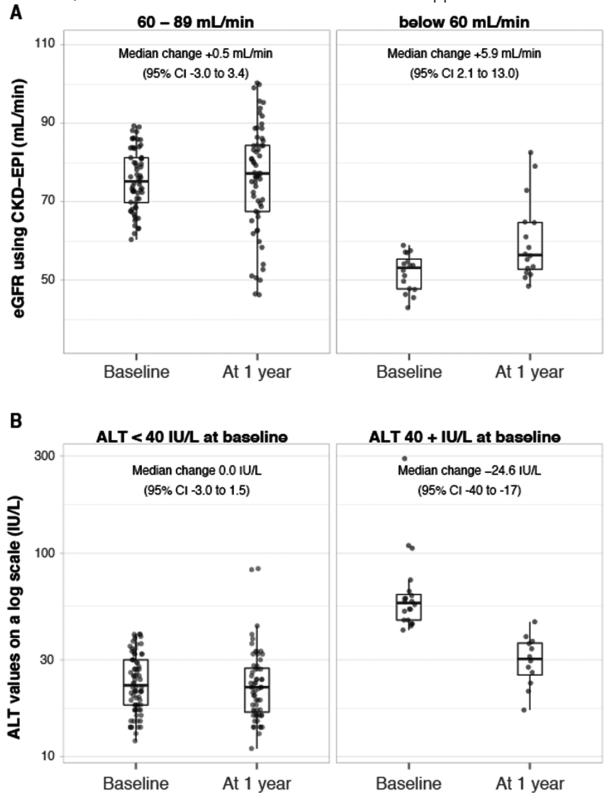
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Purpose: The impact of the use of tenofovir alafenamide (TAF) on clinical outcomes among HIV/hepatitis B virus (HBV)-coinfected individuals with renal

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dysfunction is unclear. We explored HBV outcomes and renal function after switching from tenofovir disoproxil fumarate (TDF) to TAF in a prospective nested study within the Swiss HIV Cohort Study.
Method: We included all HBsAg-positive adults who had TDF replaced by TAF while having a suppressed HIV viral load and an eGFR<90 mL/min. We assessed HIV and HBV suppression as well as HBsAg loss at 1 year after switch using descriptive statistics and evaluated changes in renal function and ALT levels with paired Wilcoxon rank-sum tests.
Results: Of 104 HIV/HBV-coinfected patients, 22 (21.2%) were female, 53 (51%) men who have sex with men, and 31 (29.8%) were of African origin. At switch, median age was 51 years (IQR 46–56), median CD4 count 600 cells/μL (IQR 422–825) and median eGFR 73.0 mL/min (IQR 61.5–81.0), with 25 patients (24%) having an eGFR<60 mL/min. At baseline, HBV was suppressed (< 50 IU/mL) in 88/92 (95.7%) with available HBV-DNA measurements, ALT was elevated (≥40 IU/L) in 20 (19.2%) individuals, and 23.8% had significant fibrosis (liver stiffness stage ≥F2). One year after switch, 74/76 (97.4%) individuals with available HIV-RNA measurements were suppressed (< 50 cp/mL). Of 50 patients with HBV-DNA follow-up measurements, 48 (96.0%) were suppressed, and 5 (4.8%) lost their HBsAg. Median eGFR remained stable among individuals with a baseline eGFR 60–89 mL/min but improved among those with a baseline eGFR<60 mL/min (Figure). Among patients with elevated baseline transaminases, ALT levels decreased over time.
Conclusion: In HIV/HBV co-infected patients with moderate renal impairment, replacing TDF by TAF was associated with improvements in renal function and ALT decline, with maintenance of HIV and HBV viral suppression.



Changes in eGFR (Panel A) and ALT (Panel B) 1 year after replacing TDF by TAF

PS12/6

Hepatic steatosis in HIV monoinfected individuals: which impact has baseline BMI and treatment with integrase inhibitors?

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Purpose: The natural history of non-alcoholic fatty liver disease (NAFLD) in HIV-infected individuals is still not fully understood and risk factors remain to be determined. This cohort study analyses factors associated with progression of hepatic steatosis (HS) in HIV-positive patients.
Method: This single-center longitudinal observational study enrolled 432 HIV-positive patients between August 2013 to July 2017. Liver stiffness and HS were assessed yearly by transient elastography using an M-probe of FibroScan (Echosens, Paris, France). Primary endpoints were progression of HS or de novo development of HS during the study period assessed by CAP values.
Results: Patients with underlying fibrosis (≥7.1 kPa) or steatosis (≥238 dB/m) at baseline were significantly older (no fibrosis/no HS : 41.6 ± 11.4 years vs HS/no fibrosis: 48.2 ± 9.5 years; p<0.001 and vs fibrosis: 51.8 ± 12.9 years; p=0.01) and had a higher baseline BMI (no fibrosis/no HS: 23.0 ± 2.8 vs no fibrosis/HS: 25.6 ± 3.4; p<0.001 and vs fibrosis: 25.1 ± 3.3; p=0.03) than those without HS and fibrosis. AUC of BMI was 0.753 (95% CI 0.694–0.813, p<0.001) revealing a cut-off value of 23.5 kg/m^2 associated with HS. Interestingly, those patients being treated with Integrase Inhibitors (INSTI) (n=88) showed significantly higher CAP values at their last visit than those receiving alternate treatment regimens (PI/r n=50; NNRTI n=84) (243 dB/m vs. 268 dB/m; p=0.01). Moreover, gain of weight over the study period (mean study period 30,8 ± 8.8 and 30.1 ± 8.8 months; 2.4 ± 7.8 kg vs. 0.5 ± 12.0 kg, p=0.007), BMI (25.9 ± 4.8 kg/m^2 vs 24.6 ± 4.3 kg/m^2; p=0.009) and weight (81.5 ± 15.9 kg vs 75.8 ± 17.5 kg; p=0.004) at last visit were significantly higher in these patients, indicating an impact of INSTIs on body weight and hereby on development and progression of HS.
Conclusion: This is the first observational longitudinal study showing, that hepatic steatosis develops in HIV-positive individuals despite a non-obese BMI (>23.5 kg/m^2). Moreover, we detected a significant effect of INSTIs on body weight and HS.

PS12/7

Evolutive NAFLD predicts frailty in people living with HIV (PLWH)

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Variable	Total	No evolutive NAFLD	Evolutive NAFLD	p
	707 (100%)	635 (89.82%)	72 (10.18%)	
Sex, male (%)	539 (76.24%)	479 (75.43%)	60 (83.33%)	0.178
Age, years, mean (±SD), [N°]	53.5 (8.15) [707]	53.24 (8.12) [635]	55.82 (8.17) [72]	0.020
BMI, kg/m^2, mean (±SD), [N°]	24.64 (4.21) [705]	24.17 (3.95) [633]	28.73 (4.19) [72]	<0.001
Waist circumference, cm, mean (±SD), [N°]	92.26 (33.05) [662]	90.84 (34.37) [595]	104.93 (11.21) [67]	<0.001
Obesity (%)	64 (9.08%)	38 (6%)	26 (36.11%)	<0.001
Mild/moderate physical activity (%)	310 (43.85%)	292 (45.98%)	18 (25%)	0.001
HIV duration, months, median (IQR), [N°]	280 (167-344) [686 (97.03%)]	275 (165.5-338) [615]	322 (229-372) [71]	0.007
Nadir CD4, median, c/μL, median (IQR) [N°]	217.5 (100-324.75) [674]	224 (100-328.75) [606]	180 (67-287) [68]	0.027
Current CD4, median, c/μL, median (IQR) [N°]	700 (539.5-888.5) [691]	700 (542.25-884.75) [622]	689 (436-891) [69]	0.394
Undetectable viral load (%)	698 (98.73%)	627 (98.74%)	71 (98.61%)	0.990
Type 2 diabetes (%)	129 (18.25%)	99 (15.59%)	30 (41.67%)	<0.001
Current exposure to NNRTI (%)	169 (26.61%)	160 (28.12%)	9 (13.64%)	0.018
AST, U/l, mean (±SD), [N°]	24.68 (12.82) [670 (94.77%)]	24.09 (12.45) [605]	30.22 (14.88) [65]	<0.001
Total cholesterol, mg/dl, mean (±SD), [N°]	179.57 (36.5) [668]	180.94 (35.64) [603]	166.88 (41.86) [65]	0.003
LDL cholesterol, mg/dl, mean (±SD), [N°]	116.7 (33.49) [664]	117.83 (32.72) [600]	106.11 (38.7) [64]	0.004
HDL cholesterol, mg/dl, mean (±SD), [N°]	50.8 (14.81) [665]	51.56 (15) [600]	43.75 (10.61) [65]	<0.001
Triglycerides, mg/dl, mean (±SD), [N°]	136.98 (92.4) [667]	133.49 (89.96) [603]	169.78 (108.2) [64]	0.002
Frailty index, mean, (±SD), [N°]	0.22 (0.09) [570]	0.2 (0.09) [512]	0.31 (0.09) [58]	<0.001
Frailty index (%) cut-off 0-0.25	387 (67.89%)	369 (72.07%)	18 (31.03%)	<0.001
Frailty index (%) cut-off 0.25-0.4	163 (28.6%)	134 (26.17%)	29 (50%)	<0.001
Frailty index (%) cut-off >0.4	20 (3.51%)	9 (1.76%)	11 (18.97%)	<0.001

Table 1. Patients' characteristics according to the presence of evolutive NAFLD

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Objective: The objective of the study was to investigate the relationship between liver steatosis and significant fibrosis alone and in association (evolutive NAFLD) and frailty in PLWH.
Methods: This was a cross-sectional study of consecutive patients attending Modena HIV Metabolic Clinic in 2018–2019. Patients with hazardous alcohol intake and HBV or HCV co-infection were excluded. Controlled attenuation parameter (CAP) and liver stiffness measurement (LSM) and were evaluated by transient elastography. Liver steatosis was diagnosed by CAP as follows: S0 (no steatosis; CAP<248 dB/m), S1 (mild steatosis; 248≥CAP<268), S2 (moderate steatosis; 269≥CAP<280), S3 (severe steatosis; CAP≥280) dB/m. Liver fibrosis was diagnosed by LSM as follows: stage F0-F1 (mild fibrosis, LSM<7.1 kPa), F2-F3 (significant fibrosis, 7.1>LSM<13), F4 (cirrhosis, LSM>13 kPa). Evolutive NAFLD was defined as the contemporary presence of liver steatosis (CAP≥248) and significant liver fibrosis or cirrhosis (stage ≥F2). Frailty was assessed using 36-Item frailty index (FI). FI was categorized as fit (< 0.25), frail (0.25–0.4), most frail (>0.4). Logistic regression was used to explore frailty predictors using steatosis and evolutive NAFLD as covariates.
Results: We analysed 707 PLWH. Mean age was 53.5 (±8.2) years, 76.2% males, current median was CD4=700 µL (IQR=539–889). Evolutive NAFLD was present in 10.2%; frail and most-frail in 18.9 % and 3.9%, respectively. Other patients' characteristics and association of evolutive NAFLD with co-morbidities are provided in Table 1 and 2, respectively. Predictors for FI were: age (OR=0.6, 0.4–0.9), steatosis (OR=2.1, 1.3–3.5) and fibrosis (OR=2, 1–3.7), evolutive NAFLD (OR=9.2, 5.2–16.8), diabetes (OR=1.7, 1–2.7), multimorbidity (OR=2.5, 1.5–4).

	Evolutive NAFLD		
	OR	IQR	p
Depression	1.78	0.93-3.31	0.07
Neurocognitive impairment	5.08	1.61-14.96	<0.01
Vitamin D insufficiency	1.94	1.18-3.24	0.01
Obesity	8.06	4.44-14.55	<0.01
Hypertension	1.59	0.95-2.7	0.08
Type 2 diabetes	3.28	1.91-5.59	<0.01
CVD	0.85	0.25-2.29	0.78
CKD	0.71	0.35-1.35	0.32
COPD	1.32	0.38-3.57	0.62
Osteoporosis	0.37	0.16-0.76	0.01
Dyslipidemia	0.92	0.47-1.92	0.8
Cancer	1.36	0.7-2.5	0.34

Table 2. Association of the evolutive NAFLD with co-morbidities

Conclusion: Evolutive NAFLD increases the risk of frailty by 9.2-fold and we may suggest it as an indicator of metabolic age. Liver steatosis alone was associated with frailty, implying that health care interventions such as lifestyle changes, should be promoted in PLWH.

Liverpool/EACS pharmacology workshop – pharmacology today and tomorrow

PS13/1

Safety and PK of subcutaneous GS-6207, a novel HIV-1 capsid inhibitor

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Purpose: GS-6207, a selective, multi-stage inhibitor of HIV-1 capsid function, is in development for the treatment of HIV-1 infection. GS-6207 is characterized by potent antiviral activity, low predicted human clearance, and low aqueous solubility, making it well suited for a sustained-release parenteral formulation. This Phase 1 study evaluated the safety, tolerability and pharmacokinetics (PK) of a subcutaneous (SC) suspension of GS-6207 in healthy volunteers.
Method: This was a randomized, blinded, placebo-controlled study with staggered single dose escalation cohorts. Within each cohort, subjects were randomized (4:1) to receive single SC doses of 30, 100, 300 or 450 mg GS-6207 (n=8/cohort) or placebo (N=2/cohort). PK parameters were estimated and summarized by dose and dose proportionality was assessed. Safety, tolerability and PK were evaluated for 24–32 weeks post-dose.
Results: 40 subjects received a single SC dose of GS-6207 (N=32) or placebo (N=8). PK was characterized by prolonged exposure, with measurable concentrations for at least 24 weeks. Across the dose range of 30–450 mg, dose-proportional increases in AUC_{inf} and C_{max} were observed. The median $t_{1/2}$ ranged from 32 to 45 days. At doses of 100 mg or greater, GS-6207 plasma concentrations exceeded the protein adjusted EC_{95} for wild type HIV-1 for at least 12 weeks.
There were no deaths, or Grade 3 or 4 adverse events (AEs). Other than injection site reactions (mild) experienced by 53% of patients, the most common AEs were headache (13%) and viral upper respiratory tract infection (8%). Most AEs were mild (Grade 1) and resolved. There were no clinically relevant laboratory findings.
Conclusion: GS-6207 was safe and well tolerated following single SC doses of up to 450 mg. Sustained exposure supports a dosing interval of at least 3 months. Safety and PK of GS-6207 supports its development as part of a long-acting antiviral regimen for people living with HIV.

PS13/2

A multicentred randomised controlled open study of the utility and acceptability of a medicines optimisation review (MOR) toolkit compared to standard pharmaceutical care in HIV outpatients

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Purpose: Polypharmacy seen in older people living with HIV (PLWH) increases risks of medicine related problems (MRP). Evidence that medicine reviews reduce MRPs in HIV outpatients is limited. We aimed to examine the utility and acceptability of a Medicines Management Optimisation Review (MOR) tool in HIV outpatients.
Method: A multicentred randomised controlled open study in 4 HIV outpatient services, randomly allocated PLWH to receive either a MOR (intervention) or standard pharmaceutical care (control). Inclusion criteria included cART use and aged>49 or aged<49 with another health condition requiring medication. Intervention patients received MOR consultations at

Table 1. HIV clinical variables

HIV clinical variable	
Age (years)*	58 (35–88)
Time on cART (years)*	15 (1–130)
Time since HIV diagnosis (years)*	20 (1–34)
CD4 cell count*	607 (98–1868)
VL<40 copies/mL	97.5%
*Median (range)	

Table 2. Type and number of MRPs seen in each group at each time point

Medicine Related problem (MRP) type	Baseline MOR N=93	Baseline Control N=2	Six-month follow-up (new MRPs) MOR N=33	Six-month follow-up (new MRPs) Control N=3
Potentials adverse drug reaction	14	0	6	2
Potential drug-drug interaction	34	1	10	0
Dose adjustment	21	0	6	0
Problem with handling or administration	10	1	2	1
Unnecessarily complex regimen	4	0	5	0
Inappropriate off label use	3	0	0	0
Undertreatment	6	0	4	0
Other	1	0	0	0

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baseline, 6 and 12 months. MOR consultations consisted of patient-orientated questionnaire promoting self-review and adherence and a MOR form designed to aid a structured patient consultation. Changes in health-related quality of life (EQ-5D-5L), acceptability, healthcare utilisation and intervention cost will be examined at 12 months. Primary outcome measure was the difference in number of MRPs between intervention and control groups at each time interval. Mean comparisons were examined using t-tests.
Results: Baseline data was collected from 200 patients (see Table 1); mean number of non-ART medications 6.6 (3.4), with the most common being statins (31%), antidepressants (25%) and analgesics (21%). Significantly more MRPs were identified at baseline and 6 months in the MOR group (1.16 ± 1.32), (0.54 ± 0.87) compared to control (0.02 ± 0.15), (0.37 ± 0.19), p<0.001 and p<0.001, respectively. Two-way ANOVA revealed no main effect of time phase on quality of life, (p=0.51)and no interaction between experimental arm and time phase on quality of life (p=0.82). Pharmacists fully resolved 42 (35%) MRPs at baseline with 67 (52%) resolved within 6 months.
Conclusion: MOR identified a significant number of MRPs compared to standard pharmaceutical care in both time phases, suggesting HIV outpatients services should consider implementing MOR for targeted populations under their care.

PS13/3

Prevalence of potential drug-drug interactions in patients of the Swiss HIV cohort study in the era of HIV integrase inhibitors

E Deutschmann[1], HC Bucher[1,2], S Jaeckel[3], S Gibbons[4], K McAllister[4], A Scherrer[5,6], D Braun[5], M Cavassini[7], A Hachfeld[8], A Calmy[9], M Battegay[2], M Cipriani[10], L Elzi[11], J Young[1], B López-Centeno[12], J Berenguer[13], S Khoo[4], G Moffa[1], C Marzolini[2,4] and The Swiss HIV Cohort Study

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Purpose: The analysis of the Swiss HIV Cohort Study (SHCS) in 2010 showed a high prevalence of potential drug-drug interactions (PDDIs) with antiretroviral drugs (ARVs) [1]. In recent years, ARVs with more favorable interaction profiles are used. We reassessed the prevalence of PDDIs with ARVs in the era of HIV integrase inhibitors (INIs).
Method: The period prevalence of PDDIs in the SHCS between 01/2018 and 12/2018 in patients receiving at least one ARV was analyzed to determine PDDIs between ARVs and non-ARV drugs. PDDIs were identified by linkage of the Liverpool drug interactions and SHCS databases and categorized as harmful (red), of potential clinical relevance (amber) or of weak clinical significance (yellow).
Results: In total, 9'034 patients were included, median age 51 years (IQR 43;57), males (72%), Caucasians (77%). Overall, 14% (1'290/9'034) of patients received a protease inhibitor (PI)-, 28% (2'561/9'034) a non-nucleoside reverse transcriptase inhibitor (NNRTI)- and 65% (5'849/9'034) an INI-based regimen. Of those, 48% (4'368/9'034) were unboosted INI regimens. Overall, 77% (6'926/9'034) of patients received≥1 comedication, and 24% (2'163/9'034) had≥1 PDDI. Among patients with comedication, 2% (159/6'926) had red, 24% (1'683/6'926) amber and 13% (920/6'926) yellow PDDIs. The most prevalent red PDDIs were between boosted ARVs and corticosteroids (25%) whereas most frequent amber PDDIs involved cardiovascular drugs (36%). Compared to 2010, more patients received≥1 comedication (68% vs 77%); but fewer received boosted PI- (46% vs 14%) and NNRTI- (38% vs 28%) based regimens leading to a 16% overall PDDI reduction, with red PDDIs remaining unchanged (2%).
Conclusion: The proportion of patients with comedications in the SHCS has increased in the past decade; however, the overall prevalence of PDDIs has decreased mainly due to the increasing use of unboosted INIs. Corticosteroids are a major component of the clinically relevant PDDIs.
Reference: 1. Marzolini C, Elzi L, Gibbons S, et al. Prevalence of comedications and effect of potential drug-drug interactions in the Swiss HIV Cohort study. Antivir Ther. 2010;15:413–23.

Cure symposium co-organised with the National Agency for AIDS Research (ANRS)

PS14/1

HIV reservoir in gut from PHI treated individuals is stable over time and correlates with blood markers of HIV reservoir and inflammation- findings from the HEATHER gut study

JP Thornhill[1,2], H Carolina[1], H Lewis[1], S Peake[1], J Hoare[1], J Fox[3], J Frater[2] and S Fidler[1]

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Purpose: Gut HIV reservoir is a key site of HIV persistence. Antiretroviral therapy (ART) in Primary HIV Infection (PHI) has been used as a strategy to limit HIV reservoir. However, tissue sampling is not routine in HIV cure studies. We present the HEATHER gut study, describing the impact of ART in PHI on gut HIV reservoir over time and identify blood correlates of the gut HIV reservoir.
Method: The HEATHER gut study is an observational cohort of individuals with PHI; commenced on ART within 3 months. Participants underwent colonoscopy with biopsies from terminal ileum (TI) and rectum. An optional second colonoscopy was performed approximately 1 year later. HIV DNA was measured using qPCR. Plasma inflammatory markers were measured using Luminex. Lasso regression models identified plasma markers associated with gut HIV DNA.
Results: 21 PHI individuals were enrolled (table 1). 10 had longitudinal sampling, with HIV DNA measured at two time points, approximately 1 year

Figure 1. Longitudinal HIV DNA levels at the time of first and second gut biopsy in the HEATHER gut study are shown for (a) terminal ileum and (b) rectum, P values were calculated using Wilcoxon's test. The jitter plot in (c) shows HIV DNA levels in the terminal ileum (TI), rectum and PBMCs using all avaliable data (n=28 observations); the line indicates the median, group comparisons in (c) were made using Friedman's test. The correlation between HIV DNA measured in PBMCs and (d) terminal ileum and (e) rectum is also shown. Non-parametric tests (Spearman's) was used to test associations. Abbreviations: CPM, copies per million; TI, terminal ileum.

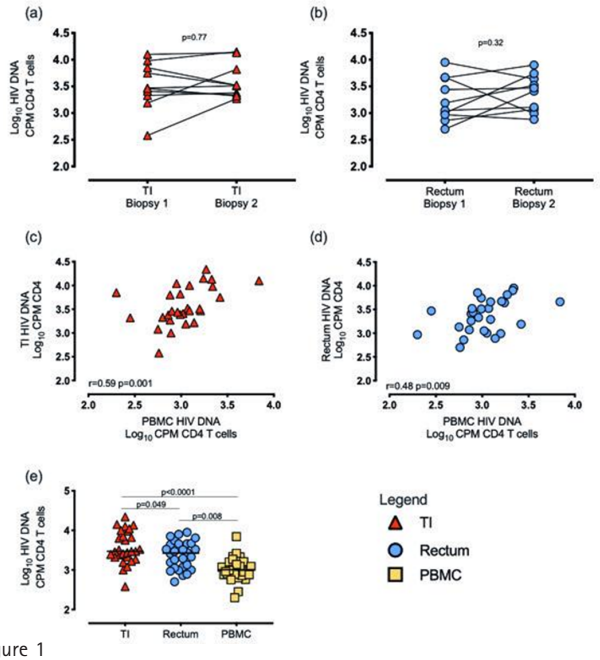


Figure 1

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apart, for these the HIV DNA levels in TI (p=0.77) and rectum (p=0.32) remained stable. HIV DNA, in log_{10} copies/million CD4 cells, from TI was higher at 3.47 (3.32–3.95) compared to 3.43 (3.06–3.66) in rectum, p=0.049. Both TI (p<0.001) & rectum (p=0.008) had higher HIV DNA compared to PBMC; 3.01 (2.88–3.21). PBMC measures of HIV DNA correlated with those in TI (r=0.59 p=0.001) and rectum (r=0.48 p=0.009), (figure 1). Lasso regression models (table 2) identified plasma markers most associated with gut HIV reservoir, including sCD40, sCD14, RANTES, MADCAM-1 for both rectal & TI HIV DNA (figure 2)

Conclusion: GUT HIV DNA is stable over time despite ART in PHI. HIV reservoir was higher in gut compared to blood. However, peripheral blood HIV DNA and markers of inflammation correlate with gut reservoir and therefore may be useful surrogate markers of gut reservoir in cure studies

HEATHER Gut Study Patient Characteristics

HEATHER Gut Study Patient Characteristics								
Study ID	Age, years	Seroconversion CD4, cells/mm^3	Seroconversion HIV viral load, *log_{10}CPM*	Time from PHI to ART start, days	Time on ART at 1st gut biopsy, months	CD4 count at 1st gut biopsy, cells/mm^3	HIV viral load at 1st gut biopsy	Time on ART at 2nd gut biopsy, months
Longitudinal (participants who had biopsies at two time points)								
GUT 1	55	705	5.53	21	18	839	<20	32
GUT 2	35	278	7.13	28	21	707	<20	34
GUT 3	56	188	5.7	17	81	957	<20	94
GUT 4	34	752	5.18	54	23	1208	<20	35
GUT 5	37	968	4.2	26	33	1396	<20	46
GUT 7	49	459	6.9	21	26	537	<20	39
GUT 9	38	412	5.92	34	15	648	<20	26
GUT 10	56	568	NA	20	3	703	<20	16
GUT 11	27	470	5.88	0	34	776	<20	46
GUT 12	23	443	3.23	28	14	476	<20	26
Participants who had one biopsy only								
GUT 6	26	300	4.62	35	34	588	<20	-
GUT 8	41	860	2.67	23	64	634	<20	-
GUT 13	44	515	4.39	10	48	382	<20	-
GUT 14	30	423	4.85	13	15	NA	<20	-
GUT 17	34	449	6.3	18	17	760	<20	-
GUT 18	36	789	5.59	46	33	687	<20	-
GUT 19	33	957	NA	27	24	1195	<20	-
GUT 20	24	450	6.7	33	96	892	<20	-
GUT 21	27	608	5.84	7	37	927	<20	-
GUT 24	24	543	4.43	7	16	957	<20	-
GUT 28	37	786	NA	0	22	1158	<20	-
Overall Median (IQR)	35 (27.38)	514 (443, 752)	5.56 (4.48, 5.91)	21 (13.28)	24 (17.24)	768 (645, 957)	<20	35 (28.44)

Abbreviations: CPM, copies per million; PHI, primary HIV infection; ART, antiretroviral therapy; VL, viral load; NA, not available. All participants were male.

Lasso regression models of gut total HIV DNA and plasma inflammatory markers

Lasso regression models of gut total HIV DNA and plasma inflammatory markers				
Model	1	2	3	4
Outcome Variable	Terminal Ileum HIV DNA (CPM gut cells)	Terminal Ileum HIV DNA (CPM CD4 cells)	Rectum HIV DNA (CPM gut cells)	Rectum HIV DNA (CPM CD4 cells)
R-squared	0.54	0.53	0.53	0.59
	Unstandardised β Coefficients*			
Variables	0.2706	–	0.5213	0.3941
sCD14	0.0079	0.0178	–	–
IL-4	0.0019	–	–	0.0032
IL-6	0.0017	–	0.0028	0.0021
MIP-1β	0.0004	0.0004	0.0004	0.0004
CD40	−0.0005	–	–	–
MCP-1	−0.0582	–	−0.6244	−0.6698
RANTES	−0.9817	−1.588	–	–
MAdCAM-1	–	–	–	–
sCD163	–	–	–	−0.005
MIP-1α	–	–	–	–
L-Selectin	–	–	–	–
IP-10	–	–	−0.0032	−0.0034
IL17A	–	–	−0.0004	–
IL12 p70	–	–	–	0.0911
IL-5	–	–	–	–
IL-15	–	–	–	–
IL-10	–	–	–	0.0026
IFN-γ	–	–	–	3.32E-06
CD40 Ligand				

*Only variables with β coefficients>0 were included in the final models are shown The prefix "s" indicates soluble. Abbreviations; CPM, copies per million

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Figure 2. The scatter plots shows the correlation between HIV DNA in the terminal ileum, expressed as CPM gut cells, and plasma (a) sCD40, (b) sCD14, (c) RANTES, (d) IL-4 , (e) IL-6 and (f) MAdCAM-1. The correlation between HIV DNA in rectum and (g) sCD40, (h) sCD14 & (i) RANTES is also shown. P values were calculated using a non-parametric test and Spearman's coefficient, r is shown. The prefix s- denotes soluble. Abbreviations; CPM, copies per million; Log, Log_{10}

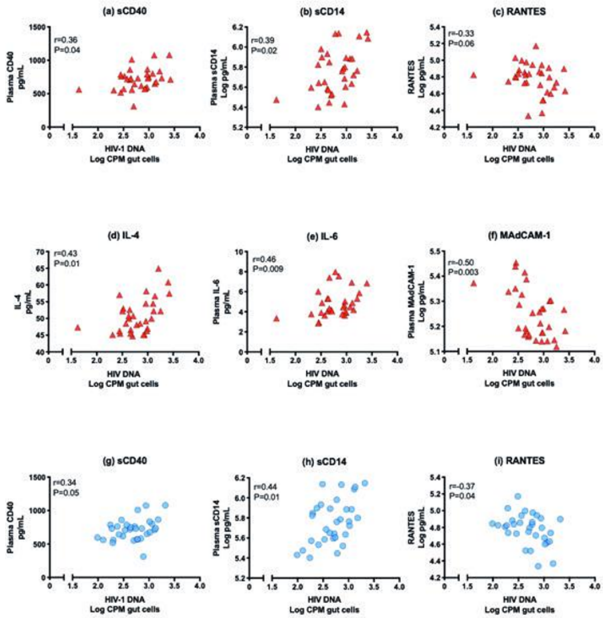


Figure 2

PS14/2

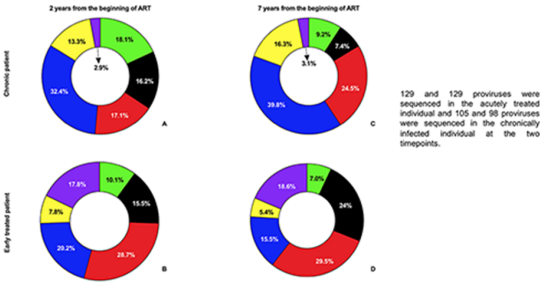
Effects of long-term ART on integrated and intact HIV-DNA in acutely treated vs chronically infected patients: is there a real advantage of treating early?

M Ceccarelli[1,2], E Venanzi Rullo[1,2], MR Pinzone[2], L Cannon[2], U O'Doherty[2] and G Nunnari[1]

[1]Università degli Studi di Messina, Department of Clinical and Experimental Medicine, Messina, Italy [2]University of Pennsylvania, Department of Pathology and Laboratory Medicine, Philadelphia, USA

Purpose: Integrated HIV-DNA declines significantly (~5-fold) in the first year of antiretroviral therapy (ART) if individuals are treated early (< 6 months from the infection) but does not decline perceptibly if the individuals are treated with ART during chronic infection (Pinzone et al, 2016; Koelsch et al, 2011, 2008; Murray et al, 2012). Herein, we investigated if early treatment results in sustained accelerated decay of intact proviral DNA after many years of ART.
Method: We measured integrated HIV-DNA in samples that were collected after 2 and 7 years of ART in an HIV infected individual treated during acute and chronic infection. From the same samples, we amplified near full length HIV-DNA at limiting dilution and performed Illumina sequencing. We then bioinformatically categorized the proviruses as intact, deleted and hypermutated (Pinzone et al, 2019).
Results: In contrast to the rapid decline detected in the first year of ART (Pinzone et al, 2016), the integrated HIV-DNA did not decline between 2 and 7 years of ART in the acutely treated subject. However, sequence analysis revealed that the decline of the intact reservoir between years 2 and 7 was ~4-fold in the chronically treated individual and ~2-fold in the acutely infected individual, despite clonal expansion and the apparent stability of the HIV-DNA. Clonal expansion was more important in the acute patient than the chronic one, especially within deleted proviruses (Fig. 1).
Conclusion: Final outcome after 10 years of ART may be a more similar intact reservoir size whether an individual is treated acutely or after chronic infection. Nonetheless, our results also suggest that treating early is beneficial because the reservoir declines more rapidly and thus these individuals are exposed to less harmful inflammation (Fig. 2).

Composition of the viral reservoir in a chronically infected patient (A, C) vs an early treated one (B, D) at two timepoints (2 and 7 years of ART), including clonal expansion.



Composition of the viral reservoir in a chronically infected patient (E, G) vs an early treated one (F, H) at two timepoints (2 and 7 years of ART), not including clonal expansion.

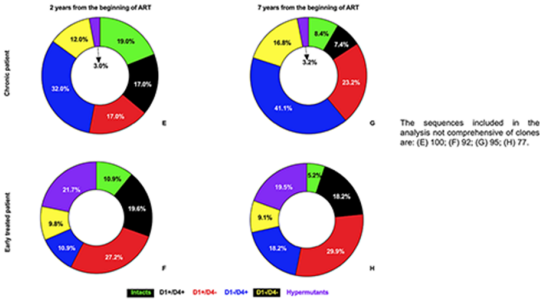


Figure 1

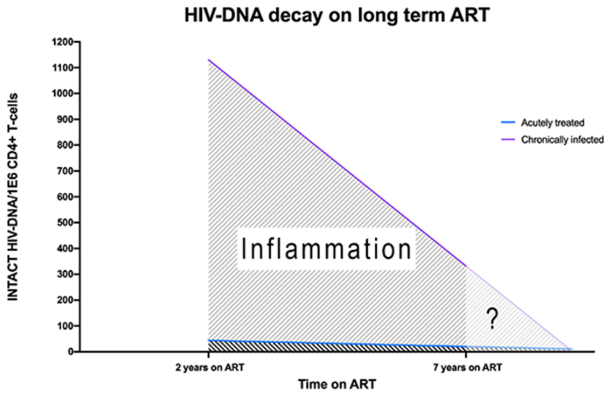


Figure 2

PS14/3

Increased frequency of cytotoxic CXCR5 + effector memory CD8 + T cells during natural control of HIV-1 infection

P Adams[1,2], G Iserentant[1], J-Y Servais[1], P Pannus[2], S Rutsaert[3], M Van Frankehuijsen[2], S De Wit[4], SD Allard[5], P Messiaen[6,7], M Moutschen[8], JL Aerts[9], L Vandekerckhove[3], G Vanham[2] and C Devaux[1]

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Purpose: Potent HIV-specific immune responses and a small latent viral reservoir are likely required to control viral replication during HIV-1 infection. Here we investigated the antiviral CD8 + T cell response of elite and viremic

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controllers (EC and VC) and antiretroviral therapy-(ART) suppressed patients at baseline and after peptide stimulation.
Method: Peripheral blood mononuclear cells of 58 patients were analyzed by 18 color flow cytometry and IFN-γ ELIspot at baseline and after 7 days of in vitro HIV peptide stimulation (PTE GAG pool, NIH). Plasmas were analyzed for IFN-γ, CXCL-10, IL1-β, IL6, TNF-a, IL-18 concentrations. Cytometry data was clustered using viSNE and analyzed by Boolean gating strategy to assess multifunctional characteristics. Statistical comparison was executed with QluCore and Prism nonparametric statistics (Kruskal-Wallis test correcting for multiple comparison).
Results: IL-18 in plasma and CD38 expression on CD4 + T cells were significantly lower in EC and ART patients with low reservoir than in VC ($p<0.05$). We observed a significant increase in IFN-γ production at baseline and after 7 days of peptide stimulation ($p<0.0005$) while CD107a and Ki67 expression were also significantly increased for ECs compared to ART patients ($p<0.001$).
Detailed phenotyping revealed that CD8 + effector memory T cells which are IFN-γ^+, Ki67$^+$, CD107a^{bright}, Perforin^{bright} and GrzB$^+$ significantly increased in EC ($p<0.005$) as compared to VC and ART patients. Similarly we observed central memory CD8 + T cells subsets with increased cytotoxic and polyfunctional features in EC ($p<0.005$). Interestingly, CD8 + T cells subsets expressing CXCR5, a homing receptor for lymph node follicles, and cytotoxic markers were significantly increased in EC as well ($p<0.005$).
Conclusion: Distinct functional subsets coexist during natural control of HIV-1 infection. Access to the B cell zone of lymph node follicles by cytotoxic CD8 + T cells might explain long-term control of the HIV reservoir.

PS14/4

HIV-1 reservoir formation, stability and dynamics during cART

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Purpose: While the continuing global HIV-related health crisis requires new approaches for sustainable therapy and towards a cure, strategies of reversing viral latency remained disappointing.
Our research strategy instead follows the changing viral properties of HIV-1 over the course of infection during suppressive therapy. We recently demonstrated that envelope properties of HIV strongly correlate with immune-recovery and disease outcome. In particular, the CXCR4-tropism of virus but also in silently infected cells, correlating with poorer outcomes in therapy-naïve individuals, appears to trigger superior HIV control during treatment. We thus aim at characterizing HIV inside the key T-cell populations during periods of suppressive therapy to identify cell populations driving such selective virus elimination and understand the preservation/re-establishment of crucial immune compartments.
Method: To study the properties of peripheral HIV-infected cells, we analyze T cell memory, the lymphoid homing potential and HIV protein expression by multi-parameter FACS, utilizing t-distributed stochastic neighborhood embedding (tsne) to identify specific target cell clusters.
Results: Although only venous blood is examined here, nave cell populations can be clearly separated from differentiated memory cells, allowing studies of cellular homing properties. Env-pos. staining (Fig. 1) reveals a phenotype of stimulated CD4 + T-cells with lymph node homing properties (CD3 + CD4 + CD28 + CCR7 +). Env-expression with co-expression of HIV-Gag discretely localizes in the tsne map (Fig. 2), hinting particle production.
Conclusion: By applying a new multi-parameter FACS staining protocol, we can now precisely map infectious cells inside bulk PBMCs of HIV positive individuals down to single cell resolution. This will guide to cell subsets with elevated viral activity, allowing to address the dormant HIV pool by reactivation and expansion of viable cells in the peripheral blood of HIV+ patients. Linking viral properties to cell homing properties will help to explain tropism-dependent pressure on the virus and clearance of these cells by cART and the recovering immune system.

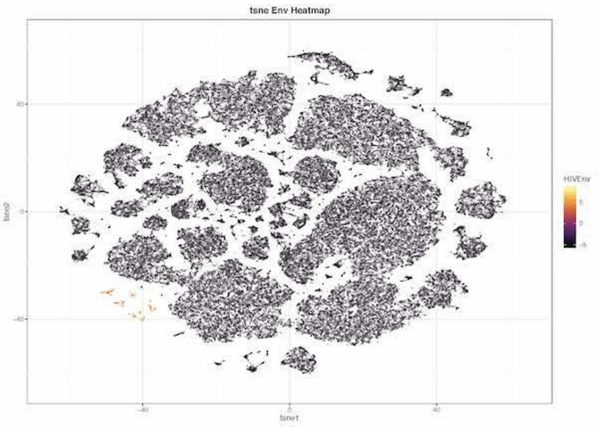


Fig 2. HIV Gag/Env co-expressing cell cluster]

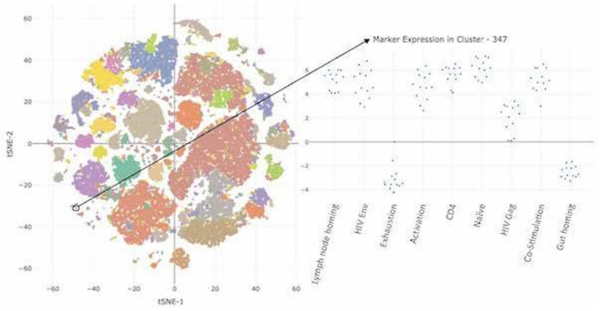


Fig 1. HIV Envelope Heatmap of tsne plot

Best poster discussion I – Antiretroviral (ARV)

BPD1/1

Causes of treatment failure in independent and industry-funded clinical trials of dolutegravir for HIV, and outcomes of unsuppressed patients continued on treatment in the ADVANCE study

T Pepperrell[1], S Sokhela[2], M Moorhouse[2], F Venter[2], A Qavi[1], B Simmons[1], V Pilkington[1], K McCann[1] and A Hill[3]
[1]Imperial College London, London, UK [2]University of the Witwatersrand, Johannesburg, South Africa [3]University of Liverpool, Liverpool, UK

Purpose: Over 20 million people living with HIV could be switched from efavirenz (EFV) to the integrase-inhibitor dolutegravir (DTG) in the coming years. ADVANCE is a randomised clinical trial (RCT) comparing tenofovir alafenamide(TAF)/emtricitabine(FTC) + DTG, tenofovir disoproxil fumarate (TDF)/FTC+DTG and TDF/FTC/EFV. This project investigated reasons for treatment failure in ADVANCE and other RCTs.

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Method: In ADVANCE, treatment failure was HIV RNA≥50 copies/mL at week-48, discontinuation for adverse events (AEs) or discontinuation for other reasons. Multiple logistic regression was used to determine clinical and sociodemographic predictors of treatment success. Each participant with HIV RNA≥50 copies/mL was followed to determine sustainment of failure.
A systematic review identified sixteen other RCTs (n=10738) for EFV and eight for DTG (n=5954).
Results: In ADVANCE, week-48 HIV RNA suppression rates were 84% for TAF/FTC+DTG, 85% for TDF/FTC+DTG and 79% for TDF/FTC/EFV. Efficacy of DTG in ADVANCE (84.3%; CI 81.7–87.0%) was lower than industry-funded RCTs (89.8%; CI 87.2–92.5%) (p<0.01).
Trials in low and middle-income countries show less AE discontinuation than trials in high-income countries for DTG (0.5% vs 1.9% [p<0.01]) and EFV (4.2% vs 10.5% [p<0.01]).
In multivariate analysis of ADVANCE, employment (OR 2.11, CI 1.50–2.96, p<0.001), older age (OR 1.04, CI 1.02–1.07, p<0.01) and DTG use (OR 1.53, CI 1.09–2.15, p<0.05) were the most important predictors of suppression. Participants on both drugs re-suppressed HIV RNA after an initial high week-48 reading (36/54), with retesting and adherence counselling (Table 1). Significantly more participants were able to re-suppress at follow-up on DTG than EFV (p<0.05)(Table 1).

	TAF/FTC+DTG (n=351)	TDF/FTC+DTG (n=351)	TDF/FTC/EFV (n=351)
HIV RNA≥50cml first week-48 reading	18 (5.1)	19 (5.4)	16 (4.6)
Follow-up results			
HIV RNA <50cml at follow-up	15 (4.3)	14 (4.0)	7 (2.0)
On sample retest	*1*	*0*	*1*
Within week-48 window	*4*	*1*	*2*
Long-term follow-up (12-weekly)	*10*	*13*	*4*
Treatment failure	2 (0.6)	3 (0.9)	7 (2.0)
HIV RNA ≥50cml at last visit	*2*	*3*	*7*
Of which treatment-emergent drug resistant	*0*	*0*	*3*
Lost-to-follow-up/missing data	1 (0.3)	2 (0.6)	2 (0.6)

Table 1. Follow-up outcomes of patients with HIV RNA≥50 copies/mL at week-48.

Conclusion: In ADVANCE, treatment failure was predicted by sociodemographic more than clinical factors. Employment and older age improved chances of suppression. Most people with HIV RNA≥50 copies/mL at week-48 re-suppressed after retesting and adherence counselling. This research promotes social protection, monitoring and adherence counselling during HIV treatment, especially for younger people.

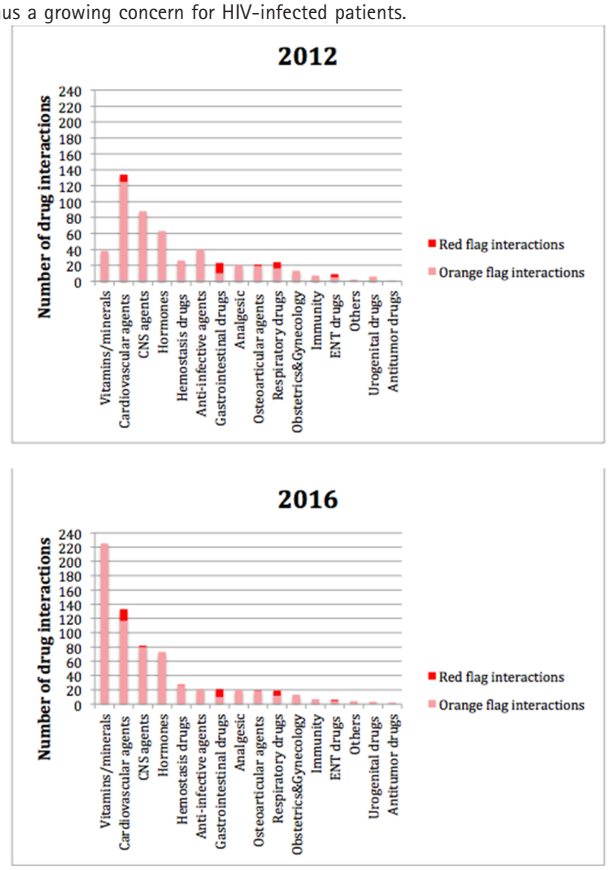
BPD1/2

Evolution of drug interactions with antiretroviral medications in HIV-infected patients

M El Moussaoui[1], I Lambert[1], N Maes[2], A-S Sauvage[1], F Frippiat[1], C Meuris[1], F Uurlings[1], M Lecomte[1], L Philippe[1], K Fombellida[1], D Vaira[3], C Vercheval[4], M Moutschen[1,3] and G Darcis[1]

[1]University Hospital of Liège, Infectious Diseases Department, Liège, Belgium [2]University Hospital of Liège, Departments of Biostatistics and Medico-Economic Information, Liège, Belgium [3]Liège University Hospital, AIDS Reference Laboratory, Liège, Belgium [4]Liège University Hospital, Department of Clinical Pharmacy, Liège, Belgium

Purpose: To investigate the extent of polypharmacy and the risk of drug interactions with antiretroviral therapy (ARV) in 2016 and to compare their evolution between 2012 and 2016.
Method: This study was retrospectively conduced with HIV-infected adults attending in Liège University Hospital (Belgium) during 2012 and 2016. The University of Liverpool HIV drug interactions database was used to determine drug interactions and classify them in red flag (contraindicated) and orange flag (potential dose adjustment and/or close monitoring required) interactions.
Results: This analysis included 1038 patients in 2016. 78% had≥1 comedication and 20.13% had polypharmacy (defined as the regular use of≥5 medications). 4.3% patients had red flag interactions and 50.7% had orange flag interactions. The non-ARV therapeutic classes involved in red flag interactions were mostly cardiovascular (41.2%) and respiratory drugs (28.2%). In contrast, vitamins and minerals represented 30.3% of the orange flag interactions. Several factors significantly contributed to both red and orange flags interactions (p<0.0001): number of non-ARV comedications and PI-based regimen ARVs. Conversely, treatment by non-nucleoside reverse transcriptase inhibitors (NNRTI) (odds ratio [OR] 1.8 95% confidence interval [CI] 1.1–3.0) and integrase inhibitors (INI) (OR 4.7 95% CI 2.9–7.6) were associated with orange flag interactions. In comparison with 2012 (914 patients), the proportion of patients with red flag interactions remained stable but patients with orange flag interactions significantly increased (42% to 57.1%. p<0.0001) due to, among others, the increased use of vitamins (5.2% to 30.9%. p<0.0001).
Conclusion: This study highlights the persistence of an alarming number of contraindicated drug interactions in 2016. We also observed an increasing number of orange flag interactions between 2012 and 2016, although some are likely of limited clinical significance. Antiretroviral drug interactions are thus a growing concern for HIV-infected patients.



Evolution of the therapeutic classes involved in drug interactions from 2012 to 2016.

BPD1/3

Drug interaction profiles for first line antiretroviral therapy and selected fixed-dose antiretroviral combinations over 20 years of the Liverpool Drug Interaction website

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Purpose: The Liverpool Drug Interactions website was launched in 1999 when the issue of drug-drug interactions was first appearing in clinical practice. With the move towards simplification of treatment regimens, a retrospective analysis was performed using the Liverpool website to determine the interaction profiles of
icurrently recommended first-line regimens,
iiregimens recommended around the time of the website launch, and
iiithe recently approved fixed dose combinations (FDCs), Delstrigo® and Dovato®.
Method: Current regimens were identified from the USA (2018), European (2018) and UK (2016) treatment guidelines; historic regimens were available

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for the USA (2000) and UK (2000). Interaction profiles for complete antiretroviral regimens were calculated using the frequency of each interaction type (red, amber, yellow, green). Interactions were grouped according to those requiring an intervention (contraindicated/do not coadminister, dose modification, monitoring; red and amber) and those not requiring such *a priori* actions (green and yellow). The interaction potential with comedications used to treat three comorbidity clusters (mental health, cardiovascular and metabolic; De Francesco *et al*, 2018) were determined for the current first line regimens and the new FDCs.
Results: A total of 16 regimens were identified in at least one of the current guidelines and 28 regimens in the historic guidelines. The percentage of interventional interactions when assessed against the comedication list (n=689) are shown for the guidelines (Table 1) and the comorbidity clusters (Table 2). Both recently approved FDCs were unboosted regimens and had interventional interaction percentages within the ranges observed for unboosted regimens in the current guidelines and in each of the comorbidity clusters.

Table 1. Percentage of interventional interactions in current and historical treatment guidelines.

	% Interventional Interactions in Guidelines	
	Current	Historic
All regimens (range)	8–54%	37–57%
PI and/or boosted regimens (mean)	45%	52%
Unboosted regimens (mean)	12%	44%

Table 2. Percentage of interventional interactions in comorbidity clusters for currently recommended first-line regimens.]

	% Interventional Interactions in Comorbidity Clusters		
	Mental Health	Cardiovascular	Metabolic
All regimens (range)	0–61%	1–55%	0–53%
Boosted regimens (mean)	52%	44%	41%
Unboosted regimens (mean)	1%	5%	6%

Conclusion: Although the interaction potential of first-line regimens has declined over the last 20 years, an awareness of possible drug-drug interactions, particularly when treating certain comorbidity clusters, remains critical for appropriate patient management.

BPD1/4

Retrospective analysis of co-medication patterns among patients treated for HIV, and potential interactions with antiviral treatment, in Norway during 2012–2018 using the Norwegian population-based prescription database

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Background: The potential for drug-drug interactions (DDIs) is an important consideration for HIV-infected individuals with concomitant medications. The aim of this study was to describe the co-administration of medication during HIV treatment, and to assess potential DDIs (pDDIs) with currently approved antiretroviral treatments.
Method: This is a retrospective cohort study using population-based data from patients prescribed antiretrovirals in the period 2012–2018. Data was sourced from the Norwegian Prescription Database. 60% of the most commonly prescribed comedications, adjusted for EACS guidelines, were cross-checked against the antiretroviral medicines in the HIV drug interaction database of the University of Liverpool. pDDIs are described as either 1) potential weak interaction, 2) potential interaction and 3) do not co-administer.
Results: 8197 patients dispensed at least one HIV treatment course were included. Median age was 51 years (< 18–81) and 65.4% were male. 56.1% of HIV-treated patients received comedications, with minimum 30 days of overlapping treatments. The most commonly prescribed comedication ATC classes were anti-inflammatory and antirheumatic products in 6.4% (292 patients), psycholeptics in 4.9% (224 patients), and drugs for acid-related disorders in 2.9% (132 patients). Among patients with comedication, 8.2% (378 patients), 25.1% (1154 patients) and 9.2% (423 patients) were prescribed at least one comedication with a pDDI in the grade 1, 2 and 3 categories, respectively. Most grade 3 pDDIs were seen in comedications with methadone, diazepam or escitalopram. When filtering the 60% most prescribed comedications and cross referencing with the EACS recommended regimens with an integrase-inhibitor as the third agent, 0.0, 0.1, 0.7 and 1.7% grade 3pDDI were observed for raltegravir, bictegravir, dolutegravir, and elvitegravir containing regimens, respectively.
Conclusion: Data from a large population-based prescription data base showed that co-administration of other drugs are frequent during antiretroviral treatment, and the potential for DDIs needs to be considered to optimize HIV care.

BPD1/5

TDF/FTC is a cost-saving maintenance option in HIV-infected people with low reservoir

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Purpose: We investigated whether tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) was able to maintain virological suppression in HIV-1-infected individuals with a low HIV reservoir on a successful TDF/FTC-based triple therapy.
Method: Academic, multicenter, open-label, non-inferiority randomized trial (margin 12%, 92% of success in both arms, power 90%; alpha 2.5%) comparing TDF/FTC once daily (experimental arm) versus triple regimen continuation (TDF/FTC with a third agent, control arm) in virologically suppressed adults with HIV DNA<2.7 log10 copies/10^6 PBMCs at screening (details at https://clinicaltrials.gov/ct2/show/NCT02302547). Primary endpoint was the percentage of patients with plasma viral load (pVL)<50 copies/mL in intention-to-treat (ITT, Non Completer = Failure, FDA Snapshot approach) at week 48 (W48). A per protocol (PP) analysis excluded patients with non-inclusion criteria and non-completers.
Results: 325 patients screened, 223 randomized to TDF/FTC (n=113) or control arm (n=110): 165 males (74%); 32 blacks (14%); age: 44.7 years (SD, 11.4); CD4 cells 739/µl [IQR, 578–912]. At W48, TDF/FTC and triple regimen continuation maintained pVL<50 cp/mL in 100/113 (88.5%) and 100/110 (90.5%) of the patients, respectively. The primary outcome difference was 2.4% with a 95% confidence interval (CI) of [−5.9 to 10.7] in ITT and 3.4% with a CI of [−4.2 to 11.0] in PP. Six virological failures occurred in the TDF/FTC arm (with mutation M184V in patient and K65R in another) versus two in

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the control arm (p=0.16 by the log-rank test). All virological failures were rapidly re-suppressed after treatment intensification. Four patients in each arm switched their antiretroviral therapy while the pVL was<50 copies/mL. The average expected antiretroviral therapy cost per patient for 48 weeks was 7,407€ (SD, 1,373) for triple regimen continuation compared to 3,820€ for branded Truvada® (French cost).
Conclusion: De-escalation to TDF/FTC is an acceptable and cost-saving strategy among virologically suppressed HIV+ patients with a low reservoir.

Best Poster discussion II – ageing: long-term complications

BPD2/1

DXA Scan vs. FRAX score for the evaluation of fracture risk in a cohort of elderly people living with HIV

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Purpose: Osteoporosis and fractures increase morbidity and mortality in people living with HIV (PLWH). EACS guidelines recommend routine assessment of fracture risk using FRAX, and dual-energy X-ray absorptiometry (DXA) scan only for those with FRAX over 10%, even though it can underestimate fracture risk in PLWH. Objective of our study was to evaluate level of concordance of DXA results (T score of the spine and of the femur) and FRAX in a population of PLWH over 50 years of age.
Methods: DXA scan results of PLWH who attended specialist Over 50's clinic in Chelsea and Westminster Hospital between January 2009 and December 2018 were collected as well as demographic and clinical characteristics. FRAX was calculated using Sheffield algorithm. Mean and standard deviation were calculated. For univariate analysis Wilcoxon test was used.
Results: 744 patients were included, 92.9% were male, mean age of 56 ± 5 years. Prevalence of osteoporosis (in the spine and/or in the femur) was 12.2% and osteopenia 63.7%. A statistically significant association was found between age and time of exposure to boosted protease inhibitors and osteoporosis in the femur (p<0.05). Two out of 744 cases FRAX major was>10% indicating need to perform DXA scan according EACS guidelines (Table 1), while 90/91 (98.9%) patients with osteoporosis had a normal FRAX score. Even when FRAX score was calculated considering HIV as a risk factor of secondary osteoporosis and using BMD results, only 1.5% (11/744) patients had FRAX score>10%.
Discussion: Our results show that the FRAX score may not be a reliable screening tool for fracture risk in PLWH. Most patients with osteoporosis in our cohort had a normal FRAX score. These findings were maintained when BMD results and HIV infection were included in the FRAX calculation tool. Bone fracture screening in PLWH over 50 years of age requires optimisation.

BPD2/2

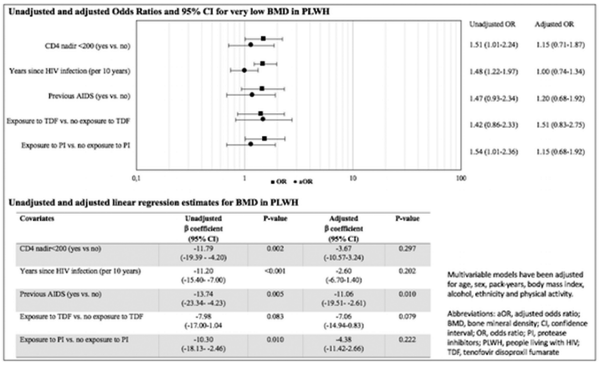
Prevalence of and risk factors for low bone mineral density assessed by central quantitative computed tomography in people living with HIV and uninfected controls

MT Thomsen[1], YL Wiegandt[2], M Gelpi[1], A Dehlbæk Knudsen[1,2], A Fuchs[2], P Ejlstrup Sigvardsen[2], J Tobias Kühl[2], B Nordestgaard[3,4], L Køber[2], J Lundgren[5], A-B Eg Hansen[6], K Fuglsang Kofoed[2], J-E Beck Jensen[7,8] and S Dam Nielsen[1]
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Purpose: Low bone mineral density (BMD) has previously been described in people living with HIV (PLWH). We determined the prevalence of low BMD measured by central Quantitative Computed Tomography (cQCT), a method that allows three-dimensional volumetric density measures of trabecular BMD, in well-treated PLWH and uninfected controls and assessed if HIV status was an independent risk factor for low BMD.
Method: Cross-sectional study including 718 PLWH from the Copenhagen Co-Morbidity in HIV infection (COCOMO) study and 718 uninfected controls matched on age- and sex from the Copenhagen General Population Study (CGPS). Trabecular BMD was determined by cQCT.
Results: Median age was 52.2 (IQR: 47.1–60.9) and 54.1 (IQR: 48.2–61.0) years in PLWH and uninfected controls, respectively, and 86% of the participants were men. Median time since HIV diagnosis was 15.8 (IQR: 8.4–23.1) years, and 96.1% of PLWH had undetectable viral replication. Median BMD was 144.2 mg/cm^3 in PLWH vs. 146.6 mg/cm^3 in controls (p=0.580). HIV was not associated with BMD in univariable- or multivariable linear analyses. However, higher prevalence of very low BMD (T-score≤-2.5) was found in PLWH (17.2% vs. 11.0% in controls, p=0.003). In unadjusted analysis HIV was associated with very low BMD (OR 1.68 [95% CI: 1.24–2.27], p=0.001), but this association was not significant after adjusting for age, sex, pack-years, alcohol, body mass index (BMI), physical activity and ethnicity. Very low BMD was associated with age, BMI and pack-years. Previous AIDS-defining disease was associated with lower BMD.
Conclusion: Using cQCT, we found a higher prevalence of very low BMD in PLWH than in controls. However, HIV status was not independently associated with BMD indicating that traditional risk factors contribute to the difference in prevalence of very low BMD. Focus on lifestyle, especially in PLWH with previous AIDS-defining disease, may prevent very low BMD in PLWH.

BMD and T-scores in people living with HIV and controls

	People living with HIV	Uninfected controls	P-value
BMD (mg/cm^3), median (IQR)	144.2 (110.7–183.8)	146.6 (119.2–177.4)	0.580
T-score, median (IQR)	−0.9 (−2.1 to 0.4)	−0.9 (−1.8 to 0.2)	0.546
T-score, categories, % (n)			
Normal, T-score>−1	50.6 (363)	52.8 (379)	0.003
Low, T-score<−1 and>−2.5	32.3 (231)	36.2 (260)	
Very low, T-score<−2.5	17.2 (123)	11.0 (79)	



Unadjusted and adjusted logistic and linear regression for BMD in relation to HIV-specific variables

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BPD2/3

Restless legs syndrome and health-related quality of life in HIV: results from the POPPY sleep substudy

K Kunisaki[1,2], D DeFrancesco[3], C Sabin[3], A Winston[4], P Mallon[5], J Vera[6], F Post[7], I Williams[3,8], E Bagkeris[3], N Doyle[4], W Khalil[1,2], S Redline[9,10,11], Pharmacokinetics and Clinical Observations in People Over Fifty (POPPY) Study

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Purpose: Restless legs syndrome (RLS) is a sleep disorder characterized by leg dysesthesias, typically relieved by movement, with sequelae that may include daytime sleepiness, mood problems, functional impairments, and decreased work productivity. RLS often responds to dopaminergic drugs, suggesting a central nervous system (CNS) etiology. Given the high burden of sleep symptoms and CNS disorders in persons with HIV (PWH), we evaluated RLS prevalence and associations with health-related quality of life (QoL) in PWH and lifestyle-similar HIV-negative controls.
Method: A subset of POPPY participants (PWH≥50 y/o, PWH<50 y/o, and HIV-negative controls≥50 y/o) completed standardized RLS and QoL questionnaires. RLS was defined using international guideline criteria. Sleep-related QoL was assessed with PROMIS questionnaires. Physical and mental health QoL was evaluated with SF-36 scores. Logistic regression was used to compare RLS prevalence in PWH and controls. QoL in those with and without RLS were compared using Wilcoxon tests.
Results: Of 435 participants (220 older PWH (median age 60 y), 99 younger PWH (45 y) and 116 older HIV-negative (60 y)), RLS criteria were met by 77 (35%), 33 (33%) and 25 (22%) of the groups, respectively. In analyses adjusted for age, sex, and race, PWH were more than twice as likely to meet RLS criteria than controls [aOR 2.4 (1.4 to 4.1), p=0.002].
Of 110 PWH with RLS (55% of whom reported symptoms at least 2–3 times/week), only 7 (6%) reported a diagnosis of RLS and 3 (3%) reported a history of RLS medication treatment. PWH with RLS reported worse sleep-related QoL and poorer physical and mental health QoL compared to PWH without RLS (Table, all p's < 0.001).
Conclusion: Among PWH, RLS is common, associated with health-related QoL impairments, and rarely diagnosed or treated. Further research is needed to understand risk factors for RLS and the effects of RLS treatment.

Table: Differences in patient-reported questionnaire scores among those with and without restless legs syndrome (RLS) as assessed by International Restless Legs Study Group criteria#. For PROMIS questionnaires, higher scores indicate more disturbance or impairment. For SF-36 measures, lower scores indicate worse quality of life.

	PWH			HIV-negative			Interaction p-value*
Questionnaire	RLS (n=110)	No RLS (n=209)	p-value	RLS (n=25)	No RLS (n=91)	p-value	
PROMIS Sleep Related Impairment	55 (50-60)	49 (44-55)	<0.001	46 (44-50)	46 (39-50)	0.27	0.06
PROMIS Sleep Disturbance	54 (49-61)	49 (44-55)	<0.001	50 (46-55)	47 (43-51)	0.06	0.26
SF-36 physical health	45 (33-54)	53 (46-57)	<0.001	55 (51-57)	56 (53-58)	0.57	0.008
SF-36 mental health	44 (35-54)	54 (44-58)	<0.001	53 (47-59)	55 (50-58)	0.54	0.03

*: Calculated using median regression
#: Answered yes to all of the following questions: 1) 'At any time in the day or night, do you have unpleasant sensations in your legs (such as unpleasant crawling or creeping sensations in the feet, calves or thighs) combined with an urge or need to move your legs?', 2) 'Do they occur mainly or only at rest?', 3) 'Do they improve with movement?', and 4) 'Are they worse in the evening or night than in the morning?'

BPD2/4

Depression and kynurenine/tryptophan ratio in people living with HIV

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Purpose: Tryptophan is a precursor for serotonin and a higher kynurenine/tryptophan ratio (KTR) has been described in People living with HIV (PLWH) resulting in lower serotonin that may predispose to depression. We aimed to determine the prevalence of depression among PLWH and to identify if KTR as well as traditional and HIV-specific risk factors were associated with depression. We hypothesized that high KTR would be associated with higher risk of depression among PLWH.
Method: 828 PLWH were recruited from the Copenhagen Comorbidity in HIV infection (COCOMO) Study. Demographic information was obtained from questionnaires. Depression was defined using Major Depression Inventory (MDI) and/or current use of antidepressant medication. Plasma kynurenine and tryptophan were analyzed by liquid chromatography-tandem mass spectrometry.
Regression models were adjusted for age, sex, origin, marital status, educational level and alcohol use.
Results: Population characteristics are presented in table 1. Depression was present in 113 (14%) of the participants with a majority having moderate depression (50%). The median KTR was 3.2 versus 3.2 (p=0.999) in PLWH without and with depression, respectively. In adjusted analyses, KTR was not associated with presence or severity of depression. Being unmarried was associated with higher risk of depression and current treatment with Efavirenz was associated with lower risk. No other associations were found between depression and traditional and HIV-specific risk factors.
Conclusion: The prevalence of depression was relatively low in this cohort of predominantly well-treated PLWH compared to previous reports. Being unmarried was and current treatment with Efavirenz were independently associated with higher and lower risk of depression, respectively. KTR and other HIV-specific risk factors were not found to be associated with depression. Our hypothesis that increased KTR would be associated with increased risk of depression was not supported, albeit a low depression prevalence in this cohort may challenge the conduction of a biomarker study.

Table 1. Characteristics of PLWH

Sex (male), n (%)	709 (86%)
Age, yrs, median (IQR)	50.2 (43.3–58.3)
Origin, n (%)	European: 695 (85%) Other: 119 (51%)
Married, n (%)	399 (51%)
Heavy drinkers, units/week, >7 female, >14 male	195 (33%)
Time since HIV diagnosis (years), median (IQR)	13.7 (6.9 - 21.5)
HIV RNA<50 copies/mL	792 (95.6%)
Treatment with cART, n (yes) (%)	814 (98.7%)
Treatment with Efavirenz (yes)	242 (29%)
Prevalence of depression (%)	113 (13.7%)

Table 2. Traditional and HIV-specific risk factors associated with depression in PLWH

Covariates	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age (per decade)	0.99 (0.97–1.01)	0.162	0.99 (0.97–1.01)	0.357
Sex (male vs. female)	0.65 (0.38–1.12)	0.121	0.67 (0.37–1.30)	0.216
Marital status (Unmarried vs. married)	1.82 (1.15–2.88)	0.010	1.79 (1.12–2.90)	0.017
Heavy drinkers, units/week, >7 (female), >14 (male)	0.73 (0.42–1.28)	0.275	0.68 (0.37–1.20)	0.200
Smoking status (Current smoker vs ex-smoker/never smoker)	1.61 (1.03–2.51)	0.037	1.59 (0.96–2.59)	0.068
KTR (only adjusted for age and sex)	1.01 (0.987–1.039)	0.340	1.02 (0.994–1.049)	0.122
Time since HIV diagnosis	1.01 (0.99–1.04)	0.353	1.03 (0.99—1.07)	0.057
Efavirenz (yes vs. no)	0.14 (0.06–0.32)	<0.0001	0.17 (0.07–0.41)	<0.0001

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BPD2/5

Antiretroviral therapy and clearance of oncogenic HPVs in HIV positive MSM

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[1]University Hospital 'Virgen de las Nieves', Infectious Diseases, Granada, Spain [2]Hospital Marina Baixa, Benidorm/Alicante, Spain [3]Complejo Hospitalario de Jaen, Infectious Diseases, Jaen, Spain [4]University Hospital 'Virgen de las Nieves', Pathology Service, Granada, Spain

Purpose: Our main objective was to determine high-risk human papillomavirus (HR-HPV) clearance and acquisition rates and related factors and their relationship with the incidence of HSILs and ASCC in anal mucosa of HIV+ MSM.
Patients and methods: The study included consecutive HIV-infected MSM between May 2010 and December 2018. Data were gathered at baseline and annually on their sexual behavior, CD4 and CD8 levels, plasma HIV viral load, and results of anal cytology, HPV PCR, and high-resolution anoscopy.
Results: Out of the 405 patients studied, 34.9 % of patients cleared oncogenic genotypes (IQR: 37–69) within 49 months, and 42.9 % acquired new genotypes within 36 months (IQR: 12–60). In multivariate analysis, clearance was only significantly influenced by the duration of antiretroviral therapy (ART) (OR: 1.016, 95% CI 1.003–1.030). The incidence of HSILs was 30.86/1,000 patient-years and that of ASCC was 81.22/100,000 patient-years; these incidences were not influenced by the acquisition (acquired: 14.9% *vs.* non-acquired: 10.4%; p=0.238) or clearance (cleared 11.4% *vs.* non-cleared: 13.2%; p=0.662) rates of these viruses.
Conclusions: The duration of ART appears to positively affect oncogenic genotype clearance in the anal mucosa of HIV+ MSM, although this clearance does not affect the incidence of HSILs or ASCC.

Best poster discussion III – hot topics

BPD3/1

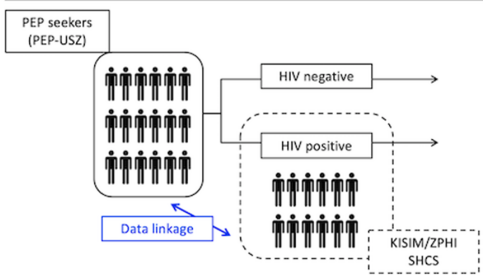
HIV infection in individuals seeking post-exposure prophylaxis (PEP): a retrospective data linkage study

F Hovaguimian[1,2], C Hauser[3], M Battegay[4], E Bernasconi[5], A Calmy[6], M Cavassini[7], P Vernazza[8], A Marzel[9], H Heinrich[10,11], M Egger[12], M Zwahlen[12], HF Günthard[1], SK Rampini[13], R Kouyos[1], JS Fehr[1,2] and the Swiss HIV Cohort Study

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Objectives: Evidence on the long term outcome of individuals taking post-exposure prophylaxis (PEP) is lacking. Therefore, we conducted a data linkage study to estimate the number of "late" HIV diagnoses (=minimum 6 months following PEP intake) in individuals who sought PEP at the University Hospital of Zurich (USZ) between 2007 and 2013.
Methods:
Design: Retrospective analysis, anonymous linkage between 4 databases ("PEP-USZ" database, USZ electronic patient record system (KISIM), Zurich Primary HIV Infection (ZPHI) cohort and Swiss HIV Cohort Study (SHCS) - figure 1). The PEP-USZ database contains data from 975 individuals; HIV diagnoses are obtained from KISIM/ZPHI/SHCS.
Primary outcome: Number of HIV diagnoses, defined as: (1) HIV infection diagnosed at the USZ (internal linkage: PEP-USZ/KISIM/ZPHI) and/or (2) enrolment in the SHCS (external linkage: PEP-USZ/SHCS).
Data linkage: external linkage using a privacy-preserving probabilistic linkage method.
Ethical approval: obtained.
Results: Internal linkage retrieved 17 potential matches. Seven were further discarded (3 duplicates, 3 HIV diagnoses at PEP consultation, 1 compatible with a PEP failure (=HIV diagnosis within 6 months of PEP intake)). Thus, late HIV diagnoses were found in 10/975 (1.03%). All were men-having-sex-with-men. Compared to seronegative PEP-seekers, those who seroconverted were more likely to take PEP repeatedly (40% *versus* 10%) and to have a strong indication for PEP (90% *versus* 54%) - table 1. There was a median of 3.8 years (IQR: 2.3 - 6.4) between PEP consultation and HIV diagnosis. Of 3 potential PEP-failures (case number 1,2 and 3 - figure 2), 2 had laboratory tests compatible with recent seroconversion (case 2 and 3). Case 1 refused PEP.
Conclusion: Although HIV diagnoses were scarce, PEP-seekers who seroconverted seem to share a specific risk profile. Nearly half of these HIV cases could have been prevented by pre-exposure prophylaxis. External linkage with the SHCS will provide further insights (expected September 2019).

Figure 1. Study plan



KISIM: USZ electronic patient record system; PEP: post-exposure prophylaxis; PEP-USZ: PEP-USZ database; SHCS: Swiss HIV Cohort Study; USZ: University Hospital of Zurich; ZPHI: Zurich Primary HIV Infection study.

Figure 2. PEP consultation(s), HIV screening and diagnosis over time in PEP seekers presenting with late HIV diagnosis (n=10)

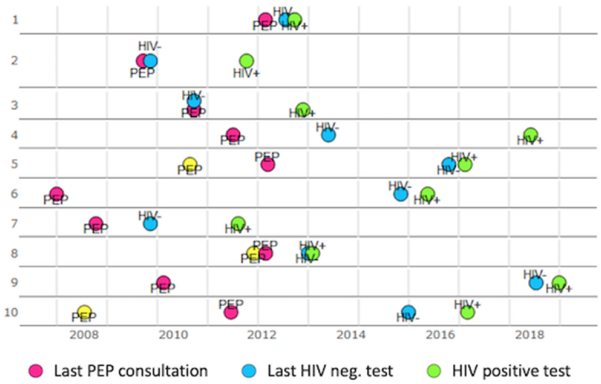


Table 1. Baseline characteristics, stratified by HIV diagnosis

	HIV negative (n=965)	HIV positive (n=10)	p-value
Age, median (IQR)	31 (26–38)	33 (23–40)	0.89
Sex, male, n (%)	791 (82%)	10 (100%)	0.22
Swiss nationality, n (%)	680 (70%)	7 (70%)	1.0
MSM, n (%)	342 (35%)	10 (100%)	<0.0001
Repeated PEP, n (%)*	93 (10%)	4 (40%)	0.012
PEP indicated, n (%)°	523 (54%)	9 (90%)	0.026

*Repeated PEP: number of individuals who received PEP prior to PEP consultation (medical history) + those who sought PEP at the USZ>1×
°PEP indicated: number of individuals for whom PEP was strongly indicated (risk assessment based on: exposure<72 h, partner with unknown HIV status AND high risk group (MSM, sex worker, IDU, endemic region), HIV+ partner with viral load>50 copies/mL)

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IDU: intravenous drug users; MSM: men having sex with men; PEP: post-exposure prophylaxis; USZ: University Hospital of Zurich.

BPD3/2

Harnessing big data on Indonesian MSM and transgender individuals using temanteman.org platforms to assess their vulnerabilities, HIV support seeking patterns and immediate HIV prevention needs

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Introduction: Indonesia is the world's largest Islamic-majority nation. Homophobia is contributing to the concentrated explosion of HIV epidemic among men who have sex with men (MSM), who for their HIV support needs resort to accessing top Google suggested websites such as TemanTeman.org, processing significant critical insights on key populations with potential for developing novel service-delivery models.
Methods: Between September 2013-June 2019, datasets spread over TemanTeman.org web-logs and databases were mined to address the gaps in our understanding on Indonesian key populations through assessing their vulnerabilities, online search patterns and immediate prevention needs.
Results: Over 3 million Indonesians engaged in TemanTeman.org platforms. 'How is HIV transmitted', 'HIV testing and treatment services', 'condoms and lubricants', 'HIV testing procedures (city-based)' were search queries originating primarily from Jakarta, Surabaya, Bandung, Medan, Makassar, Denpasar and Yogyakarta. Age demographics included 13- 17 years (1.3% - male 67%, female 33%), 18–24 years (35% - male 71%, female 29%), 25–34 years (45% - male 74%, female 26%) and>35 years (18.7% - male 60%, female 40%). TemanTeman.org videos featuring medical doctors from Indonesia's leading university hospitals garnered nearly 1.6 million views, watch-time 60,861 hours (equivalent to 6 years and 344 days), primarily via mobile phones (84% - Android 90%, IOS 7.3%), and computers (12% - Windows 95%, Macintosh 4.3%). Top video search trends included

1 HERPES - Skin/genital, causes, treatment, cure (63,903 + searches),
2 HIV/AIDS - early stage signs/symptoms/characteristics, vaccine, transmission, testing procedure and costs (59,850 + searches),
3 SYPHILIS - early symptoms, effective treatment (27,591 + searches),
4 HPV in men/women, symptoms and treatment (11,167 + searches),
5 GENITAL WARTS in male/female, treatment, surgical removal (11,090 + searches), and
6 GONORRHEA in men/women, treatment (10,848 + searches).

Conclusions: Our study shares evidence of high sexual-risk related web-searching behaviors among Indonesians. We propose intensive real-time interventions as a way to strengthen the cascade.

BPD3/3

Prescription of antimicrobials in primary health care as a marker to identify people living with undiagnosed HIV infection

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Purpose: Despite efforts in health care policies, approximately 50% of newly diagnosed HIV-infected individuals continue to present late for HIV care. Identifying factors associated with occult HIV infection is crucial in order to improve targeted HIV testing strategies and achieve earlier detection. We analysed antimicrobial prescriptions in the three years preceding the HIV diagnosis assessing whether there was a higher consumption in those diagnosed with HIV and whether the consumption was associated with increased risk of subsequent HIV diagnosis.
Method: We conducted a nested case-control study from national registers, identifying all individuals diagnosed with HIV in Denmark during 1998–2016 (N=2,784 cases) and 13 age-and gender-matched population controls per case (N=36,192 controls). Antimicrobial prescriptions were estimated as defined daily doses (DDD) per person-year (PYR). We used conditional logistic regression to compute odds ratios (OR) and 95% confidence intervals (CI).
Results: In the three years preceding the HIV diagnosis we observed a more frequent and higher consumption of some antimicrobials in cases compared to controls, with 72.4% vs. 46.3% respectively having had at least one prescription (p<0.001)(Table and Figs. 1–2). For all antimicrobial classes analysed, we found a statistically significant association between consumption and the risk of subsequent HIV diagnosis (p<0.001) (Fig. 3). The association was stronger with higher consumption, with some antimicrobials and with shorter time to HIV diagnosis. The correlation was more pronounced for males and among those presenting with late-stage HIV infection.
Conclusion: HIV-infected individuals have a significantly higher use of some antimicrobial drugs in the three years preceding HIV diagnosis than their age- and gender-matched controls. Prescription of antimicrobials in primary health care could be regarded as surrogate marker of occult HIV infection and an opportunity to consider proactive HIV testing. Further studies are needed to identify optimal prescription cut-offs, that could endorse its inclusion in public health policies.

Baseline characteristics

	HIV N=2784	Controls N=36192
Male sex, n (%)	2237 (80.4)	29081 (80.4)
Age at HIV diagnosis, median years (IQR)	39 (32–48)	39 (32–48)
CD4 + cell count at study median cells/μL (IQR)	330 (130–540)	–
VL at study inclusion, median log10 copies/mL (IQR)	4.8 (4.1–5.4)	–
Antimicrobial prescription in the study period (>=1 prescriptions)	2015 (72.4)	16750 (46.3)
Antibiotics, n (%)	1895 (68.1)	15973 (44.1)
Antiviral, n (%)	353 (12.7)	736 (2.0)
Antifungals, n (%)	382 (13.7)	1563 (4.3)

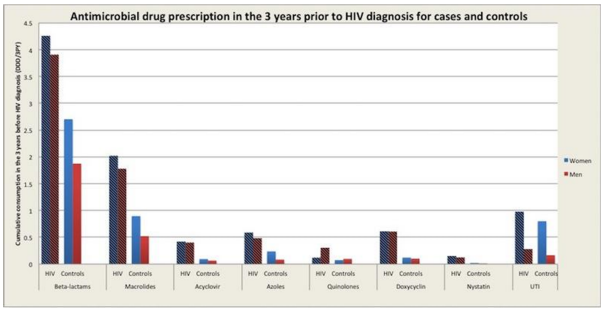


Figure 1. Antimicrobial drug prescription in the three years prior to HIV diagnosis

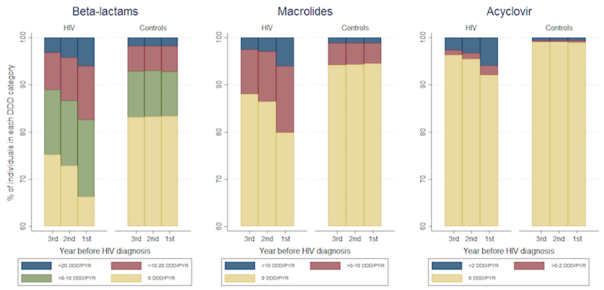


Figure 2a,b,c. Prescription of antimicrobials for cases and controls in the 3 years prior to HIV dx.

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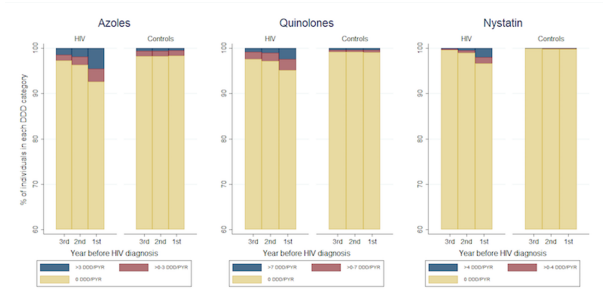


Figure 2b

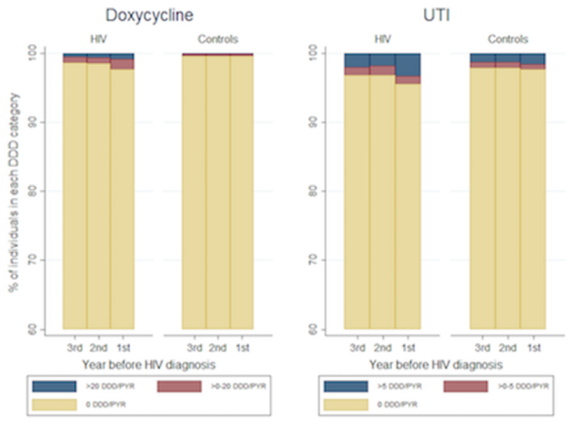


Figure 2c

DDD/3PYR	HIV (%)	Controls (%)	OR (95% CI)
Beta-lactams			
>0 vs 0	1533 (55·1)	13315 (36·8)	2·13 (1·97·2·30)
>10 vs ≤ 10	1032 (37·1)	7485 (20·7)	2·28 (2·11·2·48)
>20 vs ≤ 20	557 (20·0)	3104 (8·6)	2·70 (2·44·2·98)
>30 vs ≤ 30	333 (12·0)	1508 (4·2)	3·17 (2·79·3·60)
Macrolides			
>0 (vs 0)	932 (33·5)	5037 (13·9)	3·12 (2·87·3·40)
>10 (vs ≤10)	373 (13·4)	1494 (4·1)	3·62 (3·20·4·08)
> 20 (vs ≤20)	170 (6·1)	551 (1·5)	4·26 (3·56·5·08)
Acyclovir			
>0 (vs 0)	353 (12·7)	736 (2·0)	7·20 (6·29·8·25)
>2 (vs ≤2)	279 (10·0)	525 (1·4)	7·78 (6·67·9·08)
>4 (vs ≤ 4)	255 (9·2)	444 (1·2)	8·27 (7·03·9·72)
Azoles			
>0 (vs 0)	310 (11·1)	1448 (4·0)	3·25 (2·84·3·72)
>3 (vs ≤3)	190 (6·8)	574 (1·6)	4·65 (3·92·5·52)
>6 (vs ≤ 6)	160 (5·8)	440 (1·2)	5·01 (4·16·6·04)
Quinolones			
>0 (vs 0)	252 (9·1)	869 (2·4)	4·14 (3·52·4·81)
>7 (vs ≤7)	110 (4·0)	403 (1·1)	3·72 (3·00·4·63)
>14 (vs ≤14)	38 (1·4)	106 (0·3)	4·79 (3·29·6·97)
Nystatin			
>0 (vs 0)	122 (4·4)	164 (0·5)	10·55 (8·27·13·46)
>4 (vs ≤4)	67 (2·4)	72 (0·2)	12·53 (8·94·17·57)
>8 (vs ≤8)	33 (1·2)	25 (0·1)	17·16 (10·21·28·85)
Doxycycline			
>0 (vs 0)	132 (4·7)	386 (1·1)	4·61 (3·77·5·65)
>20 (vs ≤20)	56 (2·0)	95 (0·3)	7·87 (5·63·10·99)
>40 (vs ≤40)	28 (1·0)	45 (0·1)	8·09 (5·05·12·97)
UTI			
>0 (vs 0)	230 (8·3)	1834 (5·1)	1·80 (1·54·2·09)
> 5 (vs ≤5)	165 (5·9)	1190 (3·3)	1·95 (1·64·2·33)
>10 (vs ≤10)	94 (3·4)	635 (1·8)	2·02 (1·61·2·53)

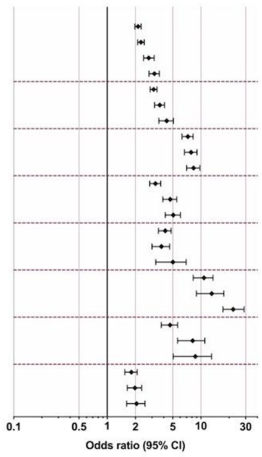


Figure 3. Association between different antimicrobial prescriptions and risk of later HIV infection

BPD3/4

Novel highly potent CD4bs bNAb with restricted pathway to HIV-1 escape

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Purpose: Broadly HIV-1 neutralizing antibodies (bNAbs) can suppress viremia in humans and represent a novel approach for effective immunotherapy. However, bNAb monotherapy selects for antibody-resistant viral variants. Thus, we focused on the identification of new antibody combinations and/or novel bNAbs that restrict pathways of HIV-1 escape.
Methods: We screened HIV-1 positive patients for their neutralizing capacities. Following, we performed single cell sorting and PCR of HIV-1 Env-reactive mature B cells of identified elite neutralizers. Found antibodies were tested for neutralization and binding capacities *in vitro*. Further, their antiviral activity was tested in an HIV-1 infected humanized mouse model.
Results: Here we report the isolation of antibody 1–18, a VH1–46-encoded CD4 binding site (CD4bs) bNAb identified in an individual ranking among the top 1% neutralizers of 2,274 HIV-1-infected subjects. Tested on a 119-virus panel, 1–18 showed to be exceptionally broad and potent with a coverage of 97% and a mean IC50 of 0.048 μg/mL, exceeding the activity of most potent CD4bs bNAbs described to-date. A 2.4 Å cryo-EM structure of 1–18 bound to a native-like Env trimer revealed that it interacts with HIV-1 env similar to other CD4bs bNAbs, but includes additional contacts to the V3 loop of the adjacent protomer. Notably, *in vitro*, 1–18 maintained activity against viruses carrying mutations associated with escape from VRC01-class bNAbs. Further, its HIV-1 env wide escape profile differed critically from other CD4bs bNAbs. In humanized mice, monotherapy with 1–18 was sufficient to prevent the development of viral escape variants that rapidly emerged during treatment with other CD4bs bNAbs. Finally, 1–18 overcame classical HIV-1 mutations that are driven by VRC01-like bNAbs *in vivo*.
Conclusion: 1–18 is a highly potent and broad bNAb that restricts escape and overcomes frequent CD4bs escape pathways, providing new options for bNAb combinations to prevent and treat HIV-1 infection.

BPD3/5

Effect of norethisterone, combined contraceptive vaginal ring (CCVR) and COCPs on HIV cervical target cells in adolescent girls: a randomized crossover study

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Purpose: Majority of new HIV infections in Sub-Saharan Africa occur in adolescent girls and young women, who are also at risk for unintended pregnancies. While a variety of contraceptives are available, the use of progestin-only injectables particularly DMPA, have been associated with increased risk of HIV acquisition. Although the ECHO trial recently revealed that women on DMPA are no more likely to acquire HIV than those using other long-acting methods. We aimed to investigate the effects of NET-EN, combined contraceptive vaginal ring (CCVR) and combined oral contraceptive pills (COCPs) on the frequencies of endocervical T cells, and their expression of CCR5, HLA-DR and CD38.
Method: Adolescent females (n=130; 15–19 years) were randomized 1:1:1 to receive either NET-EN, CCVR, or COCPs, and followed for a total of 32-weeks, crossing over to another HC at 16-weeks. Cervical cytobrush-derived T cells were analyzed by flow cytometry for the expression of CCR5 (HIV co-receptor) and activation markers (HLA-DR and CD38). Paired data was performed using the Wilcoxon signed-rank non-parametric test.
Results: Between baseline and crossover, initiation of CCVR was associated with increased proportions of cervical CD4 + T cells that expressed CD38 singly (p=0.01), and HLA-DR together with CD38 (p=0.03), despite decreased overall frequencies of CD4 + T cells compared to NET-EN and COCPs use. In addition, both CCVR and NET-EN users had increased proportions of CD8 + CD38 + T cells (p=0.01). Interestingly, expression of HLA-DR on CD8 + T cells was reduced at week 16 compared to baseline in all the HC arms.
Conclusion: Although all HC altered the phenotype of cervical CD8 + T cells, the use of the CCVR increased the activation (CD38 +) of both cervical CD4 + and CD8 + T cells in adolescent girls. The use of the CCVR in adolescents at high risk of HIV warrants further investigation.

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Access to and models of care

PE1/1

Barriers in TB services for people living with HIV and overcoming them according to the health care workers opinion in the TB facilities in Russia (sociological study)

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Introduction: The increase in HIV/TB with background of the HIV epidemic progression requires improvement in tuberculosis (TB) care for people living with HIV (PLWH). Sociological studies among specialists of TB facilities related to HIV/TB in Russia are limited. We found only one publication where, according to a questionnaire survey the activity and structure of most TB facilities in several Russian regions did not meet the required standards in TB services for PLWH.
Purpose: To identify barriers in TB services to PLWH and ways to overcome them, the opinions of specialists in TB facilities was surveyed using a questionnaire in 4 territories of Russia - St. Petersburg, Leningrad, Kaliningrad and Arkhangelsk oblasts.
Method: The total number of participants in the study was 284 people. Each respondent have signed the informed consent. The survey toolkit was a questionnaire online survey using a Google form, followed by automatic statistical processing of information. The questionnaire consisted of 19 structured questions, divided into blocks, of which 5 questions were open with the possibility of free expression of the respondent's opinion and 11 questions - closed with alternative answer for respondent choice.
Results: According to the specialists' opinion in TB facilities, the main barriers to provide TB services for PLWH are: low level of stakeholders interaction, especially with narcological dispensaries (49.0%), prison system (35.2%) and Nongovernmental Organizations (32.7%), migration (48.6% - in Kaliningrad oblast), increase in the number of injecting drug users (76.0% - in Leningrad oblast), lack of regional government support (34.9% - in total), legal acts inconsistency with reality (51.1% - in total).
Conclusion: Currently the TB services providing for PLWH are imperfect. TB system enhancing is associated with the strengthening of stakeholders collaboration, providing a full ART and TB chemoprophylaxis and effective and affordable TB treatment in patients with HIV, including establishment of low-threshold centers.

PE1/2

Investigating the impact of peer counseling intervention on access and use of sexual and reproductive health services in women Living with HIV in Nepal: a prospective cohort study

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Purpose: Women living with HIV experience inadequate access and treatment to sexual and reproductive health in resource-limited settings. Evidence is limited about the effects of peer counseling on access and use of contraceptive services, treatment of sexually transmitted infections, and unintended pregnancies in women with HIV. Therefore, this study aimed to examine the effect of HIV women led counseling to their peers on access and use of the sexual and reproductive health services in Nepal.
Method: A prospective cohort study was performed among 630 HIV-positive women (Intervention: 315; Control: 315) of major six cities of Nepal between June and November 2018. Women were provided counseling on sexual and reproductive health problems and facility-based services. Women were interviewed using semi-structure questionnaires about access, barrier, stigma, and utilization of services. Generalized estimating equation examined the effects of intervention comparing with control groups after adjusting sociodemographics.
Results: Of 630 women living with HIV, 22.2% 9n=140) reported to have Sexually Transmitted Infections, 46% (n=290) had felt stigma and 52% (n=328) women did not seek sexual and reproductive health services prior to the intervention. Women in the intervention had significantly lower level of stigma in accessing health facility compared to the control [Adjusted odds ratio (AOR): 2.8; 95% confidence interval (CI): 1.6–3.9). Condom use during last sexual intercourse also significantly increased from baseline to at the end among women in intervention compared to control (AOR: 3.4; 95% CI: 2.1–5.3).
Conclusion: Counseling and support from HIV women peer was effective to reduce self-stigma and improve use of services for sexual transmitted infections and condom use. Access and utilization of services can be improved by providing tailor made training to peers. Existing health system services can be improved through the community-based peer counseling approaches integrating in existing health system.

PE1/3

Health care delivery for HIV-positive people with tuberculosis in Europe

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Purpose: To analyze differences in tuberculosis (TB) and HIV services in Eastern Europe (EE) vs. Western Europe (WE).
Method: Twenty-three clinics completed a survey on management of HIV/TB coinfected patients in 2018 (EE: 14, WE: 9, 88% response rate). Results of the survey were compared to data from a similar survey in 2013.
Results: Delivery of health care was significantly less integrated in EE: provision of TB and HIV services in the same clinic (35.7% in EE v. 88.9% in WE; p=0.034), treatment of both diseases by the same doctor (28.6% v. 100%; p=0.002), and continued TB follow-up in one location (42% v. 100%, p=0.007). Although access to TB diagnostics and standard TB drugs was good in both regions, fewer clinics in EE reported unlimited access to rifabutin and drugs to treat MDR-TB. Opioid substitution therapy (OST) was less commonly available for all in need in EE (42.9% v. 100%; p=0.037). Integrase inhibitors based HIV treatment regimens were indicated as a possibility in 50% in EE and 100% in WE, p=0.02. In EE, routine usage of GeneXpert improved from 2013 to 2018 (53.8% v. 92.3%; p=0.073), as did access to moxifloxacin (46% v. 91%, p=0.033), linezolid (31% v. 64%, p=0.217), and bedaquiline (0% v. 25%, p=0.217), while integration of TB and HIV services (46.2% v. 38.5%; p=1.000) and provision of OST to all in need (54% v. 46%; p=0.695) did not improve.
Conclusion: Delivery of TB and HIV health care still differ between WE and EE, although availability of rapid TB diagnostics and availability of standard TB therapy improved in EE. By contrast, little progress was made towards integration of TB and HIV care, and access to drugs to treat MDR-TB remains highly variable.

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PE1/4

A survey of physicians on circumstances and factors influencing testing for HIV in Lithuania

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Objectives: Assess the circumstances and factors influencing testing for HIV among Lithuanian physicians.
Methods: Anonymous questionnaire-based survey was conducted among physicians and residents in nine clinics in four cities January-September, 2018. The test-retest of the questionnaire was conducted before the investigation to determine questionnaire reliability. Correlation coefficient was from very good (25.4%) to moderate (14.1%) in all question categories. Chi-square and exact-Fisher tests were used to compare categorical variables.
Results: 491 questionnaires were distributed, 384 returned, 371 suitable for analysis. Respondents were divided into the groups by city (Vilnius 67.7%, others 32.3%), position (physician 74.1%, resident 25.9%), specialty, work experience (0–20 years 56.1%, >20 years 43.9%), workplace (in-patient 38.8%, out-patient 36.7%, both 23.5%). Forty-one percent of respondents prescribe 0 test/month, 48% - 1–5 tests/month. HIV risk factors are the main reason for testing (84.9%), followed by indicator conditions (ICs) (63.1%). The most common of 22 given HIV ICs for which respondents would test for HIV was unexplained persistent lymphadenopathy (69.3%), unexplained leukocytopenia/thrombocytopenia (66.8%), hepatitis C (HCV) (66.3%), sexually transmitted infection (STI) (65.0%); the most uncommon - seborrheic dermatitis (5.7%), community acquired pneumonia (8.9%), severe or atypical psoriasis (10.8%). On average a physician would test for HIV in 8.4 (38%) ICs, would never test in 6.0 (27%) ICs. ICs are a more frequent testing motive for internal medicine specialists compared to other specialties (71.7% vs. 56.6%, $p<0.003$), for residents compared to physicians (75.0% vs. 61.5%, $p=0.017$). Among respondents, 49.9% indicated no barriers for testing, 20.8% - lack of knowledge, 20.2% - testing price.
Conclusion: The main reason for testing in Lithuania remains HIV risk factors. Physicians apply IC-guided testing insufficiently, but are open for integrated HIV testing in HCV infection and STIs. The lack of knowledge is the major barrier demonstrating a need for broader dissemination of information on HIV.

PE1/5

Experiences of forgiveness and unforgiveness of HIV-specific offenses among people living with HIV/AIDS in Ghana

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Purpose: To explore lived experiences of forgiveness/unforgiveness of HIV-specific offenses and meaning of these experiences among people living with HIV/AIDS.
Method: One-to-one, in-depth interviews were conducted with 15 PLWHA receiving antiretroviral therapy across the Korle-Bu, Komfo Anokye, and Tamale Teaching Hospitals in Ghana. Data were analysed using Interpretative Phenomenological Analysis.
Results: Four main themes emerged: (1) Behavioural, Spiritual, and Situational offenses; (2) Positive Personal and Interpersonal changes; (3) Restoration; and (4) Motivation for Positive and Purposeful living. Regarding theme (1), participants' most perceived HIV-related offense concerned the sexual behaviours of their partners (which led to their HIV+ status). Past risky lifestyles and discrimination by significant others were other behavioural offenses experienced. The belief that God allowed one's HIV+ status, and the financial, laboratory, and adherence demands of ART, respectively, constituted spiritual and situational offenses experienced. These often led to unforgiveness. Unforgiveness was characterized by reports of prolonged hurt, painful rumination, fear, and unhappiness, which were associated with poor concentration, social relationships, body image, and life-goal achievements. Regarding theme (2), participants described forgiveness of their perceived HIV-related offenses as personal changes in their thoughts (e.g., deciding to let go of retaliation and remove hatred/pain from their heart) and emotions (e.g., feeling free in mind, at peace, happy, and as if a burden has been lifted off); and offender-oriented, positive-behaviour changes (e.g., greeting, talking to, and laughing with offender). Regarding theme (3), to forgive meant to have one's physical/mental health, body-image, social relationships, family structure, and self-value/efficacy restored. Regarding theme (4), forgiving also meant increased motivation to live life, engage in ART-adherence and HIV-protective behaviours, and pursue significant career and family aspirations.
Conclusion: Forgiveness is one stress-relieving strategy for coping with offenses that holds implications for the health/wellbeing of PLWHA. The results hold significant implications for HIV/AIDS counselling models, collectivistic forgiveness coping, and stress-positive emotions-health research.

PE1/6

Time to antiretroviral therapy: service model adaptation during an outbreak of HIV in people who inject drugs (PWIDs)

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Purpose: There is currently an ongoing and extensive outbreak of HIV amongst people who inject drugs (PWIDs) in Glasgow City, Scotland, comprising over 150 cases. Viral sequencing revealed the majority of cases were Clade C virus with similar drug resistant mutations. Early initiation of antiretroviral therapy (ART) has both individual health benefits and population benefits as 'treatment as prevention'. This vulnerable cohort have difficulty engaging in the traditional model of care, and a new service model has been implemented, including outreach HIV clinical specialist nurses, in-reach consultant-led HIV clinic within homeless health facilities and ART dispensed by community pharmacies alongside supervised opiate substitution therapy. We aim to measure the effectiveness of this new model of care, using a surrogate marker of 'time from HIV diagnosis to ART initiation'.
Method: Patients diagnosed with HIV between April 2014 and June 2019, with the Clade C virus and resistant mutations, were included. Routine clinical data from electronic patient records was collected and analysed. Time from serological HIV diagnosis to ART initiation was recorded and comparisons were made for each calendar year.
Results: 155 patients were diagnosed between April 2014 and June 2019. 53/155(34%) were female. Mean age was 42. 10 were removed from analysis due to death or moved HIV care. The median time from HIV diagnosis to ART initiation has reduced from 324 days in 2015 to 24 days in 2019.

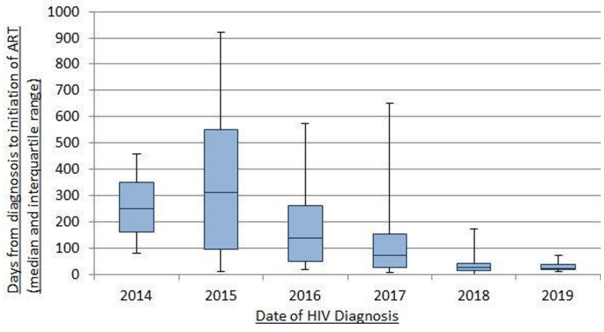


Figure 1. Time from HIV diagnosis to ART initiation by year of diagnosis

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Conclusion: In the midst of an HIV epidemic, we have shown that adaptation of service delivery can reduce time to ART initiation, with the aims of viral suppression, reduction in morbidity and prevention of onward transmission of HIV. This complex patient group require novel approaches to delivery of HIV care.

PE1/7

HIV infection hospital-based active case finding in Sardinia, Italy: results from the SHOT project

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Purpose: Many evidences suggest that some diseases occur more frequently in HIV-infected individuals and could represent target conditions to increase diagnosis in unaware patients. The aim of our study was to increase HIV-diagnosis by indicator condition based HIV-testing in Hospital settings.
Method: The SHOT project is a prospective, observational study, started in 2017. Patients were enrolled based on the presence of target conditions from the Units of Infectious Diseases (ID), Hematology, Respiratory Diseases (RD), Dermatology, Internal Medicine (IM) and Oncology (ON) of the University of Sassari. HIV positive individuals were evaluated by an ID nurse and specialist during hospitalization and linked to care.
Results: We enrolled 300 individuals during the first 27 months of study, 202 males and 98 females. The main reasons for screening were fever, non-Hodgkin lymphoma, lymphadenopathy, acute or chronic HCV/HBV infection, sexually transmitted diseases and pneumonia. We diagnosed 11/300 (3.66%) new cases of HIV infection, 4 were females and 7 were males. Five had a CD4 count<100/mm^3, one<200/mm^3, one>300/mm^3, two>300/mm^3 and two>900 mm^3. Eight out of 11 had a viral load>100.000 cp/mL. Data about CD4 count of a 41 years-old woman who has been diagnosed few days ago are pending. Among AIDS presenters, CDC stage was C3 in 4 and C2 in one patient. 90% referred a sexual exposure, 55% of them were heterosexuals.
Conclusion: We recorded an unexpectedly high number of new HIV diagnoses when considering the small number of individuals tested. Although most patients were diagnosed with advanced stage infection, at least 4 cases, including an acute HIV infection, would have been undiagnosed if not included in the study. Proactive testing may increase the diagnosis among unaware HIV-infected patients in hospital settings.

PE1/8

Retention activities based on home visits as a tool of return and keeping in care of low adhered patients. Results of work 2016–2019 Krasnoyarsk AIDS clinic

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Purpose: Retention in care of low adherent clients is one of the main challenges in HIV care. Services that address social needs of PLHIV and retention activities are recommended by WHO to be included into comprehensive integrated HIV care
Method: We analyzed efficiency of social support model developed in Krasnoyarsk AIDS center in collaboration with AHF Russia in 2016–2018 years and analyzed the number of clients who returned to HIV care, started ART and their retention. Interventions implemented in the framework of the program included : home visits, phone calls, reminder phone calls, home visits with social worker, psychologist and HIV physician follow up
Results: 4,621 clients who stopped visiting AIDS clinic more than 6 months earlier or missed ART within 3 months between 2016 and 2019, were included into this analysis. 8,430 home visits were done, 2,918 home consultation were provided, 4,370 phone consultations were provided for clients, their relatives, close friends, and partners. 2,701 (61.8%) clients returned to regular HIV clinic visits, 1,373 (51%) re-started ART within 30 days. 351 patient were provided with social support services. Out of all clients 207 deceased, 70 were found out as imprisoned, 401 (8.7%) clients refused social support. 170 clients moved to another region.
Conclusion: Social services with home visits and follow up for clients who are lost to follow up from HIV care show to be an effective way to return clients to HIV care and re-start ART. Retention in care of that group plays an essential role in the epidemic control as well as OIs and TB prevention. Social support should be adapted as integral part of an HIV care program

PE1/9

Pilot project of shared assistance with primary care for patients with HIV infection

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Purpose: Describe the results of a pilot project of shared assistance with Primary Care for patients living with HIV infection (PLWH)
Method: Prospective descriptive observational study in PLWH with regular follow up and who meet the inclusion criteria (VL undetectable last year, stable ART, current lymphocytes>350 cells // uL) are proposed to enter a Pilot Program of shared assistance with Primary Assistance (PPAC).
This project implies that the patients included should only go once a year to the hospital HIV consultations and another specific consultation is made in their Health Center (HC) after 6 months .The analytical extractions were performed in their HC, and the ART collection is performed every 4 months. The patients after 2 years of follow-up in the PPAC, filled out a satisfaction questionnaire
Results: In the first two years, 7 HC with a previous training participated, 98 patients were included, with an average age of 47.6 years (SD 11.7%), predominantly men 84.7%. The mean follow-up time in the PPAC being 446 days (SD 282). Twenty-four patients have left the PPAC (23.5%), 2 have died due to non-AIDS events, 3 were lost due to home relocation, 3 were withdrawn due to medical criteria and 15 were voluntarily withdrawn. All patients had undetectable CV during follow-up and the average TAR adherence was 99 %. No patient has had AIDS events.
Satisfaction with the PPAC at 2 years was high with an average score of 9.38, with the average score for family doctors of 9 and for the HC of 7.6. The main problems with the HC were the lack of privacy and the saturation of the mainly administrative services
Conclusion: After two years of PPAC follow-up, 23.5% left the program voluntarily, the patients who continue in the PPAC present good virological control and express their satisfaction.

Antiretroviral observational studies

PE2/1

A study of the effect of antiretroviral therapy on sexual risk behavior in a high-risk cohort of Congolese women

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Purpose: The effect of the rollout of antiretroviral therapy (ART) on global HIV epidemiology will depend, to a great extent, on the long-term effects of

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treatment on sexual risk behavior. Few studies have examined the effect of ART on sexual risk behavior in sub-Saharan Africa.
Method: We conducted a prospective cohort analysis to test the hypothesis that ART use would be associated with increased sexual risk behavior among female sex workers in Uvira, Congo, in the cohort were invited to return for monthly follow-up including a standardized interview about sexual risk behavior. They received basic HIV care, sexual risk reduction counseling, and free condoms. Data from 1993–2008 were included in this analysis. Since 2006, ART has been offered to women in the cohort who qualify for treatment according to the Congolese National Guidelines. We compared sexual risk behavior during ART-naïve versus ART-exposed follow-up using generalized estimating equations.
Results: Of the 899 HIV-seropositive women included in this analysis, 147 (16.4%) initiated ART. The women accrued 2,380 person-years of follow-up. The median number of visits was 10 (IQR 3–27) and the median interval between visits was 33 days (IQR 29–49). In analyses adjusted for calendar year, there was no increase in reported unprotected sex (aOR 0.74, 95% CI 0.53–1.02). Women on ART were significantly more likely to report 100% condom use (aOR 1.69, 95% CI 1.17–2.44) and less likely to report multiple partners (aOR 0.77, 95% CI 0.60–0.98). Sex frequency was similar during ART-naïve and ART-treated periods of follow-up.
Conclusion: In the setting of ongoing sexual risk reduction counseling and provision of free condoms, the introduction of ART did not increase sexual risk behaviour. On the contrary, while the overall level of sexual activity remained stable, condom use increased and there was a reduction in the number of sexual partners.

PE2/2

Coagulation system and HIV infection: a review

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Purpose: To understudy the coagulation system and HIV infection.
Method: Review.
Results: A review of the medical records of 36,515 patients infected with HIV who were participants in the Multistage Adult and Adolescent spectrum of Disease project reported a 1-year incidence of thrombocytopenia of 3.7% defined as a platelet count of less than 50 x109 /L. The incidence and severity of thrombocytopenia was associated with the stage of disease with an incidence of 1.7% among patients with HIV infection, but not clinical or immunologic AIDS, 3.1 % among persons with immunologic AIDS (CD4 lymphocytes<200 μL) and 8.7% in patients with clinical AIDS by logistic regression analysis, clinical AIDS, CD4 lymphocyte count of<200 μL), age>45 years, intravenous drug use, lymphoma and/or anemia was associated with a platelet count<50 x109/L
Conclusion: A number of coagulation abnormalities have been described in human immunodeficiency virus (HIV) disease. High levels of plasma von Willebrand factor have been reported in HIV disease and might be indicative of activated endothelium. Endothelium is involved in important homeostatic mechanisms of non-thrombotic vascular surfaces, vascular tone regulation and immunomodulation. Injured endothelium leads to localized inflammatory response of which the direct consequence is the occurrence of occlusive thrombosis events mediated between leucocyte recruitment and platelet adhesion and aggregation, blood clothing activation and fibrinolysis derangement. HIV infection has been associated with endothelial dysfunction. Since HIV infection is associated with endothelial dysfunction it may therefore result in activation and consumption of coagulation factors and ultimately coagulation defect.

PE2/3

Effectiveness, persistence and safety of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF), F/TAF + 3rd agent or rilpivirine/F/TAF (R/F/TAF) in treatment-naïve HIV-1 infected patients – 24-month results from the German TAFNES cohort study

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Purpose: The prospective TAFNES cohort study was initiated to evaluate the effectiveness and safety of F/TAF-based single-tablet (STR) or multi-tablet regimens (MTR) in people living with HIV (PLHIV) in a real-life setting.
Methods: The analysis population consisted of treatment-naïve (TN) PLHIV receiving E/C/F/TAF, F/TAF + 3rd agent or R/F/TAF≥21 months prior to data-cut (03/31/2019). 24-month outcome measures included ART persistence (Kaplan-Meier estimate), virologic effectiveness (HIV-RNA<50 cp/mL, discontinuation=failure, loss-to-follow-up/withdrawal consent/missing=excluded), (non-)serious adverse drug reactions (ADRs/SADRs) and health-related quality of life (HRQL).
Results: Of 247 TN patients (95% men, median age 36 years) eligible for analysis, 150 patients received E/C/F/TAF, 69 patients F/TAF + 3rd agent (86% dolutegravir, 7% darunavir/ritonavir, 4% raltegravir, 3% other), 28 patients R/F/TAF. Late presentation was common in the E/C/F/TAF and F/TAF + 3rd agent groups (Table 1).
Overall persistence was 83% (E/C/F/TAF 85%, F/TAF + 3rd agent 79%, R/F/TAF 84%); 32% of patients (n=78/247) discontinued before month 24 (including discontinuation of F/TAF-based regimens due to ADRs [3.6%], drug-drug interactions [2.4%], therapy simplification [2.0%] or virologic failure [1.6%], and loss-to-follow-up [14.2%] [Table 2]).
At month 24, 80% of patients (n=161/202) had HIV-RNA<50 cp/mL (83% of patients treated with E/C/F/TAF (n=103/124), 72% of patients treated with F/TAF + 3rd agent (n=39/54), 79% of patients treated with R/F/TAF (n=19/24)).
By month 24, 26 ADRs (including one virologic failure classified as SADR) were documented in 19 patients (7.7%).
Overall HRQL outcomes indicated improvements in HIV Symptom Index (HIV-SI) and in the mental and physical components of the SF-36 questionnaire (Table 3).
Conclusion: Persistence was high with F/TAF-based in treatment-naïve PLHIV in the TAFNES cohort. Overall virologic effectiveness was>80% two years after treatment initiation with only 2% virologic failure and low discontinuation rates (< 4%) due to ADRs. Improvements in self-reported HRQL and symptoms after 24 months of treatment illustrate the safety and effectiveness of F/TAF-based regimens in clinical routine care.

Table 1. Baseline characteristics

	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF**
N (%)	247 (100)	150 (61)	69 (28)	28 (11)
Male gender, n (%)	234 (95)	143 (95)	65 (94)	26 (93)
Age, years, median (interquartile range; IQR)	36 (30–46)	36 (30–46)	39 (30–48)	35 (30–43)
CDC stage C (AIDS), n (%)	18 (7)	8 (5)	10 (15)	0 (0)
Late presentation*, n (%)	83 (34)	43 (29)	36 (53)	4 (15)
CD4 count, cells/μl, median (IQR)	450 (253–623)	505 (317–648)	293 (153–539)	482 (382–642)
HIV-RNA, log cp/mL, median (IQR)	4.4 (4.0–5.1)	4.3 (3.9–4.9)	5.1 (4.3–5.6)	4.0 (3.7–4.5)
HIV-1 RNA>100,000 cp/mL, n (%)	71 (29)	32 (21)	39 (57)	0 (0)

*defined as<350 CD4/μL and/or AIDS; **groups not comparable due to different inclusion criteria

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Table 2. Reasons for discontinuation

		Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
Discontinuations by month 24, n/N (%)		78/247 (32)	43/150 (29)	27/69 (39)	8/28 (29)
Reason for discontinuation n (%)	ADR	9 (3.6)	5 (3.3)	3 (4.3)	1 (3.6)
	drug-drug-interaction	6 (2.4)	5 (3.3)	0 (0.0)	1 (3.6)
	virologic failure	4 (1.6)	3 (2.0)	1 (1.4)	0 (0.0)
	therapy simplification	5 (2.0)	0 (0.0)	5 (7.2)	0 (0.0)
	investigator decision	5 (2.0)	2 (1.3)	2 (2.9)	1 (3.6)
	other/unknown	9 (3.6)	5 (3.3)	3 (4.3)	1 (3.6)
	withdrew consent	5 (2.0)	3 (2.0)	2 (2.9)	0 (0.0)
	lost to follow-up	35 (14.2)	20 (13.3)	11 (15.9)	4 (14.3)

	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
BL SF-36 score, mental component[1], n, mean (+/-SD)	114, 45.9 (11.5)	68, 47.2 (11.2)	30, 42.6 (12.4)	16, 46.5 (10.0)
Change from BL in SF-36 score, mental component[1], mean (+/-SD)	+3.7 (12.7)	+3.5 (11.3)	+3.7 (16.2)	+5.0 (11.5)
BL SF-36 score, physical component[1], n, mean (+/-SD)	114, 55.0 (7.9)	68, 55.1 (7.9)	30, 55.2 (7.1)	16, 54.0 (9.2)
Change from BL in SF-36 score, physical component[1], mean (+/-SD)	+2.1 (9.1)	+2.9 (8.1)	+0.1 (10.1)	+2.4 (11.3)
BL HIV SI[2], n, mean (+/-SD)	111, 12.9 (11.8)	64, 11.3 (10.6)	33, 17.3 (13.7)	14, 9.6 (9.8)
Change from BL in HIV SI[2], mean (+/-SD)	-4.3 (9.9)	-3.1 (8.8)	-6.2 (10.8)	-5.4 (12.0)

SD, standard deviation; [1]norm based scoring, higher scores indicate higher HRQL, [2]range 0-90, higher scores indicate more bothering symptoms

Table 3. SF-36/HIV-SI outcomes in patients with completed questionnaires at baseline (BL) & month 24

PE2/4

"Attracting men" – extended clinic hours as differentiated model of care in an urban Malawian cohort

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Purpose: Male HIV patients initiate antiretroviral therapy (ART) later and are less adherent to ART than females. One known explanation is that males are the primary providers who often work during regular clinic hours. Several studies have shown that busy schedules are associated with high rates of ART treatment interruption. As a model of HIV care, Lighthouse Trust started providing extended hours as a differentiated service model targeting those who may fail to receive medications due to work.
Method: Bwaila is a large ART clinic in Lilongwe, with 21917 patients alive and on ART at the end of 2017. 36% (8242/21917) of the adult clients are males. In 2017, the clinic started offering extended service hours till 19:00. All patient data at this facility is managed in real-time using the electronic medical record system (EMR). From the EMR, we extracted HIV patients visit data for 2017. The visits were categorized into "regular hours" (06:00 to 16:30), "extended hours" (16:31 till 19:00) and "weekend". The proportion of visits attended by males in the regular hours were compared to the extended and weekend services using a two-proportion z-test.
Results: The proportion of men attending "extended hours" was 49% (6,862/14,023), significantly higher compared to the proportion of men during regular hours [36%(32,823/90,533, $p<0.001$)]. By age, the increase was most pronounced in the ages 25–34 years (38% vs. 24%, $p<0.001$) and 35–50 years (58% vs. 44%). In addition, during the weekend services, a significantly higher proportion of men were seen in the ages 35–50 (49% vs. 44%, $p<0.001$) and above 50 years (67% vs. 56%, $p<0.001$).
Conclusion: Extending clinic hours in the public ART program provide opportunity for patients on ART to have access to treatment and care beside their busy work. This seems to be particularly attractive to men.

PE2/5

HIV care in India: a systematic review of barriers to anti-retroviral therapy adherence

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Purpose: To determine the barriers to adherence to ART among HIV/AIDS patients in New Delhi, India.
Method: 21 observational studies published in India from January 2014 to March 2019 were selected which were fulfilling inclusion criteria. Searches were conducted in MEDLINE, EMBASE and PsycINFO, Searches were limited to English-language articles, using combinations of the terms: HIV, ART, adherence and barriers. Study characteristics were tabulated by summing the number of studies region wise and then stratifying by study outcome. Factors that might influence adherence like health status, beliefs and perceptions, and health risks were also studied. Ethical clearance was obtained from Institutional Ethics Committee.
Results: All studies used quantitative research methods (mainly cross-sectional study design). ART adherence outcomes were assessed using pharmacy records (pill count method, self-reported adherence and viral load. Non-adherence to ART was significantly associated with younger age, female gender, lower socio economic status, homelessness and duration of ART. Among young males, substance use were associated with poor adherence across studies, including heroin and alcohol use.
Conclusion: HIV treatment adherence is key issue of good outcome. This review suggests that urgent interventions are needed to improve treatment adherence especially among vulnerable groups.

PE2/6

Comparing NRTI-sparing dual regimens using data from the Swiss HIV cohort study

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Purpose: Nucleoside (or nucleotide) reverse transcriptase inhibitors (NRTIs) cause side effects in some patients, prompting the use of either partly or fully NRTI-sparing regimens. We used data from the Swiss HIV Cohort Study to estimate the effectiveness of two new dolutegravir dual regimens relative to the alternative NRTI-sparing dual regimens that clinicians used previously.
Method: We emulated two trials by propensity score matching case patients on the dolutegravir regimen with control patients on an alternative regimen. We analysed the case control sets using a Bayesian Cox model and estimated effectiveness as the percentage of patients still on their trial regimen without virologic failure (1 HIV RNA>1000 copies/mL or 2 consecutive HIV RNA>50 copies/mL) at 48 weeks. We did not expect our results to provide definitive answers immediately because few patients use these regimens: rather we periodically updated results, re-estimating relative effectiveness as new data accrued.
Results: In an emulated trial of partly NRTI-sparing regimens (DTG + 3TC/FTC versus DRV/r + 3TC/FTC), the estimated difference in effectiveness at 48 weeks was 15%, 12% and 15% in three sequential analyses each one year apart (Table 1). After a median follow up of 91 weeks, there were seven deaths, four virologic failures and 11 treatment changes due to toxicity. In an emulated trial of fully NRTI-sparing regimens (DTG+DRV/r versus RGV+DRV/r), the estimated difference in effectiveness at 48 weeks was 9%, 5% and 4% in the three sequential analyses (Table 2). After a median follow up of 86 weeks,

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there were no deaths, two virologic failures and eight treatment changes due to toxicity.
Conclusion: Estimates of relative effectiveness suggest that both dolutegravir regimens are not inferior to the alternative regimens used previously. Updated analyses show the stability of the earliest estimates with a slight gain in precision with each update.

Table 1. Analyses of an emulated trial comparing two partly NRTI-sparing regimens.

Partly NRTI-sparing regimens: cases on DTG and controls on DRV/r (both with 3TC/FTC).

Statistic	Initial analysis	One year later	Two years later
Events among cases	3/58	13/86	20/112
Event rate among cases, per 100PY	7.9	12	10
Events among controls	9/17	11/22	17/27
Event rate among controls, per 100PY	33	26	31
Hazard ratio (95% CrI)	0.34 (0.13, 0.83)	0.48 (0.24, 1.0)	0.43 (0.24, 0.78)
On treatment and undetectable: difference at 48 weeks (95% CrI),%	15 (2, 33)	12 (0, 26)	15 (4, 28)

Abbreviations: NRTI, nucleoside (or nucleotide) reverse transcriptase inhibitor; DTG, dolutegravir; DRV/r, darunavir boosted with ritonavir; 3TC/FTC, lamivudine or emtricitabine; PY, patient years.

Table 2. Analyses of an emulated trial comparing two fully NRTI-sparing regimens.

Fully NRTI-sparing regimens: cases on DTG and controls on RGV (both with DRV/r)

Statistic	Initial analysis	One year later	Two years later
Events among cases	6/54	13/71	17/77
Event rate among cases, per 100PY	9.5	12	11
Events among controls	12/32	14/38	15/39
Event rate among controls, per 100PY	27	20	19
Hazard ratio	0.51 (0.23, 1.1)	0.69 (0.35, 1.3)	0.74 (0.39, 1.4)
On treatment and undetectable: difference at 48 weeks (95% CrI),%	9 (−1, 21)	5 (−4, 15)	4 (−4, 13)

Abbreviations: NRTI, nucleoside (or nucleotide) reverse transcriptase inhibitor; DTG, dolutegravir; DRV/r, darunavir boosted with ritonavir; RGV, raltegravir; PY, patient years.

PE2/7

Physicians' opinions on generic antiretroviral drugs and single tablet regimen (STR) de-simplification for the treatment of HIV infection: a multicentre survey in Spain

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Objective: The aim of our study was to assess the attitudes and opinions about generic antiretroviral drugs (ARV) and single-tablet regimen (STR) de-simplification among physicians prescribing HIV treatment in the cohort of the Spanish HIV/AIDS Research Network (CoRIS).
Methods: An online questionnaire with 27 structured questions was sent to all physicians (n=199) who prescribed ARV among the 45 centers participating in the cohort.
Results: A total of 169 (84.9%) physicians answered the questionnaire. Only 4.1% of the physicians would never prescribe generic ARV, but 53.3% would not prescribe them if the number of pills per day increased and 89.3% would not prescribe them if the number of doses per day increased. However, 84.0% of the physicians agreed to prescribe generic antiretrovirals if doing so would decrease costs for the public healthcare system.
The percentages of physicians stating that generic antiretrovirals (compared to branded ones) would be associated with worse adherence, more adverse effects, or more probability of virological failure, provided that the number of pills and doses per day would not change, were low: 0.6%, 7.7% and 3.6%, respectively. However, these percentages were much higher if the generic ARV entailed breaking a STR: 63.9%, 18.9% and 42.0%, respectively. Most physicians stated that they needed more information about the effectiveness and safety of generic ARV and the price difference compared to their branded equivalents.
Conclusion: Although most physicians were confident about prescribing generic ARV, the majority had strong concerns about de-simplifying STR, and they also needed more information about generic drugs.

PE2/8

Simplifying salvage regimens with darunavir-based dual therapy in HIV-infected individuals harboring multidrug-resistance

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Purpose: We assessed the efficacy of simplifying salvage regimens with boosted darunavir plus raltegravir (DRV/b+RAL) in virologically suppressed patients with protease inhibitors (PIs) resistance-associated mutations (RAMs).
Method: Retrospective, multicenter cohort study (NCT03348449) on HIV-infected individuals switched to DRV/b+RAL who met the following criteria: plasma HIV-RNA levels<50 copies/mL for≥12 months, no previous integrase inhibitors failure or resistance, previous PIs failure, and at least one genotypic resistance test (GRT) performed. The primary endpoint was the proportion of patients maintaining HIV-RNA<50 copies/mL at week 96. Efficacy was analyzed according to darunavir genotypic sensitivity score (GSS).
Results: Overall, 228 individuals were included (mean age 50 years, men 75%) with a median time of virologic suppression before simplification of 49 months (interquartile range, IQR 39.8–63.5). Patients had a median (range) of 2 (1–3), 4 (3–6), and 5 (2–9) major mutations to non-nucleoside reverse transfer inhibitors, nucleoside reverse transfer inhibitors, and PIs, respectively. One hundred and seventy-seven individuals were darunavir full-susceptible (GSS=2), whereas 51 had reduced susceptibility (GSS<2). Individuals with reduced susceptibility to darunavir had a higher number of PIs-RAMs (9.3 vs 4.5, p<0.01), and had been suppressed for longer time (median of 61 months, IQR 29–59). At week 96, only 2 individuals (0.9%; 95% confidence interval, CI, 0.4–2.7%) failed to maintain HIV-RNA<50 copies/mL. The efficacy excluding non-virologic reasons was 94.3% (95% CI, 90.2–98.4%), without differences according to GSS (p=0.60). No individual with virologic failure had darunavir-RAMs at baseline. The median CD4/CD8 ratio increased significantly at week 96 (+9.5%; p<0.01), without differences between groups (p=0.57).
Conclusion: The simplification to a dual regimen with boosted darunavir plus raltegravir after a long period of virologic suppression was not associated with higher rates of treatment failure, even in patients with multidrug-resistant HIV infection harboring PIs-RAMs.

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PE2/9

Clinical outcomes among HIV-infected Africans with advanced disease in Spain

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Objectives: To characterize advanced HIV disease (AHD) among African people living with HIV (PLHIV), and to compare its prevalence, clinical-epidemiological characteristics, and outcomes between Africans and individuals from other regions (OtR) living in Spain.
Methods: Prospective cohort study among all adult PLHIV enrolled in Spanish AIDS Research Network Cohort, a multicenter cohort of antiretroviral therapy-naïve PLHIV enrolled in 45 Spanish centers between 2004 and 2017. AHD was defined as having CD4 cell count<200 cells/mm^3 at diagnosis; loss to follow-up (LTFU) as not having a visit>365 days since last follow-up visit; and attrition, as death / LTFU. This study is part of an international multi-cohort collaboration to characterize AHD among African PLHIV.

Table 1. Clinical-epidemiological characteristics at enrollment and Advanced HIV Disease prevalence among people living with HIV by region of origin.

	Region of origin				
	Africa	Western Europe	Other	All	P values
Characteristics at enrolment	n= 635	n= 9942	n= 3274	n= 13851	
Gender (n[%])					<0.001
Female	348 [54.8]	1202 [12.1]	597 [18.2]	2147 [15.0]	
Age, (n[%])					<0.001
[Median, IQR]	34 [28–41]	36 [29–44]	32 [27–39]	37 [29–43]	
<=30	240 [37.8]	3007 [30.2]	1377 [42.1]	4624 [33.4]	
31 – 40	244 [38.4]	3597 [36.2]	1288 [39.3]	5129 [37.0]	
41 – 50	114 [17.9]	2260 [22.7]	442 [13.5]	2816 [20.3]	
> 50	37 [5.8]	1078 [10.8]	167 [5.1]	1282 [9.3]	
HIV transmission group, (n[%])					<0.001
HSH	21 [3.3]	6345 [63.8]	2108 [64.4]	8474 [61.2]	
IDU	9 [1.4]	976 [9.8]	80 [2.4]	1065 [7.7]	
HSM	560 [88.2]	2296 [23.1]	994 [30.4]	3850 [27.8]	
Unknown	28 [4.4]	236 [2.4]	62 [1.9]	326 [2.3]	
Educational level, (n[%])					<0.001
Low	309 [48.7]	2908 [29.2]	927 [28.3]	4144 [29.9]	
Medium	126 [19.9]	2756 [27.7]	1045 [31.9]	3927 [28.3]	
High	42 [6.6]	2702 [27.2]	711 [21.7]	3455 [24.9]	
Unknown	158 [24.9]	1576 [15.8]	591 [18.5]	2325 [16.8]	
AIDS defining illness, (n[%])					<0.001
Yes	123 [19.4]	1084 [10.9]	345 [10.5]	1552 [11.2]	
CD4 cell count, cel/ul, (n[%])					
[Median , IQR]	299 [151–477]	408 [223–609]	374 [204–554]	429 [214–592]	<0.001
Advanced HIV disease					
Yes	197 [31.0]	2208 [22.2]	802 [24.5]	3207 [23.15]	<0.001
HIV Viral Load, cop/mL, (n[%])					
[Median, IQR]	49100 [8091–143000]	47900 [13505–138572]	39310 [10862–117489]	48911 [12640–132023]	<0.001
Undetectable	30 [5.3]	152 [1.6]	57 [1.8]	239 [1.8]	
HBV infection [HBsAg pos]					<0.001
Yes	57 [9.0]	284 [2.9]	134 [4.1]	475 [3.43]	
HCV infection [AcVHC pos]					<0.001
Yes	29 [4.6]	1121 [12.3]	179 [5.5]	1429 [10.3]	

IQR= interquantile range, HSH=homo/bisexual, IDU= injection drug users, HSM=heterosexual, HIV= Human Inmune Deficiency Virus, HBV= Hepatitis B virus, HCV= Hepatitis C virus , AIDS= Advanced Inmune Defiency Syndrome; P values were calculated with Kruskall-Wallis test, ANOVA or the Chi-square test, as appropiate .

Table 2. Attrition, non-AIDS comorbidities and mortality among PLHIV who presented with Advanced HIV Disease by region of origin.

	Region of origin				
	Africa	WE	Other	All	P values
Follow-up outcomes	n=197	n=2208	n=802	n=3207	
Time of follow-up					<0.001
Months [Median_IQR]	42 [15–88]	60[22–105]	47[14–91]	55 [18–100]	
Attrition [LTFU or death]					<0.001
Yes	100 [50.8]	651 [29.5]	277 [34.5]	1028 [32.0]	
LTFU (n[%])					<0.001
Yes	87 [44.2]	381 [17.3]	241 [30.1]	709 [22.1]	
Reasons for LTFU (n[%])					0.02
Lost	64 [73.6]	244 [64.0]	138 [57.3]	446 [62.9]	
Transferred	23 [26.4]	137 [36.0]	103 [42.7]	266 [37.1]	
Death during follow-up (n[%])					<0.001
Yes	13 [6.6]	270 [12.2]	36 [4.5]	319 [9.9]	
Causes of Death (n[%])					0.34
HIV/AIDS	9 [4.6]	130 [5.9]	22 [2.7]	161 [5.0]	
Cancer	2 [1.0]	35 [1.6]	7 [0.9]	44 [1.4]	
Liver	0 [0]	25 [1.1]	0 [0]	25 [0.8]	
Cardiovascular	0 [0]	10 [0.5]	0 [0]	10 [0.3]	
Non-AIDS	1 [0.5]	20 [0.9]	3 [0]	25 [0.8]	
Other	0 [0]	26 [1.2]	1 [0.1]	28 [0.9]	
Unknown	1 [0.5]	24 [1.1]	3 [0.4]	28 [0.9]	
Non-AIDS comorbidities (n[%])					0.02
Yes	24 [12.2]	732 [33.2]	130 [16.2]	899 [27.7]	
Type of comorbidities (n[%])					<0.001
Cardiovascular	2 [8.3]	87 [11.9]	6 [4.6]	96 [10.7]	
Renal	10 [41.7]	87 [11.9]	21 [16.1]	118 [13.1]	
Liver	0 [0]	66 [9.0]	2 [1.5]	68 [7.6]	
Non-AIDS malignancies	4 [16.7]	171 [23.4]	25 [19.2]	209 [23.2]	
Osteo articular	2 [8.3]	70 [9.6]	7 [13.1]	90 [10.0]	
Neurologic	3 [12.5]	122 [16.7]	28 [21.5]	153 [17.0]	
Metabolic	3 [12.5]	99 [13.5]	14 [10.7]	117 [13.0]	
Other infections	0 [0]	22 [3.0]	7 [5.4]	30 [3.3]	
pre-NonAIDS malignancies	0 [0]	8 [1.1]	10 [7.7]	18 [2.0]	

WE= Western Europe, LTFU=Lost to follow-up, NADM=Non=AIDS malignancies, HIV=Human Inmune Deficiency Virus, AIDS=Acquired Inmune Defiency Syndrome; P values were calculated with Kruskall-Wallis test , the Chi-square test and Fisher's exact test as appropiate .

Results: Overall, 13.851 subjects were analysed, including 635 (4.6%) African individuals. Compared with PLHIV from Western Europe (WE), Africans were predominantly women (55% vs. 12.1%, p<0.001), had lower median CD4 count (299 [155–477] vs 408 [223–609], p<0.001) and higher proportion of AIDS-defining illnesses (19.4% vs. 10.9%, p<0.001) at HIV diagnosis. 31% of Africans presented with AHD vs. 22.4% WE and 24.5% OtR (p<0.001). Median follow-up was 42 [15–88], 60 [22–105] and 47 [14–91] months among Africans, WE and OtR respectively. Of those with AHD, 12.2% Africans vs 33.2% WE developed non-AIDS comorbidities during follow-up. Among Africans, 42% were kidney-related (8/10, acute renal failure). 44.2% of Africans were LTFU compared with 17.3%, 30.1%,WE and OtR respectively. Mortality was documented in 6.6% Africans vs 12.2% WE. Causes of death were similar by region of origin and mainly HIV/AIDS-related.
Conclusion: AHD is a major concern among African PLHIV in Spain. The high proportion of attrition and the occurrence of renal comorbidities during follow-up are of particular relevance. The lower mortality observed among Africans is likely biased by the higher rates of LTFU in this group.

PE2/10

The Treatment of Primary HIV (TopHIV) cohort: a prospective multicenter cohort in Germany

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Purpose: Despite enormous progress in treating HIV infection, there is still no effective cure strategy. A key focus for the development of cure approaches include the exploration of HIV immune surveillance and intervention strategies prior to the establishment of the viral reservoirs.
Methods: In February 2016, we established the Treatment of Primary HIV (TopHIV) cohort, with support of the German Centre for Infection Research and the Translational Platform HIV, as a collaboration between university hospitals and HIV practices throughout Germany. TopHIV is an open multicentre cohort, enrolling newly diagnosed patients with acute and early HIV-infection. Demographic, clinical, and laboratory data as well as blood collection are performed at baseline, month 1, 3, 12, and every 12 months thereafter.
Results: To date, 305 patients are enrolled and actively followed up, including about 10,000 PBMCs and plasma samples. 22.7% (66/291) patients were diagnosed at Fiebig stage I/II, 39.9% (116/291) at stage III, and 37.5% (109/291) at stage IV/V. Our cohort mainly consist of men reporting sex with men as main risk factor (92.1%; 281/305) with a median age of 47 years (interquartile range (IQR) 42–52). Baseline HIV viral load was>1,000,000 copies/mL in 62.4% (189/303), while 8.0% (23/293) had<200 cells/mm^3 CD4 + T-cells at baseline. The most commonly prescribed first-line regimes were dolutegravir (DTG) with emtricitabine/tenofovir alafenamide (F/TAF) (19.0%, 58/305) and DTG with emtricitabine/tenofovir disoproxil (TDF/TAF) (14.8%; 45/305). Median time from diagnosis to treatment initiation was 3 days (IQR 1–7). In 164 patients with comprehensive follow-up, viral suppression (≤50 copies/mL) was achieved by 20.7%, 89.0%, and 89.0% after 1, 3 and 12 months.
Conclusion: We established a data- and biomaterial collection of a rare patient group, which allows expedited translational research. This cohort will be very valuable for future studies focussing on immune control and cure of HIV infection.

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Table 1. Variations and their statistical significance for CD4, CD8 and CD4/CD8 at switch 12, 24 and 36 months are shown in the table below

	At switch mean, IC95% (n=53)	12 months after switch mean, IC95% (n=53)	24 months after switch mean, IC95% (n=53)	36 months after switch mean, IC95% (n=46)	Difference from switch to 12 m mean, IC95% (n=53) p-value	Difference from switch to 24 m mean, IC95% (n=53) p-value	Difference from switch to 36 m mean, IC95% (n=46) p-value
CD4 Cell count cell/mm3	740 (646–834)	720 (633–806)	755 (647–863)	723 (616–831)	−21 (−87, +46) p=0.53	15 (−75, +105) p=0.73	−2 (−97, +93) p=0.96
CD8 Cell count cell/mm3	907 (786–1028)	857 (756–958)	898 (775–1021)	851 (742–960)	−50 (−130, +30) p=0.21	−9 (−98, +80) p=0.83	−65 (−166, +35) p=0.19
CD4/CD8	0.95 (0.79–1.12	0.94 (0.79–1.09)	0.99 (0.83–1.16)	0.98 (0.81–1.15)	−0.01 (−0.07, +0.05) p=0.66	0.04 (0.1,+0.9) p=0.14	0.04 (−0.05,+0.13) p=0.42

PE2/11

No decrease in CD4/CD8 ratio after 36 months therapy in patients who were switched to two dual regimens containing rilpivirine

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Purpose: The CD4/CD8 ratio has been associated with the risk of AIDS and non-AIDS events. Dual therapy is a new option for some patients but information on some aspects like immune activation control is still scarce. We evaluated the impact of two rilpivirine containing dual therapies (DT) on CD4/CD8 in the medium term.
Method: Observational, retrospective study including all the patients from an HIV Clinic at the Arnau de Vilanova Hospital in Valencia, Spain, who were switched to DTG+rilpivirine or DRNc+rilpivirine between January 2014 to December 2016. Patients should have VL<50 for at least 6 months before switch. CD4, CD8 and CD4/CD8 pre switch and after 12, 24, 36 months were recorded. Mean with IC 95%, were calculated for quantitative variables and frequencies for qualitative variables. The two tailed t-test for repeated measures was applied.
Results: From a total of 61 patients on DT, 7 were excluded because VL was not undetectable before switch. 54 patients enter in the analysis, 31 of them were on DTG+rilpivirine and 23 were on DRNc+rilpivirine. The mean (IC95%) age was 51 (49–54) and 50% were men. Patients were undetectable for a mean of 6.61 (IC95% 5.54–7.67) years before switch and the mean of CD4 at switch was 740 (646–834) cell/mm3. Mean time on DT was 33 months. During the follow up one patient had VL>50 in 2 consecutive determinations and it was due to poor adherence. No significant variations for CD4, CD8 and CD4/CD8 after 12, 24 and 36 months were found . The results did not change after stratify analysis by type of therapy (DTG+RLP or DRN+RLP).
Conclusion: In patients with suppressed viral load and sustained immune response before switching to a rilpivirine containing DT regimen we did not find any significant change in the CD4/CD8 ratio after 36 months of therapy.

PE2/12

Clinical experience of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) in real life practice: data from the Turkish HIV-TR cohort

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Objectives: Since its availability in October 2017, elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) has been widely used in Turkey. We aimed to describe the effectiveness and tolerability of E/C/F/TAF in a real-life setting.
Methods: Observational, retrospective, multicenter cohort study with treatment-naive (TN) and treatment-experienced (TE) HIV patients starting E/C/F/TAF. Clinical, immuno-virological variables, switch reasons and changes in lipids and glomerular filtration rate (eGFR by CKD-EPI formula) were analyzed at month-6 (M6) and −12 (M12). Virologic outcomes were assessed in patients with at least 6 months follow-up by a modified intention-to-treat approach (death or discontinuation of E/C/F/TAF=failure, missing data and lost to follow-up=excluded).
Results: Baseline characteristics of 1743 persons (34% TN) from 32 HIV clinics are shown in Table 1. Of the 1146 TE patients, 994 (86.7%) were virologically suppressed before switch [viral load (VL)<50 copies/mL]. Main reasons for E/C/F/TAF switch were to prevent future toxicities (46.9%), intolerance/toxicity (17.3%), treatment simplification (15.4%), provider's preference (5.7%), patient's willingness (2.9%), poor compliance (1.5%), virological failure (0.8%), and others (9.5%). At M12, 92.4% (315/341) of TN and 94.8% (674/711) of TE patients had a VL<50 copies/mL. One adverse drug reaction leading to discontinuation (bruising) and 4 deaths (3 TN and 1 TE patients) not related to E/C/F/TAF were documented during the study period. At M12, median CD4 lymphocyte count increased by 229 and 38 cells/mm^3 in TN and TE patients, respectively. In TE patients who switched from tenofovir disoproxil fumarate (TDF) to TAF, fasting lipid values increased compared to baseline while total/HDL cholesterol ratio did not change significantly. Median non-HDL cholesterol increase was 14 mg/dL at M12. Mean change in eGFR at M12 was + 1.2 mL/min/1.73 m^2 among patients switching from E/C/F/TDF to E/C/F/TAF (p<0.001).
Conclusion: E/C/F/TAF had a high virological efficacy in both TN and TE patients and was tolerated very well.

Table 1. Baseline characteristics of the study population

	Overall n (%)	Treatment-naive n (%)	Treatment-experienced n (%)
n (%)	1743 (100)	597 (100)	1146 (100)
Male, n (%)	1525 (87.5)	536 (89.8)	989 (86.3)
Age, years, median (IQR)	35 (28–44)	33 (27–43)	35 (29–45)
Pre-treatment CD4 cells/μL, median (IQR)	568 (369–784)	401.5 (263.5–554)	673 (486–870)
Pre-treatment HIV-RNA>100,000 copies/mL, n (%)	278 (15.9)	253 (42.4)	25 (2.2)
Pre-treatment CD4 count<350 cells/μL, n (%)	378 (21.7)	245 (41.0)	133 (11.6)
Transmission Mode, n (%): Heterosexual, MSM/Bisexual, IDU, Unknown/Other	837 (48.0), 617 (35.4), 4 (0.2), 285 (16.4)	287 (48.1), 204 (34.2), 4 (0.7), 102 (17.1)	550 (48.0), 413 (36.0), -, 183 (16.0)

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PE2/13

Real world utilisation of raltegravir 1200 mg once daily (The RETRO Study)

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Purpose: Raltegravir 1200 mg once daily (RAL OD) became available in England in September 2017. This study is the first to describe the population in which it is prescribed in clinical practice. Primary objectives include description of subject demographics and their baseline clinical and treatment characteristics. Antiretroviral therapy (ART) initiated with RAL OD will also be described.

Method: Retrospective data collection using standardised case report forms from 300 adult records taking≥1 dose of RAL OD from first availability and who returned for their six-month (−1/+3 months) follow-up appointment in London or Manchester.

Results: Of 300 subjects included, 255 (85%) were male, 182/255 (71%) men who have sex with men. 56% were of white ethnicity. Median age at diagnosis and RAL OD initiation was 34 (18–86) and 45 (21–96), respectively. 56 (19%) were recreational substance users, five (9%) reporting chemsex use. 286 were ART experienced (ART-E) and 14 treatment naïve (TN). Baseline (BL) viral load (VL) and CD4 + count was available for 254 and 249 ART-E subjects respectively. 94% had BL VL of<50 c/mL, and 96% < 200 c/mL. 5% of ART-E subjects had BL CD4 + < 200 vs 21% TN. At baseline, 60% took non-ART comedications and 68% experienced comorbidities, most commonly hyperlipidaemia, depression, and hypertension in 68 (23%), 56 (19%) and 51 (17%), respectively. 205 (68%) initiated TDF/FTC and 46 (15%) ABC/3TC. 5/239 (2%) with BL VL<50c/mL, and 10/300 (3%) RAL OD initiated reported VL>50c/mL at follow-up. 21 (7%) discontinued RAL OD by six months.

Conclusion: In this real world setting of individuals initiating RAL OD, subjects are predominantly white MSMs, consistent with clinical trial populations. They are however initiated at an older age, and experience significant comorbidities, with associated burden of comedications. Discontinuations and VL measures are within UNAIDS 90:90:90 targets.

Baseline Demographics

Male	255 (85%)
Female	45 (15%)
Transgender Female	3 (1%)
Age	45 (21–96)
White ethnicity	169 (56%)
Black (African)	50 (17%)
Black (Caribbean)	8 (3%)
Mixed/Other ethnicity	73 (24%)
Recreational substance use within 6 months	56 (19%)
Chemsex use	5/56 (9%)

Baseline Clinical Characteristics

ARV Treatment Experienced (ART-E)	286 (95%)
Viral Load: ART-E<50 copies/mL	239 (84%)
Viral Load: ART-E >=50 copies/mL	15 (5%)
Viral Load: ART-E Unknown	32 (11%)
Viral Load: TN<100,000 copies/mL	10 (71%)
Viral Load: TN >=100,000 copies/mL	4 (29%)
CD4 + T-cells: ART-E>200 cells/mm3	234 (82%)
CD4 + T-cells: ART-E <=200 cells/mm3	15 (5%)
CD4 + T-cells: ART-E Unknown	37 (13%)
CD4 + T-cells: TN <=200 cells/mm3	3/14 (21%)

PE2/14

Effectiveness, persistence and safety in treatment-naïve and treatment-experienced HIV-1 infected patients receiving elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) – 12-month evaluation of the French TARANIS cohort

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Purpose: Long-term tolerability of ART coupled with sustained virologic efficacy are essential for healthy ageing in HIV-infected patients. The prospective TARANIS cohort was initiated to provide evidence concerning the effectiveness and safety of using F/TAF-based regimens in routine clinical care.

Method: Treatment-naïve (TN) and treatment-experienced (TE) patients having initiated E/C/F/TAF 9–15 months prior to data-cut (04/09/2019; corresponding to the 12-month visit window) were eligible for evaluation. Month-12 (M12) outcomes comprised treatment persistence (Kaplan-Meier analysis), virologic effectiveness (HIV-1-RNA<50 cp/mL; discontinuation= failure, loss-to-follow-up/withdraw consent/missing=excluded; D=F, missing ignored), (non-)serious adverse drug reactions (ADRs/SADRs) and self-reported health-related quality of life (HRQL).

Results: The analysis population consisted of 270 patients (TN: n=57; TE: n=213) (Table 1). Of TN patients, 16% presented with<200 CD4/µl, 29% with≥100,000 HIV-1-RNA cp/mL. Of TE patients, 90% had<50 HIV-1-RNA cp/mL, 87% switched from TDF-based ART (42% from E/C/F/TDF). Main reasons for switch were ART simplification (42%) and side effects of previous ART (36%) (multiple-responses permitted).

By M12, overall estimated persistence on E/C/F/TAF was 86% (TN: 87%, TE: 86% [Figure 1]). Overall, 17% of patients (n=46/270) discontinued before M12 (including discontinuations due to ADRs [7%] [not kidney/bone related] or virologic failure [0.4%] [Table 2]).

At M12, virologic effectiveness was 80% (D=F, missing ignored; on-treatment: 94%) (TN: 84% (98%), TE: 79% (93%)). Overall, 58 ADRs and 4 SADRs were documented in 12% and 0.7% of patients, respectively. Improvements in HRQL were seen in SF-36 mental component for TN and in treatment satisfaction for TE patients (Table 3).

Conclusion: In the prospective French TARANIS cohort, persistence to E/C/F/TAF was high in TN and TE patients during the first year. Virologic effectiveness and safety of using E/C/F/TAF were confirmed in a real world setting with 7.4% discontinuations due to ADRs (not related to kidney or bone) and<1% due to virologic failure.

Table 1. Baseline characteristics of the analysis population; IQR: inter quartile range

	Overall (N=270, 100%)	TN (n=57, 21.1%)	TE (n=213, 78.9%)
Male gender, n (%)	212 (78.5)	53 (93.0)	159 (74.7)
Age, years, median (IQR)	46 (36–54)	35 (27–47)	48 (40–55)
CDC stage C, n (%)	47 (17.7)	3 (5.6)	44 (20.8)
CD4 count, cells/µl, median (IQR)	642 (414–840)	428 (287–606)	697 (459–872)
HIV-1-RNA, cp/mL, median (IQR)	34 (19–159)	40,148 (8,960–137,850)	20 (19–39)
HIV-1-RNA<50 cp/mL, n/N (%)	N/A	N/A	188/209 (90.0)
Most common INI-based previous antiretroviral regimen, n (%)	N/A	N/A	120 (57.4)
NNRTI-based	N/A	N/A	35 (16.7)
PI-based	N/A	N/A	44 (21.1)

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Table 2. Documented reasons for discontinuation of E/C/F/TAF and/or study.

	Overall (N=270, 100%)	TN (n=57, 21.1%)	TE (n=213, 78.9%)
Discontinuations by month 12, n/N (%) due to	46/270 (17.0)	11/57 (19.3)	35/213 (16.4)
ADRs	20 (7.4)	2 (3.5)	18 (8.5)
Drug-drug-interaction	2 (0.7)	0 (0.0)	2 (0.9)
Virologic failure	1 (0.4)	0 (0.0)	1 (0.5)[1]
Patient decision/withdrawal of consent	8 (3.0)	6 (10.5)	2 (0.9)
Other/unknown	11 (4.1)	3 (5.2)	8 (3.8)
Death	1 (0.4)	0 (0.0)	1 (0.5)
Loss to follow-up	3 (1.1)	0 (0.0)	3 (1.4)

[1]Patient with HIV-1-RNA of 34 cp/mL at baseline and 145 cp/mL and month 3; baseline resistance mutations: K103 and V90I

	Overall	TN	TE
BL SF-36 score, mental component[1], mean (+/−SD) [n]	43.8 (13.7) [172]	38.1 (16.5) [37]	45.3 (12.4) [135]
Change in SF-36 score, mental component[1], mean (+/−SD)	+1.5 (11.1)	+5.9 (12.4)	+0.3 (10.4)
BL SF-36 score, physical component[1], mean (+/−SD) [n]	53.3 (9.6) [172]	55.4 (9.5) [37]	52.7 (9.6) [135]
Change in SF-36 score, physical component[1], mean (+/−SD)	+1.0 (7.4)	+1.0 (8.8)	+1.0 (7.4)
BL HIV SI[2], mean (+/−SD) [n]	14.5 (12.0) [173]	14.5 (13.8) [38]	14.5 (11.5) [135]
Change in HIV SI[2], mean (+/−SD)	−1.0 (10.2)	−3.3 (12.7)	−0.3 (9.3)
BL TS (treatment satisfaction)[3], mean (+/−SD) [n]	–	–	51.0 (8.9) [131]
TS change[4], mean (+/−SD)	–	–	21.3 (10.9)

SD, standard deviation; [1]norm based scoring, higher scores indicate higher HRQL[2]range 0–80, higher scores indicate more bothering symptoms[3]range 0–60, higher scores indicate greater satisfaction[4]range −30-+30, positive scores indicate increased satisfaction.

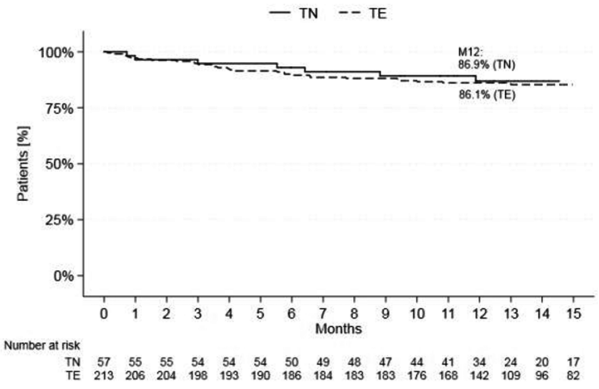


Figure 1. Persistence on E/C/F/TAF in TN and TE patients (Kaplan-Meier estimates)

PE2/15

24-month evaluation of the German TAFNES cohort - Effectiveness, persistence and safety of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF), F/TAF + 3rd agent or rilpivirine/F/TAF (R/F/TAF) in treatment-experienced HIV-1 infected patients

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Purpose: Minimizing side effects and optimizing long-term tolerability of ART are essential requirements for achieving healthy ageing in people living with HIV (PLHIV). The prospective TAFNES cohort was initiated to provide evidence concerning effectiveness and safety of using F/TAF-based regimens in routine clinical care.

Methods: Treatment-experienced adults of the TAFNES cohort receiving either E/C/F/TAF, F/TAF + 3rd agent or R/F/TAF at least 21 months prior to data-cut (03/31/2019) were included. 24-month outcomes included ART persistence (Kaplan-Meier analysis), virologic effectiveness (HIV-RNA<50 cp/mL, discontinuation=failure, loss-to-follow-up/withdrawal consent/missing=excluded), and (non-)serious adverse drug reactions (ADRs/SADRs).

Results: A total of 434 PLHIV were eligible for analysis (E/C/F/TAF: n=151; F/TAF + 3rd agent: n=146 [32% dolutegravir, 17% nevirapine, 12% darunavir/ritonavir, 11% raltegravir]; R/F/TAF: n=137). Baseline characteristics are shown in Table 1: 95% of participants had HIV-RNA<50 cp/mL prior to switch, 93% switched from TDF-based ART.

By month 24, overall persistence on F/TAF-based ART was 81%. The corresponding persistence in the subgroups using E/C/F/TAF, F/TAF + 3rd agent or R/F/TAF was 89%, 72% and 82%, respectively (Figure 1). In total, 25% of participants (n=109/434) discontinued before month-24 visit (including discontinuations due to ADRs [4.4%], therapy simplification [3.7%], virologic failure (VF) [1.2%], death [0.9%], or loss-to-follow-up [6.0%]) (Table 2).

At month-24 visit, 75% (n=296/393) had HIV-RNA levels<50 cp/mL, i.e. 84% of participants treated with E/C/F/TAF, 66% on F/TAF + 3rd agent, and 76% on R/F/TAF. Up to month-24, 26 ADRs (in 5.3% of participants [n=23]) and 6 SADRs (in 1% of participants [n=3]) were documented. Discontinuations and thereby evaluation of effectiveness in the F/TAF + 3rd agent group were driven by therapy simplification without VF (Table 3).

Conclusion: Overall persistence on F/TAF-based regimens was high in treatment-experienced PLHIV: >80% during 24 months of observation. Virologic effectiveness and safety were illustrated in a real world setting with<5% discontinuations due to ADRs and<2% due to virologic failure.

Table 1. Baseline characteristics; IQR: inter quartile range; *inclusion criteria age≥50y

	Overall (N=434, 100%)	E/C/F/TAF (n=151, 35%)	F/TAF + 3rd agent* (n=146, 34%)	R/F/TAF (n=137, 32%)
Male gender, n (%)	394 (91)	134 (89)	138 (95)	122 (89)
Age, years, median (IQR)	51 (40–58)	45 (36–54)	56 (53–61)	45 (35–52)
CDC stage C, n (%)	91 (21)	34 (23)	35 (24)	22 (16)
CD4 count, cells/µl, median (IQR)	624 (467–830)	641 (493–888)	568 (423–800)	660 (500–809)
HIV-RNA<50 cp/mL, n (%)	403 (95)	137 (93)	139 (97)	127 (95)
Most common INI-based previous antiretroviral regimen, n (%)	158 (36)	97 (64)	55 (38)	6 (4)
NNRTI-based	169 (39)	25 (17)	29 (20)	115 (84)
PI-based	83 (19)	25 (17)	45 (31)	13 (9)
Other	24 (6)	4 (3)	17 (12)	3 (2)

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Table 2. Documented reasons for discontinuation: *including switches to (other) F/TAF-based single tablet regimens (see table 3)

		Overall 109/ 434 (25)	E/C/F/TAF 27*/151 (18)	F/TAF + 3rd agent 46*/146 (32)	R/F/TAF 36*/ 137 (27)
Reasons for discontinuation n/N (%)	ADR	19 (4.4)	5 (3.3)	5 (3.4)	9 (6.6)
	Drug-drug-interaction	6 (1.4)	5 (3.3)	0 (0.0)	1 (0.7)
	Virologic failure	5 (1.2)	3 (2.0)	0 (0.0)	2 (1.5)
	Therapy simplification	16 (3.7)	0 (0.0)	16 (11.0)	0 (0.0)
	Patient decision/ withdrawal of consent	12 (2.8)	2 (1.3)	5 (3.4)	5 (3.6)
	Investigator decision	5 (1.2)	0 (0.0)	5 (3.4)	0 (0.0)
	Other/unknown	16 (3.7)	1 (0.7)	7 (4.8)	8 (5.8)
	Death	4 (0.9)	0 (0.0)	3 (2.1)	1 (0.7)
	Loss to follow-up	26 (6.0)	11 (7.3)	5 (3.4)	10 (7.3)

		Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
Patients with documentation of ART after study drug discontinuation, n		76	15	38	23
Most common regimens documented after study drug discontinuation, n (%)	D/C/F/TAF	20 (26)	0 (0)	19 (50)	1 (4)
	R/F/TDF	7 (9)	1 (7)	0 (0)	6 (26)
	DTG/ABC/3TC	7 (9)	3 (20)	1 (3)	3 (13)
	E/C/F/TAF	6 (8)	0 (0)	4 (11)	2 (9)
	other/not specified	36 (47)	11 (73)	14 (37)	11 (48)

D: darunavir; C: cobicistat; TDF: tenofovir DF; DTG: dolutegravir; ABC: abacavir; 3TC: lamivudine

Table 3. Post-study regimens in F/TAF study drug discontinuers

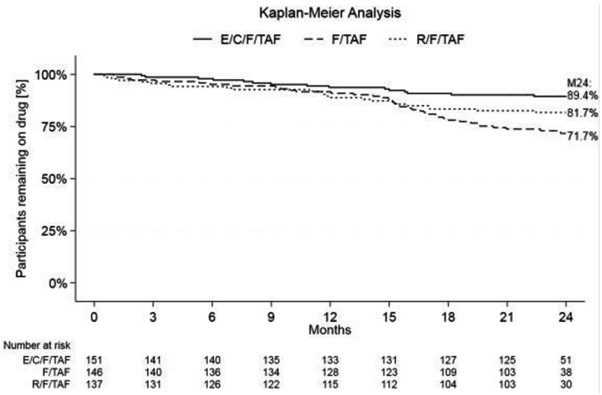


Figure 1. Drug persistence (CAVE: groups not comparable due to different inclusion criteria)

PE2/16

Effectiveness, safety and tolerability of bictegravir/ emtricitabine/tenofovir alafenamide (B/F/TAF) in HIV-1 infected adult patients in routine clinical practice – 6 months results of the BICSTaR cohort

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Purpose: In clinical studies, B/F/TAF is highly efficacious and well tolerated in both antiretroviral treatment (ART)-naïve (TN) and ART-experienced (TE) HIV-1-infected participants, with zero resistance. BICSTaR is the first cohort to evaluate the effectiveness, safety and tolerability of B/F/TAF in clinical practice.
Method: BICSTaR is an ongoing, non-interventional, prospective, multinational, cohort study planned to enroll at least 1400 adult participants. In this analysis, data from 20 German sites are presented. Outcomes included HIV-1 RNA (loss-to-follow-up/missing=excluded), drug-related (DR) adverse events (AEs) and persistence of the B/F/TAF regimen.
Results: A total of 223 HIV-1 infected participants (32 TN, 191 TE) initiated B/F/TAF and were followed-up for at least 6 months at time of data cut-off. Main reasons for starting B/F/TAF were "patient's wish" (53%, TN) and "simplification" (63%, TE). Comorbidities at baseline included neuropsychiatric disorders (23%), arterial hypertension (21%), hyperlipidemia (15.3%) and cardiovascular disorders (10%). Of those participants with available HIV-1 RNA data at month 6 (n=180), HIV-1 RNA was<50 copies/mL in 21/25 (84%) TN participants (24/25 [96%] < 200 copies/mL) and in 143/155 (92%) of TE participants (153/155 [99%] < 200 copies/mL). Median CD4 cell counts increased from 479 to 731 and from 695 to 752 cells/μL, respectively. Persistence with B/F/TAF was high (96% still on treatment) with 8 (4%; 1 TN and 7 TE) participants discontinuing B/F/TAF prior to month 6 (3 due to DRAEs). No discontinuations were due to renal or bone AEs. Overall, DRAEs and DR serious AEs were reported in 21 (10%) and 1 (0.4%) participants, respectively. Most common DRAEs were psychiatric, 7 (3%) and gastrointestinal disorders, 5 (2%).

Baseline characteristics by antiretroviral treatment status

	TN Participants N=32	TE Participants N=191
Male gender, n (%)	28 (88)	180 (94)
Age (years) Median (Q1, Q3)	38 (30, 45)	48 (39, 54)
Age≥50 years, n (%)	6 (19)	80 (42)
HIV-1 RNA $\log_{10}$cp/mL, Median (Q1, Q3)	4.8 (3.9, 5.2)	1.6 (1.3, 1.7)
HIV-1 RNA<50 cp/mL, n (%)	0	150 (88)
HIV-1 RNA>100,000 cp/mL, n (%)	12 (38)	1 (1)
CD4 count, cells/μL, Median (Q1, Q3)	479 (283, 607)	695 (463, 930)
CD4<200 cells/μL, n (%)	6 (20)	10 (6)
CDC Stage C (AIDS), n (%)	2 (6)	30 (16)

Conclusion: Consistent with randomized controlled trials, preliminary data from this observational cohort support the effectiveness, safety and tolerability of B/F/TAF in routine clinical practice, including in participants with comorbidities, and demonstrate high persistence through 6 months.

PE2/17

Short-term increase in Body Mass Index and systolic blood pressure elevation in treatment naïve persons starting INSTI-based antiretroviral therapy

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Purpose: Integrase strand transfer inhibitors (INSTI)-based ART has been associated to weight gain, but it remains unknown if this effect leads to higher overweight incidence or increases the risk of metabolic and cardiovascular disturbances. We aimed to explore the frequency of excessive weight gain in HIV+ treatment-Naïve patients starting INSTI-based regimens and to determine whether they are associated with changes in metabolic markers and blood pressure(BP).
Method: Medical records of treatment-Naïve persons starting ART at the HIV-clinic of University Hospital of Elche(Spain) between July-1991 and March-2018 were retrospectively reviewed. Standard procedures included measurements of weight, BP and comprehensive metabolic assessments at each visit. Data at baseline and post 48, 72, and 96 weeks of ART initiation were analyzed. We used Cox mixed-effects model to generate overweight predictions over time, adjusting for baseline characteristics. Generalized additive mixed models(GAMM) were used to relax the linearity assumptions and generate 95% confidence intervals(95% CI) in the multivariable adjust.
Results: Among 457 participants(median age 44.0 years, IQR=37.0–55.5; 108 females), 55(12.0%) and 402(88.0%) started ART with INSTI-based and non-INSTI-based regimens respectively. The baseline weight mean was 70.4 kg. 50% were enrolled with a BMI<25 kg/mt^2. The incidence of overweight after initiating ART was significantly greater in INSTI-based regimens: 14(35.9%) of 39 patients treated with INSTI vs 36(18.7%) of 192 treated with other ART regimens(HR 1.96; 95% CI, 1.06–3.62; p=0.032).

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Table 1. Factors Associated with the Development of Overweight post Antiretroviral Therapy (ART) initiation

Factor	Adjusted HR (95% CI)	*p-value*
INSTI-based ART	1.96 (1.60–3.62)	0.032
Baseline HIV-1 RNA>100000	1.15 (0.66–1.99)	0.620
Female	0.82 (0.46–1.45)	0.500
IDU	0.77 (0.40–1.48)	0.440
Baseline BMI	1.29 (1.22–1.36)	<0.001
Baseline CD4 + T cell count	0.97 (0.91–1.02)	0.300
Baseline CD4 + /CD8 + T cell ratio	1.16 (0.65–2.09)	0.800
Age	1.01 (0.99–1.04)	0.280

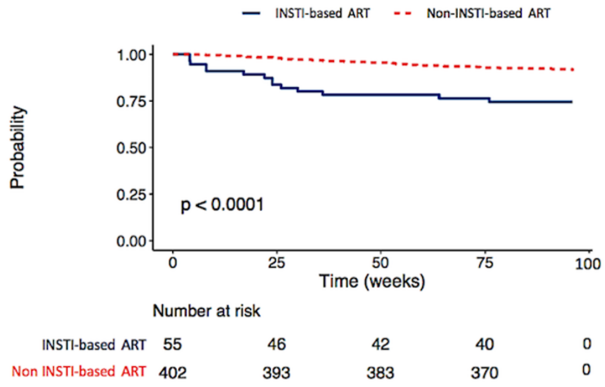


Figure 1. Overweight reached after antiretroviral therapy initiation among treatment groups

In contrast to other ART regimens, patients treated with INSTI showed a significant increase in systolic BP (SBP) (adjusted increase 6.74 mmHg; 95% CI, 1.35–12.13; p=0.014) that was weakly but significantly correlated with weight gain (Cor 0.13, 95% CI 0.10–0.12; p<0.0001).

Table 2. Multivariable Model for Factors Associated with Systolic Blood Pressure Elevation (SBP) at 48 weeks post ART Initiation

Factor	Estimated difference in SBP (95% CI)	*p-value*
INSTI-based ART	6.74 (1.35–12.13)	0.014
Baseline HIV-1 RNA>100000	6.13 (1.11–11.16)	0.016
Female	1.41 (−4.67 to 7.50)	0.647
History of Hypertension	−3.93 (−9.70 to 1.84)	0.180
History of Diabetes	−3.04 (−12.43 to 6.35)	0.523
IDU	−1.63 (−8.52 to 5.26)	0.640
Baseline BMI	2.50*	0.282
Baseline CD4 + T cell count	1.00*	0.591
Age	1.00*	0.014

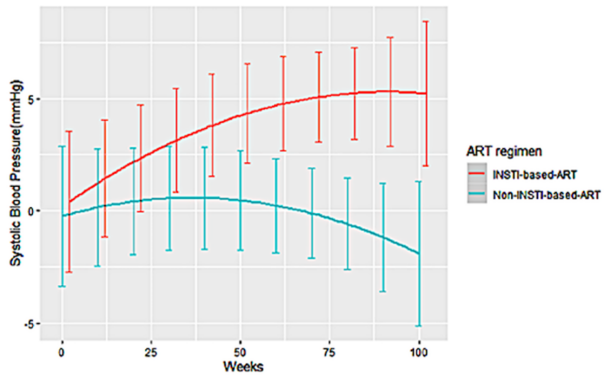


Figure 2. Predicted systolic blood pressure elevation among antiretroviral therapy regimens

We did not find differences among ART regimens in fasting blood glucose, lipid panel, and hepatic steatosis indexes.
Conclusion: INSTI-based ART was associated in the short-term with a greater risk of overweight and a modest elevation of SBP linked to weight gain.

PE2/18

Baseline characteristics in JUNGLE, a German observational cohort study of Juluca as 2-drug Regimen in virologically suppressed patients, compared to the phase-3 SWORD 1 & 2 study populations

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Purpose: Juluca, the combination of Dolutegravir (DTG) and Rilpivirine (RPV) was approved by the EMA in 2018 as the first single-tablet 2-drug regimen (2DR) for maintenance therapy in HIV-1 infected patients. The JUNGLE cohort will provide prospective real-world data regarding effectiveness and tolerability of using Juluca.
Methods: JUNGLE is an ongoing non-interventional, prospective, multi-center, German cohort study in virologically suppressed patients switched to DTG/RPV in accordance with the summary of product characteristics. Here we describe the characteristics of the study population and reasons for switch to DTG/RPV.
Results: By June 2019, 185 patients have been enrolled (90.3% men; median age 49 years; baseline characteristics see table 1). Patients had been on ART for a median time of 8 years prior to DTG/RPV (9.9% still on first-line ART, 42.9% with≥3 ART-changes); 86.1% of patients were switched from triple ART and 48.9% had been on a multi-tablet regimen. Comorbidities were common, among them hypertension (28.4%), depression (15.8%), lipid disorders (15.8%), chronic kidney disease (12.0%). Primary reasons for switch to DTG/RPV were side effects of previous ART (25.4%), switch to a single-tablet regimen (22.7%) and reduction in number of drugs (19.9%; table 2).
Conclusions: In the JUNGLE cohort, 86.1% of patients were on triple ART prior to switching to the 2DR Juluca. Main reasons for switch were side effects of previous ART, simplification to a single-tablet regimen and reduction in

Table 1. HIV related characteristics and ART history

Male, n (%)	n=185	167 (90.3)
Age, years (median, IQR)	n=185	49 (IQR 40–57)
Age≥50 years, n (%)	n=185	88 (47.6)
Time since HIV diagnosis, years (median, IQR*)	n=179	11 (5–16)
Time since start of first ART, years (median, IQR*)	n=162	8 (4–14)
Time on previous ART, years (median, IQR*)	n=166	2.6 (1.5–4.7)
CD4 T-cell count, cells/µL (median, IQR*)	n=175	714 (577–933)
History of AIDS (CDC C), n (%)	n=180	32 (17.8)

*IQR: inter quartile range; calculations based on observed data

Table 2. Primary reasons for switch to DTG/RPV

(N=181)	n (%)
Side effects of previous ART	46 (25.4)
Simplification to a single-tablet regimen	41 (22.7)
Reduction in number of drugs	36 (19.9)
Patient's preference	22 (12.2)
NRTI-free regimen	9 (5.0)
Potential/actual interactions	8 (4.4)
Pill size	1 (0.6)
Other	18 (9.9)
Calculations based on observed data	

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number of drugs. Compared to the SWORD 1 & 2 study population switched to DTG+RPV, the JUNGLE cohort is older in age (48% vs 29% >50y.), more extensively pre-treated (43% with≥3 ART-changes vs 100% on first- or second-line ART in SWORD studies, median pre-treatment time 8.0y. vs 4.3y.) and clinically more advanced in HIV disease (18% vs 11% with history of AIDS).

PE2/19

Examining the efficacy in clinical practice of the dual antiretroviral therapy regimen of boosted protease inhibitors with maraviroc

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Purpose: A focus on reducing long-term drug exposure while maintaining viral suppression has led to new strategies for treatment-experienced patients involving dual therapy. Maraviroc (MVC), a chemokine receptor 5 co-receptor antagonist, is licensed for use in treatment experienced HIV-1 positive patients. Boosted protease inhibitor (bPI) with MVC is not a recommended combination in guidelines. In the past, this option was chosen for selected patients with some declining to switch despite evidence. We set out to assess the outcomes of patients who have or are currently receiving this combination in our clinic.

Method: All patients prescribed a bPI with MVC until December 2018 were identified through our HIV database. Age, sex, and time on ART before/after switch were collected. A review of medical records determined reasons for switch off bPI/MVC where relevant.

Results: In total 114 patients (mean age 53 years (range 33–76), 80% male) had been prescribed a bPI/MVC. The median time on ART prior to bPI/MVC switch was 13 years. Patients stayed a median of 4 years on bPI/MVC; 63 (55%) patients were on MVC 300 mg dosing while 51(45%) were dosed at MVC 150 mg. At censure 69 (61%) remained on bPI/MVC, 30 (26%) had switched ART, 7 (6%) died, 7 transferred their care, and 1 was lost to follow up. Reasons for switching included hyperlipidaemia (n=6), lipodystrophy (n=2), rationalisation (n=6), drug interactions (n=5), potential toxicity (n=5), side effects (n=1), no documentation (n=1) and viral failure (n=5). Four of the five patients who failed therapy reported issues around adherence. Of patients who remained on bPI/MVC 97% (67/69) were virally suppressed (median duration 4.5 years).

Conclusion: We continue to proactively review patients on bPI/MVC and suggest contemporary alternatives but our data suggest that, if adherence is good, established patients may be reassured about the safety and efficacy of this approach.

PE2/20

Good efficacy but side effects including hypercholesterolemia and body weight gain after switching to dolutegravir plus booster protease inhibitor regimen among treatment experienced HIV-positive patients

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Purpose: In Taiwan, the regimen of antiretroviral (ARV) therapy was strictly regulated by CDC. The two-drug regimen (2-DR) with dolutegravir (DTG) and boosted protease inhibitor (bPI) was most used as a salvage therapy for treatment experienced HIV-positive patients. The efficacy and long-term adverse effects was unknown.

Method: Information on demographics and serial laboratory data were recorded retrospectively from 14 designated primary HIV care hospitals around Taiwan between September 2016 and June 2019.

Results: A total of 77 adult patients were enrolled with a mean age of 38.2 years (range 23.8 - 67.0 years) and 74 (96.1%) were male. Most patients (63/77, 81.8%) switched to 2-DR regimen due to multi-class drug resistance because of failure to first-line ARV in Taiwan. The common resistance-associated mutations included M184V (54.1%), K65R (52.5%), K103N (34.4%), Y181C (31.1%) and so on. Patients were followed up with median 374 days (28–812 days). The efficacy of DTG plus bPI was good that 93.0% (66/71) achieved viral suppression (plasma HIV RNA<40 copies/mL) at week 24 and 93.5% (43/46) maintained undetected viral load at week 48. The patients without viral suppression at week 48 included 2 patients with viral rebound due to drug interruption (one lost follow-up and the other was incarcerated) and 1 patient had persistent viremia due to poor drug compliance. After switching to study 2-DR, The mean level of cholesterol increased from 170.2 mg/dl to 196.1 mg/dl (p=0.003). Ten patients developed newly-onset dyslipidemia. In addition, patients gained 2.1 kg in average compared to the body weight before switch (p<0.001). One patient stopped study 2-DR due to recent HBV infection.

Conclusion: DTG plus bPI is efficacious for multi-class drug-resistant HIV-1-Infected patients. However, potential HBV infection and side effects including dyslipidemia and body weight gain should be concerned for the study 2-DR regimen.

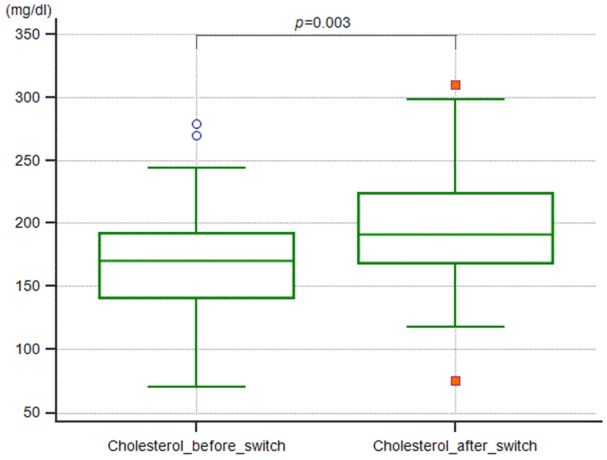


Figure 1. Increased level of cholesterol among HIV-positive patients switching to DTG plus bPI

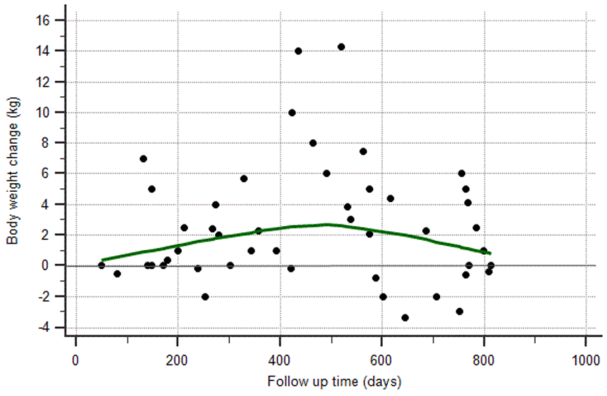


Figure 2. Body weight change among patients after switching to DTG plus bPI in the last follow-up time

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PE2/21

Rates of DTG/ABC/3TC discontinuation in a real-life setting: no surprises found in reported adverse events

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Purpose: Dolutegravir (DTG) is the most frequently used integrase inhibitor (INSTI) at our clinic. Since its widespread use, concerns grew about safety issues not clearly identified in randomized controlled trials (RCTs), namely neuropsychiatric adverse events (AE), neural tube defects in pregnancy and significant weight gain (WG).
We assessed the rates of discontinuation of the single tablet regimen (STR) of DTG + Abacavir + Lamivudine (DTG/ABC/3TC), the reasons for discontinuation and the factors associated with discontinuation.
Methods: A retrospective analysis was done of a cohort of patients starting DTG/ABC/3TC between September 2016 and June 2018. All patients had at least 52 weeks of follow-up. Primary endpoints were discontinuation and reasons for discontinuation of the STR. Treatment naïve and treatment experienced (TE) patients were included; in TE patients the reasons for switching to DTG/ABC/3TC were noted.
Results: 295 patients were identified, of which 25 were excluded from the analysis due to death, unrelated to therapy (n=10), HIV 2 infection (n=7) and transfer of care to another institution (n=8). 270 patients were included in the analysis: 33 (12.2%) were naïve and 237 (87.8%) were treatment experienced. The main reasons for TE patients to switch to DTG/ABC/3TC were simplification in 75%, virologic failure in 10.5% and AE from the previous regimen in 5%. Overall 40 patients discontinued DTG/ABC/3TC (14.8%). Of these, only 15 patients (5.5% from the total) discontinued due to AE; the second most common reason for discontinuation was being lost to follow-up (4.0%); other reasons were HBV infection and drug-drug interactions.
Conclusions: In our cohort of patients treated with DTG/ABC/3TC we observed 5.5% of discontinuations due to AE, which is higher than found in RCTs but similar to discontinuation rates described in real-life settings. The most commonly observed AE were neuropsychiatric (n=4) and WG (n=3). Some AE were unrelated to DTG.

PE2/22

Low baseline HIV viral loads with a history of PrEP use – how should these patients be managed?

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Purpose: Low baseline viral loads (VL) in newly diagnosed HIV patients, with a history of recent pre-exposure prophylaxis (PrEP) use, may present difficulties for rapid initiation of anti-retrovirals therapy (ART) due to concerns of viral drug resistance or failure of viral amplification at baseline. There is a lack of data on the optimal management for these patients and their outcomes. We have identified these cases from a single sexual health clinic in London and present the management of these cases.
Method: This is retrospective case review of newly diagnosed HIV patients with low baseline HIV VL (< 2000 copies/mL) and documented PrEP-use (within<6 months) between January 2017 - April 2019. VL threshold of<2000 copies/mL was selected due to the commonly used definition of 'viremic controllers'. Demographics, baseline investigations and initial management were recorded.
Results: Seven patients met the inclusion criteria; all were men-who-have-sex-with-men. Initial investigations and management are listed in Table 1. Prior to starting PrEP, two patients did not have a baseline HIV test, four patients did not have a baseline HIV test documented and one patient reported a baseline test elsewhere. Three patients, who initially started a protease inhibitor as the third ART agent, were switched to a integrase inhibitor. At three months post-ART initiation, five patients had an undetectable VL, one was lost-to-follow-up and one result was pending.
Conclusion: Newly diagnosed patients should have a careful PrEP history. This data shows successful VL suppression with integrase and protease inhibitors, alongside a dual nucleoside/nucleotide backbone, for six out of seven patients who started ART within 14 days of diagnosis.

PE2/23

Lamivudine-based maintenance 2-drugs regimens: an algorithm for the estimation of 2-years risk of virological failure in clinical practice

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Purpose: We developed a tool for estimating the 2-years risk of virological failure (VF) in patients switching to a maintenance regimen with lamivudine plus a boosted-protease inhibitor (bPI) or dolutegravir.
Method: From a multicentre Italian cohort of patients with undetectable HIV-RNA (according to the centre-specific threshold) and negative HBsAg-serostatus, starting lamivudine plus a bPI (darunavir, atazanavir or lopinavir) or dolutegravir, predictors of VF (i.e., a single HIV-RNA≥1000 cp/mL or 2 consecutive HIV-RNA≥50 cp/mL) at 2 years were analysed by Cox regression. The Cox-regression-based prediction scores were calculated based on variables independently associated with the outcome (as described by Sullivan et al., Statist. Med. 2004; 23:1631–1660). The discriminatory power of the point total was expressed as the area under the receiver-operator characteristic curve (ROC-AUC).
Results: The cohort included 703 patients starting lamivudine plus boosted-atazanavir (17.3%), boosted-darunavir (37.5%), boosted-lopinavir (4.1%),

Table 1. Demographics, investigations and management

ID	Age (years)	CD4 (c/ul)	VL (copies/mL)	Viral resistance test (VRT)	Time to clinic review (days)	Time to ART (days)	VRT available at time of starting ART	Last negative HIV test (days)	ART
1	32	281	603	Nil resistance	10	10	No	33	TDF, FTC, DRV/r
2	33	959	<20	Unable to amplify	11	11	Yes	76	TDF, FTC, DRV/c
3	34	1484	523	M184V	8	9	No	135	TDF, FTC, DRV/c
4	42	412	33	Unable to amplify	8	8	No	120	TDF, FTC, DRV/c
5	49	623	298	Nil resistance	1	1	No	248	TDF, FTC, DRV/c
6	54	666	40	Unable to amplify	28	88	Yes	538	ABC, 3TC, DTG
7	56	1310	24	Unable to amplify	10	10	Yes	63	TDF, FTC, DRV/c

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dolutegravir (41.2%). Characteristics of study population are summarized in table 1. Over 2 years of median follow-up, 58 VFs occurred. Prediction scores were based on the following variables (reported with hazard ratios for VF): non-B viral subtype (vs B, aHR 3.06, p=0.002), CD4 count nadir (per 100 cells/mm^3 more, aHR 0.83, p=0.063), residual HIV-RNA (per 1 cp/mL more, aHR 1.03, p=0.002), years since HIV diagnosis (per 1 year more, aHR 1.08, p<0.001) and duration of viral suppression before switch (per 1 month more, aHR 0.99, p=0.011). A point total of≤0 and≥5 reflected a risk of VF of≤5% and≥20%, respectively. The model showed moderate discrimination power: ROC-AUC was 0.69 (95% CI 0.62–0.76; p<0.001).

Conclusion: Some viro-immunological characteristics of patients switching to a lamivudine-based maintenance dual-therapy can be incorporated in a useful algorithm to identify subjects at higher risk of VF.

Characteristics of study population at baseline (N=703)

Variables	N (% or IQR)
Age	50 (42–56)
Male sex	493 (70.1)
Risk factor for HIV: - Heterosexual - MSM - IDU - Other	287 (40.8) 271 (38.5) 120 (17.1) 25 (3.6)
Years since HIV diagnosis: - 0–5 - >5–10 - >10–15 - >15–20 - >20	180 (25.6) 158 (22.5) 91 (12.9) 90 (12.8) 184 (26.2)
Zenith HIV-RNA (log10 cp/mL)	5.15 (4.68–5.66)
Nadir CD4 count (cells/mmc): - ≤ 100 - 101–200 - 201–350 - >350	167 (23.8) 134 (19.1) 267 (38.0) 135 (19.1)
Residual HIV-RNA at baseline (copies/mL): - 0–10 - 11–20 - 21–30 - 31–40	515 (73.3) 62 (8.8) 36 (5.1) 90 (12.8)
Months of viral suppression: - 0–48 - >48–96 - >96–144 - >144	531 (75.6) 104 (14.8) 55 (7.8) 13 (1.8)
Non-B viral subtype	115 (16.4)

PE2/24

Adding raltegravir to a bPI failing regimen was not associated with higher virologic suppression

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Purpose: After a failure with a NNRTI based regimen, it was previous shown that boosted protease inhibitor (bPI) combined with recycling N(t)RTI is comparable to bPI associated with INSTI in their ability to attain virologic suppression. However, adding the INSTI after a short period of N(t)RTI and bPI might evidence those patients harder to treat and direct this strategy only for them.

Method: This is a prospective, single center, single arm trial, enrolling HIV-1 infected patients who presented virologic failure to a NNRTI based regimen. Eligible patients presented at least 1 major resistance associated mutation (RAM) (IAS 2019). Visits were scheduled at 12, 24, 36 and 48 weeks after baseline. On week 24, patients with virologic failure had a resistance test. If no new RAM was detected, raltegravir was added to patient's regimen and response was analyzed at 48 weeks of follow up. VL, CD4 + , safety analysis and "detuned" HIV-1 EIA were performed in all visits.

Results: We studied 31 patients. From them, 24 (77.42%) presented virologic success (VL<40 cps/mL) at week 24. No emergency of RAM was detected in the 7 failing cases. Three patients were able to add raltegravir to their regimen. At 48 weeks, 21 (67.74%) patients sustained VL<40 cps/mL. Of 10 virologic failures, only one case had a new RAM (10I, 54V, 82F). Patients who previously failed on AZT (p=0.029) and were on ARV for longer period (p=0.01) had higher virologic control on 24 weeks. On the other side, the presence of 70E on baseline resistance test (p=0.045) and use of raltegravir were associated with lower virologic response (p=0.036) on 24 and 48 weeks, respectively.

Conclusion: Adding raltegravir to a second line failing regimen, even in the absence of RAM, was not associated with a better virologic outcome.

Table1: Sociodemographic and baseline data

Male (%)	21 (67,74)
HIV diagnosis in years (median[SD])	8 (5,30)
Age (median[SD])	22 (28-55)
Nadir CD4 cell count (median[IQR]) cel/mm^3	181 (12-615)
HIV – subtype (%)	
B	17 (54,84)
Non-B	14 (45,16)
C	10 (32,25)
F	2 (6,45)
BC	1 (3,22)
BF	1 (3,22)
Time on ARV before enrollment, in years (median[SD])	2 (3)
EFV-based regimen on failure (%)	28 (90,32)
Backbone at 1st failure (%)	
AZT + 3TC	21 (67,74)
TDF + 3TC	5 (16,12)
ddI + TDF	2 (6,45)
AZT + TDF + 3TC	1 (3,23)
D4T + 3TC	1 (3,23)
AZT + 3TC + ddI	1 (3,23)
CD4 cell count (median[IQR]) cel/mm^3	264 (11-750)
LPV/r on new regimen (%)	28 (90,32)
Backbone at second line regimen (%)	
TDF + 3TC	28 (90,32%)
AZT + 3TC	3 (9,68%)

PE2/25

Neuropsychiatric tolerability of bictegravir combined with FTC/TAF in clinical practice

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Purpose: Neuropsychiatric AEs (NPAEs) leading to dolutegravir (DTG) discontinuation were seen more frequently in real-world use than in randomized clinical trials (RCTs). The recently approved fixed dose combination bictegravir plus FTC and TAF (BIC/F/TAF) has shown comparable NPAE rates but some favourable patient-reported outcomes in RCTs. We were interested in its neuropsychiatric tolerability in routine clinical practice.

Methods: All patients starting BIC/F/TAF from June 2018 in a single center (two subcenters) were followed retrospectively. Discontinuation rates due to any AEs and NPAEs were compared with those of patients initiating DTG-based regimens.

Results: As of May 2019, a total of 943 patients (852 males, 76 females, 15 TGD) initiated BIC/F/TAF outside RCTs. After a median follow-up of 6.2 months, 50 (5.3 %) and 31 (3.3 %) patients had discontinued BIC/F/TAF due to any AEs or to NPAEs, respectively. In multivariate analysis, a pre-existing depression and subcenter remained predictive for NPAEs, but not age, gender, ethnicity, or prior DTG-related AEs. Compared to 1,043 patients treated with DTG-based regimens, the estimated NPAE-related discontinuation rate with BIC/F/TAF was comparable during the first 6 months (p=0.31). Cross-intolerance was low, and only 5/55 patients with prior DTG intolerability had to discontinue BIC/F/TAF due to NPAEs.

Conclusion: Short-term tolerability of BIC/F/TAF was comparable to DTG-containing regimens. As seen with DTG, discontinuation rates were higher than in RCT. A pre-existing depression but also physician's awareness may have an impact on tolerability and continuation of BIC/F/TAF. In contrast, prior intolerability of DTG was of limited predictive value.

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PE2/26

Real-world clinical outcomes of patients switched from complex multi-tablet regimens to TAF-based single-tablet regimens plus a boosted protease inhibitor

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Purpose: Multi-tablet regimens (MTRs) used in treatment-experienced patients are associated with increased adverse events (AEs) and non-adherence. Single tablet regimens (STRs) plus boosted protease inhibitors (PIs) are a promising treatment option for MTR-treated patients seeking simplification; however, real-world data is needed to validate this therapeutic strategy.
Method: This retrospective analysis evaluated all records from HIV-infected patients seen at the Orlando Immunology Center from 8/2012 to 12/2017 who were switched from BID regimens or regimens containing≥3 pills daily to elvitegravir/cobicistat/emtricitabine/tenofovir-alafenamide (E/C/F/TAF) plus darunavir (DRV) or rilpivirine/emtricitabine/tenofovir-alafenamide (RPV/F/TAF) plus DRV boosted with Norvir or cobicistat. Eligible patients had baseline HIV-1 RNA<50 copies/mL and at least two HIV-1 RNA measurements after switch. The primary endpoint was virologic rebound (HIV-1 RNA≥50 copies/mL) at week 48. Adherence, AEs and laboratory parameters were analyzed throughout the study.
Results: Fifty-nine patients met inclusion criteria, 54 (92%) were switched to E/C/F/TAF+ DRV and 5 (8%) were switched to RPV/F/TAF plus boosted DRV. The median age (range) was 53 (27–69) years, median baseline CD4$^+$ count (range) was 510 (87–1798) cells/mm^3, and the median number of pills taken daily (range) was 5 (3–9). At Week 48, of 41 subjects with virologic data within window, 2 (5%) had HIV-1 RNA≥50 copies/mL (Figure 1). Two patients treated with E/C/F/TAF plus DRV experienced confirmed virologic rebound during the study period however there was no evidence of treatment-emergent resistance. Median LDL cholesterol significantly increased from baseline to Week 48 (+20 mg/dL, 95% confidence interval [9, 31.8]). Treatment-related AEs occurred in 3/59 (5%) patients (all Grade 2) leading to 3/59 (5%) discontinuations.
Conclusion: In this "real-world" cohort of MTR-treated patients, switching to a TAF-based STR plus boosted PI maintained virologic control in 97% of patients and was well-tolerated, supporting potential use of this strategy for regimen simplification.

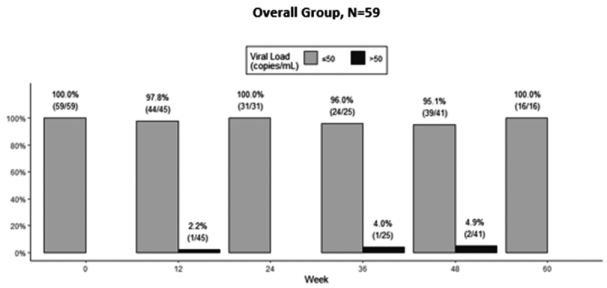


Figure 1. Virologic Outcomes through Week 60

PE2/27

Dual therapy with fixed dose combination of darunavir/ritonavir plus raltegravir in HIV-infected patients in Argentina

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Purpose: The use of dual therapy (DT) is an alternative to standard antiretroviral therapy (ART) to avoid toxicity, improve adherence or for failing regimens. There are generic fixed-dose combinations (FDC) of DRV/r 800/100 and 600/100 mg available in Argentina recommended (with NRTI backbone) for either naive or experienced patients in local guidelines. However, experience with these FDC in DT remains limited in clinical practice. We aimed to describe reasons for prescription, efficacy and tolerability of FDC DRV/r + raltegravir (RAL) 400 mg BID in real life patients.
Method: Retrospective analysis of electronic medical records of HIV-infected patients under FDC DRV/r+RAL in an HIV clinic in Argentina (period 2014–2018). Individuals were classified as:
1) "switch group" (SG): undetectable viral load (VL) with any toxicity/co-morbidity; and
2) virologic group (VG): detectable viremia and infection by multidrug-resistant HIV.

Results: Of 7380 patients on ART, 116 (1.5%) received FDC DRV/r+RAL, being 58% in SG and 42% in VG. Forty percent received DRV/r 600/100 mg dose and the rest 800/100 mg. The median (IQR) of age and CD4 T-cell count were: 52 (42–58) years, and 373 cell/μL (202–642). Ninety-eight percent were experienced in ART with a median of 3 (IQR 2–5) prior treatments; 65% were CDC category C. Main reasons for switch (SG) were renal (57%), cardiovascular (54%) and bone (14%) comorbidities. Median exposure to DRV/r+RAL was 18 months. Among patients in SG, 98% and 96% had undetectable VL at 6 and 12 months. Among those in the VG, 89% and 87% had undetectable VL at 6 and 12 months. No patient required suspension due to toxicity or intolerance.
Conclusion: In this cohort of mostly experienced HIV-infected patients, FDC DRV/r+RAL was effective and safe. Such therapy may be considered an option for patients with comorbid conditions and/or with multidrug-resistant HIV in our setting.

PE2/28

Detectability of HIV residual viremia despite therapy is highly associated with treatment with protease inhibitor

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Purpose: To better understand the complex link between clinical and treatment features and HIV persistence despite therapy.
Method: 11045 samples (from June 2009 to July 2018) from 1160 patients under combination antiretroviral therapy (cART) with unquantifiable viral load (VL, limit of quantification: 20 copies/mL) were categorized as detectable or undetectable depending on the detection of a PCR signal using a commercially-available assay. Generalized estimating equations regression was used to model viral load detectability and to assess determinants of residual viremia (RV: VL detected below 20 copies/mL) despite therapy.
Results: Low CD4$^+$ T cell nadir and high VL zenith were associated with a higher probability to have a detectable viremia under cART. Conversely, the probability to have a detectable viral load below 20 copies/mL decreased with time under therapy. Regarding therapy, protease inhibitor (PI)-based treatment was also associated with a statistically higher probability of detectable RV compared to non-nucleoside transcriptase inhibitor and integrase inhibitor.
Conclusion: PI-based treatment regimen is highly associated with an increased frequency of RV, supporting the previous evidence suggesting that PI-based cART regimens could favor an ongoing viral replication in some patients. This phenomenon could support the chronic activation of the immune system involved in the excess of aging-associated events.

Table 1. Impact of patients' characteristics on the probability to detect HIV RNA below 20 copies/ml (N=10227 samples)

	Coef. ± SE	p-value
Intercept	-1.4 ± 0.24	-
Age at sampling (per 10 years)	-0.029 ± 0.028	0.29
Gender (Ref=female)		
Male	0.12 ± 0.075	0.12
Ethnicity (Ref=caucasian)		
African	0.15 ± 0.077	0.053
Others	0.12 ± 0.18	0.51
Delay between HIV diagnosis and first treatment (per 10 days)	0.00023 ± 0.0003	0.36
CD4 T cell nadir at sampling (per 100 copies/mm³)	**-0.037 ± 0.018**	**0.038**
Treatment duration (per 10 days)	**-0.0022 ± 0.0002**	**<0.0001**
VL zenith at sampling (Log10 of copies/mm³)	**0.20 ± 0.041**	**<0.0001**

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Table 2. Effect of treatment regimens on the probability to detect HIV RNA below 20 copies/ml (N=10438)

A

	Coef.±SE	p-value	OR (95%CI)
Intercept	-1.2 ± 0.20	-	
CD4 T cell nadir at sampling (per 100 copies/mm³)	-0.028 ± 0.017	0.11	
Treatment duration (per 10 days)	-0.0022 ± 0.0002	<0.0001	
VL zenith at sampling (Log10 of copies/mm³)	0.18 ± 0.039	<0.0001	
Treatment regimen (Ref=2 NRTI, 1 PI)			
2 NRTI, 1 INI	**-0.23 ± 0.061**	**0.0002**	**0.79 (0.70 – 0.90)**
2 NRTI, 1 NNRTI	**-0.16 ± 0.066**	**0.017**	**0.86 (0.75 – 0.97)**

B

	Coef.±SE	p-value	OR (95%CI)
Intercept	-1.4 ± 0.21	-	
CD4 T cell nadir at sampling (per 100 copies/mm³)	-0.028 ± 0.017	0.11	
Treatment duration (per 10 days)	-0.0022 ± 0.0002	<0.0001	
VL zenith at sampling (Log10 of copies/mm³)	0.18 ± 0.039	<0.0001	
Treatment regimen (Ref=2 NRTI, 1 INI)			
2 NRTI, 1 NNRTI	0.074 ± 0.061	0.23	
2 NRTI, 1 PI	**0.23 ± 0.061**	**0.0002**	**1.3 (1.1 – 1.4)**

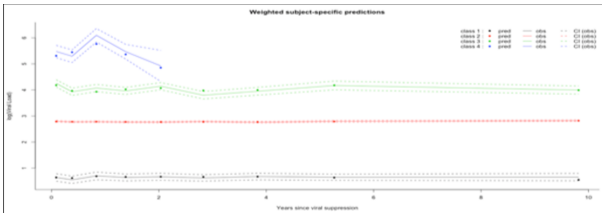
PE2/29

Prediction of virological failure in patients with low level HIV-1 viremia using a joint latent class model

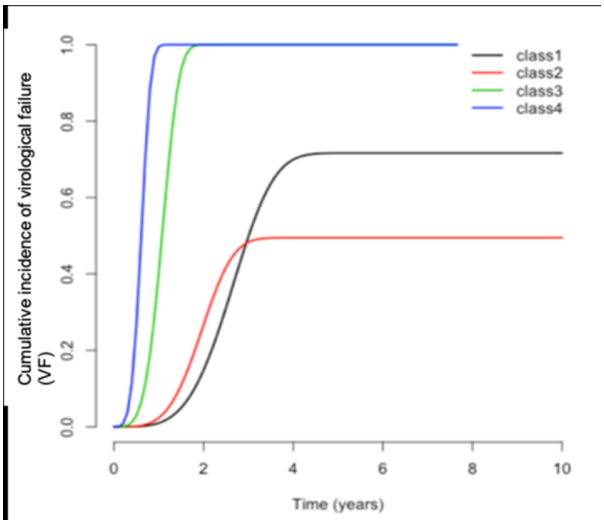
E Bernal[1], A Muñoz[1], A Alcaraz[1], MJ Alcaraz[1], S Valero[1], P Viciana[2], L García-Fraile[3], J Muñoz Sanchez[4], JA Pineda[5], MJ Galindo[6], F Gutierrez[7] and CoRIS

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Purpose: To identify HIV infected patients at risk of virological failure (VF) by generating a dynamic predictive model that takes into account their viral loads (VL) trajectories.
Method: A joint latent class and competing risk model investigating the impact of plasma VL time-trajectories after viral suppression on VF was developed. We analyzed data from the cohort of the Spanish AIDS Research Network (CoRIS) from January 2004 to 2017. Eligible patients were those who achieved plasma VL<50 copies/mL within 3–9 months after ART initiation. The capacity of the model to calculate individual predicted probabilities of VF over time was evaluated in 6.441 independent patients. The model classified the patients in latent classes with significantly different VL time profiles and different VF(2 consecutives HIV VL≥200 or 1 VL≥1000 copies/mL). Death was considered as a competitive risk. The LCMM-packages in R version 3.1.1. software were used.
Results: Four latent classes according to trajectories of viral load and cumulative incidence of VF were identified. Class 1 (4.65% of the sample) and 2 (86.58% of the sample) with mean VL time-trajectories<50 copies/mL were associated with a very low risk of VF (1% and 2.8%, resp.), whereas class 3 (4.84% of the sample) and class 4 (3.91% of the sample) with mean VL time-trajectories 54 copies/mL and 150 copies/mL resp., were strongly associated with VF (96.2% and 98.8%, resp.).
Injecting drug users, no or compulsory education, country of origin other than Spain, AIDS-diagnosis, ART regimen including 2NRTI+1PI/booster, CD4 cell count<200 cell/ul, basal HIV-1 VL≥100.000 copies/mL and HCV coinfection were higher in high-risk compared to low-risk classes (p<0.001).
The model had excellent dynamic predictive accuracy.
Conclusions: We provide an excellent dynamic prognostic tool for individual predictions in the short term, which allows us to anticipate viral failure in patients with low level HIV-1 viremia



Weighed subject-specific predictions from the final joint latent-class mixed model



Class-specific cumulative incidence of virological failurex

PE2/30

Comparing effectiveness and tolerability of emtricitabine/tenofovir alafenamide (F/TAF) with emtricitabine/tenofovir disoproxil fumarate (F/TDF) in HIV-1 infected adult patients in routine clinical practice: a cross cohort analysis

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Purpose: The aim of this cross-cohort analysis was to compare TDF- and TAF-based regimens in clinical routine care from three observational studies (TAFNES, TARANIS and STRIKE). Regimens included elvitegravir/cobicistat/F/TAF, rilpivirine/F/TAF, F/TAF + 3rd agent, elvitegravir/cobicistat/F/TDF efavirenz/F/TDF and rilpivirine/F/TDF.
Method: Individual patient-level data were pooled and month-12 (M12) outcomes of F/TDF- and F/TAF-based regimens were evaluated in both antiretroviral treatment (ART)-experienced (TE) and ART-naïve (TN) HIV-1 infected adults. Outcomes included ART persistence, virologic effectiveness, and drug-related adverse events (AEs). Multivariate logistic regression analyses [MLRA] (persistence, virologic suppression) and multivariate Poisson regression analyses [MPRA] (number of drug-related AEs) for F/TAF versus F/TDF were conducted; all were adjusted for baseline characteristics (age, sex, TN/TE status, baseline HIV-1 RNA, CDC stage, CD4).

Baseline Characteristics by Treatment (1)

	F/TDF TN=280	F/TDF TE=546	F/TAF TN=357	F/TAF TE=902
Sex, Male, n (%)	251 (89.6)	487 (89.2)	334 (93.6)	750 (83.1)
Age (yrs), Median (IQR)	38 (30–44)	41 (34–48)	36 (30–47)	50 (40–56)
Age≥50 yrs, n (%)	24 (8.6)	103 (18.9)	52 (14.6)	441 (48.9)
HIV-1 RNA log_{10} cp/mL, Median (IQR)	4.5 (4.1–4.9)	<LOQ	4.5 (3.9–5.1)	<LOQ
HIV-1 RNA<50 cp/mL, n (%)	1 (0.4)	422 (77.3)	4 (1.1)	840 (93.1)

cp: copies; IQR: Interquartile range; LOQ: limit of quantitation (median and IQR below the level of quantitation)

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Results: A total of 826 HIV-infected patients received F/TDF- and 1,259 patients received F/TAF-based regimens for up to 12 months (or discontinued before) at the time of data cut-off. Persistence was high at M12 (F/TDF: 84%, for both TN and TE, F/TAF: 88%, TN 85% and TE 89%), with a significantly lower likelihood of discontinuing F/TAF-based regimens (MLRA: odds ratio (OR) of 0.77 (95% confidence interval [CI] 0.59–0.99, p-value 0.046). No difference was observed in the likelihood of being virologically suppressed at M12 (MLRA: p-value 0.3). Significantly fewer F/TAF patients (8%) experienced at least one drug-related AE than F/TDF patients (14%) (MPRA: incidence rate ratio [IRR] 0.68 [95% CI 0.55–0.83, p-value 0.0002]).

Baseline Characteristics by Treatment (2)

	F/TDF TN=280	F/TDF TE=546	F/TAF TN=357	F/TAF TE=902
CD4 count, cells/μL, Median (IQR)	361 (266–457)	516 (360–696)	449 (255–614)	652 (470–844)
CDC Stage C (AIDS), n (%)	11 (3.9)	94 (17.2)	29 (8.1)	163 (18.1)
CD4<200 cells/μL and/or CDC Stage C1, C2 or C3	39 (13.9)	_	71 (19.9)	_
CD4<350 cells/μL and/or CDC Stage C2 or C3	153 (54.6)	_	136 (38.1)	_

IQR: interquartile range; CDC: Centers for Disease Control and Prevention

Conclusion: M12 data pooled from these observational cohort studies support the effectiveness of F/TDF and F/TAF-based regimens in routine clinical practice. F/TAF-based regimens were associated with significantly greater persistence and a more favorable safety profile than F/TDF.

PE2/31

Effectiveness of Dolutegravir-based antiretroviral therapy in a real-world setting in a Belgian cohort of 4101 HIV patients

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Purpose: To evaluate the effectiveness, durability, and tolerability of Dolutegravir (DTG)-based combined antiretroviral therapy (cART) in HIV patients in a 'real world setting'.

Method: A retrospective, observational, multi-center cohort study across Belgium. Inclusion criteria: HIV-1 patients≥18 years of age having received≥1 dose of DTG between April 1, 2014 and December 1, 2017. Primary endpoint was virologic response to DTG-based cART (HIV-1 viral load (VL)<50 copies/mL) using on-treatment analysis. Secondary endpoints included (i) durability of treatment (Kaplan-Meier survival analysis), (ii) immunological response, (iii) rates and reasons for DTG discontinuation; and (iv) change in weight.

Results: 4,101 patients were included from 6 centers. Baseline characteristics are shown on Table 1; of note 33% were female and 69% had an undetectable HIV-1 VL at DTG initiation. Through 96 weeks, 96% of study participants were virologically suppressed (Table 2), survival probability estimate of experiencing loss of virologic suppression (2 consecutive HIV-1 VL measurements of≥200 copies/mL after initial virologic suppression) was 7%, and mean increase in $CD4^+$ was 99 cells/μL. 785 patients (19.1%) discontinued DTG (Figure 1). The most frequent reason for discontinuation (Table 3) was an adverse drug reaction (ADR; 9.6%) with neuropsychiatric (NP) toxicity being the most prevalent (5.2%). Overall, the mean on-treatment weight gain was 2.01 kg at week 96, with larger weight gains observed in women (2.55 kg; p=0.036), sub-Saharan African patients (2.61 kg; p=0.006), cART-naïve patients (3.83 kg; p=0.0003), and patients with $CD4^+$ < 200 cells/μL at DTG initiation (6.3 kg; p<0.0001).

Conclusion: This large 'real-world study' confirms the high efficacy and tolerability of DTG. ADR-induced and NP toxicity-induced discontinuations were rare, albeit slightly higher than in clinical trials. Some sub-groups experienced statistically significant weight gains, however the clinical relevance of this finding remains to be evaluated.

Table 1. Baseline characteristics of the study population.

		Male	Female	Total
Number of participants (%)		2,758 (67.3)	1,343 (32.7)	4,101
Age (years)	Median	46.7	44.8	46.1
	IQR	37.4 – 54.3	37 – 52.6	37.2 – 53.8
Ethnicity, n (%)	Caucasian	2,065 (50.3)	302 (7.4)	2,367 (57.7)
	Sub-Saharan African	446 (10.9)	944 (23)	1,390 (33.9)
	Other	171 (4.1)	76 (1.9)	247 (6)
	Unknown	76 (1.9)	21 (0.5)	97 (2.4)
Weight (kg)	Median (IQR)	75 (66 – 84)	72 (61 – 81)	73.5 (64 – 83)
Mode of HIV acquisition, n (%)	Heterosexual	727 (17.8)	1,168 (28.5)	1,895 (46.3)
	Homosexual/Bisexual	1,782 (43.4)	20 (0.5)	1,802 (43.9)
	IVDU	47 (1.1)	16 (0.4)	63 (1.5)
	Transfusion related	19 (0.5)	20 (0.5)	39 (1)
	Vertical	26 (0.6)	33 (0.8)	59 (1.4)
	Other/Unknown	157 (3.8)	86 (2.1)	243 (5.9)
HIV treatment status, n (%)	Treatment-naïve	660 (16.1)	168 (4.1)	828 (20.2)
	Treatment-experienced	1,907 (46.5)	1,031 (25.1)	2,938 (71.6)
	HTE	191 (4.7)	144 (3.5)	335 (8.2)
HIV-1 viral load (copies/mL), (%)	<50	67.8	70.2	68.6
	≥50	32.2	29.8	31.4
Mean $CD4^+$ T-cell count (cells/μL), n (%)	N available (missing)	2,204 (554)	1,083 (260)	3,287 (814)
	≥500	1,266 (38.5)	620 (18.9)	1,886 (57.4)
	350-499	487 (14.8)	203 (6.2)	690 (21)
	200-349	279 (8.5)	123 (3.7)	402 (12.2)
	<200	172 (5.2)	137 (4.2)	309 (9.4)
Prior AIDS defining illness, n (%)	Yes	519 (12.7)	328 (8)	847 (20.7)
	No	2,211 (53.9)	1,010 (24.6)	3,221 (78.5)
	Unknown	28 (0.7)	5 (0.1)	33 (0.8)
Concomitant backbone, n (%)	ABC/3TC	1627 (39.7)	794 (19.3)	2421 (59)
	TDF/FTC	496 (12.1)	204 (5)	700 (17.1)
	TAF/FTC	107 (2.6)	55 (1.3)	162 (3.9)
	Other NRTI	322 (7.9)	171 (4.2)	493 (12.1)
	No NRTI	206 (5)	119 (2.9)	325 (7.9)

IQR, interquartile range; IVDU, intravenous drug user; HTE, highly treatment experienced; ABC, abacavir; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate; FTC, emtricitabine; TAF, tenofovir alafenamide; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor.

Table 2. Proportion of participants (%) with virologic suppression (HIV-1 VL<50 copies/mL). MSM, men who have sex with men; SSA, sub-Saharan African

	Week 24	Week 48	Week 96
All study participants	93	94	96
Men	93	94	97
Women	93	94	94
MSM	94	95	98
SSA patients	93	94	93
Treatment-naïve	90	93	97
Treatment-experienced	94	94	96
CD4 + T-cell count≥350 cells/μL	94	96	97
CD4 + T-cell count<350 cells/μL	85	90	93

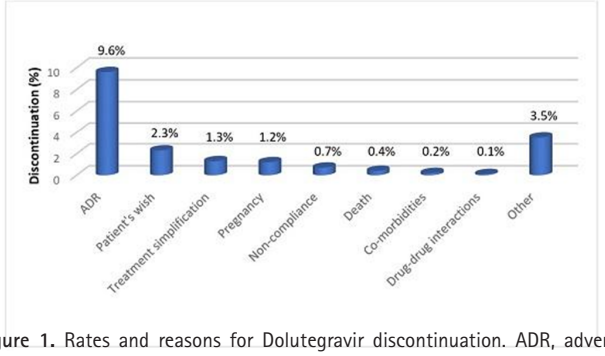


Figure 1. Rates and reasons for Dolutegravir discontinuation. ADR, adverse drug reaction.

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Table 3. Adverse drug reactions leading to Dolutegravir discontinuation.

	N	%
Neuropsychiatric toxicity	215	5.2
Gastrointestinal side effects	56	1.4
Hypersensitivity reaction	22	0.5
Abnormal fat redistribution	10	0.2
Liver toxicity	10	0.2
Renal toxicity	7	0.2
Pancreas/Endocrine toxicity	4	0.1
Hematological toxicity	1	0.02
Other	68	1.7

PE2/32

Characterizations of weight gain following antiretroviral regimen initiation in treatment-naive individuals living with HIV

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Purpose: Antiretroviral therapy (ART) regimens may be associated with weight gain. We described weight gain continuously or at various thresholds (≥3 kg, ≥5 kg, or≥5% increase from baseline) in ART-naïve people living with HIV (PLWH) initiating common core agents.

Method: ART-naïve adults initiating dolutegravir (DTG), elvitegravir/cobicistat (EVG/c), raltegravir (RAL), rilpivirine (RPV), or boosted darunavir (bDRV) for the first time between 01AUG2013 and 31DEC2017 were identified in the OPERA® cohort. Changes in weight were assessed at 6, 12, and 24 months following regimen initiation by mean change in weight, mean change in BMI, or an increase in BMI category (underweight: BMI<18.5, normal: 18.5–24.9, overweight: 25.0–29.9, obese: ≥30). Weight gain was categorized as weight increase≥3 kg, ≥5 kg, or≥5% from baseline.

Results: Among 6246 ART-naïve PLWH, demographics and weight by group varied significantly at baseline (Table 1). At 6, 12, and 24 months, mean increases in weight showed more variability than mean increases in BMI, patterns were similar (Table 2). Of PLWH with normal or overweight BMI at baseline, 15% to 33% increased by at least one BMI category at 12 months after regimen initiation. Of underweight PLWH at baseline, the majority increased to a normal BMI at 12 months (Figure 1). Obese PLWH at baseline could not increase category, by definition. Weight gain varied across thresholds: ≥3 kg (37% to 53%), ≥5 kg (23% to 41%), ≥5% (30% to 49%; Figure 2).

Conclusion: While the proportion of PLWH experiencing weight gain across groups and definitions was substantial, mean increases were relatively small across regimens over up to 24 months of follow-up; not taking into consideration baseline differences or restoration of healthy body weight in sicker patients. More research is needed to identify clinically relevant weight gain thresholds and improve the interpretability of weight gain studies.

Table 1. Baseline demographic and clinical characteristics (N=6246)

	DTG (N=2118), n (%)	EVG/c (N=2665), n (%)	RAL (N=116), n (%)	RPV (N=757), n (%)	bDRV (N=590), n (%)
Age≥50 years	237 (11.2)	287 (10.8)	40 (34.5)*	57 (7.5)*	81 (13.7)*
Female	245 (11.6)	285 (10.7)	36 (31.0)*	131 (17.3)*	99 (16.8)*
Black non-Hispanic	881 (41.6)	1225 (46.0)*	60 (51.7)*	406 (53.6)*	321 (54.4)*
Hypertension	240 (11.3)	300 (11.3)	28 (24.1)*	115 (15.2)*	82 (13.9)
Endocrine disorders	239 (11.3)	258 (9.7)	22 (19.0)*	44 (7.5)*	92 (12.2)
Meds associated w/ weight gain	228 (10.8)	245 (9.2)	26 (22.4)*	90 (11.9)	87 (14.7)*
Overweight (BMI 25–29.9)	640 (30.2)	789 (29.6)	40 (34.5)	219 (28.9)	168 (28.5)
Obese (BMI≥30)	387 (18.3)	428 (16.1)	27 (23.3)	196 (28.9)*	103 (17.5)

*Comparison to DTG, p-value<0.05

Table 2. Mean change in weight (kg) and BMI (kg/m^2) with 95% confidence intervals from baseline to 6, 12, and 24 months after core agent initiation

	DTG	EVG/c	RAL	RPV	bDRV
Mean change in weight from baseline, kg					
6 months (n=5751)	2.4 (2.1, 2.7)	2.3 (2.1, 2.5)	1.3 (0.4, 2.2)	1.5 (1.1, 1.9)	2.7 (2.0, 3.4)
12 months (n=4606)	3.6 (3.2, 4.0)	3.5 (3.2, 3.8)	2.9 (1.3, 4.5)	2.1 (1.6, 2.6)	4.7 (3.8, 5.6)
24 months (n=2427)	5.3 (4.7, 5.9)	4.2 (3.7, 4.7)	1.7 (−1.5, 5.0)	2.9 (2.2, 3.6)	5.1 (3.6, 6.6)
Mean change in BMI from baseline, kg/m^2					
6 months (n=5751)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.4 (0.1, 0.7)	0.5 (0.4, 0.6)	0.9 (0.7, 1.1)
12 months (n=4606)	1.2 (1.1, 1.3)	1.2 (1.1, 1.3)	0.9 (0.3, 1.5)	0.5 (0.2, 0.8)	1.6 (1.3, 1.9)
24 months (n=2427)	1.7 (1.5, 1.9)	1.4 (1.2, 1.6)	0.6 (−0.5, 1.7)	1.0 (0.6, 1.4)	1.8 (1.2, 2.4)

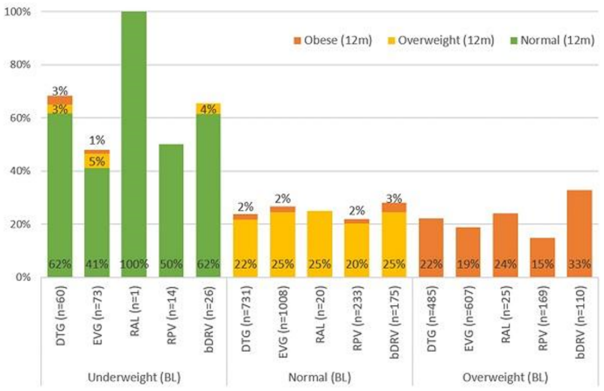
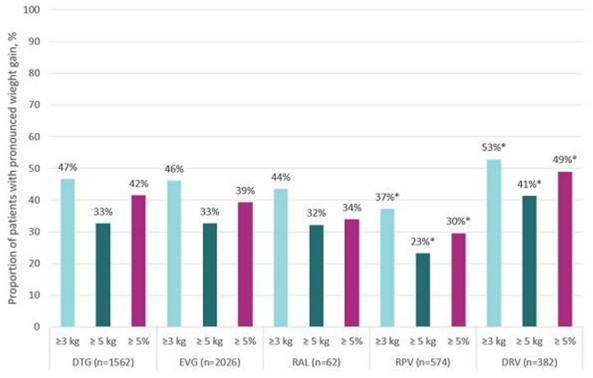


Figure 1. Proportion of PLWH with a BMI category increase at 12 months after core agent initiation



*Comparison to DTG, p-value <0.05

Figure 2. Comparison of weight gain definitions at 12 months after initiation, by core agent

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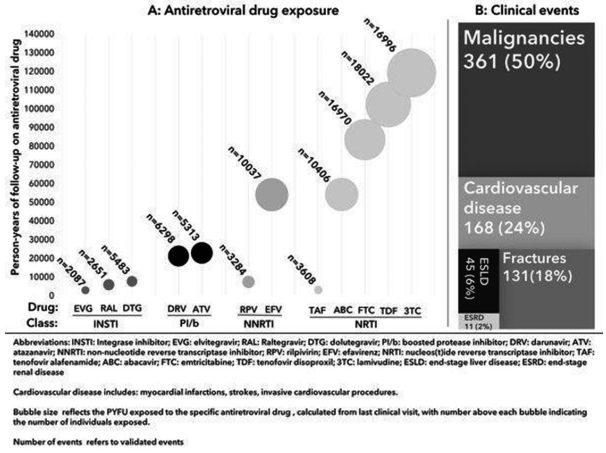
PE2/33

How to RESPOND to modern challenges for people living with HIV: a new cohort collaboration

B Neesgaard[1] and for the International Cohort Consortium of Infectious Diseases: RESPOND

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Objectives: The RESPOND cohort consortium was formed as a platform for collaborative HIV research, investigating comorbidities and outcomes of contemporary antiretroviral therapy (ART), impact of hepatitis coinfection, and public-health focused questions for people living with HIV (PLWHIV).
Methods: RESPOND uses a modular electronic data collection structure, allowing for project specific data capture, in addition to routine data collection, including: demographics, risk of HIV acquisition, viral load (VL), CD4 count and detailed information on ART. Incident cardiovascular disease, malignancies, fractures, end-stage liver- and renal diseases are reported by clinical event forms and centrally validated. Prospective enrolment of consecutive PLWHIV aged≥18 years started 1/10/17, collecting data from established cohorts back to 1/1/12. Follow-up data is collected annually.
Results: Overall, 17 cohorts from Europe and Australia joined RESPOND in 2017, supplying data from more than 26,000 individuals. At study enrolment, median age was 48 years [IQR 40–56]; 44.6% were aged>50 years. The majority was white (72.4%), males (74.3%), with the most common risk group for HIV acquisition being males-who-have-sex-with-males (43.3%); Intravenous drug use accounted for 14.9%. Coinfection with hepatitis B- and C was prevalent in 5.2% and 25.5%, respectively. At enrolment the majority had a VL<200 copies/mL (91.3%), and median CD4 count was 622 cells/μL [439–833]; 59.7% had a CD4 count>500 and 4.8% ≤200 cells/μL. CD4 nadir was≤350 cells/μL for 78.1%; ≤50 cells/μL for 16.4%. Study participants had significant exposure to contemporary ART (figure) while 5.3% were ART-naïve. Malignancies were the predominant reported clinical event, followed by cardiovascular disease and fractures (figure).
Conclusion: The RESPOND cohort study is a large, innovative and modern collaboration, using validated clinical events and detailed treatment information to assess outcomes of contemporary ART, the impact of hepatitis coinfection and to examine the continuum of care for PLWHIV, in a heterogeneous real-life setting.



Antiretroviral drug exposure and clinical events for RESPOND participants

PE2/34

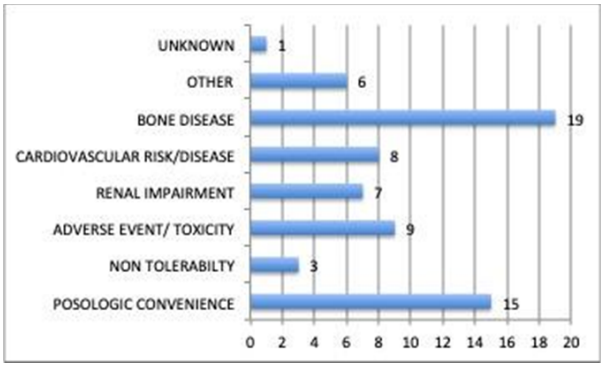
ART simplification: use of dual therapy for HIV in a public health reference center (CRT-DST/Aids) in São Paulo, Brazil

S Pereira Goulart[1], C de Albuquerque Moraes[1], A Furtado da Costa[1], M Miguel Benette[1], C Vidaurre Mendes[1], TJ Bueno Polis[1], D Lopez Teixeira[1], J Valdez Ramalho Madruga[1], LF Jamal[1] and R Schiavon Nogueira[1]

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Purpose: Evaluate the reasons for ART simplification and virological response with 2 drug regimens.

Method: We analyzed electronic data of patients under follow-up in CRT DST/AIDS and selected whose last ARV prescription until April 30th, 2019 was 3TC+DTG or 3TC+DRV/r regimens. We collected data from their charts using REDCap platform.
Results: From 6445 HIV patients, we selected 62 patients under dual therapy. Profile: mean age, mean time of ART use and mean time of infection (from HIV diagnosis until the beginning of dual therapy) was 57.9 (37- 87), 13.9 and 16 years, respectively. None of them was ART naive and the mean number of previous schemes were 3.7 (1–12). Therapy was simplified to 3TC+DTG for 47 patients (75.8%) and to 3TC+DRV/r for 15 (24.2%). Reasons for ART simplification are described in the graphic. There were no switches due to failure or drug interactions. The main reason was bone disease (osteopenia or osteoporosis) in 30.6%. Prior to dual therapy, HIV viral load was not detected in 87.1% patients and under the detection limit (40 copies) in 12.9%, CD4 was above 500 cells/mm^3 in 61 patients and only one had CD4<200. After 6 months, viral load was available for 35 patients: 34 not detected and one had a blip of 60 copies. Viral load after 12 months were available for 10 patients, all not detected or under limit.
Conclusion: Simplification of ART regimens might be a secure option when we need to reduce toxicity considering ageing of HIV patients, multi-morbidity and polypharmacy, especially in a country where TAF is not available in the public health system. This is an early analysis and we need a longer follow-up to evaluate maintenance of virological suppression.



Reasons for ART simplification

PE2/35

Simplification to dual (2D) antiretroviral therapy (ART) with lamivudine and dolutegravir in HIV-infected patients with solid organ transplantation (SOT): a preliminary single-center experience

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Purpose: Dolutegravir is a non-boosted integrase inhibitor that theoretically has no pharmacokinetic interactions (DDI) with immunosuppressant drugs. In addition, dual ART treatment (2D) with lamivudine and dolutegravir is as effective and safe as triple ART in naïve patients (Cahn P. Lancet, 2019) and in simplifying studies (Joly V. JAC, 2018). Therefore, this strategy could be useful in HIV-infected solid organ transplant (SOT) recipients, since it would avoid DDI and the potential bone and kidney toxicity of tenofovir and the cardiovascular risk associated with abacavir. The aim was to analyze the efficacy and safety of the simplification of triple-to-dual ART with lamivudine and dolutegravir in HIV-infected patients with SOT at the Hospital Clínic, Barcelona
Method: A retrospective single-center study of SOT recipients who had to stop tenofovir or abacavir from triple ART due to toxicity and simplified to lamivudine and dolutegravir in HIV-infected SOT recipients at the Hospital Clínic. Exclusion criteria: previous failure to ART, resistance to lamivudine or raltegravir and HBV co-infection
Results: The clinical characteristics of the six included patients are described in the table. Five patients were receiving effective ART with two NRTI and raltegravir (4 cases) or rilpivirine (1 case) and switched to dolutegravir plus

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lamivudine (2D). One patient (case 6) was on dual therapy pre-transplant. Renal function (creatinine, glomerular filtration) stabilized or improved in all cases. There were no significant changes in the dose of calcineurin inhibitors (either cyclosporin or tacrolimus) or mycophenolic acid. All remained suppressed and none had an episode of acute rejection. One patient (case 4) with positive anti-core HBV antibodies and negative HBsAg, HBeAg and plasma DNA-HBV, developed acute HBV two years after simplification

Demographic and clinical characteristics

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age, years	57	58	50	56	51	54
Gender	Male	Male	Female	Male	Male	Male
Type of solid organ transplant	Liver	Liver	Kidney	Liver	Heart	Kidney
Previous ART	TDF+FTC+ RAL	TDF+FTC+ RAL	TDF + 3TC+ RAL	TDF+FTC+ RAL	TDF+FTC+ RPV	DTG-3TC
Reason for ART change	Acute renal toxicity	Chronic renal toxicity	Chronic renal toxicity Ischemic cardiopathy	Chronic renal toxicity	Chronic renal and liver toxicity	Chronic renal toxicity

Immunological and virological evolution and immunosuppressive therapy

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
CD4 count (cells/mm3)/HIV-RNA (copies/mL)						
Basal	226/<50	297/<50	412/<50	416/<50	543/<50	947/<50
6 months	365/<50	231/<50	695/<50	490/<50	553/<50	1013/<50
12 months	417/<50	193/<50	671/<50	684/<50	735/<50	
24 months	520/<50	254/<50	616/<50	426/<50	565/<50	
36 months	237/<50	261/<50	794/<50		875/<50	
Levels of IS before / after the change of ART (ng / mL)	Tacrolimus	Tacrolimus	Tacrolimus	Tacrolimus	Cyclosporin	Tacrolimus
	2.6/2.1	7.9/7.4	7.8/8.6	7.8/4.7	222/259	/12.8

Conclusion: Simplification to lamivudine and dolutegravir was effective and safe in the short/medium term in HIV-infected SOT recipients who had no history of active/past infection with HBV

PE2/36

Comparable effectiveness of Raltegravir-based dual therapy versus other regimens in patients switched for maintenance

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In clinical practice Raltegravir is used in nuke-free dual therapy. Here, we compared profiles and 48-week treatment outcomes of patients on RAL-based dual versus other RAL-based ART in a historical German real-life cohort.
The WIP study was a real-life, prospective, observational cohort study with data collection from 2010–2014. Safety and efficacy outcomes of RAL-based ART in a population enriched for aging patients (274, 61% ≥50 years) were documented. Detailed methods are described elsewhere (Naumann et al., J STD AIDS 2016).
The cohort included 77 (17%) patients on dual and 372 patients on other ART. 85% were male, no differences by treatment group. Compared to patients on other ART, patients initiated on RAL-based dual therapy were on average 3.9 years older and suffered more likely from hypertension (26% vs. 18%), coronary artery disease (12% vs. 4%) and renal insufficiencies (10% vs. 4%) at baseline. They were less frequently therapy-naïve (17% vs. 22%) or pretreated with suppressed viral load (VL) (45% vs. 51%) but more often failing (35% vs. 22%). Dual therapies mainly included a PI (94%, 72/77); most other regimens combinations included NRTI (77%, 287/374). Treatment outcomes of dual vs. other ART differed slightly: 48-week virologic response (VL<50 c/mL; early DC (discontinuation)=failure) was numerically lower in therapy-naïve patients (69% vs. 76%). However, in virologically suppressed patients switched for maintenance efficacy of RAL-based dual therapy was high and comparable to other RAL-based regimens (83% vs. 81%; Table 1).

Table 1. Therapeutic outcomes at week 48

	Dual therapy			Other regimens		
	VL<50 c/mL N (%)	VL≥50 c/mL N (%)	early DC N (%)	VL<50 c/mL N (%)	VL≥50 c/mL N (%)	early DC N (%)
Therapy-naive	9 (69%)	1 (8%)	3 (23%)	63 (76%)	9 (11%)	11 (13%)
Pretreated - suppressed	29 (83%)	2 (6%)	4 (11%)	156 (81%)	10 (5%)	26 (14%)
Pretreated - failing	18 (67%)	7 (26%)	2 (7%)	54 (64%)	13 (15%)	17 (20%)
Pretreated - ART interruption	1 (50%)	1 (50%)	0 (0%)	7 (47%)	4 (27%)	4 (27%)
Total	57 (74%)	11 (14%)	9 (12%)	280 (75%)	36 (10%)	58 (16%)

Patients on RAL-based dual vs. other ART showed differing comorbidity profiles and RAL utilization patterns. While outcomes in therapy-naïve and pretreated failing patients were less favorable, response rates in virologically suppressed patients were high and comparable supporting the concept of maintenance switch to RAL-based dual therapy to avoid drug toxicities or intolerances.

PE2/37

Comparison of a two-drug regimen (dolutegravir/rilpivirine) to standard three-drug regimens in virologically suppressed, treatment experienced individuals in the real world

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Purpose: Dolutegravir/rilpivirine (DTG/RPV) was the first single tablet, once daily regimen containing only two antiretrovirals to be approved. The objective of this study was to compare the effectiveness and durability of DTG/RPV to standard three-drug regimens (3-DR) in a real-world population.
Method: People living with HIV-1 (PLWH) who initiated DTG/RPV or 3-DR, defined as one core agent and two NRTIs, were identified in the OPERA Database. Those who initiated therapy between 1/1/2018–6/30/2018, were ART experienced, age≥13 years, and suppressed (< 50 copies/mL) at start were analyzed. Discontinuation (d/c) was defined as cessation of DTG/RPV or 3-DR.

Table 1. Baseline Characteristics

Characteristic n (%)	DTG/RPV (n=259)	3-DR (n=2,792)	p-value
Age≥50 years	143 (55.2%)	1,093 (39.1%)	**<0.0001**
Female sex	38 (14.7%)	534 (19.1%)	0.2303
African American race	78 (30.1%)	1,131 (40.5%)	**0.0011**
Hispanic ethnicity	88 (34.0%)	719 (25.8%)	**0.0041**
Care in Southern US	172 (66.4%)	1,355 (48.5%)	**<0.0001**
Hx of AIDS	68 (26.3%)	777 (27.8%)	0.5880
CD4 Count>500 cells/ μL	205 (79.2%)	1,986 (71.1%)	0.1100
Hx of Syphilis	72 (27.8%)	1,001 (35.9%)	**0.0094**
Any Comorbidity	224 (86.5%)	2,218 (79.4%)	**0.0067**

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Table 2. Durability, Sustained Suppression & Viral Failure

	DTG/RPV (n=259)	3-DR (n=2,792)	p-value
Durability			
Weeks on regimen, median (IQR)	36.4 (29.9 - 43.1)	37.7 (28.3–48.4)	**0.0252**
Discontinuations, n (%)	25 (9.7%)	438 (15.7%)	**0.0096**
Sustained Suppression Among Those Tested			
Last VL<50 copies/mL in all follow up, n (%)	209 (92.1%)	2,003 (90.0%)	0.3139
Last VL<200 copies/mL in all follow up, n (%)	222 (97.8%)	2,134 (95.9%)	0.2083
Virologic Failure Among Those Tested			
n (%) of Virologic Failures	3 (1.3%)	44 (2.0%)	0.7972
Incidence Rate per 100 PY (95% CI)	1.7 (0.6, 5.4)	2.3 (1.7, 3.1)	0.6937

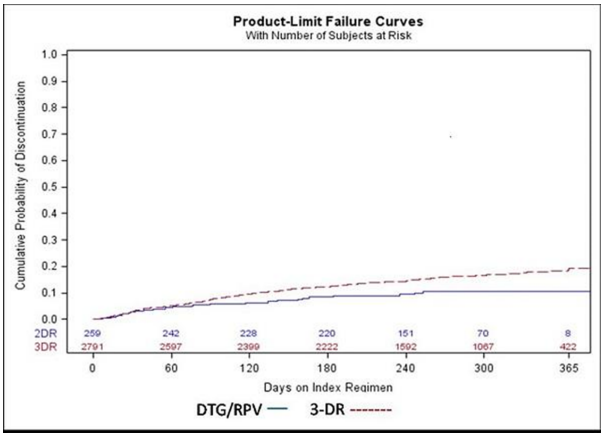


Figure 1. Unadjusted Cumulative Probability of Regimen Discontinuation

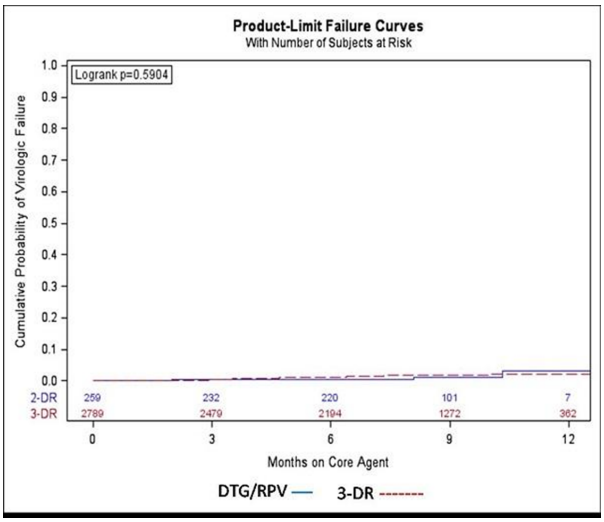


Figure 2. Unadjusted Cumulative Probability of Virologic Failure

Sustained suppression was defined as last viral load (VL)<50 copies or<200 copies. Virologic failure (VF) was defined as either 2 consecutive VL≥200 copies/mL OR 1 VL≥200 copies/mL + d/c. The population was observed through 12/31/2018. Baseline characteristics were described using Pearson's chi-square, Fisher exact, or Wilcoxon rank-sum tests. Kaplan-Meier methods were used to describe d/c and VF. Cox Hazards models compared time to VF.

Results: Among 259 PLWH who initiated DTG/RPV and 2,792 PLWH who initiated 3-DR, DTG/RPV users were older, more likely to be Hispanic, to live in the southern US, and have comorbidities (Table 1). DTG/RPV users were followed for less time and experienced fewer discontinuations and did not differ in sustained suppression compared to 3-DR users (Table 2, Figure 1). VF rates per 100 patient-years (95% CI) did not differ either (DTG/RPV: 1.7 (0.6, 5.4) vs. 3-DR: 2.3 (1.7, 3.1)) (Table 2, Figure 2). Differences in the risk of virologic failure between 3-DR, DTG/RPV initiators in adjusted Cox models were not significant (p=0.8085).

Conclusion: Among ART-experienced, virologically suppressed PLWH initiating DTG/RPV or standard 3-DR, there was no observed difference in their ability to remain suppressed or risk of virological failure in a real-world setting.

PE2/38

Effectiveness of the combination elvitegravir/cobicistat/tenofovir/emtricitabine (EVG/COB/TFV/FTC) plus darunavir in treatment-experienced patients: a multicentre cohort study

I Suárez-García[1,2], C Moreno[3], B Alejos[3], M Ruiz-Alguero[3], MJ Pérez Elias[4], M Navarro[5], M Díez Martínez[6], P Viciana[7], C Amador Prous[8], I Jarrín[3] and Cohort of the Spanish HIV/AIDS Research Network (CoRIS)

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Objective: The aim of this study was to investigate the effectiveness of the combination elvitegravir/cobicistat/tenofovir/emtricitabine plus darunavir (EVG/COB/TFV/FTC+DRV) in treatment-experienced patients from the cohort of the Spanish HIV/AIDS Research Network (CoRIS).

Methods: Treatment-experienced patients starting treatment with EVG/COB/TFV/FTC+DRV during the years 2014–2018 and with more than 24 weeks of follow-up were included. TFV could be administered either as tenofovir disoproxil fumarate or tenofovir alafenamide. We evaluated virological response (defined as viral load<50 copies/mL) and change in CD4 count at 24 and 48 weeks after starting this regimen.

Results: We included 39 patients (12.8% women). Median CD4 count at the start of the regimen was 437 (IQR: 108–740) cells/microl. Patients had been receiving ARV for a median of 5.3 (IQR: 2.5–7.5) years, had received a median of 3 (IQR: 2–6) previous antiretroviral regimens and were receiving a median of 2 (IQR: 1–5) pills per day. Ten (25.6%) patients had viral load<50 copies/mL at the start of EVG/COB/TFV/FTC+DRV, and the most frequent reasons for changing to this regimen were treatment failure in 14 (35.6%) and simplification in 10 (25.6%) patients.

The patients received EVG/COB/TFV/FTC+DRV for a median of 391 (IQR: 205 to 514) days. At their last follow-up visit, 18 patients continued receiving the regimen and 21 had changed to another regimen (nine [23.1%] changed due to simplification, 6 [15.4%] due to treatment failure, 1 [2.6%] due to toxicity, and 5 [12.8%] due to nonadherence, interactions or other reasons). Treatment outcomes are shown in the table.

Conclusions: EVG/COB/TFV/FTC+DRV was well tolerated and effective in treatment-experienced patients with undetectable viral load as a simplification strategy, allowing once-daily, two-pill regimen with three antiretroviral drug classes. Effectiveness was low in patients with detectable viral loads. This is the largest cohort published to date showing results from "real-life" clinical practice with this treatment regimen.

Outcome	24 weeks	48 weeks
Virological response: n/total (%)		
Viral load<50 copies/mL	6/7 (85.7%)	4/5 (80%)
Viral load >=50 copies/mL	11/23 (42.3%)	9/27 (40.9%)
CD4 change, cells/microl: median (IQR)		
Viral load<50 copies/mL	29 (14 - 48)	8 (−85 to 50)
Viral load >=50 copies/mL	-6 (−134 - 107)	-16 (−116 - 77)

Outcomes of patients at 24 and 48 weeks after starting EVG/COB/TFV/FTC+DRV, stratified by viral load at the start of the regimen

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PE2/39

High persistence of dolutegravir-containing 2-drug regimens in routine clinical care

S Noe[1], C Jonsson-Oldenbuettel[1], S Heldwein[1], C Wiese[1], A von Krosigk[1], F Schabaz[1], H Jaeger[1], E Wolf[2] and ArcHIV
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Purpose: To describe the persistence of DTG-containing 2DR and three-drug-regimens (3DR) in people living with HIV from real-life cohort data.
Method: Monocentric time-on-treatment analysis. The 2DR-group consisted of patients initiated on DTG+ rilpivirine (RPV) or lamivudine (3TC) between 2014–2018 with or without history of DTG-containing 3DR. Of all others, patients initiated on DTG with abacavir (ABC)/3TC or tenofovir [alafenamide (TAF) or disoproxil fumarate (TDF)]/emtricitabine (FTC) were included into the 3DR-group. In Kaplan-Meier analysis, discontinuation of 2DR or 3DR was defined as event (excluding switches from DTG-containing 2DR or 3DR to another 2DR or 3DR in the absence of virologic failure. Associations of covariates with time-on-treatment were analyzed using Cox regression analysis.
Results: Of 617 patients, 134 (21.7 %) received a 2DR. 79.1% and 76.3% of patients on 2DR and 3DR were male (p=0.473), median age was 52 and 46 years (y.) (p<0.001), median time since HIV-diagnosis was 16 and 7y. (p<0.001), respectively; 4 (3.0%) and 163 (33.8%) of patients had been treatment-naïve. Persistence on 2DR and 3DR was not significantly different (p=0.245) with 94.9% (93.0%) and 91.1% (88.8%) after 48 weeks (96 weeks). After adjusting for age<50y., time since HIV-diagnosis<10y., HIV-RNA<50 cps/mL, treatment-naïvety, CD4 cells<200/µL, 2DR wasn't associated with a higher risk of discontinuation (HR 0.7 (95% CI: 0.3–1.6); p=0.427), while only CD4<200/µL (HR 2.2 (95% CI: 1.2–4.0; p=0.009) was.
Conclusion: Persistence of 2DR was comparable to 3DR up to>200 weeks. Experienced HIV-centers seem to identify potential candidates for 2DR well, with 2DR being as effective as 3DR in routine clinical practice.

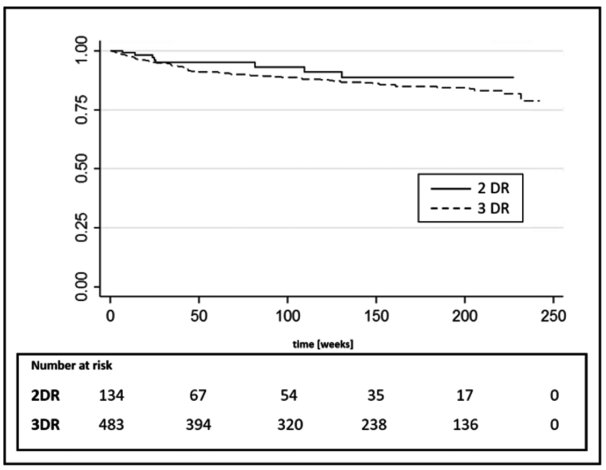


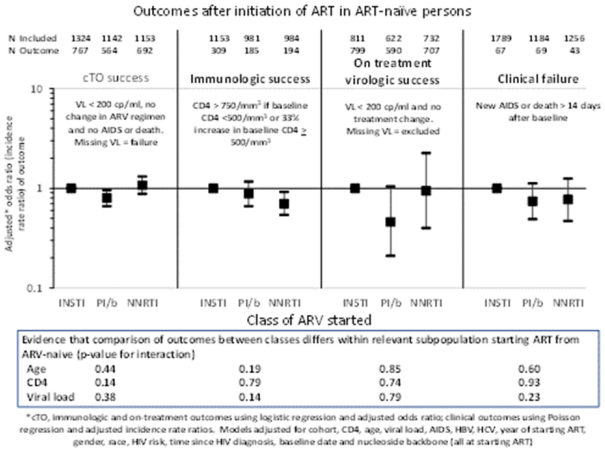
Table 1. Kaplan-Meier graph of persistence on DTG-containing 2DR or 3DR

PE2/40

Virologic, immunologic and clinical outcomes in antiretroviral treatment (ART) naïve individuals in the RESPOND cohort collaboration

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Purpose: Although outcomes of modern ART use have been evaluated in randomized controlled trials, experiences from subpopulations defined by age, CD4 count or viral load (VL) in heterogeneous real-world settings are limited.
Method: Logistic regression compared virologic and immunologic outcomes at 12 ± 3 months after first starting ART with an integrase inhibitor (INSTI), non-nucleoside reverse transcriptase inhibitor (NNRTI) or boosted protease inhibitor (PI/b) with 2 nucleos(t)ides after 1/1/2012. Composite treatment outcome [cTO] defined success as VL<200 cp/mL with no regimen change, AIDS or death. On-treatment analysis (success: VL<200 cp/mL) excluded individuals with unknown VL/any regimen change. Immunologic success was defined as a CD4>750 cells/mm^3 or 33% increase where baseline CD4>500 cells/mm^3. Poisson regression compared clinical outcomes (failure: AIDS/death occurring≥14 days after starting ART). Interactions between ARV class and subpopulations (defined by age, CD4 count, VL) were determined for each endpoint.
Results: Of 4249 ART-naïve persons in RESPOND, 42.4% started INSTIs, 28.0% PI/b and 29.6% NNRTIs. After adjustment, compared to those starting INSTI, those treated with a PI/b had lower odds of cTO success. In contrast, those treated with an NNRTI had lower odds of immunologic success than those on INSTI (Figure). During 10566 persons-years-of-follow-up the rates of new AIDS/death were similar across all drug classes (Figure). Virologic or immunologic success and clinical failure were completely consistent across age groups (≤ 40, 40–50 and>50 years), CD4 count at starting ART (≤ 350 versus>350 cells/mm^3) or VL at starting ART (≤100,000 versus>100,000 cp/mL) with all interactions non-significant (p>0.1).
Conclusion: Virologic, immunologic and clinical outcomes ART naive participants were similar across subpopulations defined by age, immune suppression or VL at ART initiation suggesting that these subpopulations will equally benefit from ART, regardless of ART class. Confounding by indication cannot be excluded.



PE2/41

A retrospective analysis of the EuResist data set assessing HIV dual therapy success in a real-life context

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Purpose: Assess if dual therapies after switch are non-inferior to comparable triple therapies in a real-world context. Several clinical trials have shown non-inferiority already, the added Value of this study is to see if this holds true in a real-world context and on a longer time frame.
Method: This retrospective study uses the EuResist Integrated Database. EuResist is a meta database containing data from>81.000 HIV patients,

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including>100,000 genotypes, >170,000 treatments, >1 million viral load and>1 million CD4 values.
Patients were selected into either the dual therapy or triple therapy treatment group. Both groups need to have a VL (viral load) measurement short before switch with VL under 50 cp/mL and multiple viral load measurements while on therapy. Viral failure was defined as two consecutive VL measurements with VL over 200 or one measurement above 1000.
The triple therapy cases were then selected via propensity score matching to contain similar covariates gender, age, route of transmission, CD4 at start, time on ART and time before switch with VL below 50.
Those data were used to generate Kaplan Meier curves for the dual and triple therapy groups. Afterwards, a TOST (two-one-sided-t-test) was performed comparing the Kaplan Meier estimator at 48 weeks, the endpoint for most prospective studies in this area.
Results: In contrast to older dual therapies, we found no significant difference between INI containing dual and triple therapies in the Kaplan Meier curve. The two-one-sided-t-test at week 48 showed that dual-therapy was significantly non-inferior compared to triple-therapy.
Conclusion: Our results showed that in a real-life clinical setting, INI containing dual therapies have a similar success rate compared to INI containing triple therapies. Therefore, we consider dual therapy as a valuable addition in HIV management.

PE2/42

The real-world impact of switching to tenofovir-alafenamide (TAF) on metabolic co-morbidities in PLWH aged over 60s

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Purpose: Studies have shown that when patients are switched from Tenofovir disoproxil fumarate (TDF) to Abacavir/ Lamivudine or TAF this has caused lipid elevation (Arae et al 2016) suggesting that TDF has lipid-lowering properties [Tungsiripat et al 2010].
Method: Electronic notes and results were retrospectively reviewed of all PLWH aged over 60 regularly attending a HIV clinic in London in 2017, documenting estimated glomerular filtration rate (eGFR), lipid profiles, and body weight measurements.
Analysis was stratified by groups: (1) Those remaining on tenofovir disoproxil fumarate (TDF)-based antiretroviral (ARV) regimens, (2) switched from TDF to TAF, (3) switched from non-TDF to TAF, and (4) Neither on TAF or TDF during the evaluation period. Baseline visits were as the last visit prior to TAF switch, or last visit in 2017 for non-TAF groups, and differences in markers compared to the most recent visit within 24 months were measured. One-way ANOVA and logistic regression performed for univariate and multivariate analysis respectively using Minitab.
Results: Of 279 PLWH included, 59% switched to TAF-based regimen. Mean age, ethnicity and sexual orientation were similar. Switch to TAF was only significantly associated with a change in total cholesterol (TC) (Group 2: +0.1754 (SD 0.802), Group 3: −0.6545 (SD 1.084), p<0.0001). The association remained after adjusting for age, ethnicity, 3rd ARV class, or use of lipid-lowering therapy (Coef 0.367, p=0.012). There were no significant differences seen in mean changes in eGFR, TC:HDL ratio, and body weight. Univariate results are summarised in Table 1.
Conclusions: Switch from TDF to TAF is associated with a small increase in TC. However, switching from non-TDF to TAF regimes was also associated with small improvements in TC, and reassuringly did not affect overall changes in TC:HDL ratio. TAF did not significantly impact changes in eGFR or weight gain in this cohort.

Table 1. Differences in baseline eGFR, and changes in outcomes stratified by ARV groups

	Group 1: Remain on TDF n=56	Group 2: TDF to TAF n=135	Group 3: Non-TDF to TAF n=29	Group 4: Neither on TDF or TAF n=59	p-value
Mean baseline eGFR (SD) mL/min	77.4 (13.7)	71.5 (20.0)	58.8 (15.0)	68.1 (26.0)	<0.0001
Mean change in eGFR (SD)	4.47 (9.22)	5.75 (11.39)	5.31 (15.15)	3.5 (10.94)	0.634
Mean change in total cholesterol (TC) (SD)	-0.0963 (0.640)	0.1754 (0.802)	-0.6545 (1.084)	-0.005 (1.136)	<0.0001
Mean change in TC:HDL ratio (SD)	-0.0299 (0.721)	-0.0335 (0.7342)	-0.111 (0.814)	0.08 (1.08)	0.76
Mean change in body weight (SD)	1.306 (5.247)	1.571 (4.642)	0.82 (6.27)	0.43 (4.425)	0.573

PE2/43

Effect of simplification to INSTI-based dual therapy on residual inflammation and viral reservoir

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Purpose: Whether dual regimens (2DR) might reduce the control over immune activation/inflammation has not been fully addressed. We aimed to describe the trend in pro-inflammatory markers and monocyte activation over 1 year of observation after a switch to INSTI-based dual therapy with VL≤50 copies/mL.
Method: Inclusion criteria: (i) cART-treated HIV+ patients (HIV-RNA<50cp/mL) in Icona cohort, (ii) switched from triple combinations to INSTI-containing 2DR for any cause, iii) on a stable triple cART for >= 12 months prior to the switch and iv) availability of plasma samples at switch (T0) and 12 ± 6 months post-switch (T1). Laboratory: circulating sCD14, C Reactive Protein (CRP), IL-6 (Luminex); HIV-DNA (ddPCR).
Statistics: paired T-test, non- parametric Spearman correlation.
Results: We included 50 patients, with median (IQR) CD4, HIV-RNA and cART duration of 732 cell/mmc (568–920), 15 cp/mL (1–37), 4 years (2–10) respectively. 18 switched from INSTI triple, 13 from boosted-PI, 19 from NNRTI (Table 1). 17 (34%) patients simplified to RAL-based dual, 33 (66%) to DTG-based dual therapy. Median follow-up between T0 and T1: 15 months (IQR: 12–18). Simplifying to 2DR resulted in a slight CD4 increase (p=0.038) coupled with a parallel decrease in sCD14 (p<0.001), the latter being more relevant in patients switching to DTG- vs RAL-containing regimens (p interaction p=0.014), and evident only in patients switching from other than INSTI-containing regimens. Upon switch to 2DR, no changes in CD8, CD4/CD8 ratio, HIV-RNA and HIV-DNA, as well as other pro-inflammatory markers were shown (Table 2). No correlations between inflammatory markers and viro-immunologic parameters were found.
Conclusion: In our cohort of long-treated HIV+ patients, simplification to INSTI-based 2DR appeared to reduce sCD14 - slightly increasing CD4 - notwithstanding stable HIV reservoirs, suggesting no disturbance to immune balance, rather an amelioration of the immune and inflammatory profile, during the first year of dual INSTI-based regimens.

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Table 1. Epidemiological and Clinical Features of the Study Population

Characteristics	Total
	N= 50
Age, years, Median (IQR)	49 (42, 59)
Gender, female, n(%)	17 (34.0%)
Nationality, not Italian, n(%)	3 (6.0%)
Smoking, n(%)	
No	24 (48.0%)
Yes	21 (42.0%)
Unknown	5 (10.0%)
HCVAb, n(%)	
Negative	42 (84.0%)
Positive	4 (8.0%)
Not tested	4 (8.0%)
Mode of HIV Transmission, n(%)	
IDU	3 (6.0%)
Homosexual contacts	20 (40.0%)
Heterosexual contacts	25 (50.0%)
Other/Unknown	2 (4.0%)
Calendar year of baseline-Median (IQR)	2015 (2014, 2016)
CD4 count, cells/mmc, Median (IQR)	732 (568, 920)
CD4 count nadir, cells/mmc, Median (IQR)	293 (166, 420)
CD4 count nadir≤200 cells/mmc, n (%)	15 (30.0%)
CD8 count, cells/mmc, Median (IQR)	724 (537, 1049)
Viral load, copies/mL	
Median (range)	15.00 (1.00, 39.00)
Median (IQR)	15.00 (1.00, 37.00)
AIDS diagnosis, yes, n(%)	3 (6.0%)
CVD diagnosis, yes, n(%)	2 (4.0%)
Diabetes, yes, n(%)	6 (12.0%)
Use of statins, yes, n(%)	12 (24.0%)
Use of blood pressure lowering drugs, yes, n(%)	14 (28.0%)
Time from HIV diagnosis to date of HBV serology test, months Median (IQR)	57 (36, 138)
Follow-up time, months	15 (12, 18)
cART duration, years, Median (IQR)	4 (2, 10)
Pre-switch cART regimens, n(%)	
PI/r-based	13 (26.0%)
NNRTI-based	19 (38.0%)
INSTI-based	18 (36.0%)

Table 2. Changes in viro-immunologic and pro-inflammatory markers upon INSTI-based switch

	HIV-related markers				Pro-inflammatory markers			
	CD4, n	CD8, n	Ratio CD4/CD8	HIV-DNA, Log cp/10^6CD4	IL-6, pg/ml	CRP, ug/ml	sCD14, ug/ml	
Whole sample (n=50)								
T0	762.9 (656.3, 869.5)	863.5 (722.8, 1004)	1.03 (0.88, 1.18)	2.44 (2.23, 2.65)	1.65 (1.16, 2.13)	1.73 (1.21, 2.26)	1.25 (1.12, 1.38)	
T1	823.1 (716.4, 929.9)	1082 (703.1, 1461)	1.06 (0.91, 1.22)	2.43 (2.17, 2.68)	1.99 (1.15, 2.83)	1.58 (1.09, 2.07)	1.05 (0.94, 1.15)	
Variation	60.39 (3.41, 117.0)	218.7 (-161, 598.3)	0.03 (-0.05, 0.12)	-0.02 (-0.17, 0.12)	0.35 (-0.59, 1.28)	-0.15 (-0.54, 0.25)	-0.20 (-0.30, -0.10)	
p-value*	0.038	0.253	0.416	0.764	0.463	0.454	<.001	
INSTI-free previous regimen (n=32)								
T0	727.8 (576.7, 879.0)	791.9 (638.7, 945.1)	1.06 (0.84, 1.28)	2.42 (2.17, 2.68)	1.64 (1.12, 2.17)	1.77 (1.19, 2.36)	1.26 (1.09, 1.44)	
T1	775.3 (629.3, 921.4)	933.6 (546.3, 1321)	1.10 (0.88, 1.32)	2.47 (2.22, 2.73)	2.06 (0.87, 3.25)	1.71 (1.13, 2.29)	1.04 (0.89, 1.19)	
Variation	47.50 (-18.5, 113.5)	141.7 (-244, 527.8)	0.04 (-0.07, 0.15)	-0.02 (-0.22, 0.18)	0.42 (-0.77, 1.61)	-0.06 (-0.57, 0.45)	-0.22 (-0.36, -0.09)	
INSTI in previous regimen (n=18)								
T0	825.3 (685.7, 964.8)	990.7 (696.3, 1285)	0.97 (0.78, 1.17)	2.48 (2.00, 2.97)	1.65 (0.59, 2.71)	1.65 (0.53, 2.78)	1.23 (1.02, 1.43)	
T1	908.1 (754.3, 1062)	1346 (498.3, 2194)	1.00 (0.78, 1.22)	2.32 (1.61, 3.04)	1.87 (0.74, 2.99)	1.34 (0.39, 2.30)	1.06 (0.92, 1.21)	
Variation	82.78 (-31.9, 197.4)	355.5 (-509, 1220)	0.02 (-0.12, 0.16)	-0.02 (-0.22, 0.18)	0.21 (-1.48, 1.91)	-0.31 (-1.05, 0.42)	-0.16 (-0.31, -0.01)	
Interaction p-value	0.642	0.917	0.801	0.612	0.151	0.857	0.690	
RAL in dual (n=17)								
T0	687.4 (466.6, 908.1)	883.1 (688.3, 1078)	0.89 (0.61, 1.16)	2.67 (2.32, 3.03)	1.06 (0.67, 1.45)	2.22 (1.29, 3.15)	1.28 (1.06, 1.50)	
T1	790.8 (553.9, 1030)	899.6 (688.7, 1111)	0.96 (0.70, 1.22)	2.71 (2.35, 3.07)	1.80 (1.33, 2.27)	2.12 (1.54, 3.09)	1.12 (0.87, 1.36)	
Variation	103.4 (28.31, 178.5)	16.59 (-53.1, 86.28)	0.07 (-0.06, 0.20)	0.04 (-0.33, 0.40)	0.74 (0.14, 1.34)	-0.10 (-1.02, 0.81)	-0.16 (-0.32, -0.01)	
DTG in dual (n=33)								
T0	801.8 (679.7, 924.0)	853.4 (658.1, 1049)	1.10 (0.91, 1.29)	2.34 (2.07, 2.61)	1.95 (1.25, 2.65)	1.48 (0.82, 2.13)	1.24 (1.07, 1.41)	
T1	839.8 (723.7, 955.9)	1176 (603.0, 1749)	1.11 (0.91, 1.32)	2.29 (1.96, 2.63)	2.09 (0.82, 3.36)	1.30 (0.74, 1.86)	1.01 (0.90, 1.13)	
Variation	37.94 (-40.5, 116.4)	322.8 (-259, 904.3)	0.01 (-0.10, 0.12)	-0.05 (-0.21, 0.11)	0.14 (-1.27, 1.56)	-0.18 (-0.62, 0.26)	-0.22 (-0.36, -0.09)	
Interaction p-value	0.196	0.776	0.873	0.287	0.949	0.725	0.014	

*paired t test. Data are presented as mean (95% CI)

PE2/44

Changes in LDL after switch from TDF to TAF in the U.S.

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Purpose: Increases in lipids have been observed in people living with HIV (PLWH) switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF). We assessed changes in LDL over time following a switch from TDF to TAF.

Method: Adults switching from TDF to TAF, including those who maintained all other components of their antiretroviral regimen, with≥1 lipid measure on TDF taken≤6 months prior to switch and≥1 lipid measure≥7 days after switch to TAF were identified in the OPERA® cohort (84 clinics in 18 U.S. states/territories). Predicted changes in lipids over time on TAF were assessed with multivariable linear regression using generalized estimating equations to account for repeated measures. Months on TAF was modeled flexibly with linear splines (knots at 3, 9, 16 months).

Results: 6,451 PLWH switched from TDF to TAF (main population), of whom 4,328 maintained all other ARVs (sensitivity population, Table 1). Over 80% had normal or borderline abnormal LDL values at their last lipid panel on TDF (Figure 1). Among switchers, LDL values increased significantly by 1.40 mg/dL per month over the first 3 months of TAF exposure, continued to increase significantly, though less rapidly, by 0.33 mg/dL per month between 3 and 9 months, and plateaued beyond 9 months (Table 2). Similar patterns were

Table 1. Demographic and Clinical Characteristics at the Time of Switch from TDF to TAF in the Main and Sensitivity Populations

	Main population: All switches (N=6,451), Median (IQR) or n (%)	Sensitivity population: Maintained other ARVs (N=4,328), Median (IQR) or n (%)
Months on TDF pre-switch	29.2 (13.8, 51.5)	27.7 (14.0, 46.4)
Age	48 (38, 55)	47 (37, 54)
Female	1,010 (15.7)	674 (15.6)
HIV viral load≥50 copies/mL	1,103 (17.2)	620 (14.0)
PI Use	1,272 (19.7)	815 (18.8)
Boosting agent use	4,019 (62.3)	2,520 (58.2)
Concomitant hormone use	554 (8.4)	372 (8.6)
Concomitant statin use	1,112 (17.2)	732 (16.9)
Concomitant non-statin lipid lowering agent use (omega-3, fibrate, etc.)	425 (6.6)	267 (6.2)

Table 2. Rates of Change in LDL Over Time After Switch to TAF, Estimated from a Multivariable Linear Regression* in the Main and Sensitivity Population

	Main population: All switches (N=6,451)	Sensitivity population: Other ART components maintained (N=4,328)
Months on TAF	Changes in LDL over time, mg/dL per month (95% CI)	Changes in LDL over time, mg/dL per month (95% CI)
0–3 months	+1.40 (1.19, 1.60)	+1.72 (1.47, 1.96)
3–9 months	+0.33 (0.20, 0.46)	+0.27 (0.11, 0.42)
9–16 months	+0.06 (−0.05, 0.16)	+0.10 (−0.03, 0.23)
16 + months	+0.03 (−0.07, 0.12)	-0.00 (−0.11, 0.11)

* Adjusted for baseline LDL (cubic splines, knots at 79, 96, 117 mg/dL), age (cubic splines, knots at 40, 50, 55 years), months on TDF (cubic splines, knots at 15, 28, 49 months) and sex; time-updated HIV viral load≥50 copies/mL and concomitant hormone, statin, non-statin lipid lowering agent, PI and boosting agent use

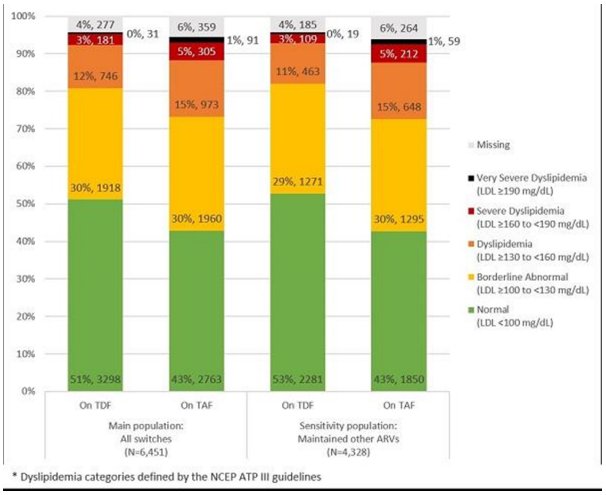
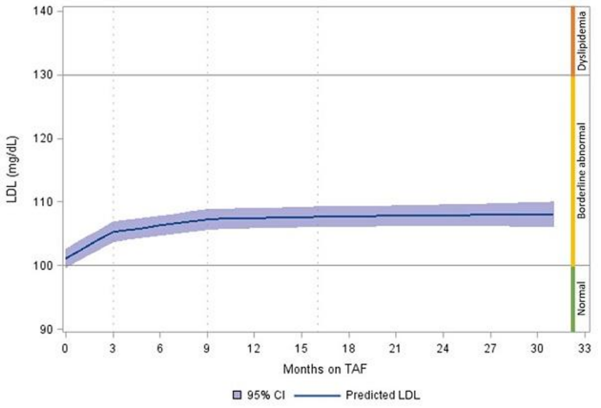


Figure 1. Dyslipidemia Categories* at the Last Lipid Panel on TDF or the First Lipid Panel on TAF in

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observed among PLWH who maintained all other ARVs (Table 2). Average predicted LDL values remained borderline abnormal throughout follow-up (Figure 2).

Conclusion: In this large, diverse cohort of PLWH in care in the U.S., switching from TDF to TAF was associated with an increase in LDL over the first 9 months on TAF, followed by a plateau at higher LDL levels. The observed LDL increases cannot be attributed to changes in other ARVs as indicated by a sensitivity analysis restricted to PLWH who maintained all other ARVs.



* Adjusted curves for predicted LDL values over time on TAF for individuals with specific characteristics at baseline (LDL: 98, age: 45, sex: male, months on TDF: 24) and throughout follow-up (VL: <50, hormones: none, statins: none, non-statins lipid lowering agents: none, boosting agent: none, PI: none)

Figure 2. Adjusted* Predicted LDL Over Time After Switch from TDF to TAF in the Main Population (All)

PE2/45

A retrospective analysis of the EuResist data set assessing if NRTI resistance impairs INSTI based treatment with NRTI backbone

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Purpose: Antiretroviral combination therapy (cART) normally contain two nucleotide reverse transcriptase inhibitors (NRTIs) and an integrase inhibitor (INSTI). But there is still a lack of studies showing how baseline resistance to NRTIs affects the risk of virologic failure in this constellation. We assess whether NRTI resistance can impair INSTI based treatment with NRTI backbone.

Method: This retrospective study uses the EuResist Integrated Database. EuResist is a meta database containing data from>81.000 HIV patients, including>100,000 genotypes, >170,000 treatments, >1 million viral load and>1 million CD4 values.

Selected patients had a recorded first-line therapy and a baseline sequence within 1 month of the therapy start. Only therapies after 2009 were selected, the onset of dual therapies in the data set. NRTI resistance mutations where obtained by the Stanford HIVdb program. The cases were then classified as either no NRTI mutation or>1 NRTI mutation. Virologic failure was defined as after 6 months or after first virologic suppression a VL viral load measurement of over 1000 cp/mL. This resulted in 497 INSTI therapies without NRTI resistance and 38 INSTI therapies with NRTI resistance.

Kaplan Meier plots were generated both for the overall risk of viral failure stratified by NRTI mutation and specifically for INSTI based ARTs.

Results: The Log-rank test for the Kaplan Meier curve depicting overall viral failure shows a significant difference between no NRTI mutation and >=1 NRTI mutation p=0.048. The log-rank test for INSTI-based ARTs was p=0.003. For INSTI based ARTs the risk of viral failure was 13% in the resistant group and 4% in the non-resistant group.

Conclusion: Our results point in the direction that NRTI resistance in first-line integrase therapies does indeed increase the risk of viral failure.

PE2/46

Impact of archived M184V/I mutations on the effectiveness of switching to coformulated elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide among virologically suppressed HIV-positive patients

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Purpose: Real-world experience with the effectiveness of coformulated. elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) as a switch regimen among patients with HIV-1 harboring M184V/I mutations with or without other thymidine analogue-associated mutations (TAMs) are lacking.

Method: In this multicenter, retrospective matched cohort study, patients who were switched to E/C/F/TAF after having achieved viral suppression (plasma HIV RNA load [PVL] < 200 copies/mL) for 6 months or longer were included. Patients with archived M184V/I mutations (case patients) were matched to controls without previous M184V/I mutations by a 1:4 ratio. Those who had a previous history of virological failure or resistance to integrase inhibitor were excluded. The primary end point was PVL<50 copies/mL at week 24 of switch using FDA snapshot analysis.

Results: In total, 101 case patients with known M184V/I mutations were identified, including 6 (5.9%) with K65R and 19 (18.9%) with at least 1 TAM, and were matched to 404 controls in terms of age (mean, 41.3 vs 40.1 years), gender (male, 98.0% vs 98.0%) and cumulative exposure duration to tenofovir disoproxil fumarate (median, 138 vs 140 weeks). At week 24, the rate of virological non-success (PVL>50 copies/mL) among case and control patients was 5.1% (5/101) and 2.7% (11/404), respectively (difference, 2.3%; 95% CI, −1.2–8.7%). The rate of virological success (PVL≤50 copies/mL) was 84.8% vs 84.1% among the case and control patients, respectively. Discontinuations of E/C/F/TAF occurred in 4.0% (n=4) of the case patients due to adverse effects and missing scheduled blood testing occurred in 7.9% (n=8) at week 24, who continued to receive E/C/F/TAF, while the respective rate of discontinuations and missing blood testing was 4.0% (n=16) and 9.4% (n=38) among the control patients.

Conclusion: Among virally suppressed HIV-positive patients, E/C/F/TAF is effective in maintaining viral suppression at week 24 despite archived M184V/I mutations with or without TAMs.

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Central nervous system (CNS) side effects and viral blips post cART switch from atazanavir boosted with ritonavir (ATZ/r) to atazanavir boosted with cobicistat (ATZ/c)

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Purpose: Cobicistat is a weaker inhibitor of the P-gp and BCRP efflux pumps expressed at the blood-brain barrier limiting the entry of protease inhibitors (Ronaldson et al., 2008). Atazanavir penetration is low in CSF (Best et.al, 2009). Clinic experience of cases of CNS symptoms post switch to ATZ/c triggered a review.
Method: PLWH who had their PI switched from ATZ/r to ATZ /c were randomly selected from pharmacy audit data retrospectively and followed up to a maximum of 6 months to analyse data on CNS side effects and viral loads post switch. A comparative arm for DRV/r to DRV/c switch was selected.
Results: ATZ/r to ATZ/c switch group: A total of 41 patients [M23, F18; Mean CD4 count at switch 662 cells/ul; HIV viral load at switch : < 50 (n=37), < 100 (n=3), >100 copies/mL (n=1)] were included.
5 (12%) experienced CNS side effects reported at 1 month follow up (Headache, numbness of fingers, excessive sweating, anxiety, transient headache) which resolved only on discontinuation of cobicistat (n=3). All 5 maintained viral load<50 copies/mL.
4 (9%) out of 41 experienced viral blips during follow up period with previous undetectable viral load (< 50 copies/mL).
DRV/r to DRV-c switch group: 50 patients [M32, F18: Mean CD4 count at switch 567 cells/ul; HIV viral load at switch: < 50 (n=36), < 100 (n=3), >100 copies/mL (n=11)] were included. 1 person developed low level viremia post switch. 2 developed CNS side effects (vivid dreams, increased appetite) reported at one month follow up and resolved without discontinuation of cobicistat.
Conclusion: Higher CNS side effects and viral blips are observed on ATZ/r to ATZ/c shift. This could be due to variable compartmental concentration of boosted atazanavir within CNS and other viral reservoir sites. Further studies are required to explore this association.

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Quantitation of cellular HIV-1 DNA levels by droplet digital PCR in virologically-suppressed patients switching to dolutegravir plus lamivudine: a prospective study

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Purpose: The aim of this study was to assess HIV-1 cellular reservoir size in virologically-suppressed patients switching to dolutegravir (DTG) plus lamivudine (3TC).
Method: This was a single-arm, prospective study that enrolled 40 patients without previous virological failure, with HIV-1 RNA<50 copies/mL for≥48 weeks and CD4>200 cells/μL switching from 3-drug cART to DTG 50 mg + 3TC 300 mg once daily. We assessed total blood-associated HIV-1 DNA levels at baseline (BL) and 48 weeks (T48) after switch by droplet digital PCR using a 5' nuclease assay targeting the HIV-1 LTR region. Results were expressed as $\log_{10}$ HIV-1 DNA copies/10^6 leukocytes. Paired T-test was used to compare the means between the two time-points. Regression analyses were applied to assess the correlations.
Results: A subset of 31 subjects with a complete follow-up was analyzed: 81% males, mean age 53 years, mean CD4 count 688 cells/μL, previous regimen NNRTI-(42%), INSTI-(39%) and PI-based(19%). The mean BL HIV-1 DNA was 2.16 (95% CI 1.97; 2.35). At T48 the mean HIV-1 DNA was 2.04 (95% CI 1.85; 2.23), with a significant mean decrease from BL of −0.13 (95% CI −0.006;-0.25) (p=0.041). BL and T48 HIV-1 DNA levels were highly correlated (p<0.001). No demographical, clinical and viro-immunological variable was associated with HIV-1 DNA changes. Zenith $\log_{10}$ HIV-1 RNA, mean change + 0.350 per + $1\log_{10}$, 95% CI 0.157/ 0.542 (p<0.001) and BL CD4, mean change −0.132 per + 100 cells/ μL, 95% CI −0.178/-0.087 (p<0.001) were independently associated with BL HIV-1 DNA. No significant change in CD4 count and HIV-1 RNA levels was observed during the study, albeit one patient experienced a virological failure at T48.
Conclusion: Our data suggest that in virologically suppressed patients switching to DTG + 3TC may have a favorable impact on the cellular HIV-1 DNA reservoir. These results need to be confirmed by larger controlled studies.

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Evaluation of weight gain in incarcerated individuals living with HIV/AIDS after switching to a raltegravir-based regimen

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Purpose: Integrase Strand Transfer Inhibitors (INSTIs) are a class of antiretrovirals (ARVs), commonly used with other ARV classes, to achieve virologic suppression. However, recent data have demonstrated the potential for weight gain with the addition of an INSTI. The primary objective was to assess average weight change, in kilograms, before/after raltegravir (RAL) initiation. Secondary outcomes included change in body mass index (BMI) and BMI categorization.
Method: A retrospective cohort study was performed in incarcerated adults living with HIV in Illinois, USA, from January 1, 2011, through June 30, 2014. Included subjects were≥18 years old, on a non-INSTI regimen prior to switching to RAL-based therapy, and received routine CD4, HIV-RNA, and weight monitoring at least 6 months prior and post switch to RAL. Subjects were excluded if previously receiving an INSTI, ARV-naïve, or released prior to obtaining appropriate follow-up. Statistical analysis included paired t-tests and descriptive statistics.
Results: Among 29 patients placed on RAL, the majority were male (97%) with an average age of 41.9 years (range 20–57). Mean time on a pre-INSTI regimen was similar to time on RAL (13.4 and 13.7 months, respectively). Twenty-six patients (90%) experienced weight gain with an average increase of 4.1 kg (p=0.0006) regardless of previous regimen (NNRTI or PI-based) or virologic suppression (p=0.9593). Twenty-three subjects (79.3%) received concomitant tenofovir while 20.7% (n=6) received NRTI-sparing regimens. Patients with CD4≥200 cells/mm^3 were more likely to experience an increase in their weight from baseline (p=0.0012). BMI data were available for 25 patients. BMI increased by an average of 0.932 (pre-RAL=25.344 vs. post-RAL=26.276) (p=0.0031) with 6 subjects re-categorized into an increased BMI classification.
Conclusion: Switching to RAL-based therapy may be associated with significant weight gain. Further studies should assess clinical consequences of increased weight with INSTI-regimens.

PE2/50

Determinants of viral non-suppression among people living with HIV (PLHIV) in rural setting, Neno: a retrospective cohort study

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Purpose: Early establishment of viral suppression status among patients on ART, is key for early detection of treatment failure and identification of patients in need of intensive adherence counseling. Viral suppression is defined as viral load (VL)<1000 ribonucleic acid (RNA) copies/mL. There is limited data on determinants of viral non-suppression among ART clients. This study investigated factors associated with viral non-suppression among PLHIV in Neno, Malawi.
Method: We conducted a retrospective cohort study using routinely collected HIV program data from 2007 to 2018. We extracted VL, defined as having VL in past four years, along with demographic variables in Electronic Medical Records (e.g., gender, age, presence of at least one NCD, BMI, ART duration, and default outcome). Viral non-suppression served as outcome variable in

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analysis. Multivariate logistic model was used to identify determinants of viral non-suppression

Results: We reviewed 14680 clients, of these, 53% (7847/14680 had VL, and 6% were not virally suppressed. After adjusting for covariates; age, default outcome, ART duration and BMI, likelihood of having non-suppressed VL decreases with increase in age, with 5 times higher among those below 20 years (AOR=5.00, 95% CI 2.36–10.57), 2 times higher (AOR=2.35, 95% CI 1.61–3.37) among those aged 20–25 compared to 25 + years. Defaulting outcome was associated with 4 times increase in non-suppressed VL (AOR=4.61, 95% CI 3.35- 6.35) compared to non-defaulting. The odds of having non-suppressed VL was 62% higher among those on treatment for below 1 year compared to 7 + years. Viral non-suppression was 46% higher among underweight (< 18.5) compared to normal weight (18.5–24.9).

Conclusion: Specific and specialized programs targeting clients who are young, having history of defaulting, underweight, and in first year of ART treatment with comprehensive range of interventions including psycho-social support and treatment literacy are needed to further improve viral suppression outcomes.

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Risk of developing HIV resistance in patients with low level viraemia in a large London cohort

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Purpose: Management of low-level viraemia (LLV) in patients on combined antiretroviral therapy (cART) remains a challenge. LLV is an independent risk factor for virological failure. We examined resistance patterns and management of patients with LLV in our clinic cohort.

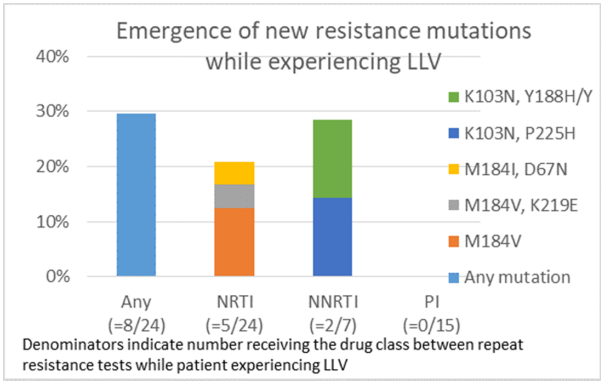
Method: All individuals attending our HIV clinic who experienced LLV between 2015–2019 were included. LLV was defined as≥2 consecutive detectable viral loads of 21–200 cps/mL. Characteristics at the time of first detectable VL were summarised. Development of new mutations were summarised among those with repeat resistance tests whilst experiencing LLV.

Results: 84 experienced LLV during follow-up, representing 2% of the total clinic population. Characteristics are shown in table 1, with most (59%) receiving PI-based ART. 67 (79.8%) had at least one resistance test performed, of which 6 (9.0%) were unable to be amplified. Of those with a result, 15/61 (24.6%; 95% CI 14.5%-37.3%) had resistance to at least one-class (4 [6.6%; 1.8–15.9%] PI-associated, 11 [18.0%; 9.4%-30.0%] NNRTI-associated, 7 [11.5%; 4.7%-22.2%] NRTI-associated, 0 [0.0%] triple-class). 24 patients went on to have a second resistance test whilst experiencing LLV, a median (IQR) of 5 (3, 7) months later; 8 (33.3%; 95% CI 15.6%-55.3%) had a new major mutation detected (Figure). There were 5 new M184V/I mutations detected, 2 new K103N and one each of K219E, D67N, P225H, Y188H/Y and low-level resistance to INSTI.

Conclusion: Low level viraemia in our cohort was rare. A high level of baseline resistance was seen in our LLV group. Repeat resistance testing during LLV was not done routinely. Of those with repeat resistance tests during LLV, a third developed a new major mutation. LLV at this level may represent assay variation, but suggests that in the cART era LLV remains a risk factor for resistance and possible virological failure. The optimum management strategy of LLV needs clarifying.

Table 1. Characteristics of PLWH experiencing low level viraemia, 2015–2019

	N (%) or Median (IQR; range)		N (%) or Median (IQR; range)
Total	84 (100%)	CD4 nadir (cells/mm3)	224 (111, 328; 10, 783)
Age (years)	51 (45, 56; 20, 91)	Subtype (n=69) A B C CRF01_AE CRF01_AG D F G Complex recombinant	8 (11.6%) 28 (40.6%) 17 (24.6%) 1 (1.5%) 8 (11.6%) 1 (1.5%) 2 (2.9%) 2 (2.9%) 1 (1.5%)
Gender Male Female	67 (79.8%) 17 (20.2%)	Ever hepatitis B/C co-infected	11 (13.1%)
Ethnicity White Black Other	35 (41.7%) 43 (51.2%) 6 (7.1%)		
Time since diagnosis (years)	9 (5, 15; 0, 29)		
Time from diagnosis to starting ARVs (years) CD4 nadir (cells/mm3)	1 (0, 3; 0, 17) 224 (111, 328; 10, 783)		
Total ARVs in regimen (excluding RTV/cobi) 1 2 3 4	2 (2.4%) 2 (2.4%) 75 (89.3%) 5 (6.0%)		
NRTI backbone Tenofovir+ emtricitabine Abacavir+lamivudine 0 or 1 NRTIs	60 (71.4%) 16 (19.1%) 8 (9.5%)		
"Third" drug Efavirenz Rilpivirine Nevirapine Etravirine Darunavir Atazanavir Dolutegravir Raltegravir Maraviroc	13 (15.5%) 6 (7.1%) 3 (3.6%) 1 (1.2%) 38 (45.2%) 12 (14.3%) 6 (7.1%) 10 (12.9%) 6 (7.1%)		



Emergence of new resistance mutations while experiencing low level viraemia

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Virological outcomes of first line regimens in women living with HIV from Icona cohort: comparison with clinical trial data

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Purpose: Aim of this analysis was to verify in a real-life setting the efficacy of newer cART regimens and to compare results with those obtained by WLWH-specific RCTs.

Methods: Naïve WLWH enrolled in Icona from 2006 starting a ATV/r-, DTG-, EVG/c-, DRV/r or DRV/c -, RAL-, RPV-based regimens regardless of backbone and with at least 1 follow-up HIV-RNA were included. Primary endpoint was treatment failure (TF) (confirmed HIV-RNA>200 c/mL after 24 weeks or discontinuation for any reason but simplification). Secondary endpoints: 1) first line discontinuation for any reason; 2) first line discontinuation for toxicity; 3) virological failure; 4) virological success at week 48 [Modified FDA Snapshot Algorithm]) for regimens mimicking WLWH-RCT.

Cox regression model was used to estimate the hazard risk (HR) of various outcome according to different cART regimens, after adjusting for main confounders.

Results: 1084 WLWH were included (median FU: 1.9 yrs [IQR 0.9–3.2]). 258 WLWH (26%) started ATV/r, 166 (16%) DTG, 115 (11%) EVG/c, 219 (21%) DRV/r or DRV/c, 71 (7%) RAL, 219 (21%) RPV. Study population's

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characteristics are reported in table 1. At multivariable regression, women on ATV/r showed higher risk of TF; the other factor associated to higher risk of TF was AIDS (HR 1.58, 95% CI 1.13–2.20, p=0.007). HRs of different outcomes for each third drug of the regimen are reported in figure 1. 404 WLWH started regimens included in WLWH-RCT, the proportions of virological success were 50.7% in ATV/r (81% Waves and 71% ARIA), 79.2% in EVG/c (87% Waves) and 74.7% in DTG (vs 82% ARIA).

Conclusions: In a real-world cohort of WLWH, treatment failure is still an issue, particularly in case of PI/r based regimens. Results from clinical practice are far from those obtained in trials and suggest the need for focused intervention on adherence and vulnerability support in this population.

Table 1. General characteristics of study population

	ATV/b N=258	DGV N=166	EVG N=115	DRV/b N=219	RAL N=71	RPV N=219	p
Age, median (IQR)	36 (30-44)	45 (33-55)	39 (32-50)	39 (31-47)	44 (32-52)	38 (29-49)	<0.001
Mode of HIV infection, n(%)							
heterosexual	215 (83.3%)	139 (83.8%)	99 (86.1%)	186 (84.9%)	62 (87.3%)	184 (84.0%)	0.297
IVDU	27 (10.5%)	11 (6.6%)	10 (8.7%)	21 (9.6%)	1 (1.4%)	21 (9.6%)	
other/unknown	16 (6.2%)	16 (9.6%)	6 (5.2%)	12 (5.5%)	8 (11.3%)	14 (6.4%)	
Nationality							
Italian	132 (51.2%)	87 (52.4%)	59 (51.3%)	124 (56.6%)	40 (56.3%)	134 (61.2%)	<0.001
not Italian	125 (48.4%)	58 (34.9%)	39 (33.9%)	88 (40.2%)	24 (33.8%)	68 (31.0%)	
missing	1 (0.4%)	21 (12.7%)	17 (14.8%)	7 (3.2%)	7 (9.9%)	17 (7.8%)	
AIDS diagnosis, n(%)	26 (10.1%)	25 (15.1%)	16 (13.9%)	45 (20.6%)	9 (12.7%)	7 (3.2%)	<0.001
HCVAb, n(%)							
negative	198 (76.7%)	128 (77.1%)	91 (79.2%)	174 (79.4%)	59 (83.0%)	172 (78.5%)	0.153
positive	35 (13.6%)	9 (5.4%)	9 (7.8%)	21 (9.6%)	6 (8.5%)	22 (10.1%)	
missing	25 (9.7%)	29 (17.5%)	15 (13.0%)	24 (11.0%)	6 (8.5%)	25 (11.4%)	
HBsAg, n(%)							
negative	224 (86.8%)	131 (78.9%)	92 (80.0%)	187 (85.4%)	63 (88.7%)	182 (83.1%)	0.386
positive	9 (3.5%)	5 (3.0%)	6 (5.2%)	5 (2.3%)	2 (2.8%)	9 (4.1%)	
missing	25 (9.7%)	30 (18.1%)	17 (14.8%)	27 (12.3%)	6 (8.5%)	28 (12.8%)	
CD4, n(%)							
0-200	80 (31.0%)	64 (38.5%)	43 (37.4%)	94 (42.9%)	26 (36.6%)	17 (7.8%)	<0.001
201-350	85 (33.0%)	30 (18.1%)	24 (20.9%)	59 (26.9%)	14 (19.7%)	41 (18.7%)	
351+	88 (34.1%)	66 (39.8%)	46 (40.0%)	60 (27.4%)	29 (40.9%)	158 (72.1%)	
missing	5 (1.9%)	6 (3.6%)	2 (1.7%)	6 (2.8%)	2 (2.8%)	3 (1.4%)	
HIVRNA, n(%)							
<100.000	156 (60.5%)	103 (62.0%)	74 (64.3%)	107 (48.9%)	41 (57.8%)	209 (95.4%)	<0.001
>=100.000	96 (37.2%)	57 (34.4%)	40 (34.8%)	103 (47.0%)	27 (38.0%)	5 (2.3%)	
missing	6 (2.3%)	6 (3.6%)	1 (0.9%)	9 (4.1%)	3 (4.2%)	5 (2.3%)	
NRTI backbone, n(%)							
TDF/FTC	219 (84.9%)	64 (38.6%)	95 (82.6%)	176 (80.4%)	58 (81.7%)	202 (92.3%)	<0.001
TAF/FTC	0	5 (3.0%)	20 (17.4%)	3 (1.4%)	1 (1.4%)	6 (2.7%)	
ABC/3TC	39 (15.1%)	97 (58.4%)	0	40 (18.2%)	12 (16.9%)	11 (5.0%)	
Causes of discontinuation, n(%)							
failure	14 (7.6%)	4 (9.8%)	2 (14.3%)	4 (3.2%)	0	5 (14.3%)	<0.001
toxicity	64 (35.0%)	9 (22.0%)	7 (50.0%)	24 (19.4%)	3 (8.8%)	12 (34.2%)	
semplification	32 (17.5%)	4 (9.8%)	0	37 (29.8%)	15 (44.1%)	2 (5.7%)	
patient's decision	12 (6.6%)	3 (7.3%)	1 (7.1%)	4 (3.2%)	4 (11.8%)	1 (2.9%)	
other	28 (15.3%)	8 (19.5%)	2 (14.3%)	17 (13.7%)	8 (23.5%)	11 (31.5%)	
missing	33 (18.0%)	13 (31.6%)	2 (14.3%)	38 (30.7%)	4 (11.8%)	4 (11.4%)	

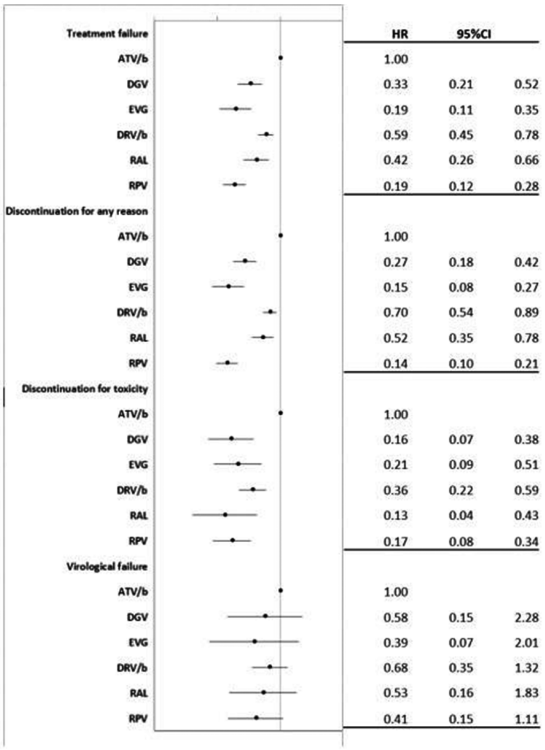


Figure 1. Hazard ratio of various outcome according to third drug of the regimen from 4 separate Cox models, after adjustment for AIDS diagnosis, nationality, CD4 cell count, plasma HIV-RNA, HCV-Ab status, NRTI backbone and calendar year of cART initiation.

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Well-being in people living with HIV/AIDS (PLWHA) according to cART exposure: data from IOCONA cohort

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Purpose: Patient-reported outcome measures (PROMs) are now being collected within a subset of the ICONA cohort. To evaluate one of a selection of PROMs suitable for PLWHA regardless of time since diagnosis, to examine differences associated with exposure to cART.

Methods: PROMs were administered to PLWHA not on cART (no-cART) or on cART (>6 months, without previous virological failure). PROMs included the W-BQ16, a measure of 4 aspects of well-being plus overall general well-being. Independent samples t-tests and Pearson's r correlations were used with alpha set at 0.05.

Results: Participants included 318 PLWHA(72/246 no-cART/cART). Median CD4 cell count: 453/mmc and 678/mmc; median HIV-RNA: 39202 and 29 copies/mmc in no-cART or on cART PLWHA (median time on cART: 0.8 y

Table 1. Sociodemographic characteristics of all PLWHA and according to cART exposure

	On cART (N=246)	No cART (N=72)	p	Total (N=318)
Age, years, mean(SD)	46 (12)	39 (12)	<0.001	44 (13)
Sex, n(%)			0.508	
Women	31 (12.6)	7 (9.7)		38 (11.9)
Men	215 (87.4)	65 (90.3)		280 (88.1)
Ethnic group, n(%)			0.916	
Caucasian	226 (91.9)	67 (93.1)		293 (92.1)
Black	3 (1.2)	1 (1.4)		4 (1.3)
Other	17 (6.9)	4 (5.6)		21 (6.6)
HIV transmission route, n(%)			0.245	
Heterosexual	70 (28.5)	16 (22.2)		86 (27.1)
IDU	18 (7.3)	2 (2.8)		20 (6.3)
MSM	143 (58.1)	47 (65.3)		190 (59.7)
Other/unknown	15 (6.1)	7 (9.7)		22 (6.9)
Employment, n(%)			0.392	
Employed	131 (53.2)	37 (51.4)		168 (52.8)
Unemployed	13 (5.3)	7 (9.7)		20 (6.3)
Other/Unkwon	102 (41.5)	28 (38.9)		130 (40.9)
Education, n(%)			0.104	
College	85 (34.5)	21 (29.2)		106 (33.3)
Primary School	5 (2.0)	0 (0.0)		5 (1.6)
Secondary School	30 (12.2)	10 (13.9)		40 (12.6)
University	43 (17.5)	22 (30.6)		65 (20.4)
Unknown	83 (33.7)	19 (26.4)		102 (32.1)

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Table 2.: Aspects of well-being and difference according to cART exposure

Outcome	cART group	N	Mean	SD	t	p
Well-being						
Negative Well-being	No cART	67	3.48	3.07	3.153	0.002
	cART	236	2.31	2.57		
Energy	No cART	66	7.61	2.63	-0.47	0.639
	cART	234	7.76	2.37		
Positive Well-being	No cART	70	7.29	3.26	-2.184	0.030
	cART	244	8.19	2.99		
Stress	No cART	71	4.87	3.16	1.782	0.076
	cART	235	4.16	2.91		
General Well-being	No cART	61	30.77	9.55	-2.274	0.024
	cART	220	33.6	8.34		

Note: Greater well-being is indicated by higher scores on General Well-being, Energy and Positive Well-being and lower scores on Negative Well-being and Stress.

[95% CI 0.4–2.0]); no-cART pts had fewer years since HIV diagnosis (0.8 [2.8] vs 6.7 [6.8], p<0.001).Treatment groups differed significantly on age (those on cART were older) but not on other demographic characteristics (Table 1). Participants on cART reported significantly less negative well-being, greater positive well-being and better overall general well-being than those not on -cART, (Table 2). Mean scores for energy and stress followed the same (but non-significant) pattern. Correlational analyses revealed no association between age and well-being scores (r=0.003 - 0.036, ns) which, together with findings of no treatment-group differences in effects of sex or ethnicity, suggests these demographic variables are not confounding the effects of treatment group on well-being.

Conclusion: PROMS provide patient-centered outcomes for use alongside biomedical markers to support patient care. PLWHA on cART reported significantly better well-being than PLWHA not yet receiving cART, suggesting cART treatment not only improves biomedical markers but is also associated with improved psychological well-being. Longitudinal follow-up will allow exploration of HIV-specific PROMs as well as well-being and other generic PROMs associated with different cART regimens.

PE2/54

Body composition changes in HIV: do INSTI matter?

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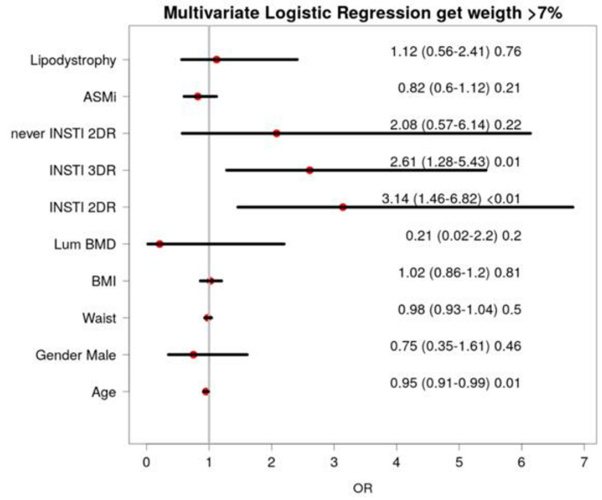
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Objectives: The aim was to assess weight gain (WG) and body composition changes in people living with HIV (PLWH) switching to INSTI-based regimens in comparison to INSTI-naïve patients. We assessed WG impact on incidence of co-morbidities.

Methods: In a prospective observational study, we included ART-experienced INSTI-naïve PLWH from 2007 to 2019. Patients were divided in two groups: patients who remained INSTI naïve and patients who switched to an INSTI regimen either in 3-drugs regimens (3DR) or in 2-drug regimens (2DR). The groups were matched for sex, age, baseline BMI and switch duration. WG was defined as an annualized increase of 7% in BMI. Predictors of WG were analyzed in a multivariable regression model comparing INSTI naïve 3DR to INSTI naïve 2DR, and patients who switched to INSTI either in 3DR or 2DR.

Results: A total of 1158 PLWH (68.7% males) were analyzed at baseline and at 4 years (±2.23) follow-up. Patients who switched to INSTI showed significant changes in age, BMI, waist circumference (WC), fat-free mass index (FFMI), appendicular skeletal muscle index (ASMI) and leg fat % (p<0.001). Mixed lipodystrophy, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) did not change over time. INSTI naïve showed significant changes in age, BMI, WC, FFMI, ASMI, leg fat %, sarcopenia, VAT and SAT. Higher prevalence of WG was observed in patients who switched to INSTI (68.9% vs. 31.2%, p<0.001). Figure describes independent predictor of WG. PLWH who experienced WG had higher incidence of T2DM (1.97 vs 1.22), CVD (1.67 vs 0.53), HTN (13.2 vs 7.07), CKD (6.82 vs 3.49), COPD (3.4 vs 1.06) cases per 100 patient-year, with the latter being the only statically significant.

Conclusions: We observed WG both in 3DR and 2DR in INSTI-based switch. Clinical relevance of this phenomenon needs to be explored in larger cohorts.



Multivariate regression model for weight gain

PE2/55

Dolutegravir-based regimens are associated with weight gain over two years following ART-initiation in ART-naïve people living with HIV (PLWH)

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Purpose: Previous studies have suggested that PLWH who initiate integrase inhibitor-based regimens may gain more weight than those who initiate other antiretroviral therapy (ART). These studies have often examined classes not individual agents, been small, combined ART-experienced and naïve PLWH, and did not address key potential confounders such as regimen backbone. We evaluated weight change among PLWH initiating ART in the current treatment era.

Method: Across 8 CNICS sites we identified ART-naïve PLWH initiating ART between 2012–2018, including efavirenz (EFV, n=404), rilpivirine (RPV, n=347), atazanavir (ATV, n=90), darunavir (DRV, n=245), raltegravir (RAL, n=89), elvitegravir (EVG, n=981), and dolutegravir (DTG, n=295)-based regimens with a tenofovir (TDF)/emtricitabine (or lamivudine) backbone. We also examined dolutegravir-based regimens with abacavir/lamivudine (ABC, n=338). Weight change was estimated using linear mixed models adjusted for time on regimen, time on regimen x regimen interaction, age, sex, race, hepatitis C, hepatitis B, nadir CD4, smoking, diabetes, anti-psychotic medication use, and site.

Results: Mean follow-up was 2.0 years. Compared with EFV, DTG/TDF was associated with a 2.6 kg (95% CI: 1.6–3.6) per year greater weight gain while DTG/ABC was associated with a 2.1 kg (95% CI: 1.4–2.8) per year greater gain. Other integrase inhibitor-based regimens showed less weight gain per year. Weight gain on DTG was statistically significantly

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greater than EFV, RPV, ATV, and EVG, but not DRV (1.8 kg per year, 95% CI: 0.9–2.7). Generalized additive model plots suggested that weight gain on DTG occurred in the first two years following regimen initiation (Figure 1).

Conclusion: DTG users had the greatest two-year weight gain, regardless of backbone, although weight gain was not significantly higher than in DRV users. For ART-naïve PLWH, potential weight gain should be considered in conjunction with the benefits of viral suppression when comparing DTG to other ART regimens.

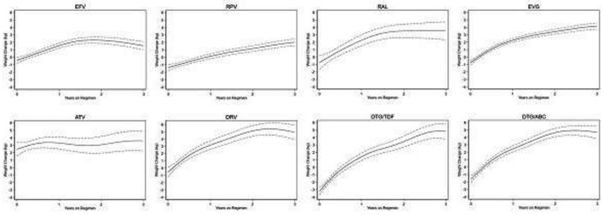


Figure 1. Generalized additive model plots of weight gain over time for each regimen

PE2/56

Efficacy and safety of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in combination with boosted darunavir (DRV) in treatment experienced patients with HIV

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Purpose: We report the safety and efficacy of B/F/TAF with boosted DRV in antiretroviral (ARV) experienced patients with HIV.

Method: Retrospective chart review at a single academic center. Inclusion criteria were having started on B/F/TAF in combination with boosted DRV (cobicistat or ritonavir) between 2/2018 and 6/2019. Excluded were patients taking this combination with additional ARVs, those with less than 24 weeks of follow up who did not discontinue the regimen, and those without viral load (VL) data at or beyond 24 weeks. Patients who discontinued the regimen prior to completing a week 24 VL were excluded from the efficacy analysis only.

Results: Forty-one patients were included in the analysis, of whom five discontinued the regimen prior to completing a week 24 VL. Table 1 and 2 show demographics, baseline virologic data, and treatment/resistance history. The cohort was highly treatment experienced, with 63.4% resistant to at least two classes of ARVs and 7.3% with documented integrase resistance. Of the 21 patients with a VL of<50 copies/mL, 85.7% remained<50 copies/mL. Fifteen patients had a VL>50 copies/mL at time of switch (mean 416,578 copies/mL), of whom 66.7% achieved a VL of<200 copies/mL and 20% achieved<50 copies/mL at week 24. Mean change in CD4 count was + 22 cells/mm^3 at week 24. Ten patients discontinued the regimen, two due to adverse events (rash, diarrhea). The mean baseline serum creatinine (SCr) was 1.08 mg/dL and the mean change in SCr after 24 weeks was 0.01 mg/dL.

Conclusion: The combination of B/F/TAF with boosted DRV was effective in maintaining viral suppression in those with VL<50 copies/mL and in achieving VL<200 copies/mL in those with detectable viremia. There were few discontinuations due to adverse effects with no safety concerns after 24 weeks of treatment.

Table 1. Demographics of study population (n=41)

Median Age (range)	54 (31–67)
Gender (%): Male, Female, Transgender	33 (80.5), 6 (14.6), 2 (4.9)
Race (%): White, Black, Asian, Other	26 (63.4), 4 (9.8), 1 (2.4), 10 (24.4)
Ethnicity (%): Hispanic, Non-Hispanic	15 (36.6), 26 (63.4)

Table 2. Virologic and treatment/resistance history for study population (n=41)

Pharmacokinetic enhancer (%): Cobicistat, Ritonavir	40 (97.6), 1 (2.4)
VL<50 copies/mL at time of switch (%)	24 (58.5)
CD4 + T-cell count (cells/mm3) (median, range)	449 (13–1099)
Number of previous ARVs (mean, 95% CI)	10.8 (9.6–12.0)
Number of previous ARV classes (mean, 95% CI)	3.9 (3.7–4.0)
Years on ARV (mean, 95% CI)	18.2 (15.9–20.1)
Number of ARV class resistance (%): Unknown, 1, 2, 3, 4	4 (9.8), 4 (9.8), 7 (17.1), 14 (34.1), 11 (26.8), 1 (2.4)
Documented integrase inhibitor resistance (%)	3 (7.3)
Reason for regimen change (%): Side effects, Poor adherence/resistance, Low level/ongoing viremia, Regimen simplification, Drug interaction	4 (9.8), 14 (34.1), 5 (12.2), 16 (39.0), 2 (4.9)
Follow up time (days) (mean, 95% CI)	315 (285–346)

PE2/57

Real world data of using Triumeq (dolutegravir/abacavir/lamivudine; DTG/ABC/3TC): final outcomes of the 3-year German TRIUMPH cohort show good virologic effectiveness and safety in clinical routine

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Background: TRIUMPH was a prospective, 3-year observational German cohort study in ART-naïve and pre-treated adult HIV-infected patients receiving Triumeq, an one-pill regimen consisting of DTG/ABC/3TC.

Methods: Primary and secondary outcomes included the rate of monitoring measures per patient year (PPY), virologic effectiveness using a modified ITT snapshot approach (HIV-RNA<50 cp/mL (visit-window ≥month 33), discontinuation=failure, missing/loss-to-follow-up=excluded) and on-treatment (OT) analysis, persistence of DTG/ABC/3TC, and incidence of (non-)serious adverse drug reactions (ADRs/SADRs).

Results: The analysis population consisted of N=387 patients (40.1% ART-naïve). Of ART-naïve patients, 12.9% had<200 CD4/µl, 18.1% had≥100,000 HIV-RNA cp/mL. Of pre-treated, 84.9% had<50 HIV-RNA cp/mL, 19.4% had≥3 prior regimens and 47.8% switched from PI-based regimens. Comorbidities were documented in 44.2% of patients (Table 1).

At last follow-up (≥month 33), in 36.2% of patients premature study discontinuation was reported, including 13.4% lost to follow-up, 5.7% patient decision/withdrawal of consent and 18.3% discontinuing DTG. ADRs and virologic failure were the reasons for DTG discontinuation in 9.6% and 0.8% of patients, respectively (Table 2).

After 3-year follow-up, virologic effectiveness was 73.1% (mITT; 244/334) [ART-naïve 72.8 (99/136), pre-treated 73.2% (145/198)]. In OT analysis, HIV-RNA was<50 cp/mL in 95.3% (244/256) [ART-naïve 94.3% (99/105), pre-treated 96.0% (145/151)]. Physician visits and monitoring measures are shown in Table 3.

Overall, 92 ADRs (incl. 11 SADRs) were reported resulting in an event rate of 0.097 PPY; 77.2%, 12.0% and 10.9% of ADRs occurred in years 1, 2 and 3.

Conclusion: During the course of the 3-year TRIUMPH cohort, the good safety profile and high virological effectiveness of DTG/ABC/3TC in clinical trials was confirmed in real-life with discontinuation rates for intolerance or virologic failure of 9.6% and 0.8%, respectively. Moreover, ADR rates decreased over time. Monitoring measures were mainly related to

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routine quarterly controls of HIV-disease, reflecting local HIV treatment guidelines.

Table 1. Baseline characteristics

	Overall (N=387)	ART-naïve (N=155, 40.1%)	Pre-treated (N=232, 59.9%)
Sex, male, n (%)	348 (89.9)	147 (94.8)	201 (86.6)
Age, years, median (interquartile range)	42 (33–50)	38 (29–48)	45 (35–52)
CDC stage C, n (%)	60 (15.5)	8 (5.2)	52 (22.4)
HIV-1 RNA, median (interquartile range)	1.7 (1.7–4.3)	4.4 (3.9–4.9)	1.7 (1.7–1.7)
CD4 cell count, median (interquartile range)	533 (368–760)	450 (282–613)	600 (434–834)
Presence of comorbidities, n (%)	171 (44.2)	45 (29.0)	126 (54.3)
Comorbidities in>10% of patients			
Depression, n (%)	76 (19.6)	18 (11.6)	58 (25.0)
Hypertension, n (%)	43 (11.1)	14 (9.0)	29 (12.5)

Table 2. Study or DTG/ABC/3TC discontinuations and most common reasons (multiple responses permitted)

	Overall N=387	ART-naïve patients N=155	Pre-treated patients N=232
Patients with study discontinuation, n (%)	140 (36.2)	53 (34.2)	87 (37.5)
Loss to follow-up, n (%)	52 (13.4)	18 (11.6)	34 (14.7)
Patients stopping DTG, n (%)	71 (18.3)	24 (15.5)	47 (20.3)
Reasons for stopping DTG, n (%)			
ADRs (adverse drug reactions), n (%)	37 (9.6)	15 (9.7)	22 (9.5)
Patient wish, n (%)	33 (8.5)	8 (5.2)	25 (10.8)
Virologic failure, n (%)	3 (0.8)	2 (1.3)	1 (0.4)
Comorbidity /comedication, n (%)	2 (0.5)	1 (0.6)	1 (0.4)
Other, n (%)	9 (2.3)	1 (0.6)	8 (3.4)

Table 3. Physician visits and monitoring measures per patient year (PPY)

	Overall N=387
Documented physician visits PPY, median (IQR*)	4.6 (4.1 – 5.4)
Referrals to specialists (excl. infectiologists), median (IQR*)	1.0 (0.5 – 1.7)
Monitoring measures PPY, median (IQR*)	
- HIV-RNA/CD4 cell	4.0 (3.5 – 4.3)
- Blood count	4.1 (3.6 – 4.5)
- Serum chemistry	4.1 (3.6 – 4.5)
- Urine tests	1.8 (0.0 – 3.8)
- Microbiological tests (including one or multiple tests)	1.0 (0.0 – 2.3)

*IQR: inter quartile range

PE2/58

The effectiveness of E/C/F/TAF in treatment-naive (TN) or treatment-experienced (TE) adult HIV-infected patients in a real-world setting, results from southern Turkey

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Purpose: In Turkey, elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) is a recommended regimen for first-line treatment of HIV infection and for some TE patients, but limited data are available from real-world experience. This retrospective cohort study was done in southern Turkey to evaluate the effectiveness of E/C/F/TAF when used in TN or TE adult HIV-infected patients in a real world setting.

Method: All patients who received E/C/F/TAF for at least 6 months were included in this multicenter, retrospective study. Patient characteristics, reasons for selection of E/C/F/TAF, virological efficacy and reasons for discontinuations/modifications were evaluated.

Results: A total of 562 patients were included in the analysis population; 167 patients were TN, 395 patients were TE. In the TN group 24 (14.5%) patients were late presenters (Table 1). Patients were switched to E/C/F/TAF; 73.7% of them had previously used INSTI (Table 1). Overall 2.1% (12/562) of patients discontinued/modified study medication before M12 visit. Reasons are shown in Table 1.

At M6 visit 89.2% (n=501/562) had HIV RNA levels<50 cp/mL. At M12; 105 TN patients had treatment results, follow-up of 58 patients was not completed yet, 4 patients were lost to follow-up. 90.5% of patients (95/105) achieved HIV RNA<50 cp/mL at 12 months. In the TE group, virological suppression was 95.8% in 263 patients with M12 data (see Figure 1).

The most common reason for switch to E/C/F/TAF was to minimize long-term toxicity (n=207, 52.4%) (Table 2).

In TN patients at M12 there was no difference in viral suppression after stratification by baseline variables (p: 0.3). (Figure 2)

Conclusion: In TN and TE patients, 6 and 12 month data from this real world cohort confirmed the effectiveness E/C/F/TAF in routine practice. This virological effectiveness was unaffected by baseline HIV RNA and CD4 levels.

Table 1. Baseline characteristics

Participant Characteristics	Overall Median (IQR) or Proportion (N=562)	Treatment Naive (TN) Median (IQR) or Proportion (N=167)	Treatment Experienced (TE) Median (IQR) or Proportion (N=395)	p
Age, y, median (IQR)	34.0 (28.0–44.0)	31.0 (26.0–41.0)	36.0 (28.0–46.0)	0.000
Age, y≥50, n (%)	89 (15.8)	18 (10.8)	71 (18.0)	0.042
CD4 cells/μL, median (IQR)	566.0 (361.0–806.0)	378.0 (268.0–540.0)	683.0 (468.75–926.50)	0.000
CD4<200 cells/μL, n (%)	39 (7.1)	24 (14.5)	15 (3.8)	0.000
HIV RNA log10, median (IQR)	4.6 (2.8–5.2)	4.9 (4.5–5.6)	2.1 (1.7–3.1)	0.000
HIV RNA<50 copies/mL, 50-<200 copies/mL 200–100 000 copies/mL>100 000 copies/mL	330 (60.7) 22 (4.0) 114 (21.0) 78 (14.3)	- - 88 (52.7) 75 (44.9)	330 (86.6) 22 (5.8) 26 (6.8) 3 (0.8)	
Previous Antiretroviral Treatment INSTI NNRTI PI Other	NA NA NA NA	NA NA NA NA	291 (73.7) 72 (18.2) 31 (7.8) 1 (0.3)	
Reasons for modification / discontinuation, n (%) Patient's wish Clinician's preference Obstetric Virological failure Other	12 (2.1) 1 (8.3) 1 (8.3) 1 (8.3) 4 (33.3) 5 (41.7)	4 (2.4) - - - 4 (100.0) -	8 (1.4) 1 (12.5) 1 (12.5) 1 (12.5) - 5 (62.5)	

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Table 2. Reasons for switch to E/C/F/TAF, n (%)

Reasons for drug modification and/or discontinuation	n (%)
Treatment simplification	77 (19.5)
Patient preference	10 (2.5)
Intolerance/toxicity Gastrointestinal intolerance	31 (7.8) 1 (3.2) 2 (6.5) 7 (22.6)
Hyperlipidemia Osteopenia Osteoporosis Central Nervous System Nephrotoxicity	3 (9.7) 4 (12.9) 14 (45.1)
Minimize long-term toxicity	207 (52.4)
Other	70 (17.7)

Figure 1. Virologic effectiveness in patients with E/C/F/TAF

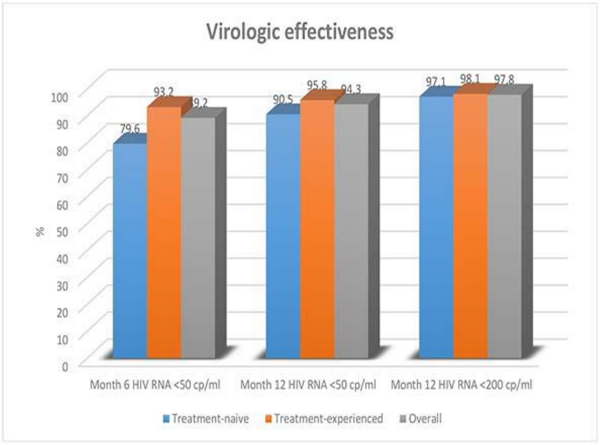
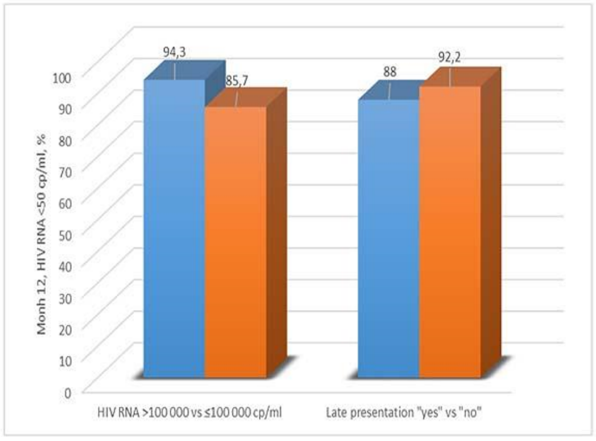


Figure 2. Month 12 HIV RNA <50 cp/ml stratified by baseline variables, only TN patients



PE2/59

Comparison of efficacy and safety of a switch to fixed-dose combination FTC/TDF-TAF/RPV versus fixed-dose combination 3TC/ABC/DTG in HIV-1-infected, treatment experienced and virologically suppressed patients: a cohort study

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Purpose: Comparison of efficacy and safety of switching to single tablet with FTC/TDF-TAF/RPV (RPV-STR) or 3TC/ABC/DTG (DTG-STR) in virologically-suppressed (VS), antiretroviral therapy (ARV) experienced HIV-positive patients.
Method: This is a retrospective-monocentric cohort-study analyzing all ARV experienced HIV-infected patients with HIV-RNA level<50 copies/mL, switching to RPV-STR or to DTG-STR since 2013 and 2015 respectively. Study entry was drug-intaking date, study exit was virologic failure (VF) date or the discontinuation date due to any cause or loss to follow-up (FU)/death. VF was defined as consecutive detection of two HIV-RNA level>50 copies/mL. X^2/Fisher's and Wilcoxon signed rank test were used where appropriate. Kaplan-Meier for the probability of VF/discontinuation and Poisson model for regression analysis were employed.
Results: We included 396 patients (244 with RPV-STR, 152 with DTG-STR).
Conclusion: few VF occurred in patients switched to DTG-STR or to RPV-STR. A significative more risk of discontinuation due to toxicity within 3 months from switch was observed in DTG-STR compared to RPV-STR.

Table 1. Clinical/demographic characteristics of the study population grouped by the different single tablet regimen

	FTC/TDF-TAF/RPV group (N=244)		3TC/ABC/DTG group (N=152)		p
Italians, n (%)	221	90.6	126	82.9	0.024
Sex Female, n (%)	54	22.1	29	19.1	0.029
Age at entry, median [IQR]	49	[43–56]	51	[42–58]	0.136
Years of undetectable viremia, median [IQR]	5	[2–7]	4	[1–8]	0.594
AIDS diagnosis, n (%)	41	16.8	35	23.0	0.126
HCV Ab positivity, n (%)	53	21.7	29	19.1	0.528
HIV RNA Zenit, Log10 copies/mL, median [IQR]]	5.09	[4.67–5.49]	5.12	[4.74–5.54]	0.585
Nadir CD4 (cells/mL), median [IQR]	265	127–370	281	125–405	0.488
Years of HIV, median [IQR]	13	[7–19]	10	[4–18]	0.063

Table 2. Outcome of the study population grouped by the different single tablet regimen

	FTC/TDF-TAF/RPV group (N=244)		3TC/ABC/DTG group (N=152)		p
End-of-follow-up therapy outcome, n (%)					
Ongoing	167	68.4	123	80.9	0.011
Change for toxicity	23	9.4	19	12.5	
Change for other causes	18	7.7	5	3.3	
Virologic failure	16	6.6	2	1.3	
Self-suspension of therapy	6	2.5	2	1.3	
Lost to follow-up	11	4.5	1	0.7	
Dead	3	1.2	0	0	

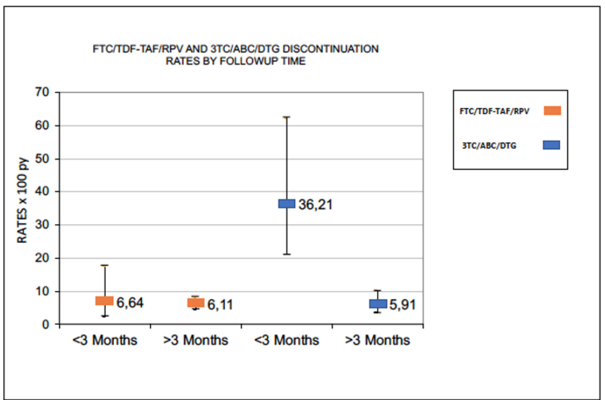


Figure 1. FTC/TDF-TAF/RPV and 3TC/ABC/DTG discontinuation rate by follow-up time

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COPEDOL: a 2-year French multicentric, observational, longitudinal retro-prospective study, in pretreated HIV-1-infected patients starting dolutegravir based regimen due to treatment failure

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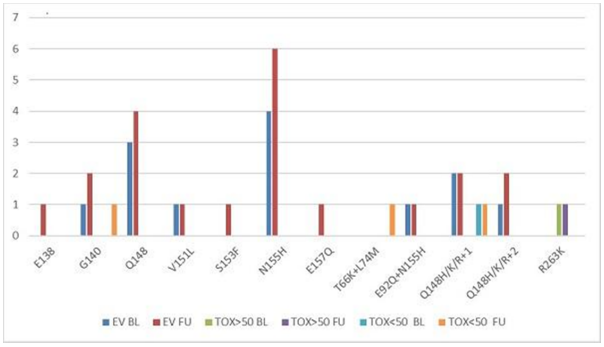
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Purpose: The main objective of this study was to assess the virological response in patients switched to dolutegravir based regimen (DBR) at the time of their treatment failure. The main secondary objectives were to assess the Virological sustained response in addition to the safety.
Method: COPEDOL is a 2-year, French multicentric, observational, longitudinal, retro-prospective study in which patients were stratified in two groups according to the reason of their failure. Patients in EV group had failed due to virological reason and patients in TOX group had failed due to toxicity of previous treatment regimen. TOX patients were studied according to their virological status (detectable or not at the time they started DBR). To be included HIV patients were to have started DBR between February 2014 and September 2016.
Results: 50 centers included 459 patients (EV N=222 and TOX N=237). The mean age was 50 years (+/- 11 years; range 16–82) with 64.1% of men and 21.8% presented 3 or more comorbidities. The median time since HIV diagnosis was 18 years and the median duration of treatment was 14 years. The mean CD4 nadir was 198 cells/mm3 (±182). At DTG introduction, 30.7% and 27.2% had GSS≤1 (genotypic sensitivity score) in the EV and TOX groups respectively.

Virological response (VL<50cp/mL) through 24 months

		1 month N=136	3 months N=147	6 months N=178	12 months N=180	24 months N=153
EV group	n	117	138	172	173	148
	yes	78 (66.67%)	99 (71.74%)	137 (79.65%)	137 (79.19%)	113 (76.35%)
		1 month N=11	3 months N=7	6 months N=14	12 months N=14	24 months N=8
TOX group (≥50 mL/cp)	n	9	6	14	13	6
	yes	6 (66.67%)	4 (66.67%)	11 (78.57%)	11 (84.62%)	6 (100.00%)
		1 month N=77	3 months N=124	6 months N=172	12 months N=168	24 months N=143
TOX group (< 50 mL/cp)	n	69	108	163	161	135
	yes	67 (97.10%)	101 (93.52%)	158 (96.93%)	155 (96.27%)	128 (94.81%)

At DTG introduction (BL) 37 patients had INSTI resistance mutation (1 mutation: 11.4%, 2 mutations: 54.3%, more than 2: 34.13%). Major resistance mutations to DTG occurred in 5 patients during follow up (FU).



Emergence of mutations associated with resistance to DTG

Conclusion: The results obtained in real life conditions are aligned with those observed in clinical trials in pretreated patients in terms of efficacy and safety and few patients experienced virological failures with emergent resistance mutation to DTG.

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Drug-drug interactions with recommended first-line antiretroviral therapy in real-world settings

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Purpose: Extended life expectancy of patients with human immunodeficiency virus (HIV) necessitates treatments for their comorbidities. Given the complex metabolic pathway of antiretroviral therapies (ARTs), polypharmacy may increase the risk of drug-drug interactions (DDIs), leading to detrimental clinical outcomes. Therefore, we investigated the DDIs with recommended first-line ARTs using claims data from National Health Insurance.
Method: This was a nationwide cross-sectional study with HIV patients receiving ART in 2016. Potential or contraindicated DDIs with recommended first-line ARTs were identified from University of Liverpool drug interaction database. The DDIs were defined as having at least one-day overlap of comedications within an ART exposure period. Fisher exact or chi-square test was used to determine a significant association between categorical variables.
Results: A total of 25,863 HIV-infected individuals were identified, including 5,877 TDF/FTC/EFV users, 3,519 TDF/FTC/RPV users and 2,517 ABC/3TC/DTG users. Highest percentage of potential DDIs was observed among patients receiving TDF/FTC/EFV (50%), followed by TDF/FTC/RPV (32%) and ABC/3TC/DTG (15%). Most frequently co-prescribed medications related to potential DDIs were diclofenac and polyvalent cation-containing antacids. The percentage of patients with more than one contraindicated DDI was low, with the highest percentage of DDIs observed for TDF/FTC/RPV (4%), followed by TDF/FTC/EFV (2%) and ABC/3TC/DTG (1%). The most commonly co-administered medications for contraindicated DDIs were midazolam and dexamethasone. Compared to patients without DDIs, those with potential or contraindicated DDIs were more likely to be elder, and had more comorbidities and comedications.
Conclusion: Our study showed low prevalence of contraindicated DDIs in the HIV population, suggesting that most physicians in Taiwan aware of the severe DDI issue. However, strategies used to avoid potential DDIs and maintain the effectiveness and safety of medications should be implemented. Future research that focuses on long-term clinical impact of the potential DDIs is warranted.
Abbreviations: TDF-tenofovir; FTC-emtricitabine; EFV-efavirenz; RPV-rilpivirine; ABC-abacavir; 3TC-lamivudine; DTG-dolutegravir

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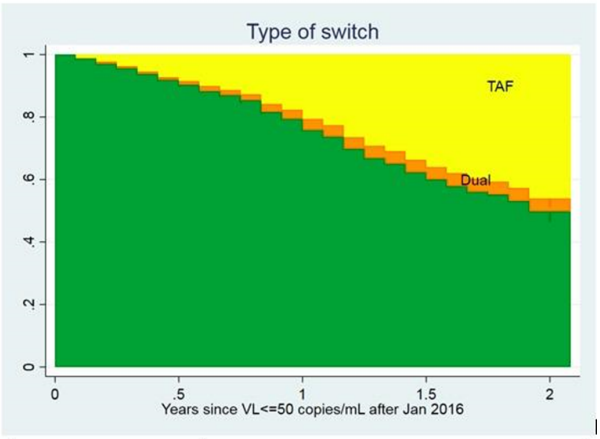
Determinants of switching to TAF-based cART or dual combinations (DC) from TDF-based regimens in a cohort of HIV-infected individuals with controlled viral load≤50 copies/mL

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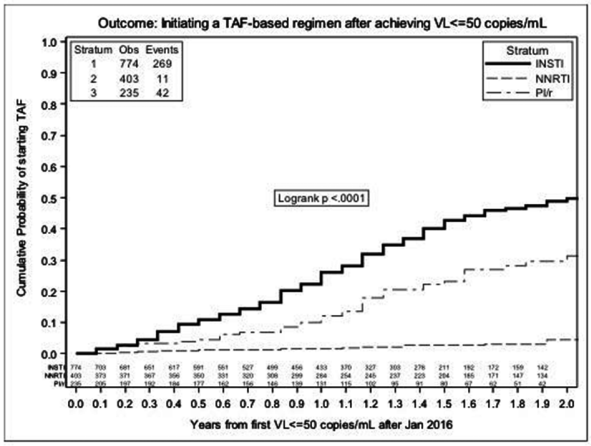
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Purpose: The main aim of this analysis was to evaluate the impact of recent results of randomised studies on the shift between TDF to TAF-based regimens or dual combinations (DC) therapy in real-life.
Method: HIV+(HBsAg-negative) patients in the Icona Cohort, who achieved a VL≤50 copies/mL for the first time on a TDF-based regimen after January 2016 are included. Kaplan-Meier (KM) curves and (unweighted and weighted) Cox regression models were used to separately estimate the time to switch from TDF to either TAF or DC. A competing KM risk analysis was conducted to jointly model both switches. The main association of interest was between eGFR and the probability of switching after controlling for confounding factors (Tables 1 and 2). An alternative analysis was performed excluding switches to TAF/F/EVG/c as they could be triggered by reasons not strictly related to renal toxicity.
Results: A total of 1.412 participants were included, 20% female, median (IQR) age of 36(30–42) years, CKD-EPI eGFR 99.1(85.8–111.1) mL/min/1.73 m^2, 86% acquired HIV through sex. At baseline, the most commonly used anchor drugs were RPV(27%), EVG/c(26%), DTG(20%) and DRV/r(13%). By 2 years from baseline, the probability of switching was 4% (95% CI 2.3–4.6) to DC and 21% (95% CI 18.8–23.7) to TAF-based cART (Figure 1). A significant higher probability of switching to TAF-based regimen was found for those receiving INSTI at baseline (KM estimates: 49.8%;95% CI 45.2%,54.5% by 2 years, log-rank p<0.0001; figure 2),not confirmed in the alternative analysis. A eGFR<60 mL/min/1.73 m^2 both as time-fixed at baseline or as current value, was associated with a higher probability of switching to DC but not to TAF-based cART (Table 1).
Conclusion: A consistent proportion of people with a VL≤50 copies/mL have switched from TDF to alternative strategies (20% to TAF-based and 4% to DC by 2 years). eGFR does not seem to change the probability of switching to TAF-based regimens.



	2-year KM estimate (95% CI)
DC	3.5% (95% CI 2.3-4.6)
TAF-based regimen	21% (95% CI 18.8-23.7)

Figure 1. Kaplan Meier plot of competing therapy initiation



	Kaplan-Meier estimates of probability of switching to TAF-based cART	
	No. switches by 24 months	2-year percent (95% CI)
Other	11	4.6 (1.7, 7.4)
PI/r	42	31.3 (22.7, 40.0)
INSTI	266	49.8 (45.2, 54.5)
Total	232	21.2 (18.7, 23.6)

Figure 2. Kaplan Meier plot of time to TAF initiation by anchor drug class

Table 1. HR of TAF-based therapy initiation after excluding switches to EVG/c from fitting a Cox-regression model-association with time-dependent eGFR

Hazard Ratios of switching to TAF-based regimens - TAF/F/EVG/c not counted as an event			
Hazard Ratio (95% CI); p-value			
eGFR (mL/min/1.73 m^2)	Unadjusted	Adjusted1	Adjusted2
Baseline value			
60+	1.00	1.00	
0–59	2.46 (1.12, 5.37); 0.024	1.88 (0.76, 4.66); 0.173	
Most recent value			
60+	1.00		1.00
0–59	2.07 (0.98, 4.34); 0.055		1.34 (0.59, 3.04); 0.484

**(1)Adjusted for gender, age, mode of HIV transmission, nationality, AIDS diagnosis, hep C-coinfection status, calendar year of VL<=50 copies, number of drugs failed prior to baseline, type of anchor drug of TDF-based regimen, number of concomitant co-morbidities and current CD4 count, HIV-RNA as time dependent variables **(2)Adjusted for gender, age, mode of HIV transmission, nationality, AIDS diagnosis, hep C-coinfection status, calendar year of VL<=50 copies, number of drugs failed prior to baseline, type of anchor drug of TDF-based regimen, number of concomitant co-morbidities and current CD4 count, HIV-RNA using inverse probability weighting

Table 2. HR of DC from fitting a Cox regression model- association with time-dependent eGFR

Hazard Ratios of switching to DC regimens			
Hazard Ratio (95% CI); p-value			
eGFR (mL/min/1.73 m^2)	Unadjusted	Adjusted1	Adjusted2
Baseline value			
60+	1.00	1.00	
0–59	6.91 (2.65, 18.03); <0.001	6.01 (2.10, 17.24); <0.001	
Most recent value			
60+	1.00		1.00
0–59	7.78 (3.38, 17.9); <0.001		6.28 (2.30, 17.15); <0.001

**(1)Adjusted for gender, age, mode of HIV transmission, nationality, AIDS diagnosis, hep C-coinfection status, calendar year of VL<=50 copies, number of drugs failed prior to baseline, type of anchor drug of TDF-based regimen, number of concomitant co-morbidities and current CD4 count, HIV-RNA as time dependent variables **(2)Adjusted for gender, age, mode of HIV transmission, nationality, AIDS diagnosis, hep C-coinfection status, calendar year of VL<=50 copies, number of drugs failed prior to baseline, type of anchor drug of TDF-based regimen, number of concomitant co-morbidities and current CD4 count, HIV-RNA using inverse probability weighting

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An early proactive switch to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/T/TAF) is effective in maintaining virologic control and improving quality of life (QoL) in patients with a primary HIV-1 infection (PHI). An interim analysis of a phase IV clinical trial (ESTER study)

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Purpose: The aim of this study was to evaluate virologic and immunologic efficacy, adherence, and QoL of an early simplification strategy in HIV+ patients starting ART during PHI.
Method: ESTER is a pilot 96-week (w) single-arm trial enrolling HIV+ patients who achieved virologic suppression on a 4-drug ART regimen of darunavir 800 mg boosted with ritonavir or cobicistat + raltegravir 400 mg + tenofovir disoproxil fumarate/emtricitabine started during PHI. Included pts were switched to E/C/F/TAF. Virologic failure (VF) was defined two consecutive HIV-1 RNA test≥40 copies/mL. Evolution of residual viremia from baseline was assessed by ultrasensitive HIV-RNA<5 cp/mL and HIV-DNA evaluated at w24 and w48. QoL was assessed through both a visual analogue scale and the 30-item version Medical Outcome Study-HIV Health Survey (MOS-HIV) score.
Results: 30 participants were enrolled, of whom 18 have completed 48 weeks: 97% male, 87% MSM, median age 34 yrs, baseline CD4 count 667 cells/mm^3. At 48w both CD4 count and CD4/CD8 ratio significantly improved compared to baseline (Table 1). At 48w 55% patients achieved undetectable ultrasensitive HIV-RNA compared to 15% at baseline (p=0.011). Median HIV DNA decreased from 3.3 at baseline to 3.0 $\log_{10}$ copies/10^6 PBMC at 48w (p=0.135) (Table 1). 2/30 (6.6%) pts experienced VF, of whom none developed drug resistance mutations and all achieved resuppression without ART changes. There was a non-significant trend toward improved health perception and adherence over time (Tables 2). Pain and physical functioning scores significantly improved from baseline to w24 (p=0.046; p=0.049).

Table 1. Viro-immunological outcomes at W24 and W48. *n (%); ** median (interquartile range); *** mean (SD)

N=23	BL	W24	p value
CD4**	653 (520–759)	701 (582–839)	0.026
CD4/CD8**	0.87 (0.80–1.34)	1.07 (0.78–1.34)	0.176
log HIV DNA cp/mL***	3.2 (0.69)	3.0 (0.49)	0.265
US HIV RNA<5cp/mL*	4 (16.7%)	10 (41.7%)	0.059
N=18	BL	W48	p value
CD4**	650 (586–773)	766 (616–884)	0.024
CD4/CD8**	1.00 (0.81–1.34)	1.11 (0.73–1.55)	0.035
log HIV DNA cp/mL***	3.3 (0.7)	3.0 (0.61)	0.135
US HIV RNA<5cp/mL*	3 (15%)	11 (55%)	0.011

Quality-of-life and patients-reported adherence at W24 and W48. *n (%); **mean (SD)

N=23	BL	W24	p value
Missed doses*	5 (21.7%)	2 (8.7%)	0.083
>1 day treatment interruption*	1 (0.80–1.34)	0 (0%)	0.180
Adherence perception (VAS)**	98.5 (5.5)	98.5 (3.9)	0.718
Health perception (VAS)**	82.5 (20)	88 (18.5)	0.173
N=18	BL	W48	P value
Missed doses*	5 (29.4%)	2 (11.8%)	0.180
>1 day treatment interruption*	0 (0%)	0 (0%)	1
Adherence perception (VAS)**	98.6 (5.9)	98.9 (3.2)	0.968
Health perception (VAS)**	83.7 (20.5)	87.8 (17.3)	0.283

Conclusion: Although not recommended from guidelines, starting ART with an intensified quadruple regimen in patients with PHI has represented a clinical practice in recent years. In those patients an early switch to E/C/F/TAF showed to be effective in maintaining virologic control, reducing low level viral replication and in continuing immunological recovery.

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Prevalence of neuropsychiatric conditions in patients living with HIV-1 treated with antiretroviral therapies – a perspective from US Medicaid

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Objective: Neuropsychiatric events have been reported in patients living with HIV, treated with antiretroviral therapy (ART). Such events may lead to poor adherence, treatment interruptions, or change of therapy regimens; yet, the prevalence of such events is not well-understood. This study aimed to describe the demographics and clinical characteristics of patients living with HIV-1 who were newly initiated on ART and to estimate the prevalence of neuropsychiatric conditions (NPCs) of interest in this population.
Methods: A retrospective cohort study was conducted using administrative claims data from the IBM MarketScan® Multi-State Medicaid Database (MDCD, 1/1/2014–12/31/2017). The database includes hospital and outpatient diagnoses, procedures and pharmacy claims for Medicaid enrollees. Adults (≥18 years) with a diagnosis of HIV-1, were newly initiated on ART (no pharmacy claims 12 months prior) and had continuous health plan enrollment for 12 months prior to (baseline period) and at least 6 months following the start of ART (post-period) were included. Demographics and clinical characteristics were described, and period prevalence of NPCs 6- and 12-months post ART initiation was calculated.
Results: Among 1,971 included patients [mean age (SD) 38.5 (12.7) years, 41.4% female; 59.7% Black, 16.8% White and 1.6% Hispanic], the mean (SD) Quan-Charlson Comorbidity Index (QCI), a measure of comorbidity burden to which presence of HIV/AIDS contributes 4 points, was 4.2 (2.2). NPC period prevalence at 6- and 12-months post treatment initiation are presented in Table 1.

Table 1: Period Prevalence of NPCs in ART-treated Patients with HIV at 6- and 12-months post treatment initiation

	6 months (N=1,971)	12 months (N=1,335)
≥1 NPC	51.4%	61.9%
≥2 NPC	25.1%	36.6%
≥3 NPC	11.7%	19.3%
≥4 NPC	5.2%	10.4%

NPC = neuropsychiatric condition (anxiety, major depressive disorder, other depression, bipolar disorder, dizziness, fatigue, headache, insomnia/sleep disorder, trauma and stressor related disorders, cognitive impairment/poor concentration [combined diagnosis codes for specific memory loss, mild cognitive impairment, and other specified cognitive deficit], suicidal ideation, suicide attempt.)

Conclusion: In this study of Medicaid patients living with HIV-1 who were newly initiated on ART, NPCs during follow up were common, with 1 in 2 patients having evidence of at least 1 condition during the 6-month follow up; over the longer follow up period (12 months), NPCs were more common. Further studies are needed to investigate potential factors influencing the frequency of neuropsychiatric events, including the effects of ART.

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Switch to dolutegravir dual regimens and inflammation mediated by annexin

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Background: The toxicities associated with long-term use of NRTIs have led to the assessment of dual therapy approaches that reduce an NRTI component.

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Several strategies of treatment optimization and simplification gained interest, with the objectives of improving quality of life, minimizing ART-related toxicity and drug-drug interactions. The ART de-escalation from 3 to 2 drugs (dual-) therapies has mainly been evaluated in virologically suppressed patients. Due to its interesting pharmacokinetic profile, good tolerability and high genetic barrier to resistance, dolutegravir (DTG) is often used in simplified treatment regimens. Several studies evaluating DTG-based dual therapy showed a high virological efficacy, but no data are currently available on circulating Annexins, such as Annexin A1(AnxA1) and Annexin V(AnxV) that play an anti-inflammatory role. In addiction low AnxV levels are related to a greater atherosclerotic and thrombotic risk in systemic diseases.
The aim of this study is to evaluate the levels of plasmatic AnxV and AnxA1 before and after 48 weeks in a population which switched from triple standard therapy without DTG to a dual therapy DTG-based (plus lamivudine or rilpivirine).
Methods: A total of 16 HIV-positive male outpatients on cART attending the Infectious Diseases Clinics of Chieti and Roma were enrolled. Demographic and anamnestic data were collected, blood and immunological parameters were measured and AnxA1 and V were analyzed. Framingham risk score was calculated.
Results: The data were summarized in table 1. All patients was virologically suppressed at time of the enrollment(T0) and after 48 weeks(T1). At T0 AnxA1 was 16.9 + /-12.2 ng/mL and AnxV was 1.56 + /-0.55 ng/mL and at T1 AnxA1 was 16.2 + /-14.7 ng/mL and AnxV was 1.44 + /-0.71 ng/mL, no significant different were found.
Conclusions: Annexins levels were not altered after 48 weeks DTG-based dual therapy switch, indicating that there are no inflammatory and endothelial changes after switch. These data will be confirmed in a larger population.

Table 1

	Enrolment time (T0)	After 48 weeks (T1)	p
Age (years)	52.7 ± 11.5	53.7 ± 11.8	ns
CD4 + /CD8 + ratio	0.83 ± 0.38	0.85 ± 0.36	ns
eGFR (mL/min/1.73 m^2)	93.6 ± 22.9	93.1 ± 16.7	ns
GOT (UI/mL)	30.6 ± 15.8	23.6 ± 6.7	0.06
Total cholesterol (mg/dL)	168.1 ± 50.8	197.4 ± 56.6	ns
HDL (mg/dL)	46.7 ± 15.0	49.3 ± 15.4	ns
LDL (mg/dL)	92.1 ± 45.9	117.1 ± 50.0	0.07
Triglycerides (mg/dL)	146.3 ± 88.0	154.7 ± 124.9	ns
Framingham risk score	13.1 ± 10.3	14.2 ± 10.7	ns

PE2/66

Efficacy of dual antiretroviral therapy (ART) as intermittent short cycle regimen in virologically suppressed HIV-infected patients: an observational cohort

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Purpose: Intermittent triple therapy given 5 or 4 days per week (4D/5D) is highly effective in maintaining control of HIV replication in virally suppressed patients. Here we aimed to assess the efficacy of intermittent two drug regimens (2-DR).
Method: This observational single-centre study enrolled all virologically suppressed patients who were switched to intermittent 2-DR defined as 5D/4D 2-DR regimens. Primary outcome was the strategy success rate (plasma viral load [pVL] < 50 copies/mL with no regimen change) at W24. Secondary outcomes were the strategy success rate at W48, and evolution of HIV-DNA level from D0 to W48 in a subset of patients.
Results: Forty-five patients were included: men: 39/45 (87%), history of AIDS: 10/45 (22%), median age: 58 years (IQR 49–63), CD4 nadir: 245/mm^3 (127–322), ART duration: 21 years (12–23), duration of virological suppression: 6.8 years (3.6–10.6), CD4: 635/mm^3 (509–757), CD4/CD8 ratio: 0.80 (0.55–1.02). Baseline regimens included: 2-DR given 7 days per week (n=43; 95%), 4D triple therapy (n=1) and PI/r monotherapy (n=1). All patients were switched to intermittent 2-DR consisting of: INSTI/NNRTI (n=27), 2NRTI (n=6), PI/r-based 2-DR (n=6), INSTI/NRTI (n=5) and INSTI/PI/r (n=1). The median follow-up was 51 weeks (IQR 35–88); 29/45 patients (64%) had follow-up of≥48 weeks. All patients remained virally suppressed with no virological failure and no regimen change, leading to a strategy success rate of 100% (CI95% [92;100]) at W24 and 100% (CI95% [88;100]) at W48. In 13 evaluated patients, baseline median HIV-DNA level was 2.23 log_{10} copies/10^6 cells (IQR 1.94–2.51) and remained stable at W48 (−0.01 log_{10} copies/10^6 cells, CI95% [−0.25; +0.27], p=0.96).
Conclusion: Intermittent 2-DR given 5 or 4 days per week was highly successful (100%) in maintaining viral suppression in a cohort of 45 aviremic patients mainly under a daily 2-DR. Such strategies should be evaluated in larger prospective studies.

PE2/67

Modelling time varying viral load and CD4 cell counts response to antiretroviral therapy in a cohort of HIV naive patients

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Purpose: This study aims to evaluate the dynamics of HIV viral load and CD4 cell count over time in response to different antiretroviral therapy (ARV) regimens in a cohort of HIV naïve patients and to investigate the factors associated to the inability to achieve viral load suppression.
Method: A cohort of 1044 HIV infected patients who started a first ARV regimen based on INSTI, NNRTI or PI classes was evaluated with a mean of 5.6 (range: 1–16) measurements of CD4 counts and viral load over 2 years of follow-up. Longitudinal linear mixed-effect models were used to evaluate changes in viral load and CD4 cell count over time according ARV classes, among other predictors. To investigate the determinants associated to non-virologic suppression (evaluated after 6 months of treatment) propensity score-based weighted method, calculated with the generalized boosted method, was used.
Results: Lower mean CD4 cell count was found for NNRTI and PI treated patients compared with INSTI based ARV (−130/mm3 and −194/mm3, respectively), after adjusting for other determinants of CD4 count variation as age, MSM related transmission and presence of opportunistic infection at ARV initiation. HIV Viral load variation over follow-up time was significantly and independently associated with the presence of an opportunistic infection and MSM related transmission. Mean viral load was higher in NNRTI and PI treated patients compared with those treated with INSTI based ARV, without statistical significance. Compared with INSTI, PI based ARV was significantly associated with risk of non-virologic suppression (OR=2.9; 95% CI: 2.1–3.9) after accounting for the effect of treatment compliance, basal viral load and CD4 cell count, age, mode of transmission and presence of opportunistic infections.
Conclusion: This real-world study evidenced higher effectiveness of INSTI based ARV when virologic and immune response was evaluated using multiple measurements over time, with significant better CD4 cell count trajectory.

PE2/68

Impact of switching to E/C/F/TAF on lipid profile and renal function in HIV-infected patients

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Purpose: Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) is a recommended and widely used regimen for HIV infection. In this

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study we aimed to determine the impact of switching to E/C/F/TAF on the lipid profile and renal function in HIV-infected patients.
Method: ACTHIV-IST Study Group produced a database and 5 dedicated HIV centers in Istanbul entered data on HIV patients who switched from any tenofovir disoproxil fumarate-containing regimen to E/C/F/TAF. Viral parameters, lipid studies, renal function tests, adverse events, and adherence to the treatment were recorded.
Results: The study included 171 patients; 93% (159/171) were male and mean age was 41 years (SD: 11 years). Among them, 48% (83/171) described themselves as men who have sex with men. Median duration of HIV infection was 40 months (interquartile range-IQR 53–31). Median duration of E/C/F/TAF use was 18 months (IQR 20–15).
HIV-RNA was undetectable at months 6 and 12 in 88% (151) and 87% (149), respectively. Median CD4 counts were 729 cells/μL (IQR: 931–595) and 789 cells/μL (IQR: 970–580).
Renal functions tests and lipid profile at month 12 were available in 84% and 60% of the patients, respectively. Patients with abnormal lipid parameters and kidney functions with treatment were given in Table 1.
There were trends toward a decrease in serum creatinine and an increase in eGFR at month 12.
Median total cholesterol levels at baseline and month 12 were 162 and 204 mg/dL; LDL-cholesterol 103 and 135 mg/dL; HDL-cholesterol 38 and 45 mg/dL; and triglycerides 99 and 129 mg/dL, respectively. The total cholesterol/HDL ratio at baseline and month 12 were 4.4 at both time points.
Conclusion: Switching to E/C/F/TAF was associated with stable renal functions. Its use was associated with increases in LDL-cholesterol, triglycerides and also in HDL cholesterol levels at month 6; these effects were diminished at month 12.

Patients with abnormal lipid parameters and kidney functions with treatment

	Baseline	Month 6	Month 12	p
Creatinine level, median (IQR)	0.87 (0.98–0.75)	0.86 (0.97–0.79)	0.85 (0.96–0.77)	NS
High creatinine*	0.6% (1/167)	2.1% (3/145)	1.4% (2/143)	NS
eGFR, median (IQR)	105.97 (115.9–94.2)	105.4 (113.2–95.0)	107.2 (116.2–96.0)	NS
Low eGFR** Stage 2 (60–89) Stage 3 (30–59) Stage 4.5 (<30)	18.7% (31/166) 1.2% (2/166) 0/166	15.9% (23/144) 1.4% (2/144) 0/144	14.8% (21/142) 1.4% (2/142) 0/142	NS NS -
TC>200 mg/dL	16.7% (25/150)	58.1% (68/117)	53.4% (55/103)	<0.0001
LDL>130 mg/dL	15.5% (22/142)	51.8% (59/114)	56.3% (54/96)	<0.0001
Low HDL***	74.6% (106/142)	50.4% (57/113)	43.0% (43/100)	<0.0001
TG>200 mg/dL	14.9% (22/148)	27.4% (31/113)	19.0% (19/100)	<0.05

Antiretroviral randomized clinical trials

PE3/1

Genital HIV-1 RNA and DNA shedding in virologically suppressed individuals switching from triple- to dual- or monotherapy: pooled results from two randomized controlled trials

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Purpose: Increasing HIV-infected individuals benefit from less-drug regimens (LDRs). Exploring viral genital shedding during LDRs is crucial to ensure their safety.
Method: We pooled genital sub-studies from two clinical trials in this area. Patients were randomized 1:1 to continue abacavir / lamivudine / dolutegravir or switch to dolutegravir (MONCAY trial), or to continue tenofovir / emtricitabine + 3rd agent or to switch to tenofovir / emtricitabine (TRULIGHT trial). Participants whose plasma HIV-RNA remained<50 copies/mL had sperm or cervicovaginal lavage collected between weeks 24 and 48. RNA- and HIV-DNA were amplified by ultrasensitive PCR. The main objective was the proportion of participants who had no detectable HIV in genital fluids according to each strategy, then in an aggregated analysis (LDR versus triple therapies).
Results: Sixty-four participants (35 males, 29 females) were included: 16 dual therapies and 16 triple therapies in TRULIGHT; 16 monotherapies, 16 triple therapies in MONCAY. In TRULIGHT, 13/15 (87%) of evaluable participants on dual therapy had no detectable HIV in their genital fluid, versus 14/15 (93%) under triple therapy (p=1.0). In MONCAY, this figure was 12/15 (80%) on monotherapy versus 13/16 (81%) on triple therapy (p=1.0). In the pooled analysis, a similar proportion of participants in LDR and triple therapy groups had no detectable HIV: 25/30 (83%) and 27/31 (87%), respectively (p=0.73).
Conclusion: In our experience, LDRs did not increase the risk of detecting RNA- or HIV-DNA in genital fluids of people who maintained undetectable plasma HIV-RNA.

PE3/2

Comparison of the Ease of Swallowability of B/F/TAF placebo compared to DTG/ABC/3TC placebo

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Purpose: People living with HIV require daily adherence to lifelong antiretroviral therapy (ART) regimens to achieve long term treatment success. However, patient medication preferences for ART pill size have not been well studied. The study aims to assess the factors associated with the ease of swallowability and tolerability of two placebo pills representing BIC/FTC/TAF (BPP) and DTG/ABC/3TC (DPP).
Method: Fifty ART naïve patients (1 seropositive/49 negative) were recruited from the Infectious Diseases Clinic at Henry Ford Hospital in Detroit, MI, and randomized into 2 groups, and then administered the 2 placebo pills in different order by group assignment. Questionnaires using Likert scale (1–5) were administered regarding factors influencing the ease of swallowability, adherence, home medications, pill preferences and their perceptions of the placebo tablets. Comparisons were done using Student t-tests and ordinal regression.
Results: Participants were 64% female, 61% white, mean(+/-) age 43(14.6) years, mean of 1.7 comorbidities and taking a mean(median) of 4(1) pills/day. BPP was reported to be easier to swallow than DPP 1.76 vs. 2.42 (p<0.001). Pill size for DPP was correctly perceived as larger than BPP (p<0.005); with both pills perceived as smaller than actual size (p<0.005). BPP ease of swallowability was associated with the size of the largest home pill and how easy to swallow that pill was reported (p=0.021, p<0.05, respectively). DPP swallowability was only correlated with ease of swallowing of the largest home pill (p=0.003). No differences were found by gender, race, age, number/size of home medications or order of administration for ease of swallowability for either placebo pill.
Conclusion: A BIC/FTC/TAF placebo pill was perceived as easier to swallow and better tolerated than the larger DTG/ABC/3TC placebo pill. Patient's perceptions of swallowability can affect medication adherence, especially in HIV, a chronic medical condition that requires life-long daily adherence.

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PE3/3

Evaluation of total HIV-DNA changes in HIV-1 infected patients who continue a 2-drug regimen with dolutegravir plus one reverse transcriptase inhibitor or switch to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide enrolled in the Be-One Study

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Purpose: To investigate changes in HIV-DNA through 48 weeks (W48) in virologically suppressed HIV-1 infected patients randomized to continue a 2-drug regimen (2DR) with dolutegravir (DTG) plus one reverse-transcriptase-inhibitor (RTI) or to switch to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF).
Methods: This is a randomized, single-center, open-label, 96-week superiority study (NCT03493568; Be-One Study). Total HIV-DNA was measured with a standardized in-house ddPCR-assay and normalized for CD4 + T-cells. Spearman correlation coefficients were calculated to assess linear relationship between HIV-DNA and several immunological parameters (including D-Dimer, CRP, %CD8 + CD38 + HLA-DR+, %CD4 + CD38 + HLA-DR+, CD4 + T-cells, CD8 + T-cells, CD4/CD8) both at baseline and at W48. Results were described by median (IQR) and n (%). Differences in HIV-DNA levels were evaluated by using Wilcoxon signed-rank test among patients within the same arm or Mann-Whitney test between the two arms.
Results: HIV-DNA measurements at baseline and at W48 were available for 40/50 patients (Figure).

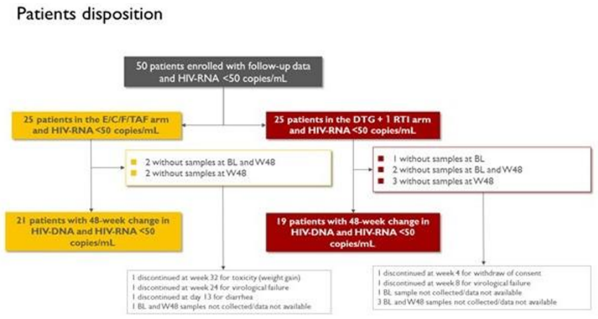


Figure 1. Flow diagram of patients enrolled the NCT03493568 study for whom HIV-DNA was quantified

	HIV-DNA at BL (copies/10^6 CD4+T-cells)	p-value*	HIV-DNA at W48 (copies/10^6 CD4+T-cells)	p-value*	Change in HIV-DNA at W48 from BL (copies/10^6 CD4+T-cells)	p-value*
Overall (n=40)	2247 (767 - 4268)		1587 (556 - 3543)	-	-162 (-1086; 611) p=0.264[§]	-
DTG+1RTI (n=19)	3077 (781 - 6030)	0.448	1922 (982 - 3804)	0.330	-226 (-1189; 890) p=0.465[§]	0.968
E/C/F/TAF (n=21)	1971 (632 - 3270)		1053 (458 - 3105)		-137 (-983; 133) p=0.334[§]	
With RV through 48 weeks of follow-up (n=16)	2168 (579 - 4922)	0.999	966 (478 - 6254)	0.793	-162 (-1202; 238) p=0.404[§]	0.999
With no RV through 48 weeks of follow-up (n=24)	2247 (898 - 4268)		1830 (1033 - 3138)		-177 (-1086; 849) p=0.403[§]	
DTG+1RTI with RV through 48 weeks of follow-up (n=5)	3225 (3077 - 6030)	0.547	5782 (883 - 6726)	0.488	414 (-2194; 3501) p=0.999[§]	0.611
DTG+1RTI with no RV through 48 weeks of follow-up (n=14)	2571 (781 - 4360)		1680 (1084 - 3171)		-229 (-983; 331) p=0.268[§]	
E/C/F/TAF with RV through 48 weeks of follow-up (n=11)	1190 (525 - 3813)	0.805	944 (458 - 3875)	0.751	-187 (-983; -67) p=0.067[§]	0.699
E/C/F/TAF with no RV through 48 weeks of follow-up (n=10)	2205 (1176 - 3270)		2246 (421 - 3105)		3 (-1534; 1220) p=0.999[§]	
With RV through 48 weeks of follow-up among treated with DTG+1RTI (n=5)	3225 (3077 - 6030)	0.428	5782 (883 - 6726)	0.497	414 (-2194; 3501) p=0.999[§]	0.821
With RV through 48 weeks of follow-up and E/C/F/TAF (n=11)	1190 (525 - 3813)		944 (458 - 3875)		-187 (-983; -67) p=0.067[§]	
With no RV through 48 weeks of follow-up and DTG+1RTI (n=14)	2571 (781 - 4360)	0.838	1680 (1084 - 3171)	0.977	-229 (-983; 331) p=0.268[§]	0.619
With no RV through 48 weeks of follow-up and E/C/F/TAF (n=10)	2205 (1176 - 3270)		2246 (421 - 3105)		3 (-1534; 1220) p=0.999[§]	

Results described by median (interquartile range, IQR) or n (%), as appropriate
Total HIV-DNA was quantified by Droplet Digital PCR (ddPCR). Viral load was assessed by standard Abbott Real time PCR; residual viremia (RV) was defined ad any detectable HIV-RNA <50 copies/mL trough week-48
Abbreviations. BL: baseline; DTG: dolutegravir; E/C/F/TAF: elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide; RV: residual viremia; No RV = target not detected; RTI: reverse transcriptase inhibitor; W48: week 48

Table 1. HIV-DNA load adjusted for CD4 + T-cells, overall and according to the study groups and RV

Overall, HIV-DNA was 2247 (767–4268) and 1587 (556–3543) copies/10^6 CD4 + T-cells at baseline and at W48, respectively, without any significant difference between arms (Table 1). No significant correlations were found between HIV-DNA levels and the immunological parameters, neither at baseline nor at W48. At W48, a modest decrease in HIV-DNA from baseline was observed in both arms: −226 (−1189; 890) copies/10^6 CD4 + T-cells (p=0.465) in the DTG + 1RTI-arm and −137 (−983; 133) copies/10^6 CD4 + T-cells (p=0.334) in the E/C/F/TAF-arm, without significant differences between the two arms (p=0.968).
HIV-DNA slightly increased from baseline to W48 in some patients of both arms (DTG + 1RTI: 8/19; E/C/F/TAF: 7/21, p=0.745). Interestingly, in the DTG + 1RTI-arm a≥4-fold increase in HIV-DNA (15 to 429 and 320 to 1210 copies/10^6 CD4 + T-cells, respectively) was observed in two individuals.
Conclusion: Changes in HIV-DNA from baseline to W48 in virologically suppressed individuals who switch from a 2DR with DTG + 1RTI to E/C/F/TAF did not significantly differ from changes in those who continue with the ongoing 2DR.

PE3/4

Phase-3 trials of new antiretrovirals are not representative of the global HIV epidemic

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Purpose: People living with HIV (PLWH) are mainly African or Asian, the majority female. In contrast, pharmaceutical companies typically conduct phase-III regulatory clinical trials in high income countries (HICs), where PLWH are mainly white males. Regulatory authorities can be conservative about including pregnant people in trials, discouraging female participation. Some adverse events are more common in females. Most drugs have insufficient safety data in pregnancy and non-white people even after regulatory approval. This analysis compared race and sex demographics of phase-III clinical trials of dolutegravir (DTG), bictegravir (BIC) and tenofovir alafenamide (TAF) with global HIV epidemic demography.
Method: National epidemic sizes by sex were extracted from UNAIDS 2018 data. National demographics were used to estimate prevalence by race. PLWH by national socioeconomic status were calculated from World Bank data. Race and sex demographics for 11 trials of DTG (n=8257), 4 BIC (n=2414) and 6 TAF (n=6483) were extracted from clinicaltrials.gov.
Results: Black females (42%) and black males (30%) have highest prevalence globally. Caucasian males comprise 6% of PLWH. Over 60% PLWH live in low or low-middle income countries, 68% of whom are black and 23% Asian. 76% of DTG trial centres were in high income countries (HICs) (5% global burden) and 23% in upper-middle income countries (UMICs). DTG trials were unrepresentative of PLWH even within the UMIC/HIC setting (49% white male versus 31% income band). Caucasian males were over-recruited by + 48% to DTG, BIC and TAF trials in comparison to prevalence. Black females were underrepresented by −38%.

Racial demographics of DTG, BIC and TAF clinical trials compared with the global HIV epidemic.

	Epidemic	DTG trials	BIC trials	TAF trials
Black				
Male	30%	19%	25%	19%
Female	42%	6%	4%	3%
Caucasian				
Male	6%	49%	55%	58%
Female	3%	15%	8%	9%
Other				
Male	11%	9%	7%	10%
Female	7%	3%	1%	2%

Conclusion: Phase-III clinical trial populations for new antiretrovirals comprised 54% white males, vastly disproportionate to the global HIV epidemic (6%). Females and non-white people are underrepresented. Female safety data are insufficient despite drug approval in Europe and USA. HIV trials must be located in regions representing the global epidemic with no gender-based selection.

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PE3/5

Impact of susceptibility scoring on virologic response in heavily treatment-experienced participants with HIV-1 receiving a fostemsavir-based antiretroviral regimen: results through week 96 from the randomized cohort of the Phase 3 BRIGHTE study

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Purpose: Fostemsavir (FTR) is an investigational, first-in-class, attachment inhibitor prodrug of the active moiety temsavir (TMR).[1] BRIGHTE is a Phase 3 study evaluating FTR in heavily treatment-experienced (HTE) participants with multidrug resistant HIV-1 who cannot form a viable regimen from remaining fully active ARVs (FAAs; based on historical/screening resistance activity). Virologic response by subgroups was previously reported.[2]

[1] J Pharm Sci. 2013;102(6):1742–1751.

[2] IAS2018 Amsterdam. IAS2019 Mexico City.

Method: HTE participants failing their current antiretroviral (ARV) regimen (≥400c/mL) were assigned to the Randomized Cohort if they had 1 or 2 FAAs to pair with FTR. Following 8-days of functional monotherapy (FTR + failing ARV regimen), participants commenced open-label FTR plus optimized background therapy (OBT). Virologic response (< 40 c/mL, Snapshot) was analyzed by baseline susceptibility including: GSS (genotypic susceptibility score), PSS (phenotypic susceptibility score), OSS (overall susceptibility score), and OSS-new (net assessment of genotypic + phenotypic susceptibility [Fully active=1, Partially active=0.5, and Resistant=0] and previous exposure to an ARV.

Results: Participants had 1 (52%) or 2 (42%) available FAAs in the initial OBT per historical/screening resistance. Participants with baseline OSS-new>2 had higher rates of virologic response compared to participants with lower baseline OSS-new. At Week 96, 88% of participants with OSS-new>2 achieved<40 c/mL; rates decreased with decreasing scores [>1-2=68%, >0–1=58%, 0=31%]. This trend was less pronounced for OSS and inconsistent for GSS, PSS, and number of FAAs. Among most common ARVs in initial OBT, inclusion (vs. non-inclusion) of fully active dolutegravir yielded the greatest difference in virologic response by OSS and OSS-new (Table 2).

Table 1. HIV-1 RNA<40 copies/mL (Snapshot Analysis, ITT-E) at Week 96 by Susceptibility Scores for the Initial OBT - Randomized Cohort

Factors		N	Randomized Cohort, Total N=272, n (%)		
			Week 24	Week 48	Week 96
Total Randomized Cohort		272	144 (53)	146 (54)	163 (60)
Fully Active and Available ARVs (FAA)[a]	ARV = 0[b]	16	5 (31)	5 (31)	3 (19)
	ARV = 1	142	80 (56)	82 (58)	92 (65)
	ARV = 2	114	59 (52)	59 (52)	68 (60)
	ARV > 2	0	0	0	0
Susceptibility Subgroups[c]					
Genotypic Susceptibility Score (GSS)					
	0	1	0	0	0
	>0 to 1	55	28 (51)	26 (47)	31 (56)
	>1 to 2	142	83 (58)	86 (61)	92 (65)
	>2	65	33 (51)	34 (52)	39 (60)
Phenotypic Susceptibility Score (PSS)					
	0	0	0	0	0
	>0 to 1	20	13 (65)	11 (55)	12 (60)
	>1 to 2	130	70 (54)	72 (55)	77 (59)
	>2	112	60 (54)	62 (55)	72 (64)
Overall Susceptibility Score (OSS)					
	0	0	0	0	0
	>0 to 1	27	13 (48)	12 (44)	14 (52)
	>1 to 2	131	71 (54)	72 (55)	77 (59)
	>2	99	54 (55)	56 (57)	65 (66)
OSS-new[d]					
	0	35	12 (34)	12 (34)	11 (31)
	>0 to 1	105	56 (53)	57 (54)	61 (58)
	>1 to 2	101	59 (58)	59 (58)	69 (68)
	>2	17	11 (65)	12 (71)	15 (88)

a. FAA is determined by the number of fully active (per historical and baseline resistance) and available (by intolerance, contraindication, or other safety concern) ARV agents included in the initial OBT

b. The 16 participants with 0 fully active ARVs in initial OBT include those who: never started OBT (n=5); were not treated with a fully active ARV in their initial OBT despite having a fully active ARV available (n=6); or were a protocol deviation (inadvertently assigned by the investigator to the randomized cohort despite having no fully active ARV available; n=5).

c. The susceptibility scoring subgroups (GSS, PSS, OSS) are calculated by summing the genotypic, phenotypic and net assessment rating of the individual ARV agents used in the initial OBT and based on baseline Monogram resistance results:
- PhenoSense GT Plus Integrase assay used for PIs, NRTIs, NNRTIs, and INIs. Scoring: 1 (sensitive), 0.5 (partially sensitive), 0 (resistant)
- PhenoSense Entry assay used for enfuvirtide. Scoring 1 (susceptible), 0 (reduced susceptibility)
- Trofile assay used for maraviroc. Scoring 1 (CCR5 antagonist activity is yes), 0 (activity is no)
- Missing (non-reportable or missing sample).

d. OSS-new is the overall susceptibility score for new (not previously taken) agents in the initial OBT. If an agent was taken as part of a prior regimen, then the susceptibility rating for that component is 0.

Table 2. HIV-1 RNA<40 c/mL (Snapshot Analysis, ITT-E) at Week 96 by Most Common Fully Active ARVs in Initial OBT - Randomized Cohort

Most Common Fully Active ARV of note – Randomized Cohort	Fully Active ARV of Note Included in Initial OBT[a] n/N (%)		Fully Active ARV of Note is Not Included in Initial OBT[b] n/N (%)	
	OSS	OSS-new	OSS	OSS-new
Dolutegravir	127/190 (67)	118/167 (71)	36/82 (44)	45/105 (43)
Darunavir	50/79 (63)	25/31 (81)	113/193 (59)	138/241 (57)
Etravirine	34/48 (71)	29/39 (74)	129/224 (58)	134/233 (58)
Maraviroc	24/49 (49)	19/36 (53)	139/223 (62)	144/236 (61)
Enfuvirtide	13/26 (50)	6/13 (46)	150/246 (61)	157/259 (61)

a. Denominator refers to participants who are using the fully active ARV of note in their initial OBT. A fully active ARV has an individual susceptibility score (OSR or OSR-new) of 1.

b. Denominator refers to participants (1) who are using the noted ARV in their initial OBT, but it is either partially active (OSR or OSR-new score = 0.5) or resistant (OSR or OSR-new = 0) or the OSR or OSR-new score of the noted ARV is missing, or (2) who are not using the noted ARV in their initial OBT.

Conclusion: Durability of virologic response in an HTE population receiving FTR-based antiretroviral therapy may be better forecast by considering a combination of baseline net assessment plus prior ARV exposure (OSS-new) compared to baseline genotypic (GSS), phenotypic (PSS), net assessment (OSS), or FAA results alone.

PE3/6

Reversibility of dolutegravir/lamivudine/abacavir neuropsychiatric toxicity after 24 weeks of switching to elvitegravir/cobicistat/emtricitabine/tenofovir-alafenamide (EVG/c/FTC/TAF). The DREAM Clinical Trial

I Perez Valero[1], A Cabello[2], P Ryan[3], S de la Fuente Moral[4], I Santos[5], MJ Vivancos[6], M Gorgolas[2], G Cuevas[3], A Diaz De Santiago[4], L García-Fraile[5], JI Bernardino[1], E Valencia[1], M Montes[1], G Rua[1], M Yllescas[7] and A Gonzalez[1]

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Objective: To assess whether neuropsychiatric symptoms observed in some patients treated with dolutegravir/lamivudine/abacavir (DTG/3TC/ABC) are true drug-related adverse events (AEs) that improve after DTG/3TC/ABC discontinuation or AEs related to other concomitant conditions.

Methods: Open-label, randomized (1:1), multicenter clinical trial designed to assess, in participants with suppressed HIV viral-load (>6 months) on DTG/3TC/ABC and either developed a new treatment-emergent neuropsychiatric AE or had worsening of an existing neuropsychiatric AE, improvement of these AEs after switching DTG/3TC/ABC to elvitegravir/cobicistat/emtricitabine/tenofovir-alafenamide (EVG/c/FTC/TAF).Participants were randomized to either immediately switch to EVG/c/FTC/TAF for 24 weeks or defer the switch for 4 weeks followed by EVG/c/FTC/TAF for 24 weeks. At each visit, a grading of neuropsychiatric AEs score (DREAM) was obtained and each participant completed the Hospital Anxiety & Depression Scale (HADs) and the Pittsburgh Sleep Quality Index (PSQI) questionnaires. Raw results on DREAM, HADs and PSQI scores were normalized (0–100) and changes from baseline were compared at each visit using t-test, McNemar test or generalized estimating equations (for longitudinal linear models). We analyzed differences at week 4 between study arms (primary objective) and changes in the DREAM, HADs and PSQI scores after 4, 12 and 24 weeks of switching to EVG/c/FTC/TAF (secondary objectives).

Results: 19 participants with similar baseline characteristics were included in each arm (table 1). At week 4, compared to the deferred arm, participants in the immediate-switch arm had significant improvements in DREAM, HADs and PSQI scores (table 2). After switching to EVG/c/FTC/TAF, we observed a consistent and continuous improvement in neuropsychiatric symptomatology up to week 24 (figure).

Conclusions: Our study supports existing evidence that DTG/3TC/ABC is associated with neuropsychiatric AEs that improve after switching to EVG/c/

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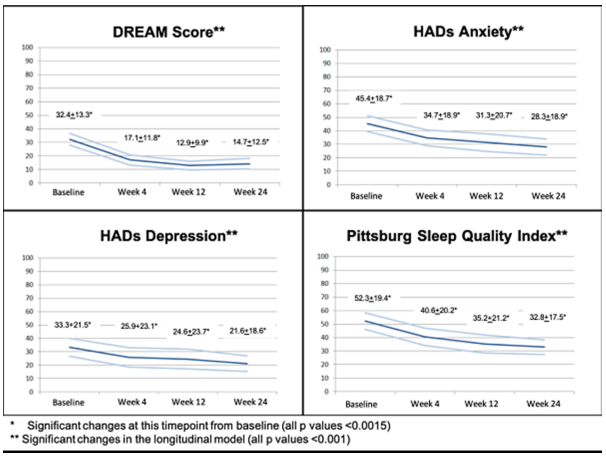
FTC/TAF and confirms the improvement observed in neuropsychiatric symptomatology in some cohorts after DTG/3TC/ABC discontinuation and in the GS-US-380–1844 clinical trial after switching to bictegravir/FTC/TAF.

Table 1. Baseline characteristics

	Immediate switch to EVG/c/FTC/TAF n=19	Deferred switch to EVG/c/FTC/TAF n=19
Gender (male), n (%)	19 (100)	18 (94.7)
Age (years), mean (SD)	40.2 (10.1)	45.6 (8.9)
Years since HIV diagnosis, mean (SD)	9.4 (9.2)	9.0 (7.9)
Weeks of HIV RNA<50 cop/mL, mean (SD)	235.9 (216.3)	292.5 (257.1)
Weeks on DTG/3TC/ABC, mean (SD)	67.1 (38.3)	83.7 (35.3)
CD4 Nadir, mean (SD)	416 (218)	413 (225.5)
History of illicit drug consumption, n (%)	6 (31.6)	5 (26.3)
History of psychiatric conditions, n (%)	4 (21.1)	5 (26.3)
Neurocognitive impairment, n (%)	5 (26.3)	5 (26.3)

Table 2. Changes at week 4 in neuropsychiatric symptomatology by study arms

	Immediate switch to EVG/c/FTC/TAF arm n=19	Deferred switch to EVG/c/FTC/TAF n=19	P value
Neuropsychiatric AEs (DREAM) Score, mean change (SD)	−14 (9.8)	−1 (9.1)	<0.001
HADs Anxiety subscale, mean change (SD)	−11.9 (16.4)	−1 (9.6)	0.021
HADs Depression subscale, mean change (SD)	−5.8 (11.1)	1.8 (10.8)	0.041
Pittsburg sleeping questionnaire, mean change (SD)	−14 (13.4)	−1 (12.0)	0.008



Changes in neuropsychiatric scores after switching to E/C/F/TAF

PE3/7

A switch to dolutegravir in combination with boosted darunavir is safe and effective in suppressed patients with HIV – a predefined psychosocial subanalysis of the DUALIS study

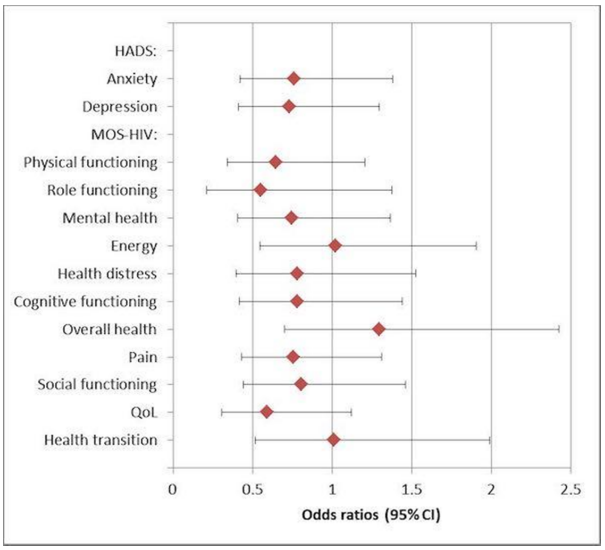
J Ronel[1], B Bührlen[2], F Fischer[2], C Boesecke[3], T Kümmerle[4], J Schneider[5], C Cordes[6], H Heiken[7], H-J Stellbrink[8], I Krznaric[9], S Scholten[10], B Jenssen[11], C Spinner[5] and TDS Group

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Purpose: The DUALIS study assessed a combination of Dolutegravir (DTG) and boosted Darunavir (bDRV) (2DR) for maintaining HIV-suppression and demonstrated non-inferiority as compared to 2NRTI+bDRV(3DR). A predefined psychosocial sub-analysis focused on psychopathology and health related quality of life (HRQoL).

Methods: The study sample of the exposed intention to treat (ITTe) population consisted of n=263 predominantly male Caucasian persons with a mean age of 46.7 years. All patients completed a sociodemographic questionnaire together with two validated outcome instruments: the Hospital Anxiety and Depression Scale (HADS) with two scales and the Medical Outcomes Study HIV Health Survey (MOS-HIV) with 11 scales characterizing HRQoL. Multiple logistic regressions were carried out for each outcome criterion at the last visit (48 months after enrollment) with treatment arms as group factor and baseline value of the outcome, age, sex, population size of the patients' area of residence, current occupation and current or earlier treatment for mental disorder as predictors. Odds ratios (OR) and their 95% confidence intervals for the 2DR group as compared to the 3DR group were computed.

Results: The study population did not differ in regards to sociodemographic factors. Odds ratio (OR; 95% confidence interval) of the two HADS subscales, anxiety (0.76; 0.42–1.38) and depression (0.73; 0.41–1.30), as well as the OR of the 11 HRQoL scales of the MOS-HIV scale, including physical functioning (0.64; 0.34–1.21), role functioning (0.55; 0.21–1.38), mental health (0.75; 0.41–1.37), energy (1.02; 0.52–1.90), health distress (0.78; 0.40–1.53), cognitive functioning (0.80; 0.42–1.44), overall health (1.30; 0.70–2.42),



Forest plot of HADS and MOS-HIV outcomes with Odds ratio (OR) and corresponding 95% CI

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pain (0.75; 0.43–1.31), social functioning (0.81; 0.44–1.46), quality of life (0.60; 0.31–1.12) and health transition (1.01; 0.51–1.99), until 48 weeks of treatment did not show significant differences (Forest plot of . . .).
Conclusion: A switch to a 2DR regimen consisting of DTG+bDRV does not lead to any significant differences, neither in anxiety nor depression, nor in HRQoL outcome measures.

PE3/8

Tenofovir alafenamide versus tenofovir disoproxil fumarate – is there a true difference in safety?

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Purpose: Plasma tenofovir is associated with renal and bone adverse events (AEs) in treatment of HIV and HBV. Lower plasma and higher intracellular tenofovir concentrations are achieved with tenofovir alafenamide (TAF) than tenofovir disoproxil fumarate (TDF). Pharmacokinetic boosters ritonavir and cobicistat increase plasma tenofovir concentration, compounding existent safety concerns for tenofovir formulations. We assess TAF versus TDF safety with and without booster co-formulation.
Method: A systematic review identified eight phase-3 and two phase-2 clinical trials which recruited HIV patients, and two which recruited hepatitis B patients. TAF and TDF safety were compared in predefined boosted and unboosted subgroups. Safety endpoints included all AEs, serious AEs and AE discontinuation. Individual AEs investigated included bone mineral density (BMD) change, fractures, all gastrointestinal AEs, serious gastrointestinal AEs, nausea, and discontinuation for bone or renal AEs. Pooled risk differences were calculated using random-effects models with Mantel-Haenszel's methods.
Results: There were no significant differences in boosted or unboosted subgroups between TAF and TDF for all AEs, serious AEs, AE discontinuation, nausea, or serious gastrointestinal AEs. Boosted TDF caused more fractures ($p<0.05$), larger BMD decreases ($p<0.001$), and more bone ($p<0.05$) and renal ($p<0.01$) discontinuations than boosted TAF. Unboosted TDF caused more gastrointestinal AEs than unboosted TAF ($p<0.05$), however, this reversed with booster co-formulation ($p<0.05$); boosted TAF caused more gastrointestinal AEs than boosted TDF ($p=0.11$).
Conclusion: Ritonavir-/cobicistat-boosted TDF was associated with higher bone and renal AE risk than boosted TAF. However, unboosted TAF and TDF risk differences were marginal. Boosted TAF caused higher gastrointestinal AE risk than boosted TDF. Both formulations have booster-dependent AEs. The broadcasted health economic benefits of TAF versus generic TDF may be reduced without boosters. Systematic bias from boosted and unboosted trial result grouping needs to be dispelled.

PE3/9

Biologic sex is not the only difference between men and women: data from the Doravirine phase 2/3 clinical trials

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Purpose: Doravirine (DOR) is a recently approved NNRTI for the treatment of HIV-1, available as a single entity and a fixed-dose combination with lamivudine and tenofovir disoproxil fumarate (DOR/3TC/TDF). Differences in baseline characteristics between men and women, beyond biological sex, in DOR phase 2/3 clinical trials (Protocol 007, DRIVE-FORWARD, and DRIVE-AHEAD) were examined.
Method: Antiretroviral-naïve adults with pre-treatment HIV-1 RNA≥1,000 copies/mL received once-daily DOR 100 mg or efavirenz 600 mg (EFV) with FTC/TDF in P007; DOR 100 mg or darunavir/ritonavir 800 mg/100 mg with FTC/TDF or ABC/3TC in DRIVE-FORWARD; and DOR/3TC/TDF or EFV/FTC/TDF in DRIVE-AHEAD. All treatment groups were combined for this analysis, which included all randomized participants who received≥1 dose of study therapy. Differences in proportions were analyzed using the Miettinen-Nurminen method. Association between sex and race was investigated using Pearson's chi-square test. For continuous variables, linear regression models were used to investigate difference for age (with no adjustment); for baseline body weight, body mass index (BMI), CD4 + T-cell count, CD4/CD8 ratio, and HIV-1 RNA (adjusted for age); and for treatment compliance (adjusted for age and study group).
Results: Racial distribution was significantly different between men and women, with Black or African Americans representing 40.6% of women vs. 16.6% of men. Statistically significant differences were also found for age, weight, BMI, CD4 + T-cell count, HIV-1 RNA, and medication use (table). Despite these differences, DOR demonstrated similar efficacy and safety in men and women in the phase 2/3 clinical trials.
Conclusion: Women in the phase 2/3 clinical trials of DOR were statistically significantly different from their male counterparts in certain baseline characteristics beyond biological sex. Although women had similar efficacy and safety results, women represented 15% of participants. Increased enrollment of women in clinical trials or women-only trials should be considered to further understand antiretroviral efficacy and safety in this important population.

Characteristics of Women and Men in Doravirine Clinical Trials

	Female		Male		
Characteristic	n	Mean (95% CI)	n	Mean (95% CI)	p-value
Age	249	37.0 (35.6, 38.3)	1461	34.0 (33.5, 34.5)	<0.0001
Baseline Weight	249	70.2 (68.0, 72.3)	1461	75.7 (74.9, 76.5)	<0.0001
Baseline BMI	249	26.4 (25.6, 27.2)	1460	24.5 (24.3, 24.7)	<0.0001
Baseline CD4 + T-cell counts	249	380.2 (353.5, 407.0)	1461	433.5 (422.6, 444.4)	0.0008
Baseline log10 HIV-1 RNA	249	4.3 (4.2, 4.4)	1460	4.5 (4.4, 4.5)	<0.0001
Baseline HIV-1 RNA≤100,000 copies/mL, n (%)	249	206 (82.7)	1461	1125 (77.0)	0.065
Any concomitant medication, n (%)	249	145 (58.2%)	1461	666 (45.6%)	<0.001
≥3 concomitant medications, n (%)	249	58 (23.3%)	1461	236 (16.2%)	0.006

PE3/10

No metabolic or renal benefits when switching to an NRTI-free dolutegravir-containing 2 drug regimen (2DR) – a subanalysis of the DUALIS study

C Boesecke[1], T Kümmerle[2], J Schneider[3], C Cordes[4], H Heiken[5], H-J Stellbrink[6], I Krznaric[7], S Scholten[8], B Jensen[9], H Jessen[10], C Schulz[11], P Spornraft-Ragaller[12], P Khaykin[13], E Wolf[14], C Spinner[3] and on behalf of the DUALIS Study Group
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Purpose: The DUALIS study assessed efficacy and safety of switching to Dolutegravir (DTG) and boosted darunavir (bDRV) (2DR) and has demonstrated non-inferiority as compared to 2 NRTI+bDRV (3DR). Here we present a post-hoc subanalysis on changes in metabolic and renal parameters.
Method: In DUALIS PLWH with HIV-RNA<50cps/mL on 2 NRTI+bDRV (3DR) for≥24 weeks (one accepted blip<200cps/mL) were randomized to switch to

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DTG 50 mg+DRV 800 mg (with 100 mg Ritonavir or 150 mg Cobicistat) or remain on 3DR.
Results: Overall, 266 subjects were randomized and treated (2DR: n=133, 3DR: n=133). Over 48 weeks, patients in the 2DR arm gained median + 2.0 kg in body weight (IQR: −0.2–+4.0) vs. +0.2 kg (−1.9–+2.1) in the 3DR arm (p=0.0006 comparing 2DR and 3DR); median increase in BMI was + 0.6 kg/m^2 (−0.1–+1.2) for 2DR and + 0.1 kg/m^2 (−0.5–+0.7) for 3DR (p=0.0006). After 48 weeks, total cholesterol had increased by a median of + 20.0 mg/dL (+3.0–+35.5) in 2DR vs. no increase, i.e. 0.0 mg/dL (−18-+15.5), in 3DR (p<0.001); LDL increased by + 13.3 mg/dL (−3.0–+31.3) in 2DR vs. 0.0 mg/dL (−14.0–+18.0) in 3DR (p=0.0003). HDL increased by + 4.9 mg/dL (−1.0–+10.4) in 2DR vs. a decrease of −1.0 mg/dL (−5.0–+4.0) in 3DR (p<0.001).
Changes in MDRD-eGFR over 48 weeks were −7.8 mL/min/1.73 m² (−17.4–−0.3) in 2DR vs. −0.4 mL/min/1.73 m² (−8.8-+5.7) in 3DR (p=0.0002); changes in Creatinine-CKD-EPI-eGFR were −8.0 mL/min/1.73 m² (−17.0–−0.6) in 2DR vs. −0.7 mL/min/1.73 m² (−9.4–+4.5) in 3DR (p=0.0002). CKD-EPI Creatinine-Cystatin eGFR decreased by −6.7 mL/min/1.73 m² (−14.4–+5.3) in 2DR vs. −2.7 mL/min/1.73 m² (−10.0-+4.3) in 3DR (p=0.1572).
Conclusion: While being non-inferior with regard to virologic suppression, a switch to a 2DR consisting of DTG+bDRV does not yield significant metabolic or renal advantages by substituting the NRTI components of a comparative 3DR antiretroviral therapy.

PE3/11

Sustained viral suppression with dolutegravir monotherapy during 9,899 patient weeks of follow-up in individuals starting combination antiretroviral therapy during primary HIV infection (EARLY SIMPLIFIED): a randomized, controlled, multi-site, non-inferiority trial

DL Braun[1,2], T Turk[1,2], B Hampel[1,2,3], C Grube[1], T Bühler[1], N Lutz[1], A Plate[1,2], S Brugger[1], C Depmeier[4], H Kuster[1], M Flepp[5], K Metzner[1,2], J Böni[2], R Kouyos[1,2] and H Günthard[1,2]

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Purpose: Dolutegravir (DTG) monotherapy has been criticized because of the risk of long-term failure. Our EARLY-SIMPLIFIED trial showed that at week 48 DTG monotherapy was non-inferior to combination antiretroviral therapy (cART) in patients who started cART during primary HIV-1 infection (PHI) and had a HIV-1 RNA<50 cp/mL plasma for>48 weeks (Braun et al, CID 2019). Here we report on the intermediate results at week 108 and beyond.
Method: EARLY SIMPLIFIED is a randomized, open label, non-inferiority trial. Inclusion criteria were documented PHI, start of cART<180 days after estimated date of infection, and HIV-1 RNA<50 cp/mL plasma for>48 weeks. Exclusion criteria were previous virological failure. We randomly assigned patients (2:1) to DTG monotherapy 50 mg once-daily or to continuation of cART. The trial continues for 4 years in total (ClinicalTrials.gov, NCT02551523).
Results: 101 patients were assigned to DTG monotherapy (n=68) or continuation of cART (n=33). After week 48 data had been analyzed, 16 patients from the cART group demanded to switch to DTG monotherapy. One patient from the DTG monotherapy group switched back to cART because of extensive weight gain. There was no virological failure occurring in both groups during the 9,899 and 4,316 person weeks of follow-up (PWFU) in the per-protocol population for the DTG monotherapy and the cART group, respectively. One patient with virological failure from the DTG monotherapy group was excluded from the per-protocol analysis because he did not fulfill the criteria of PHI at the time of first cART start.
Conclusion: No virological failure was observed during the observational period of 9,899 PWFU after switching to DTG monotherapy in patients who started cART during PHI and were fully suppressed for>48 weeks. DTG monotherapy might be a safe and sustainable maintenance therapy in patients who started cART during PHI.

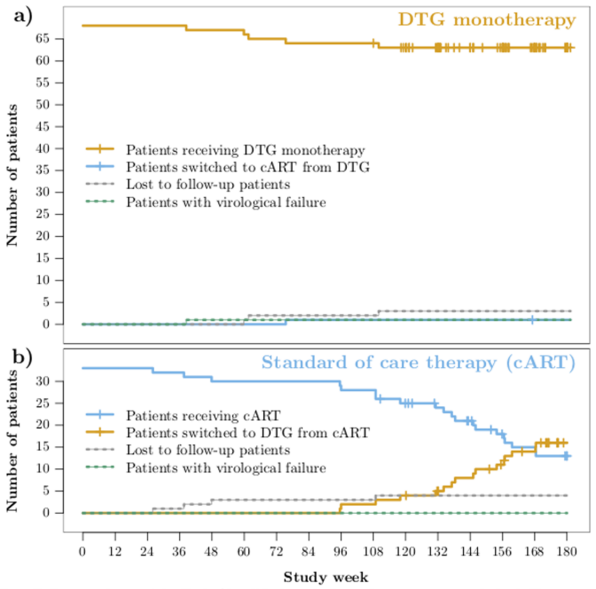


Fig1: Follow-up times of the Early Simplified study (intention-to-treat population). The upper (**a**)) and the lower (**b**)) panels summarize the follow-up times according to the HIV-1 RNA measurements in the dolutegravir (DTG) monotherapy group and the standard of care therapy group, respectively. Blue color indicates the number of patients on combination antiretroviral therapy (cART) and the orange color shows the patients on DTG monotherapy. The dotted lines indicate cumulative number of patients who have been excluded from the study or are lost to follow-up, whereas the vertical bars (|) indicate the last study visit (all with HIV-1 RNA <50 cp/ml) of active participants at the time of abstract submission. **a) DTG monotherapy group**. The single patient who experienced a viral rebound violated the inclusion criteria as he was chronically infected at the start of cART. One patient switched to cART after 75 weeks due to side effects and three were lost-to follow-up with last HIV-1 RNA <50 cp/ml before week 120. 63 of 68 patients have reached week 120. **b) cART group**. Sixteen patients switched to DTG monotherapy, four patients were lost to follow-up with last HIV-1 RNA <50 cp/ml and there was no virological failure. 28 of 33 participants have reached week 120.

Follow-up times of the Early Simplified Study (intention-to-treat population)

PE3/12

Rapid initiation of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in patients with human immunodeficiency virus (HIV)-1 infection: age, race/ethnicity, and gender subgroup analyses from the DIAMOND study

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Objective: To evaluate Week 48 efficacy and safety results from the DIAMOND study across age, race/ethnicity, and gender subgroups.
Methods: DIAMOND (NCT03227861), a phase 3, single-arm, prospective study, assessed efficacy/safety of rapidly initiating D/C/F/TAF 800/150/200/10 mg. Adults enrolled within 14 days of HIV-1 diagnosis and started D/C/F/TAF without baseline laboratory results. Patients not meeting predefined stopping rules continued treatment, as per study protocol. Efficacy/safety were assessed across subgroups based on age (18–25/26–50/>50 years), race/ethnicity (white/black or African American/other; Hispanic/non-Hispanic), and gender (women/men). Virologic response rates (HIV-1 RNA<50 copies/mL) were assessed by intent-to-treat FDA snapshot and an observed analysis (excluding patients with missing samples).
Results: Overall, 109 patients enrolled (median [range] age: 28 [19–66] years; 32% black/African American; 44% Hispanic/Latino; 13% women); 97 (89%) patients completed the study with no discontinuations due to virologic failure or developed resistance. Demographic characteristics, virologic response, and D/C/F/TAF-related adverse events (AEs) by subgroup are shown (Tables 1–3). Across age subgroups, Week 48 virologic response rates were high and similar. No D/C/F/TAF-related renal or bone AEs were reported, including among patients aged>50 years. Virologic response rates were also similar across race/

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ethnicity subgroups, while virologic response rates by FDA snapshot (but not observed) analysis were lower among women versus men. The latter should be interpreted with caution given the small sample size of women (see Table 2 footnote). Patients>50 years, black/African Americans, and women had numerically lower rates of related AEs versus other subgroups.
Conclusion: In the first phase 3 study of a single-tablet regimen in a rapid initiation model, DIAMOND enrolled patients synonymous with the population most affected by HIV-1 infection today. D/C/F/TAF resulted in high virologic response rates across a variety of baseline demographics. Treatment was safe and well tolerated, indicating D/C/F/TAF as a preferred antiretroviral therapy option for rapid initiation.

Table 1. Baseline Demographic Characteristics by Subgroups*

	Age			Race/Ethnicity					Gender	
Parameter, n (%)	18-25 y	26-50 y	>50 y	White	Black/ African American	Other	Hispanic	Non-Hispanic	Women	Men
n	38	58	13	65	35	9	48	61	14	95
Age, median (range), y	22 (19-25)	33 (26-49)	60 (52-66)	30 (19-66)	28 (19-65)	27 (20-53)	27 (19-62)	30 (19-66)	33 (25-63)	27 (19-66)
18-25 y, n (%)	38 (100)	0	0	21 (32)	13 (37)	4 (44)	19 (40)	19 (31)	2 (14)	36 (38)
26-50 y, n (%)	0	58 (100)	0	36 (55)	18 (51)	4 (44)	25 (52)	33 (54)	11 (79)	47 (49)
>50 y, n (%)	0	0	13 (100)	8 (12)	4 (11)	1 (11)	4 (8)	9 (15)	1 (7)	12 (13)
Race, n (%)										
White	21 (55)	36 (62)	8 (62)	65 (100)	0	0	45 (94)	20 (33)	6 (43)	59 (62)
Black/African American	13 (34)	18 (31)	4 (31)	0	35 (100)	0	0	35 (57)	7 (50)	28 (29)
Other	4 (11)	4 (7)	1 (8)	0	0	9 (100)	3 (6)	6 (10)	1 (7)	8 (8)
Gender, n (%)										
Women	2 (5)	11 (19)	1 (8)	6 (9)	7 (20)	1 (11)	4 (8)	10 (16)	14 (100)	0
Men	36 (95)	47 (81)	12 (92)	59 (91)	28 (80)	8 (89)	44 (92)	51 (84)	0	95 (100)

*Percentages may not total 100% due to rounding.

Table 1. Baseline Demographic Characteristics by Subgroups*

Table 2. Virologic Response (HIV-1 RNA <50 copies/mL) at Week 48 by Subgroups

	Age			Race/Ethnicity					Gender	
Parameter, n/N (%)	18-25 y	26-50 y	>50 y	White	Black/ African American	Other	Hispanic	Non-Hispanic	Women	Men
ITT-FDA snapshot	32/38 (84)	50/58 (86)	10/13 (77)	55/65 (85)	29/35 (83)	8/9 (89)	42/48 (88)	50/61 (82)	9/14 (64)*	83/95 (87)
Observed analysis	32/32 (100)	50/52 (96)	10/12 (83)	55/58 (95)	29/30 (97)	8/8 (100)	42/44 (95)	50/52 (96)	9/10 (90)	83/86 (97)

ITT, intent-to-treat; FDA, Food and Drug Administration.
*Among the 5 women who did not achieve HIV-1 RNA <50 copies/mL at Week 48, 1 had HIV-1 RNA ≥50 copies/mL (77 copies/mL) at Week 48, 1 had HIV-1 RNA ≥50 copies/mL at early discontinuation, and 3 did not have data in the window.

Table 2. Virologic Response at Week 48

Table 3. Related Adverse Events Through Week 48 by Subgroups

	Age			Race/Ethnicity					Gender	
Related AE, n (%)	18-25 y	26-50 y	>50 y	White	Black/ African American	Other	Hispanic	Non-Hispanic	Women	Men
n	38	58	13	65	35	9	48	61	14	95
≥1 AE	14 (37)	20 (34)	2 (15)	26 (40)	6 (17)	4 (44)	22 (46)	14 (23)	2 (14)	34 (36)
≥1 SAE	0	0	0	0	0	0	0	0	0	0
≥1 grade 2 AE	2 (5)	5 (9)	0	6 (9)	1 (3)	0	3 (6)	4 (7)	0	7 (7)
≥1 grade 3 AE	1 (3)	1 (2)	0	2 (3)	0	0	2 (4)	0	1 (7)	1 (1)
≥1 grade 4 AE	0	0	0	0	0	0	0	0	0	0

AE, adverse event; SAE, serious adverse event.

Table 3. Related Adverse Events Through Week 48

PE3/13

A systematic review and meta-analysis evaluating the risk of central nervous system adverse events in randomised controlled trials of dolutegravir

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Purpose: Dolutegravir was recently added as the recommended first-line treatment for HIV-1 infection by the World Health Organisation. With the changes in guidelines and the generic manufacturing of dolutegravir, it is anticipated that there will be a mass roll out of the drug in low- and middle-income countries (LMIC). Results from observational studies have demonstrated safety issues relating to the drug. The purpose of this review was to evaluate the risk of central nervous system (CNS) adverse events observed in randomised controlled trials of dolutegravir in patients with HIV-1 infection.
Method: Embase, Medline and Global Health databases were searched using word variants of "dolutegravir" and "randomised controlled trial" from the earliest possible start date until 11th March 2019. Phase 3 clinical trials with at least one treatment arm containing dolutegravir were included. CNS adverse events were extracted and analysed, then stratified for switch studies versus non-switch studies and efavirenz versus other antiretrovirals. Relative risk for the comparisons were calculated and a Mantel-Haenszel random-effects model was applied to the meta-analysis.
Results: 17 studies of unique randomised controlled trials were included in the review, with a combined total of 11,138 participants. A meta-analysis was conducted on 14 of the 17 included studies; results are shown in the tables below. There was a higher risk of insomnia for dolutegravir compared to other antiretrovirals (RR=1.32, p=0.006). The results for suicide related adverse events showed no significant differences between dolutegravir and either efavirenz or other antiretrovirals, across each analysis.

Table showing insomnia related adverse events in each subgroup used for the analysis of clinical trials of dolutegravir.

	Dolutegravir Arm		Comparison Arm	
Subgroup	Total Events/ Number of Participants	Percentage, %	Total Events/ Number of Participants	Percentage, %
Switch Studies	31/794	3.90	18/793	2.27
Non-switch Studies	194/2726	7.12	138/2348	5.88
Efavirenz Comparison Arm	104/1185	8.78	64/814	7.86
Other Antiretroviral Comparison Arm	121/2335	5.18	92/2327	3.95

Table showing suicide related adverse events in each subgroup used for the analysis of clinical trials of dolutegravir.

	Dolutegravir Arm		Comparison Arm	
Subgroup	Total Events/ Number of Participants	Percentage, %	Total Events/ Number of Participants	Percentage, %
Switch Studies	2/794	0.25	5/793	0.63
Non-switch Studies	23/3080	0.75	24/2709	0.89
Efavirenz Comparison Arm	5/1185	0.42	8/814	0.98
Other Antiretroviral Comparison Arm	20/2689	0.74	21/2688	0.78

Conclusion: Overall, this analysis shows an increased risk of insomnia for dolutegravir. Although cases of suicide related adverse events have been seen in patients taking dolutegravir, this was not significant when compared to other antiretrovirals. With the anticipated roll out of dolutegravir based regimens in LMICs, it is essential to closely monitor patients for adverse events.

PE3/14

Long-term efficacy and safety of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in ART-naïve adults

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Purpose: To evaluate comparative efficacy and safety of B/F/TAF and dolutegravir (DTG)-containing regimens through 144 weeks (W).
Method: We conducted two randomized, double-blind, active-controlled phase 3 studies of B/F/TAF in treatment-naïve adults living with HIV. Study 1489 randomized HLA-B*5701-negative adults without HBV to receive B/F/TAF or DTG, abacavir, and lamivudine (DTG/ABC/3TC). Study 1490 randomized adults to B/F/TAF or DTG+F/TAF. Participants were pooled into three groups: B/F/TAF (Studies 1489, 1490), DTG/ABC/3TC (Study 1489), and DTG+F/TAF (Study 1490). A pre-specified pooled analysis at W144 assessed efficacy as the proportion with HIV-1 RNA<50 c/mL (FDA Snapshot) and safety; proteinuria and bone mineral density (BMD) were measured in 1489 only.
Results: 1274 adults were randomized/treated (634 B/F/TAF, 315 DTG/ABC/3TC, 325 DTG+F/TAF), 89% male, 33% Black. Baseline characteristics were similar across groups. At W144, 82% on B/F/TAF, 84% on DTG/ABC/3TC, and 84% on DTG+F/TAF achieved HIV-1 RNA<50 c/mL (table 1). No participant

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developed resistance. The proportion with drug-related adverse events of any grade was 26% (B/F/TAF), 42% (DTG/ABC/3TC), and 29% (DTG+F/TAF). Adverse events led to discontinuation for 1% (B/F/TAF), 2% (DTG/ABC/3TC), and 2% (DTG+F/TAF). Changes in eGFR at W144 were similar across groups. In Study 1489, comparing B/F/TAF to DTG/ABC/3TC, changes in proteinuria and renal biomarkers were similar and mean percentage change from baseline in hip and spine BMD by DXA at W144 were similar. Small treatment differences in changes from baseline in fasting LDL, HDL, and TC:HDL ratio were observed with B/F/TAF vs DTG/ABC/3TC but not vs DTG+F/TAF.

Conclusion: Through 3 years of follow-up in ART-naïve adults, use of B/F/TAF resulted in high rates of virologic suppression through W144. B/F/TAF was well tolerated, had fewer drug-related adverse events compared with DTG/ABC/3TC, and no clinically relevant effect on bone and renal safety or fasting lipids.

	B/F/TAF (N=634)	ABC/DTG/3TC (N=315)	DTG + F/TAF (N=325)	P-value B/F/TAF vs ABC/DTG/3TC	P-value B/F/TAF vs DTG+F/TAF
HIV-1 RNA <50 c/mL					
Full analysis set, n (%)	518 (82)	265 (84)	273 (84)	–	–
Difference in % (95% CI)	–	-2.7% (-7.8% to 2.4%)	-1.9% (-7.0% to 3.1%)	0.31	0.46
Per protocol analysis set, n/N (%)	513/515 (100)	260/262 (99)	270/273 (99)	–	–
Difference in % (95% CI)	–	0.3% (-1.4% to 2.0%)	0.8% (-1.0% to 2.5%)	0.55	0.20
Change or % change from baseline in renal safety parameters, median (Q1, Q3)*					
eGFR, mL/min	-9.2 (-19.8, -0.2)	-11.7 (-22.7, -0.6)	-11.0 (-22.0, 0.1)	0.13	0.28
UACR*, %	+2.6 (-33.4, 62.9)	-1.6 (-29.6, 61.8)	–	0.94	–
Urine RBP:Cr ratio*, %	+19.6 (-13.4, 60.3)	+15.4 (-20.5, 66.9)	–	0.83	–
Urine β2M:Cr ratio, %	-26.4 (-69.5, 18.7)	-34.2 (-68.8, 0.9)	–	0.41	–
% change from baseline in BMD, mean (SD)†					
Hip[a]	-1.02 (3.76)	-1.29 (3.11)	–	0.39	–
Spine[a]	-0.37 (4.44)	+0.04 (3.52)	–	0.26	–
Change from baseline in fasting lipid parameters, median (Q1, Q3)					
Total cholesterol, mg/dL	+13 (-6, 32)	+10 (-10, 27)	+12 (-12, 33)	0.057	0.51
LDL, mg/dL	+20 (2, 40)	+14 (-2, 32)	+19 (1, 38)	0.005	0.35
HDL, mg/dL	+4 (-2, 10)	+6 (0, 13)	+5 (-1, 12)	0.01	0.33
Total cholesterol:HDL ratio	0.0 (-0.6, 0.4)	-0.3 (-0.8, 0.3)	-0.1 (-0.6, 0.4)	0.001	0.23
Triglycerides, mg/dL	+5 (-23, 37)	+5 (-20, 31)	+2 (-25, 31)	0.56	0.43

[a] n=314 (B/F/TAF), n=615 (ABC/DTG/3TC)
[b] n=236 (B/F/TAF), n=240 (ABC/DTG/3TC)
[c] n=243 (B/F/TAF), n=244 (ABC/DTG/3TC)
*Renal biomarkers and BMD measured for Study 1489 only
P-value for the superiority test comparing the percentages of subjects with HIV-1 RNA <50 c/mL between treatment groups was from the CMH test stratified by baseline HIV-1 RNA stratum (≤100,000 vs. >100,000 c/mL) and region stratum (US vs. Ex-US). The difference in percentages of participants with HIV-1 RNA <50 c/mL between treatment groups and its 95% CI were calculated based on the Mn-p proportion adjusted by baseline HIV-1 RNA stratum (≤100,000 vs. >100,000 c/mL) and region stratum (US vs. Ex-US).
P-values were from the 2-sided Wilcoxon rank sum test to compare the 2 treatment groups for eGFR, renal biomarkers, and lipid parameters.
P-values were from the ANOVA model including treatment as a fixed effect for BMD comparison.

Table 1. Key efficacy and safety results at week 144

PE3/15

Switching from a 3-drug tenofovir alafenamide (TAF)-based regimen (TBR) to a 2-drug dolutegravir/lamivudine (2DR, DTG/3TC FDC) was not associated with a higher frequency of intermittent viremia in suppressed patients in the TANGO study

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Purpose: TANGO is a 200-week, Phase III, randomized, open-label trial to evaluate efficacy and safety of replacing TBR with a 2DR of DTG/3TC in HIV-1-infected adults, with HIV-1 RNA<50 c/mL and without prior virologic failure or historical NRTI or INSTI major resistance mutations. Switching to DTG/3TC was non-inferior to continued TBR through Week 48 using a 4% non-inferiority margin for Snapshot virologic failure.

Method: Frequency of elevated viral loads (VL, HIV-1 RNA>50 c/mL) was assessed over 48 weeks of therapy overall and in a subset of participants with archived M184V/I and K65R. Proviral DNA genotyping was conducted retrospectively on baseline samples using GenoSure Archive assay by Monogram Bioscience. Participants with>1 post-baseline VL (Intent-to-Treat Exposed, ITT-E population) were categorized as described in Table 1. Results are generated using all available on-treatment VL through Week 48 visit.

Results: 741 participants were randomized and exposed (DTG/3TC, 369; TBR, 372). At baseline, M184V/I was detected in 1% (7/626) participants by proviral genotype, and K65R was present in<1 % (1/626). One participant (< 1%) on TBR met confirmed virologic withdrawal criteria with no resistance mutations observed at failure. Through Week 48, the occurrence of elevated VL (see Table 1) was low and comparable across arms; most frequently observed VL rebounds are in category 1a. Elevated VLs (regardless of category) were not observed in the low number of participants with archived M184V/I or K65R (see Table 1).

Conclusion: Incidence of intermittent viremia through 48 weeks was low and similar between the two treatment arms. Frequency of archived M184V/I or K65R at baseline was very low and did not increase the risk of elevated VL in either treatment arm with no participants exhibiting intermittent viremia through Week 48. Switching from a 3-drug TBR to a DTG/3TC 2DR was not associated with higher frequency of intermittent viremia.

Elevated Viral Load Categories for Participants in ITT-E population	DTG/3TC FDC (N=369) n (%)	TBR (N=372) n (%)
1. Participants with VLs between 50-200 c/mL and no viral load ≥200 c/mL	11 (3%)	22 (6%)
1a. VLs between 50-200 c/mL with adjacent values <50 c/mL (defined as "blips")	9 (2%)	18 (5%)
1b. ≥ two consecutive VLs between 50-200 c/mL	2 (<1%)	4 (1%)
2. Participants with at least one VL ≥200 c/mL	3 (<1%)	3 (<1%)
2a. a single VL ≥200 c/mL and no two consecutive viral loads ≥ 50c/mL	3(<1%)	1 (<1%)
2b. ≥ two consecutive VLs ≥ 50 c/mL with at least one >200 c/ml	0	2* (<1%)
Total (all categories)	14 (4%)	25 (7%)
Participants with Baseline Resistance Testing Data Available	N=318**	N=308**
M184I/V (Occurrence of Elevated VL)	4 (0)	3 (0)
K65R (Occurrence of Elevated VL)	0 (0)	1 (0)

Footnote: * one subject met Confirmed Virologic Withdrawal Criteria (CVW) by Week 48. CVW was defined as 2 consecutive on-treatment viral-load measurements of >=50 copies/mL with the 2nd one ≥ 200 c/mL. **Out of 741 participants in the ITT-E population, baseline proviral DNA resistance testing was performed on participants with available whole blood sample and consent, on-treatment post-baseline HIV-1 RNA and no withdrawal due to protocol deviations. 77 participants had non-reportable results due to assay failure.

Table 1

PE3/16

Phase 3 randomized, controlled DISCOVER study of daily emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV pre-exposure prophylaxis (PrEP): week 96 results

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Purpose: In the 48-week (W) primary endpoint analysis, tenofovir alafenamide (TAF) delivered higher intracellular tenofovir (TFV)- DP and lower plasma TFV levels resulting in non-inferior HIV PrEP efficacy and improved renal and bone safety compared with TDF. We report W96 secondary endpoint results from an ongoing, randomized, double-blinded, active-controlled, non-inferiority (NI) phase 3 trial comparing F/TAF to F/TDF in men who have sex with men (MSM) and transgender women (TGW).

Method: 5387 participants were randomized 1:1 to receive blinded F/TAF (200/25 mg) or F/TDF (200/300 mg) and matching placebo. Primary outcome was HIV incidence rate ratio (IRR) of F/TAF to F/TDF at W48. IRR was evaluated as a secondary endpoint when 100% completed W96. Assessments included adherence by pill count, self-report, and dried blood spot (DBS) TFV-DP levels and comparative safety by six pre-specified renal and bone outcomes. Sexually transmitted infections were assessed at each study visit.

Results: At W96, 82% remained on study drug, 8% discontinued by participant choice, and 8% were lost to follow up. After 10,081 person-years (PY) of follow-up in 2,670 and 2,665 participants on F/TAF and F/TDF respectively, 23 acquired HIV; F/TAF 8: IR: 0.16/100 PY (95% CI: 0.069, 0.313) vs F/TDF 15: IR 0.30/100 PY (95% CI: 0.166, 0.490), confirming continued non-inferiority of F/TAF vs. F/TDF (IRR: 0.54 [95% CI 0.23, 1.26]). Both regimens were well-tolerated through W96; F/TAF was superior to F/TDF on six pre-specified bone and renal endpoints (table 1). With high (versus medium or low) adherence by DBS testing, the OR associated with HIV acquisition were 0.05 (95% CI: < 0.001, 0.40) with F/TAF and 0.15 (95% CI: 0.03, 0.55) with F/TDF. STI rates remained high (table 1).

Conclusion: At 96 weeks, F/TAF remains non-inferior to F/TDF and superior in bone and renal safety for HIV prevention, as it is for HIV treatment.

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	F/TAF (N=2694)	F/TDF (N=2693)	p-value
Change or % change from baseline in renal safety parameters, median (Q1, Q3)[a]			
Serum Creatinine (mg/dL), mean (SD)	0.01 (0.114)	0.03 (0.117)	<0.001[a]
$eGFR_{CG}$ (mL/min), median (IQR)	−0.6 (−10.8, 9.6)	−4.1 (−13.4, 5.3)	<0.001[b]
On-study, Treatment-emergent Proteinuria by Urinalysis (Dipstick)	23%	26%	0.003[c]
Participants who Developed UPCR >200 mg/g[d]	1%	1%	0.22[c]
Urine β2M:Cr (µg/g), %	−14.6 (−45.4, 23.9)	14.2 (−26.1, 99.7)	<0.001[b]
Urine RBP:Cr (µg/g), %	0.2 (−27.1, 35.6)	21.4 (−13.7, 73.6)	<0.001[b]
% change from baseline in BMD, mean (SD)			
Hip[e]	0.645 (2.9600)	-1.013 (2.9692)	<0.001[a]
Spine[e]	0.950 (3.3991)	-1.386 (3.5385)	<0.001[a]
Lab-assessed GC/CT incidence, number of participants with STI (rate: number of STI event/100 PY)[a,f]			
Any Gonorrhea or Chlamydia	1562/ (85.7)	1604 (83.1)	–
Gonorrhea (oral, urethral or rectal)	1107 (45.1)	1107 (43.0)	–
Chlamydia (oral, urethral or rectal)	1120 (40.6)	1136 (40.1)	–
Syphillis, n (%)	394 (15)	406 (15)	–

[a] P-value was from the analysis of covariance (ANCOVA) model including baseline F/TDF for PrEP and treatment as fixed effects and baseline serum creatinine as a covariate
[b] P-values were from the Van Elteren test stratified by baseline F/TDF for PrEP to compare the 2 treatment groups
[c] P-value was from the rank analysis of covariance adjusting for baseline category and baseline F/TDF for PrEP to compare the 2 treatment groups
[d] Participants had UPCR <200 mg/g at baseline
[e] P-value was from ANOVA model with baseline F/TDF for PrEP and treatment as fixed effects
[f] n=140 (F/TAF), n=137 (F/TDF)
[g] n=144 (F/TAF), n=140 (F/TDF)
[h] Rates include multiple STI events per participant
[i] n=2670 (F/TAF), n=2665 (F/TDF)

Table 1. Key renal, bone, and STI results at week 96

PE3/17

Single doses of long-acting capsid inhibitor GS-6207 administered by subcutaneous injection are safe and efficacious in people living with HIV

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Purpose: GS-6207 is a novel, long-acting, HIV-1 capsid inhibitor. In HIV-negative volunteers, a single dose of subcutaneous (SC) GS-6207 (30–450 mg) was well tolerated and maintained systemic exposure≥24 weeks.
Method: This is an ongoing, phase 1b, randomized, double-blind, placebo-controlled, proof-of-concept study in people living with HIV who are ART-naïve or -experienced but capsid inhibitor naïve. A single SC dose of GS-6207 (20, 50, 150, 450, or 750 mg) or placebo was administered. The primary endpoint was maximum reduction of HIV-1 RNA through day (D) 10. We present antiviral activity (through D10) and blinded safety (through at least D16) for the 50, 150, and 450 mg cohorts. Pharmacokinetics (PK) of GS-6207 were assessed.
Results: Eighteen participants received GS-6207 (n=6/cohort) and 6 placebo (n=2/cohort). In each cohort, mean maximum reduction in HIV-1 RNA by D10 ranged from 1.76 to 2.20 $\log_{10}$ copies/mL (figure), which were all significantly greater compared with placebo (all $p<0.0001$) and comparable across cohorts. All participants receiving GS-6207 had at least 1 $\log_{10}$ copies/mL reduction (range: 1.16 to 2.86). At these doses, the inhibitory quotients (mean GS-6207 concentrations/protein-adjusted EC_{95} for wild type HIV-1) on D10 ranged from 1.1 to 9.9. No serious AEs, AEs leading to discontinuation, Grade 3 or 4 AEs, or clinically relevant Grade 3 or 4 laboratory abnormalities were reported. The most common AEs were mild or moderate injection site reactions (63%; 15 of 24). Available data from remaining cohorts will be presented.
Conclusion: These preliminary data demonstrate proof-of-concept for in vivo antiviral activity via capsid inhibition. Following a single SC dose, potent antiviral activity was observed in all participants who received GS-6207 at 50, 150, or 450 mg through D10. GS-6207 was generally safe and well tolerated. These results support further evaluation of GS-6207 as a long-acting antiretroviral agent in people living with HIV.

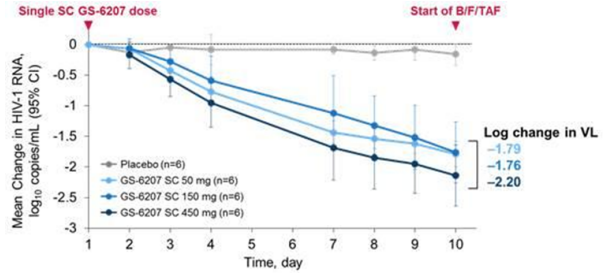


Figure 1. Antiviral activity of GS-6207 through day 10

PE3/18

Long-term safety and efficacy of rilpivirine plus nucleoside/nucleotide reverse transcriptase inhibitors in HIV-1 infected patients: 7-year roll-over study from phase 2 and 3 clinical studies

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Purpose: Evaluate long-term safety, tolerability and efficacy of rilpivirine (RPV) plus background regimen of two nucleos(t)ide reverse transcriptase inhibitors (N(t)RTIs) in human immunodeficiency virus type-1 (HIV-1) infected patients.
Methods: In this open-label study, RPV-treated HIV-1 infected adults rolled-over from phase 2–3 studies and received continued access to RPV 25-mg once-daily with two N(t)RTIs. Adverse events (AEs), viral load, and genotypic data were assessed. Time to virologic failure (rebound, viral load≥50 copies/mL) was analyzed using Kaplan-Meier estimates.
Results: Of 482 enrolled patients, majority were men (74.1%), aged<50 years (85.5%), and white (59.5%). At 7 years data cut-off (RPV exposure: 1374.8 patient-years; maximum: 336 weeks), 437 (90.7%) patients had already discontinued, of which 371 (77%) switched to commercially available RPV, 14 (2.9%) discontinued due to AE, and 6 (1.2%) had virologic failure. Overall, 102 (21.2%) reported any AE, most were grade 1–2 (87 [18%]); most common: pregnancy (7 [1.5%]) and syphilis (5 [1%]). Grade 3–4 AEs: n=17 (3.5%), no grade 3–4 rash observed. AEs at least possibly related to RPV: n=23 (4.8%), most frequent: increased blood triglycerides, n=3. There were 23 SAEs and 2 deaths, none considered RPV-related. AEs of special interest: n=39 (8.1%), most frequently neuropsychiatric events (14 [2.9%]). Majority (80%; 95% CI: 75%, 84%) maintained virologic suppression (< 50 copies/mL) through 288 weeks of treatment, beyond which data considered insufficient for meaningful conclusions. Throughout the study, rebound rate per 100 patient-years (95% CI) was 5.5 (4.4; 6.9) corresponding to 68/482 (14.1%) patients (mostly during first 24 weeks, n=39); 4/68 patients with virologic rebound had genotypic data available with RPV-associated mutations in 3 patients (E138K, Y181C, M230L).
Conclusion: Long-term treatment with once-daily RPV and two N(t)RTIs was well-tolerated with no new safety findings and with sustained virologic suppression in HIV-1 infected patients.

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PE3/20

Prevalence of archived HIV-1 DNA resistance-associated mutations (RAMs) and their lack of effect on virologic outcome at week 96 in antiretroviral treatment (ART)-experienced, virologically suppressed patients receiving the once-daily, single-tablet regimen (STR) darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in the EMERALD phase III trial

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Purpose: Through 96 weeks in EMERALD (ART-experienced, virologically-suppressed adults; NCT02269917), D/C/F/TAF 800/150/200/10 mg showed high virologic response (91% [692/763] viral load [VL]< 50c/mL) and low virologic failure (VF; 1% VL≥50c/mL) rates, with no emergence of darunavir, primary protease inhibitor (PI), tenofovir or emtricitabine RAMs. We examined baseline archived RAMs and their effect on virologic outcome through week 96 in the D/C/F/TAF arm.

Method: HIV-1 proviral DNA from baseline samples (VL<50c/mL) was analysed post-hoc (GenoSure Archive®) to assess prevalence of archived RAMs in the D/C/F/TAF subgroup with prior VF (n=116) or protocol-defined virologic rebound (PDVR; cumulative confirmed VL≥50c/mL) (n=24), i.e. patients most likely to have baseline resistance. If historical genotypes were available, patients with darunavir RAMs were excluded; Patients with emtricitabine and tenofovir RAMs were eligible for inclusion.

Results: In EMERALD, 59% of D/C/F/TAF patients had multiple prior antiretroviral experience; 15% had VF prior to screening. Of those VFs, 7% had previously failed≥1 PI, 12% ≥1 N(t)RTI, 7% ≥1 NNRTI and 1% ≥1 integrase inhibitor. Predicted phenotype showed that 100% were susceptible to darunavir, 63% to emtricitabine and 78% to tenofovir. At baseline, in 98 D/C/F/TAF patients with prior VF and genoarchive data, 4 (4%) had archived darunavir RAMs, 4 (4%) tenofovir RAMs, 19 (19%)≥3 TAMs and 35 (36%) emtricitabine RAMs, mainly at position M184, 31 (32%) (Table 1). All these patients with archived resistance maintained virologic response at week 96 or last on-treatment VL and no VF was observed. None of the 22 D/C/F/TAF patients with PDVR and baseline geno-archive data had archived RAMs to darunavir, emtricitabine or tenofovir.

Conclusion: In EMERALD, in ART-experienced, virologically-suppressed patients, baseline archived darunavir, emtricitabine and tenofovir RAMs had no effect on virologic response/failure rates through 96 weeks, confirming the efficacy and high genetic barrier of D/C/F/TAF.

Table 1. EMERALD: Prevalence of baseline RAMs in HIV-1 proviral DNA for patients with previous virologic failure

	D/C/F/TAF once daily; N=763
Patients with previous virologic failure (VF), N	116
Patients with previous VF and geno-archive data at baseline, N	98[a]
Genotypic Susceptibility[b], n (%):	
All PIs[c]	80 (82)
Darunavir/r	98 (100)
All N(t)RTIs[c]	53 (54)
Emtricitabine	62 (63)
Tenofovir	76 (78)
All NNRTIs[c]	56 (57)
All integrase inhibitors	86 (88)
≥1 primary PI RAMs, n (%)	20 (20)
≥1 darunavir RAMs[d], n (%)	4[e] (4)
L76I/V	1 (1)
I84I/V	4 (4)
≥1 N(t)RTI RAMs, n (%)	46 (47)
≥1 tenofovir RAMs[d], n (%)	4 (4)
K65K/R	4 (4)
≥3 TAMs[d,f], n (%)	19 (19)
M41M/L	18 (18)
L210L/W	9 (9)
≥1 emtricitabine RAMs[d], n (%)	35 (36)
K65K/R	4 (4)
M184M/I/V	31 (32)
≥1 NNRTI RAMs, n (%)	44 (45)
≥1 Primary integrase inhibitor RAMs, n (%)	5 (5)

[a]Denominator for the prevalence of baseline RAMs (IAS-USA 2017 mutation list)
[b]Genotypic susceptibility assessment based on the Monogram GenoSure®Archive report
[c]All currently commercially available antiretrovirals
[d]Observed mutations were concatenated
[e]In one patient 2 darunavir RAMs were observed (I84I/V and L76L/V)
[f]Multi-N(t)RTI resistance: Thymidine analogue-associated mutations (TAMs)

Table 1

PE3/21

Islatravir efficacy and safety for selected demographic and baseline subgroups from a Phase 2 trial in treatment naïve adults with HIV-1 infection

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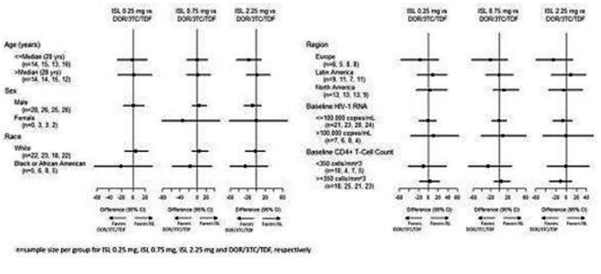
Purpose: Islatravir (ISL, MK-8591) is the first nucleoside reverse transcriptase translocation inhibitor (NRTTI) in development for treatment of HIV-1 infection. We analyzed the week 48 results of a Phase 2 ISL trial in treatment naïve adults with HIV-1 infection by pre-specified subgroups for efficacy and safety.

Method: In this randomized, double-blind, dose-ranging trial, participants were initially assigned to receive ISL (0.25 mg, 0.75 mg, or 2.25 mg) with doravirine (DOR, 100 mg) and lamivudine (3TC, 300 mg) or a fixed-dose combination of DOR, 3TC, and tenofovir disoproxil fumarate (DOR/3TC/TDF) once daily. Participants receiving ISL who achieved HIV-1 RNA<50 copies/mL at Week 20 or later stopped taking 3TC at their next visit and continued DOR+ISL at initial dosage; most participants stopped 3TC at Week 24. Efficacy endpoints included the overall proportion of participants at week 48 with HIV-1 RNA<50 copies/mL. For the current analysis, efficacy results were summarized within pre-specified subgroups (age, sex, race, region, baseline HIV-1 RNA, baseline $CD4^+$ T-cell count) using the Observed Failure Approach (excludes participants with data missing for reasons other than lack of efficacy).

Results: 121 participants received study drug and were included in analyses (mean age 31 yr, 92.6% male, 76.0% white, 49.6% Hispanic or Latino, 22% HIV-1 RNA>100,000 copies/mL, median $CD4^+$T-Cell Count 456 cells/mm^3). At week 48, 92.9% (26/28), 93.1% (27/29), 85.7% (24/28), of participants achieved HIV-1 RNA<50 copies/mL in the 0.25 mg, 0.75 mg, 2.25 mg dose of ISL respectively, compared to 92.9% (26/28) with DOR/3TC/TDF. Across the pre-specified and selected demographic and baseline subgroups, proportions of participants with HIV-1 RNA<50 copies/mL at week 48 were comparable between all treatment arms (Figure 1). In the safety analysis, similar adverse event rates between treatment groups were observed across subgroups.

Conclusions: At week 48, across all baseline subgroups, the ISL regimens demonstrated similar efficacy and safety comparable to DOR/3TC/TDF.

Figure 1: Analysis of the Difference in Proportions with HIV-1 RNA <50 copies/mL at Week 48 by Subgroup



n=sample size per group for ISL 0.25 mg, ISL 0.75 mg, ISL 2.25 mg and DOR/3TC/TDF, respectively

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Antiretroviral therapy preclinical

PE4/1

Discovery of novel pyrazole based dual inhibitor of HIV and HCV together with attenuation of oxidative stress

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Purpose: HIV-infected people are on average six times more prone to HCV infection than HIV-uninfected people, which warrants need to improve integrated HIV/HCV services together with affordable newer medications. HIV infection has been associated with a high oxidative stress via depletion of protective system, activation of immune signalling molecules (cytokines and chemokines) and an increased production of free radicals leading to activation of lymphocytes and phagocytising cells, chronic inflammation. Therefore, the present study was intended to discover novel pyrazole based dual inhibitor of HIV and HCV infection.
Method: The compounds were developed via facile synthetic route and subsequently tested for anti-HIV activity using TZM-bl cell lines along with Luciferase expression profile of the TZM-bl cells after infecting with NL4.3 virus and MTT assay for the cytotoxicity determination. The anti-HCV activity was also determined by capability to obstruct the HCV replicase (HCV NS5B) activity in vitro and HCV replication in a cell culture system carrying replicating HCV subgenomic RNA replicon. The DPPH assay was conducted to determine the antioxidant activity of the molecules.
Results: It has been found that compound 8a showed utmost 97 % inhibition of HIV with K_i = 523.45 nM against HIV-RT. Rest of the molecules showed also showed significant inhibition pattern. The target molecules also found to exhibit potent inhibition of RNA dependent RNA polymerase (RdRp) activity of HCV replicase in vitro with IC_{50} 15.21 μg/mL. Compound 8c, significantly inhibited HCV replication in culture system which leads to reduction in HCV RNA titer and translation level of viral proteins in concentration-dependent manner. In DPPH assay, molecules showed significant reduction of oxidative stress.
Conclusion: As a concluding remark, we have developed novel pyrazole based dual inhibitor of HIV and HCV infection, while presenting no considerable toxicity at the test dosages.

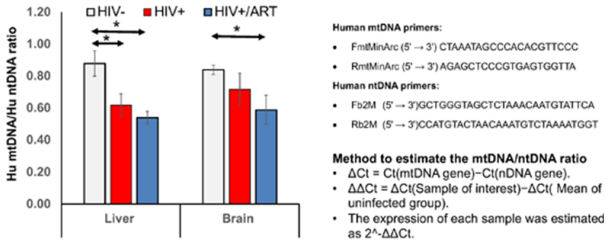
PE4/3

In vivo dissection of the effects of HIV and antivirals on mitochondrial function in chronic treated HIV

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Purpose: The mechanisms that drive comorbidities in chronic treated HIV remain unclear. Mitochondria are responsible for creating the energy needed for function of organs. Mitochondrial dysfunction likely plays a role in aging in chronic treated HIV. Given that observational human studies cannot dissect the differential effects of HIV versus antivirals (ART) on mitochondria, we used a physiologically relevant humanized mouse model of chronic treated HIV to determine HIV-1 and/or ART-driven mitochondrial dysfunction in vivo.
Method: The C57BL/6 Rag2−/−γc−/−CD47−/− Bone Marrow/Liver/Thymus mice do not develop early graft versus host disease. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice (n=20) were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. The groups were: A (n=5): uninfected (HIV-); B (n=10): HIV+; C (n=15): HIV+, ART. Reduction in mitochondrial DNA (mtDNA) levels compromises cellular function and the mtDNA/ntDNA ratio was determined by real-time PCR (Figure). Results are described as mean and SEM and t-test was used for statistical analysis.
Results: HIV-1 induced a mean 26% reduction in human mtDNA/ntDNA ratio in the liver of infected compared to uninfected mice ($p<0.05$) but did not affect the human and murine mtDNA/ntDNA ratio in the brain (data not shown). Potent ART for 12 weeks suppressed viremia within 4 weeks and induced a mean>20% reduction in human and mouse (not shown) mtDNA/ntDNA ratio in the liver and human mtDNA/ntDNA ratio in the brain of infected compared to uninfected mice ($p<0.05$).
Conclusion: HIV-1 and/or potent ART had a differential impact on mitochondria at the tissue level in vivo. Potent ART consistently induced mitochondrial dysfunction in both liver and brain and in both human and murine cells and may be a more important (than HIV-1) instigator of mitochondrial dysfunction in chronic treated HIV.



Figure

PE4/4

The main barriers to "Test and Start" in Central Asia from the service providers' and patients' point of view

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Purpose: Under the Test and Start (T&S) guidelines being introduced in Central Asian countries (Kazakhstan, Kyrgyzstan and Tajikistan), all people living with HIV (PLHIV) are eligible for antiretroviral therapy (ART), regardless of CD4 cell count. T&S strategy has been approved by the MOH in three countries, but only about 70% actually start ART within 30 days after HIV diagnosis. To assess the readiness of local HIV service providers and patients to move towards T&S, ICAP conducted an assessment of HIV service providers' capacity and a patient flow analysis in the three largest AIDS centers.
Method: During May-June 2018 ICAP conducted individual semi-structured interviews with clinical staff and PLHIV, carried out mapping of PLHIV visits and patient-flow observations, and reviewed government documents in three AIDS centers in Kazakhstan, Kyrgyzstan and Tajikistan.
Results: We interviewed 20 clinical staff and 161 PLHIV, including 152 on ART. The results of interviews showed that clinical staff and most patients are supportive and understand the benefits of early ART initiation. However, assessment identified several key challenges to effective roll-out of T&S, including lack of appropriate space for confidential examination and counseling of patients, limited number of nurses and insufficient information about ART provided to the patients. PLHIV still have fears about potential side-effects of ART, treatment complexity, privacy violation and, therefore, are not fully supportive of the prompt ART initiation.
Conclusion: There are several barriers to the effective roll-out of T&S in Central Asia. Key opportunities to overcome these barriers are to improve the management of patient flow by scheduling of clinical visits, implementation of "fast tracking" of stable patients on ART, and improving patients' understanding of ART. Facility staff should invest more time in explaining the benefits of ART and the way ART is provided and should actively involve community organizations and peers in these information sessions.

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PE4/5

Preclinical aspects of an anti-HIV molecule targeting vimentin

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Purpose: Host proteins are essentials for HIV replicative cycle. We have identified vimentin, an intermediate filaments forming protein, as a potential target for inhibiting HIV-1. The present work exposes a preclinical characterization of a vimentin targeting peptide.
Method: The HIV replication in presence of a synthetic peptide capable of modifying vimentin intermediate filaments was evaluated. Flow cytometry, fluorescence and electron microscopy and circular dichroism spectrometry analysis were applied to study the effect of the peptide on the supramolecular structure of vimentin and its cell penetration capacity. The peptide safety was assessed through the macroscopic and microscopic analysis of the organs and the evaluation of immune system functionalities in mice. The pharmacokinetic profile and the bio-distribution were investigated in rodents.
Results: A synthetic peptide, derived from human keratin 10, was capable to change the structure of vimentin intermediate filaments. The peptide exhibited a high anti-HIV activity with a half maximal inhibitory dose at the nanomolar range and a low cytotoxicity. The capacity of the peptide to penetrate in human cell lines of different origins was demonstrated. A mostly disordered structure in aqueous solution, with an estimated alpha helical content of less than 5% was determined. The peptide safety was evidenced in repeated doses schemes, in mice. The half-life of elimination from blood was 4 hours. The peptide was found in HIV relevant tissues like lymph nodes.
Conclusion: The results show a synthetic peptide with a dose-dependent HIV inhibitory activity, a low cytotoxicity and a good cell uptake. Since this peptide targets a genetically conserved host factor there is low probability of selecting drug-resistant viruses. The preclinical data suggests a favorable pharmacokinetic and biodistribution profile for this potential drug candidate against HIV-1 infection.

PE4/6

PK/PD modelling of bnAbs for HIV treatments identifying knowledge gaps

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Purpose: Broadly neutralizing antibodies (bnAbs) are a potential HIV monoclonal antibody (mAb) therapy whose clinically effective dose often exceeds its in vitro potency by more than 10-fold. Pharmacokinetic and pharmacodynamic (PK/PD) modelling is critical for drug development and is used for

1) Candidate progression into clinical trials,
2) Characterizing processes critical to treatment success, and
3) Drug combination trials.

Application of relevant antibody models to bnAbs, incorporating pre-existing HIV and mAb knowledge, has the potential to identify knowledge gaps and solutions.
Method: A review of infectious disease models identified a unified PK/PD scaffold, adapted to model published in vivo bnAb (BNC117) PK and PD data. A non-linear mixed effects model predicted bnAb data obtained from patients with detectable viral load. Sensitivity analyses evaluated the impact of tissue biodistribution, accelerated antibody clearance and resistance on parameter and dose estimation.
Results: The model predicted bnAb PK/PD data estimating dose-dependent effects on viral depletion and expansion. The influence of tissue biodistribution, enhanced clearance, and the presence of resistant viral quasispecies could not be estimated due to data paucity and model specification issues. The model identified a clinically 'effective' IC50 that was approximately 10-fold higher than the in vitro assessment. Viral suppression was maintained when plasma concentrations exceeded the 90th percentile of the 'effective' IC95 (determined from the 'effective' IC50). Sensitivity analyses indicated: tissue biodistribution could have a significant impact on estimating IC50, some emerging resistance and antibody clearance can be mitigated with increased doses.
Conclusion: The bnAb model had a structure similar to other infectious disease models including resistance development and the maintenance of effective drug concentrations. A difference in in vitro and in vivo potency was quantified that was dependent on biodistribution. Future characterisation of influential processes like biodistribution, presence of virus and effectors of PK will improve forecasting of bnAb effectiveness.

PE4/7

A new inhibitor of HIV-1 infection exploiting host intracellular signaling to alter viral RNA processing

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Purpose: The ability of HIV-1 to evolve resistance to current antiretroviral drugs has stimulated research into alternative means of modulating infection. We assayed>60 modulators of RNA splicing to identify novel inhibitors of HIV-1 RNA processing—a segment of the viral lifecycle that is not targeted by current drugs.
Method: Cell-based inhibitor screening and protein/RNA quantification assays, SUnSET, RNA-Seq, and LC-MS/MS.
Results: We identified compound 191 as a potent inhibitor of both wild-type (*IIIB/nL4–3/N54*) and drug-resistant strains of HIV-1 in CD4 + T cells (IC_{50}: ~700 nM), *LAI* in HeLa cells (IC_{50}: 750 nM), and *BaL* in CD4 + primary T cells (IC_{50}: 1.8 μM) with insignificant effects on cell viability at concentrations tested. 191 dramatically reduces expression of four essential HIV-1 structural/regulatory proteins (Gag/Env/Tat/Rev) without affecting total protein synthesis. These results are associated with altered viral RNA accumulation and transport: reducing unspliced and singly-spliced HIV-1 RNAs by 60% and loss of Rev. Consistent with perturbing HIV-1 RNA processing, 191 affects the abundance (and modification) of serine/arginine-rich splicing factors 1, 3, and 4. Decreased expression of Tat, but not Gag/Env, by 191 treatment was reversed by a proteasome inhibitor, suggesting that this compound also promotes degradation of this key viral factor. In contrast, 191 causes only 0.25% and 0.01% perturbation (resp.) in alternative splicing and expression of host RNAs and 0.02% alteration in abundance of host proteins. Inhibition of HIV-1 expression by 191 requires G protein-coupled receptor and Raf-MEK1/2-ERK1/2 signaling. Supporting this hypothesis, pre-treatment with G-protein α-subunit or MEK1/2 inhibitors rescued 191's inhibition of HIV-1 Gag and unspliced/singly-spliced RNA expression. Conversely, exogenous expression of variants of the small G protein, N-Ras, inhibited expression of these viral products.
Conclusion: These findings reveal the potential of modulating host intracellular signaling, with minimal consequences observed to cells, as an alternative approach for controlling HIV-1 infection.

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Behavioural interventions

PE5/1

Close group social media network and social gatherings for comprehensive HIV services among adolescent MSM in Lagos Nigeria

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Purpose: Men who have sex with men (MSM) in Nigeria contribute significantly to the national HIV epidemic. In Lagos, Nigeria, the prevalence of HIV among MSM is as high as 41%. Adolescent MSM are more at risk. As effort to achieve UNAIDS 90:90:90 target, this project focused on adolescent MSM, to facilitate their access to comprehensive HIV Testing Services (HTS) and educate them on how to access biomedical HIV prevention tools.
Method: Target group were adolescent MSM aged 15–19 years. The targets were reached through close group social media networks using the snowball approach. Focus group discussions were conducted once a week during strategic social gathering for sixteen weeks to facilitate HTS. Ten main topics on HIV, AIDS, sexual and reproductive health, biomedical HIV prevention tools, PrEP, PEP and microbicides including their uses, accessibility, common myths and misconceptions were covered over sixteen weeks. Skills building were included in the training activities.
Results: Close group social media network complemented with targeted face to -face meetings during social gatherings/parties using snowball approach can facilitate comprehensive HIV services for adolescent MSM. Face-to face meetings is important to facilitate access to HTS. Of the 52 adolescent MSM reached, 45 (86%) completed the educational sessions and learnt about new HIV prevention tools. Ninety-two percent (92%) had access to HTS for their first time. Fourteen tested HIV positive and were all (100%) linked to HIV treatment. Adolescent MSM require constant assurance of confidentiality before they open up and discuss personal sexual and reproductive health issues. Follow up of adolescent MSM is challenging as most had unfavorable time schedules to seek care.
Conclusion: Close group social media network with targeted social gatherings can improve comprehensive HIV services for adolescent MSM. There is need for more targeted interventions tailored to the specific needs of adolescent MSM in the State.

PE5/2

Good hygiene practices post circumcision: a case for low adverse events in VMMC

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Purpose: Kenya continues to implement Voluntary Medical Male Circumcision (VMMC) for HIV prevention due to its cost effectiveness and projected long term benefits. However, provision of VMMC in resource limited settings raises safety concerns of VMMC services. This study sought to determine the rates and correlates of adverse events among men at Migori County hospital, Kenya.
Method: This was a quantitative cross sectional study of men attending VMMC follow up visits between November 15 2015 and December 20 December 2015. Participants were examined by a clinician for adverse events and interviewed by the Investigator for data on hygiene.
Results: A total of 138 men, with an average age of 22 years were enrolled into the study. A total of 4 participants (2.9%) had moderate adverse events. A total 52(43%) showered daily after circumcision while 25(18%) showered once every two days, and an additional 47(34%) showered at least once in three days and only 4(3%) showered after more than 3 days. A total of 122 (89%) participants wore underpants after circumcision while 15(11%) participants did not. A total of 55(45%) reported a daily change of underpants, 44(36%) changed the underpants after two days. 17(14%) changed underpants after three days while 6(5%) did not change or wash their underpants post-circumcision. Infrequent bathing ($p=0.001$) and not wearing of underpants
($p<0.005$) was associated with infection and swelling. Additionally men who never changed their underpants were more likely to experience infection and delayed healing ($p=0.001$).
Conclusion: Despite the standard practice of counseling and provision of information on post circumcision practices, there is a need for further evaluation on what messages are provided and how they are understood by clients. There may be a need for specific instructions on the frequency of bathing and the wearing, changing and washing of underpants.

PE5/3

Challenges of implementing HIV counselling and testing (HCT) campaigns for higher education distance learning students at University of South Africa

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Purpose: Higher education distance learning institutions do not usually have students who are physically present on campus as is the case with residential higher education institutions. Therefore, the purpose of this study was to investigate the challenges faced by implementers of HIV Counselling and Testing (HCT) campaigns for higher education distance learning students at University of South Africa.
Method: This study used a qualitative approach supported by exploratory and case study techniques to collect and analyse data. In-depth interviews and observations at research sites uncovered rich data elucidated by Health Belief Model approach
Results: It has been concluded that the administrative planning procedures of HCT campaigns were not properly followed, which resulted in the following difficulties: defining the roles and responsibilities of stakeholders, using limited resources, and the inability to reach all the students, in order to get them to actively participate in the campaigns. Lack of coordination of HIV and AIDS activities and the absence of monitoring and evaluation also impacted negatively on the success of HCT campaigns.
Conclusion: This study recommended that HCT campaigns at University of South Africa should have a proper task team constituting of experts in HCT campaign operations, in order to strategically plan and coordinate all the campaigns activities. The implementers should also monitor and evaluate these activities on a regular basis.

PE5/4

Enhancing effective HIV prevention among girls by fighting child marriage and sexual and gender based violence in Karonga district, Malawi

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Purpose: In Malawi, early sexual debut and marriages, initiation and marriage systems, intergenerational and transactional sex, multiple partners, and sexual coercion expose youth especially girls to HIV. More than half of Malawian youth marry while still in their teens and 69% of sexually-active young people have multiple partners. Example, 30% of young women aged 15–19 years have first sexual intercourse before they were 15 years old making themselves more vulnerable to HIV and AIDS, STIs and maternal death. Similarly, in TA Kilupula, Karonga district, youth especially girls were affected by the situation. Cases of Sexual and Gender Based Violence (SGBV), early child marriages (CM) among girl children exposed girls to HIV infections while denying their education rights. The situation was influenced by culture, poverty and ignorance.
Therefore, FOHOP implemented a project purposed to enhance protection of 3500 girls from Early child Marriages and SGBV situations which were increasing the rate of new infections of HIV.
Method: Baseline data from 10 health facilities and 4 schools was collected. Trained 50 girls in HIV infection, early childbearing, marriages prevention; Established 10 girls' clubs of 10 members each, Trained 11 young women as paralegals, Conducted 12 awareness campaigns, Trained community leaders, teachers, in child marriages, SGBV and HIV prevention.

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Facilitated linkages to care and treatment for HIV infected and/or victims of child marriage/SGBV.
Results: 8 child marriages were divorced and girls were retained at school. 143 girls went for HIV testing, Reduced cases of SGBV by 90%.
Improved communication between parents and children on HIV.
47300 people were sensitized on HIV infection in connection to Child marriage and SGBV.
Increased support from religious and local leaders.
Conclusion: Enhancing effective HIV prevention among girls by fighting child marriage and sexual and gender based violence is possible and improves girls' health.

PE5/5

Effectiveness of rapid HIV and HCV testing programmes based on mobile units

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Purpose: Increasing coverage of HIV and hepatitis testing by increasing the availability of services.
Method: In the "Humanitarian action" fund's programs rapid testing is carried out in mobile units. The team of each unit includes health workers, peer consultants and case managers. Testing is free and anonymous, accompanied with before and after test counseling. All clients who have received a positive result of the rapid HIV or HCV test are accompanied to the specialized medical services. Testing and consultations take no more than 15 minutes. Mobile units park in the places with large gatherings of people: shopping centers, subway, etc.
Results: According to the professional community, in Russia 50% more people live with HIV than indicated in the official statistics. Thus, in 2015–2018, 38 thousand people were examined for HIV infection, 1,900 new cases of HIV infection were detected and more than 1,500 people were treated at mobile units of the Fund "Humanitarian action". According to official data, detectability during testing in medical institutions does not exceed 3%, in our projects it is 5% of the total number of tested. We also tested 600 people for HCV, of which 347 new cases were identified, which is more than 50% of the total number tested.
Conclusion: Based on these figures, we can conclude that the mobile service is more effective than in-patient testing for HIV and HCV, in identifying these infections among the population.

PE5/6

It can't happen to me – tackling cognitive mistakes and HIV using a national campaign

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Purpose: National campaign It can't happen to me was conducted from October to December 2018 by CAHIV, pointing out a general assumption that bad situations happen more likely to others than to yourself. Rather, it is important to assess the risk reflecting on the past sexual behaviors. To do that, citizens were invited to assess their risk by an expert at CheckPoint Zagreb (CPZ). The idea was promoted using various sources - from educative videos and talk shows to engagement of influencers and promoting mobile application Spolno zdravlje (Sexual health), inspired by the experiences in CPZ. It was also possible to assess the risk through a calculator inside the application.
Method: Data was collected individually for each CPZ user in order to assess risk. In case of high-risk, person was tested for HIV. To measure effects better, frequency data was drawn from the named mobile application's Risk calculator.
Results: Excerpt of the data in table 1. shows risky behavior increase in CPZ during the time of a campaign - namely, high-risk users who have never been tested for HIV, other STDs and who have been practising anal and vaginal sex. A number of HIV+ results remains steady at 1 or 2 per month, but with increasing success.

Table 1. Characteristics of high-risk CPZ users May-Dec 2018

	May	Jun	Aug	Sep	Oct	Nov	Dec
High-risk users	86	72	40	109	127	119	61
MSM	46.5%	45.8%	50.0%	47.7%	43.3%	48.7%	39.3%
Chemsex users	22.1%	37.5%	37.5%	21.1%	22.8%	35.3%	27.9%
HIV never tested	43.0%	58.3%	47.5%	23.9%	55.9%	52.9%	50.8%
Other STDs never tested	64.0%	63.9%	60.0%	31.2%	74.8%	65.5%	83.6%
Practising anal sex	57.0%	52.8%	62.5%	56.0%	59.1%	67.2%	55.7%
Practising vaginal sex	55.8%	62.5%	50.0%	61.0%	65.4%	59.7%	68.9%
Practising oral sex	91.9%	97.2%	100%	95.4%	96.1%	100%	96.7%
HIV+ results	2.3%	1.4%	0.0%	1.9%	1.2%	1.7%	2.4%

Also, risk calculator use skyrocketed during the time of a campaign, as seen in figure 1.

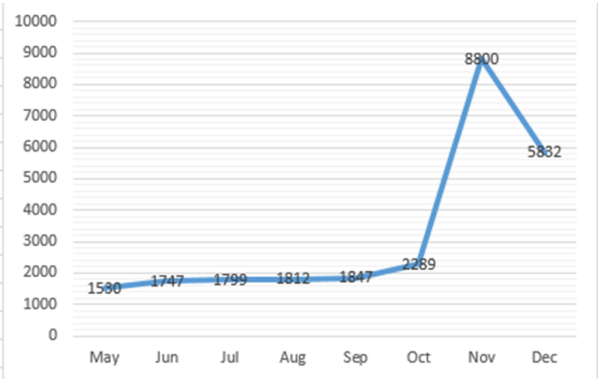


Figure 1. Risk calculator users May-Dec 2018

Further analysis was conducted on various other key populations in order to track success of a campaign.
Conclusion: A campaign was organised to emphasize high risk of getting infected by an STD due to risky behavior. Data shows the importance of understanding why risky behaviors happen, as focusing on cognitive mistakes may contribute to better perception of personal risk and motivate people to seek help, hence prevent getting infected or further spreading the STD infections.

PE5/7

Is mobility still a HIV/STI associated vulnerable factor in the changing sex work dynamics among female sex workers in India? – Emerging evidence

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Background: Mobility for sex work poses increased vulnerability for HIV/STI among Female Sex workers (FSWs) in India. In addition, there is limited evidences on the FSWs who are reported to be travelling for sex work, not associated with HIV prevention program and in context of changing solicitation practices.
Objective: This analysis attempts to explore association between mobility and various factors including new mode of solicitation, association with HIV prevention programs, sexual risk behavior and violence among FSWs.
Method: A cross sectional study, mixed method study at 14 districts spread over seven states of India. This analysis focused on quantitative part, 1750 FSWs, recruited between January-March 2019. Study broadly, observed FSWs soliciting through NACO identified approaches, defined as traditional and all other solicitation approaches defined as non-traditional approaches.

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Univariate, bivariate and binary logistic regression has been applied to address objectives.
Results: Among 1750, 33% (578) reported of practicing non-traditional, including 20% (350) exclusively through social network applications and 13% (228) through new physical spaces. 21% (368) via traditional approaches, while remaining 46% (804) has reported more than one approach of solicitation. 23% (394) FSWs has travelled outside district for sex work and they were more likely (OR=3.62, 95% CI 2.4–5.3) to solicit through non-traditional mode. Further, these FSWs were found to be significantly associated with not using condom with clients (OR=1.58, 95% CI, 1.23–2.03), engages in anal sex in last one month (OR=2.24, 95% CI, 1.72–2.08), *reported violence (*OR=1.84, 95% CI, 1.46–2.32) whereas it is not significant with consumption of *alcohol* before *and* during sex (OR=1.38, 95% CI, 0.94–2.03).
Conclusions: National HIV program should consider new approaches such technology and new physical spaces, for reaching out FSWs not associated with HIV programs. Adapting these newly identified solicitation approaches would facilitate for sharing information on importance of safe-sex and educating them on HIV/STI risk reduction strategies.

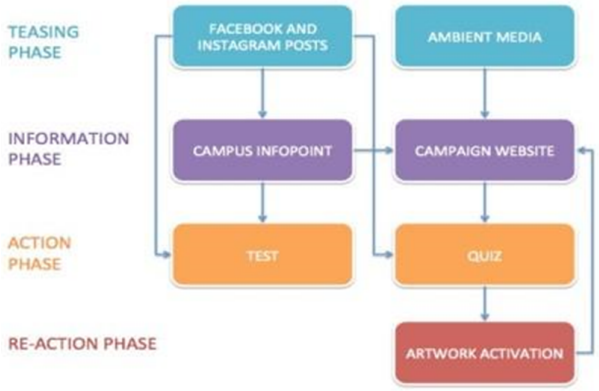
PE5/8

"Amare con Sapienza": an Italian digital ambient media prevention campaign in one of the largest European University to increase U=U, PreP, TasP knowledge

S Vita[1], M Lichtner[2], G Morlino[3], L Celani[2], MA Zingaropoli[2], V Perri[2], S Valeri[2], F Cogliati Dezza[2], L Santinelli[2], G Masci[2], M Falciano[2], A Salotti[2], O Turrizziani[2], G Antonelli[2], CM Mastroianni[2] and V Vullo[2]
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Purpose: Purpose of the study is the evaluation of the effectiveness of digital ambient media in promoting the prevention of HIV infection.
Methods: The project included 3 phases:
- the pre-evaluative: a questionnaire was sent to Sapienza employees and students by email. It included 20 items focused on transmission and preventive measures including PreP, TASP and U=U concept and HIV test.
- the informative campaign via social networks and digital ambient media installed in the campus, both routing target people to the project website where they could get information about the infection and actively contribute to the campaign playing quiz-games that, when correctively solved, animated a digital opera in the campus heart (Fig. 1).
- the post- evaluative: the same questionnaire of the 1st phase was sent, the number of access to the nearby hospital to perform HIV test, the number of visits to the website, of post impressions were counted.
Non-parametric tests were used for statistical analysis.
Results: A total of 7263 persons replied to the questionnaires. We compare the answers before and after the campaign that was set up for 2 months in the campus (Table 1). Overall after the informative campaign an increase in all new HIV knowledge was observed. Through the website and the social campaign were reached about 16.000 persons.
Interestingly in the 2 months period of the campaign, an increase of 31% of the HIV tests and 22% of the new HIV diagnosis was registered in the nearby hospital comparing the same period of the previous years (Fig. 2).
Conclusion: The university population have poor knowledge of recent achievements in HIV prevention. The use of unconventional communication was effective in improving the new knowledge of HIV prevention strategy and in the access to HIV test.
Responses to the questionnaire before and after the digital ambient media campaign

Knowledge	Pre-evaluation questionnaire	Post-evaluation questionnaire	p
U=U (% of correct answer)	30%	46%	<0.001
PreP (% of correct answer)	25%	32.2%	<0.001
PEP (% of correct answer)	22.3%	35.9%	<0.0001
People who never did a HIV test (% of correct answer)	68.3%	57.7%	<0.0001
People who knows that the test is available in pharmacy (% of correct answer)	18.1%	31.2%	<0.0001



Informative campaign phases

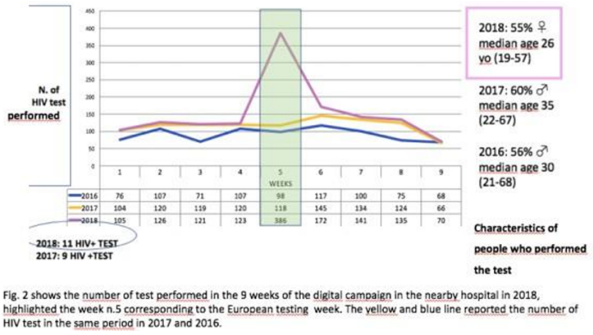


Fig. 2 Number of test performed in the 9 weeks of the digital campaign

PE5/9

Assessing high risky sexual behaviors in vulnerable women in northern Uganda: baseline results of "Pe Atye Kena, no longer alone" study

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Purpose: HIV infection among vulnerable women (VW) has been attributed to unfavourable power relations and limited access to sexual and reproductive health information and services. Objective of the study is to assess sexual high risk behaviors (SHRB) among VW in a rural area of North Uganda in order to plan intervention.
Methods: Cohort pilot, intervention study on VW (aged 18–49 y) in the municipality of Gulu actively recruited by community outreach. HIV-Ab (4th generation Alere™ HIV Combo)and electronic comprehensive questionnaire on SRB and HIV awareness (by ODK system, 110 questions) performed at baseline and every 6 months up to 3 y, educational interventions planned every 6 m. The baseline analysis reported here is performed by uni- and multivariable regression models.
Results: 468 VW were enrolled (mean age: 29 (SD 7.7)). 40/468 (8.5%) were found to be HIV-Ab + . 231 (49%) had a primary level of education; 242 (51%) did not use condom in the last 12 m, 13 (2.7)% have a HIV+ stable sexual partner, median sexual partners in the last 12 m were 1.05 (SD 1.2), 30 (6%) did transactional sex at least once; Factors associated to a recent HIV diagnosis are reported in table 1. After controlling for several sociodemographic, behavioral and knowledge variables, the likelihood of engaging in SHRB (defined as not having used condom in the last 12 m or

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having done transactional sex at least once) was significantly higher among those not knowing the protective role of a monogamous union (AOR 11.3, 95% CI 2.2–58.3, p=0.003), and not thinking that a healthy-looking person may have HIV infection (AOR 18.3, 95% CI 1.84–183.5, p=0.01).
Conclusions: In this cohort of VW HIV prevalence is considerably high and sexual risky behaviors are multifaced; HIV prevention should be tailored through educational approaches focused on health information and avoiding stigma.

	Univariate			Multivariable		
	OR	95%CI	p	OR	95%CI	p
Age>34 y (vs <24y)	1.2	1.1-2.7	0.01	11.4	1.1-117.3	0.01
Last HIV-Ab test > 12 m (vs <12m)	5.1	2.3-11.2	0.001	8.8	1.8-41.5	0.01
Think that sexual partner is HIV-negative	18.1	6.1-54.3	<0.001	40.7	4.9-334.3	0.002
Use of condom at first intercourse	3.13	1.4-5.0	0.007			
Do transactional sex at least once	2.7	1.02-7.28	0.04			
Reduce HIV acquisition by monogamous union	4.5	4.2-8.1	0.01			

Sociodemographic, behavioral and knowledge factors associated to recent HIV diagnosis in uni- or mul

PE5/10

HIV/AIDS educational program for secondary school female students in Iran: a school-based randomized controlled trial

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Purpose: Adolescents form a particularly important target group for primary prevention against HIV/AIDS. The aim this study was to assess the effectiveness of TBP training based program on attitude, norms, parental control, behavioral control and intention among high school female students in Tehran.
Method: A randomized controlled trial was conducted in Tehran, among female high school students aged 12–16 years in 2015–16. They were selected using multistage random cluster sampling and then were randomly assigned to the experimental (n=289) and control (n=289) groups. The Theory of Planned Behavior (TPB) is the basis of both education and evaluation. During the study, the experimental group received an HIV training program based on a modified TPB. Respondents in the two groups completed a questionnaire both at baseline and 6 months follow up.
Results: In the experimental group, significant improvement was shown in attitude (16.6%, 95% CI=14. 4 to 18.8), subjective norm (16.8%, 95% CI=12. 9 to 20.6), perceived behavioral control (19.1%, 95% CI=16. 2 to 22.1), perceived parental control (17%, 95% CI=13. 8 to 20.2), behavioral intention (19%, 95% CI=16. 3 to 21.6) and behavior (17.3%, 95% CI=13. 9 to 20.6) compared to the control group (p<0.001 for all dimensions).
Conclusion: Theory-based HIV/AIDS intervention may be effective in reducing high risk behaviors related to HIV/AIDS among adolescent girls. Routine educational programs need to be replaced by these active educations about HIV/AIDS in school systems.

Cascade of care

PE6/1

Self-reported non-receipt of HIV test Results a silent barrier to HIV epidemic control in Mozambique

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Purpose: People living with HIV (PLHIV) and who are aware of their HIV status can access and benefit from antiretroviral therapy (ART) with subsequent individual and public health benefits; however, many PLHIV are unaware of their HIV status. We assessed the magnitude and determinants of self-reported non-receipt of HIV test results in adults aged 15–59 years old in Mozambique.
Method: We performed a secondary analysis of data from the 2015 Mozambique Immunization indicators, Malaria and HIV/AIDS Survey (IMASIDA 2015). Adults (aged 15–59 years) were interviewed and data on sociodemographic characteristics, HIV knowledge, attitudes and behaviors, and HIV testing history were collected. Multivariable logistic regression assessed factors associated with self-reported non-receipt of HIV test results. Population representative estimates were calculated.
Results: A total of 6,654 (51.1%) respondents had previously been tested for HIV and were included in the analysis. Of these, 308 (4.6%; 95% CI: 3.70–5.77) self-reported not having received HIV test results. In the multivariable analysis, previous sexually transmitted infection (aOR: 2.76; 95% CI: 1.44–5.31), HIV stigmatizing attitudes (aOR: 1.96; 95% CI: 1.14–3.37), and lack of decision-making power towards health care seeking (aOR: 2.51; 95% CI: 1.39–4.52) were associated with non-receipt of HIV test results. Whereas, secondary or higher education (aOR: 0.25; 95% CI: 0.12–0.54), higher HIV knowledge (aOR: 0.47; 95% CI: 0.26–0.86), and age between 30–34 and 35–39 years old (aOR 0.47; 95% CI: 0.28–0.80; and aOR: 0.49; 95% CI: 0.27–0.90, respectively), were associated with receipt of HIV test results.
Conclusion: In this nationally representative survey, self-reported non-receipt of HIV test results was high and of public health relevance. These findings suggest adaptation of HIV counseling and testing programs emphasizing individualized approaches that target the youngest, least educated and the poorest individuals, especially those living in rural areas.

PE6/2

Improvement in ART initiation in different regions of Ukraine from 2010 to 2014

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[1]Alliance for Public Health, Kiev, Ukraine [2]Independent Consultant, Kiev, Ukraine

Purpose: Ukraine is affected by one of the most severe HIV epidemics in Europe with HIV prevalence around 0.67% of adult population and AIDS death rate 25 per 100.000. ART therapy massively came in Ukraine in 2009 covering 25% of the need. ART Protocol has been changing in order to prioritize treatment initiation based on CD4 cell counts from 250 to 350 cells till 2015. HIV case reporting in Ukraine is paper based thus limited data available for analysis. The study describes the major changes in ART uptake between 2010 and 2014.
Methods: We analyzed clinical data routinely collected at regional AIDS centers, HTS points, and ART sites. The study dataset contains only depersonalized clinical information on patients receiving HIV care between 2010 and 2014 in at 18 (out of 25) regions in Ukraine. Study observed information about 27841 HIV-positive persons diagnosed from 2010–2014. We used Kaplan-Meier estimator to determine the time between HIV diagnosis and treatment initiation and log-rank test to assess the difference between years and regions.
Results: Annual ART coverage has increased moderately from 54% in 2010 to 60% in 2014, while average and median time decreased significantly: average time from 45.4 months (95% CI: 44.7–46.2) to 28 month (95% CI: 27.1–28.9); median from 58 (95% CI: 55–61) to 10 (95% CI: 9–11). Improvement in some regions even more prominent (see Tables 1 and 2).

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Average and median time for ART start in 5 years cohort observation

Cohort	N, people	Started ART, people	Started ART, %	Average time, month	95% CI	Median time, month	95% CI
2010	5335	2901	54%	45.4	44.7–46.2	58	55–61
2011	539	2958	55%	41.3	40.5–42.1	47	44–50
2012	5489	3326	61%	33.2	32.4–34.0	25	23–27
2013	5875	3609	61%	29.7	28.8–30.5	16	14–18
2014	5745	3473	60%	28	27.1–28.9	10	9–11

Median time/month before ART start in 5 years cohort observation by regions

Region	2010, month	2011, month	2012, month	2013, month	2014, month	log-rank test
Volyn	52	30	14	24	5	<0.001
Dnipro	65	54	33	18	14	<0.001
Zakarpatya	70	42	32	3	3	<0.001
Kyiv reg	50	44	20	18.5	7	<0.001
Lviv	39	37.5	4	2	2	<0.001
Sumy	68	60	27	24	22	<0.001
Kharkiv	43	27	10	6	4	<0.001
Chernigiv	51	40	24	28	11	<0.001
Kyiv city	56	43	21	7	4	<0.001

Conclusion: Due to changes in ART protocol treatment coverage increased slowly, while the speed of treatment initiation increased sharply in the majority of observed regions. Current ART protocol has changed to criteria of 500 cells in 2015 while ART coverage remains low: 37% of estimated HIV cases or 62 of registered HIV cases. More radical changes in country ART protocol and regulations are needed to get WHO targets on early treatment initiation.

PE6/3

The HIV treatment cascade in Azerbaijan, 2018

N Zulfugarov[1]

[1]*Republican AIDS Centre, Monitoring and Evaluation, Baku, Azerbaijan*

Purpose: The treatment cascade model has been an effective tool to evaluate HIV/AIDS control programs throughout the world. Diagrams of the 'treatment cascade' provide a useful way of visualizing problems with the implementation of 'treatment as prevention' in specific contexts, and of identifying reasons why HIV treatment may not have as great an impact as could be hoped. Purpose of research to study the main problems in the cascade of treatment of PLHIV, to identify ways and mechanisms to overcome them.
Method: Analysis of the final reports of the AIDS centre, databases, monitoring of ARV therapy. Spectrum software.
Results:

1 The estimated number of PLHIV in Azerbaijan -8100;
2 The number of diagnosed PLHIV -6193;
3 Number of PLHIV receiving ART -4397;
4 The number of persons with suppressed viral load - 3312

As can be seen from the figures, in Azerbaijan the number of people who know their positive HIV status is 76.5% of the estimated number of PLHIV (6193 out of 8100 PLHIV). 4397 people receiving ART (71% of the registered patient and 22%).
The number of people receiving ART and having a viral load below 1000 copies/mL was 3,312 people.
There are large gaps exist between the number of people who have HIV, those who know that they have HIV, those attending medical services, and those receiving effective treatment. HIV treatment cascade shows that only 41% (3312 out of 8100 PLHIV) of living with HIV have a suppressed viral load.
Conclusion: To achieve goal 90–90–90, it is necessary to eliminate the main problems identified in the following stages: testing coverage, retention on ART, to achieve viral suppression.

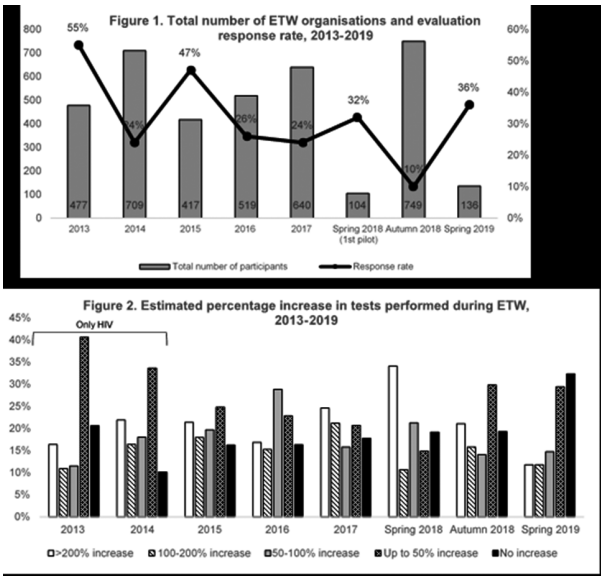
PE6/4

Seven years of European Testing Week: impact of a regional awareness campaign on increase in awareness and testing activities in Europe

L Combs[1], **B Collins**[2], **V Delpech**[3], **D Simões**[4,5], **JK Rockstroh**[6], **D Raben**[1] **and on behalf of the EuroTEST Steering Committee and European Testing Week Working Group**

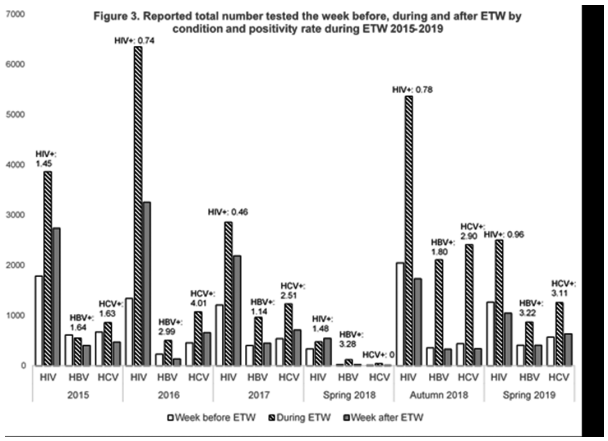
[1]*CHIP, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark* [2]*ReShape/International HIV Partnerships, London, UK* [3]*Public Health England, London, UK* [4]*EPIUnit - Institute of Public Health of the University of Porto, Porto, Portugal* [5]*Grupo de Ativistas em Tratamentos, Lisbon, Portugal* [6]*University Hospital Bonn, Department of Medicine I, Bonn, Germany*

Purpose: European Testing Week (ETW) started in 2013 to unite organisations across Europe to increase testing efforts and awareness of earlier testing for HIV and in 2015, also viral hepatitis. We present the effectiveness and impact of ETW over the past 7 years.
Method: To participate, interested organisations sign up on the ETW website. At the completion of ETW, all participants are asked to complete an online evaluation recording types of activities, targeted key groups, details on testing activities, promotion activities, satisfaction with ETW and challenges. Organisations who conducted testing are invited to submit aggregated data on people tested, reactive results and linkage to care. Results from all surveys (2013 - 2019) were included.
Results: With the exception of 2015, where there was miscommunication regarding sign-up renewal, the number of organisations signed-up to participate increased on average 29% per year (Figure 1). Participating organisations on average overall are NGOs/CSOs (63%), 19% health care, 11% government and 7% other organisations. Over the years, the most common ETW activity have been testing activities followed by awareness raising and are targeted towards key populations including MSM (60%), PWID (41%) and the general population (66%). Of those who reported testing activities from 2015–2019, an average of 85% of survey respondents reported an increase of at least 50% in testing during ETW in comparison to a regular week (Figure 2). Aggregated testing data indicated an average percentage increase in ETW testing of 155% for HIV, 228% for HBV and 192% for HCV compared to the previous week. The average positivity rate during ETW is 1.0 for HIV, 2.3 for HBV and 2.4 for HCV (Figure 3).
Conclusions: Now in its seventh year, ETW has established itself as a well-known European campaign which now occurs biannually and has proven impact on increasing awareness and testing rates.



European Testing Week – Figures 1 and 2

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European Testing Week – Figure 3

PE6/5

Impact of integrated family planning and HIV services on early postpartum contraceptive use among women with HIV in the Eastern Cape, South Africa

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Purpose: Integrated model of one-stop access to family planning services and HIV care in South Africa was considered as a cost-effective strategy with potential to impact on unplanned pregnancy rate and elimination of mother-to-child transmission of HIV. This study examined the impact of the integrated model on early uptake of family planning services among parturient women living with HIV in the Eastern Cape, South Africa.
Method: This was a part of a large prospective cohort study which enrolled a total of 1709 HIV-infected mother/infant pairs in the Eastern Cape between 2015 and 2016. Descriptive statistics and multinomial regression were used to determine prevalence of early contraceptive use and determinants of uptakes of short acting, long active and permanent contraceptive methods.
Results: Nearly all the women (93%) received one form of contraception. Age, place of residence, educational status, employment, parity and abortion history were not significantly associated with early postpartum contraceptive utilisation. Caesarean section delivery [AOR: 0.62; CI: 0.41–0.94] and having more than two children [AOR: 0.54; 0.34–0.85] were associated with a lower likelihood of using short-acting contraceptive method while pre-conception awareness of HIV serostatus [AOR: 2.91; CI: 1.48–5.72] and never used alcohol [AOR: 1.57; CI: 1.04–2.36] were associated with a higher likelihood of using short-acting contraceptive method. Caesarean section delivery [AOR: 7.59; CI: 3.95–14.59], and pre-conception awareness of HIV serostatus [AOR: 3.75; CI: 1.31–10.75] were significantly associated with a higher likelihood of using long-acting contraceptive method. Older Age (>30 years) [AOR: 5.41; CI: 2.63–11.10], Caesarean section delivery [AOR: 5.41; CI: 2.93–10.01], having more than two children [AOR: 4.45; CI: 2.32–8.55], ever terminated pregnancy [AOR: 2.11; CI: 1.05–4.25] and pre-conception awareness of HIV serostatus [AOR: 5.80; CI: 1.40–23.97] were significantly associated with a higher likelihood of permanent contraceptive method.
Conclusion: Integration of family planning services into HIV care has significantly improved access to early postpartum contraceptive among women living with HIV in this setting.

PE6/6

The first report of Prevention of Mother-to-Child Transmission (PMTCT) of HIV in Islamic Republic of Iran

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Purpose: The integration of reproductive health programme and Prevention of Mother-to-Child Transmission of HIV (PMTCT) programme in Iran was conducted as a pilot project three years ago. Therefore, this study is an attempt to thoroughly evaluate the PMTCT programme in Iran through assessing the current situation of PMTCT programme.
Method: Pilot phase of PMTCT was launched in early September 2014 in selected centers included 170 health centers and 40 selected hospitals in 16 medical universities. A checklist for gathering the study data was developed after ethic approval (IR.MUK.REC.1397.5006) then checklists were filled out through interview by the university AIDS expert for all new diagnosed HIV-positive pregnant. Data was analyzed by SPSS 19 software.
Results: Overall, 69.4% of eligible pregnant women were enrolled in the pilot phase. From 134 reactive cases, 76 (56.7%) were confirmed as HIV positive. In 10 (13.2%) of HIV positive pregnant women, consumption of ARV was irregular. Also, 82.5% had CD4 count more than 350 after treatment with an average of 55.5% increase in the number of CD4 in comparison to the base, and 84.8% had viral load suppression (< 200 copies/mL). Counselling with husbands was done in 75% of the husbands/partners of which, 15 (39.5%) of the spouses were identified as new cases of HIV and 23 (60.5%) were known as previously registered HIV patients. One (1.5%) of the infants was diagnosed as HIV positive.
Conclusion: The implementation of rapid HIV testing in pregnant women in Iran is a strength in the national HIV control program. Conducting such a pilot, before its integration into the national program, can prevent major problems and increase the knowledge about the defects and the processes of the program. To achieve the EMTCT stage, it is necessary to carefully examine and resolve the problems observed in the pilot phase.

PE6/7

New HIV diagnosis and linkage to care in two outpatient units in South Europe

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Purpose: Southern European countries, as Italy and Spain, share epidemiological aspects and therapeutic approach to HIV infection. Aim of the study is to evaluate any differences in linkage to care and timing of first cART administration.
Method: We analyzed epidemiological, clinical and virologic parameters and access to care in two HIV populations, first diagnosed from January 2015 to December 2017, in Madrid (M), Spain and in Catania (C), Italy. Data were collected at diagnosis, at first cART beginning and one month later.
Results: Globally 330 subjects (85.5% males) were enrolled. Among M group, 225 (87.6%) were men, median age 33 years; 74.4% were MSM. C group included 105 patients, 85 (81%) male, median age 30 years, 60.8% MSM. Comparing the two groups no significant differences were found in median age, mode of transmission, chemsex habit, CD4 cell-count and viral load before and after a month of cART, CDC stage and late presentation at diagnosis. The time between first positive ELISA test and first visit appears shorter in C group ($p<0.0001$), while the M group starts earlier cART ($p<0.0001$). Single Tablet Regimens were more frequently administrated in M group ($p<0.0001$), in particular containing INI ($p<0.001$). Educational level was higher in M group ($p<0.0001$). After one month of cART, M patients showed more frequently an undetectable viremia ($p=0.019$).
Conclusion: Results obtained show some critical aspects due to different clinical and lab organization. Longer time for linkage to care in Madrid should

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be in-depth analyzed and reduced to guarantee a better health assistance. Madrid patients, maybe due to an efficacious network with lab, were treated more quickly with cART obtaining a better virological response at the first month. At the same time, Catania outpatient unit should reduce laboratory timing to achieve more rapidly cART administration with optimal regimens.

PE6/8

The HIV- and HCV-cascade in Swiss opioid agonist treatment (OAT) patients – the SAMMSU-cohort

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Background: To end the HIV/AIDS-epidemic by 2030, until 2020, 90% of all HIV-infected people should be diagnosed, 90% of those diagnosed should receive antiretroviral treatment (ART) and 90% of those treated should achieve viral suppression (90–90–90 targets of UNAIDS). To reach HCV-elimination by 2030, the WHO considers 80% treatment-uptake to be necessary. However, a 90–90–90 target is also discussed for viral hepatitis.
Objectives: To describe the HIV- and HCV-cascade in Swiss opioid agonist treatment (OAT) patients and compare the HCV-cascades in HIV-negative and HIV-positive people.
Methods: The Swiss Association for the Medical Management in Substance Users (SAMMSU)-Cohort is an open cohort with yearly follow-up enrolling OAT patients in eight different centres throughout Switzerland.
Results: Between 2014 and 05/2019, 906 patients have been enrolled (78% male, median age: 48 years, 81% ever intravenous drug use). For 904 (99.8%), the HIV/HCV-serostatus was known. HIV- and HCV-seroprevalence were 12.8% and 68.5%, respectively. Of the 116 HIV-positive patients, 114 (98.3%) received ART, with 108 (94.7%) of them virologically suppressed (HIV-RNA<50 cop/mL), resulting in an overall HIV-RNA-prevalence of 0.9% (8/906). For 96.1% (595) of the 619 HCV-positive patients, the HCV-RNA-status was known. 397 (79.4%) of the 500 patients with ever chronic hepatitis C ever received treatment (interferon-based or interferon-free). In 327 (82.4%) of them SVR was documented. The overall HCV-RNA-prevalence was 13.8% (125/906). In HIV-positive patients (all but three HCV-coinfected), HCV-RNA-prevalence was higher: 26.7% (31/116) versus 11.9% (94/790) and HCV-treatment-uptake lower: 69.5% (66/95) versus 81.7% (331/405).
Conclusions: In Swiss OAT patients of the SAMMSU-cohort, the 90–90–90 target is met for HIV, but not for HCV. The WHO-goal of 80% HCV-treatment-uptake has been achieved in HCV-mono-infected, but not in HIV-HCV-coinfected patients. Accordingly, one out of four HIV-positive patients is still HCV-RNA-positive (i.e. infectious) compared to only one out of eight HIV-negative patients.

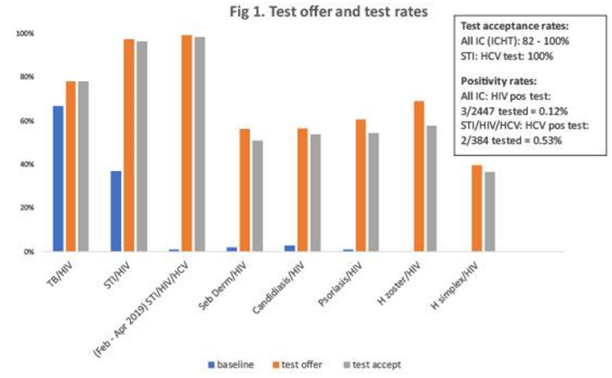
PE6/9

Increased Integrated testing for HIV and HCV in health care facilities: examples from the INTEGRATE activities in Lithuania and Romania

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Purpose: To improve HIV and HCV testing rates in health care settings through implementing Indicator Condition guided HIV testing (ICHT) in a dermato-venereology clinic in Lithuania and tuberculosis clinic in Romania.
Method: A baseline audit was conducted in both clinics on HIV testing performance and questionnaires on staff attitudes towards HIV testing were completed by clinic staff. Data on testing was collected monthly to monitor progress. Training of staff and PDSA (Plan-do-study-act) cycles were frequently performed and a patient information leaflet (PIL) on reasons for HIV testing was introduced to ease consent process in Romania. After 7 months of HIV testing HCV testing was added routinely for all STI patients in Lithuania.
Results: HIV testing rates increased significantly after the introduction of ICHT and test acceptance rates were high (fig 1). Overall HIV testing rate baseline in Lithuania (12 months before) was 10.6%: the highest (37%) for STIs, the lowest (0%) for *Herpes* infection. HIV testing rate during the pilot study (10 months) increased to 67%: the highest (96%) for STIs, the lowest (38%) for *H. simplex*. HIV/HCV combined testing was effectively introduced with test acceptance rates of 100% and overall testing rate of 99%, although baseline HCV testing for STIs was 0.8%. Three new cases of HIV and 2 of HCV positivity were identified. All patients were linked to care. For tuberculosis the introduction of a PIL improved the testing rates from 67.4% before the INTEGRATE project to 87% after the introduction of the PIL.
Conclusion: ICHT and HIV/HCV combined testing are feasible and acceptable methods to increase HIV and HCV testing rates in health care settings and methods to implement ICHT has proven transferable to implement combined HIV/HCV testing. Introduction of a PIL can ease work for consent and increase the number of HIV tests among TB patients.



PE6/10

AIDS and late presentation follows testing gaps in Poland – data from Test and Keep in care (TAK) Polska project

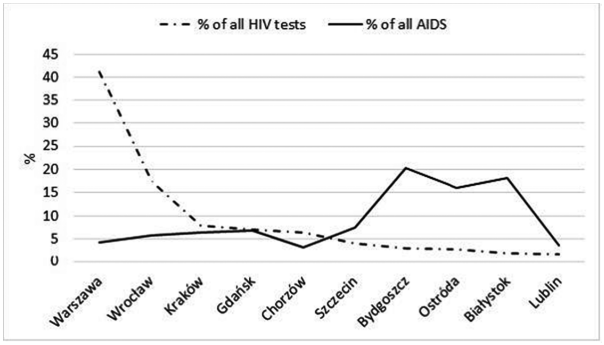
JD Kowalska[1], E Jabłonowska[2], M Bielecki[3], E Firląg-Burkacka[4], B Szetela[5], M Bociąga-Jasik[6], E Mularska[7], G Barałkiewicz[8], M Hlebowicz[9], M Jankowska[9], A Cybula[10], M Suchacz[11], A Olczak[12], A Grzeszczuk[13], D Bielec[14], A Kocbach[15], M Ankiersztejn-Bartczak[16] and M Parczewski[17]

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Background: Data on late presentation (LP) in Poland are not available from surveillance authorities, while to date it is the most effective measure of HIV testing access and linkage to care. To address this gap clinical centres initiated TAK Polska project to assess the prevalence and characteristics of AIDS and LP in the country.
Methods: Clinical and demographic data were collected retrospectively on predefined questionnaires for all patients newly registered in 13 HIV centres in 2016 and 2017. Data were cleaned and queried centrally. LP was defined as AIDS and/or CD4 count<350 cells/mm3 at first visit. Information on number of HIV tests performed in 2016 in voluntary counselling and testing centres (VCTs) in the region represented by each clinical centre were acquired from national VCTs system. In statistical analyses logistic regression models were used to identify factors associated with AIDS and LP.
Results: Data on 1751 patients were received (89.6% men, 64% infected through MSM contacts). The median age was 33.1 (IQR: 27.5–39.8) years, CD4 count 383 (210–552) cells/mm3. Information about AIDS at baseline was available for 1535 (87.7%) of patients: 693 (45.1%) patients were LP and 184 (11.7%) presented with AIDS. The prevalence of AIDS was highest in cities from regions with lowest number of HIV tests in VCTs (Figure).



The relation between HIV test coverage and AIDS at diagnosis in Poland stratified by cities

The most common AIDS conditions: pneumocystis pneumonia (25.2%), candidiasis (22.4%), tuberculosis (14.7%) and wasting syndrome (14.0%). The odds of AIDS/LP were higher for each 10 years older (aOR 1.65[1.41–1.92] / 1.15 [0.7–1.74]), persons infected through heterosexual contacts (2.07 [1.31–3.22] / 2.18 [1.00–4.94]) and injecting drug use (4.11 [1.29–7.88] / 3.13 [1.29–7.88]).
Conclusions: LP/AIDS at first clinical visit is still common in Poland with large variation between the centres. This indicates suboptimal testing for HIV in certain regions of the country and for some groups, especially injecting drug users.

PE6/11

Loss to follow-up and re-linkage to care in a single cohort study: who do we re-link to care?

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Purpose: Describe the HIV-infected patients lost to follow-up (LTFU) at our Centre and identify variables that might predict a subsequent re-linkage to care (RLTC).
Method: We conducted a single center, retrospective study including patients followed at the Infectious Diseases Clinic of San Martino Policlinico Hospital, Genoa. LTFU was defined as missing appointments for both visits and exams for≥12 months. All patients LTFU during the year 2015, who were already in care at the beginning of the previous year, were included. All RLTC up to December 2018 were registered. Data were retrieved through medical records and the electronic MedInfo database. The possible association of different variables with RLTC was assessed through univariable logistic regression model.
Results: Sixty-three patients were enrolled, of whom 32 (50.8%) re-entered care. Median time between LTFU and RLTC was 1 year (range 1–3 years). Median viral load at RLTC was 46.5 copies/mL (IQR 0–1500 copies/mL). Seventeen patients (53.1%) had undetectable viral load (HIV RNA<50 copies/mL) at RLTC. Other characteristics of the two populations are illustrated in table 1. At univariable logistic regression, only age showed a statistically significant association with RLTC (OR 0.9; 95% CI 0.9–1.0; p=0.033). No multivariable analysis was performed due to the small sample size.
Conclusion: To maintain linkage to care is crucial in the cascade of care of HIV-infected patients.
Half of the patients we LTFU in 2015 re-entered care after a median time of 1 year; half of them had an undetectable viral load upon re-linkage, testifying that they carried on antiretroviral treatment despite the apparent LTFU. Younger age was the only factor we found could predict the re-entrance in care.
Limitations to the interpretability of our data stem from the small sample size and the retrospective design of the study, with a consistent amount of missing data.

Table 1. Characteristics of LTFU and RLTC populations with unadjusted odds ratio and corresponding 95% confidence intervals.

	LTFU, n=63 (100%)	RLTC, n=32 (50.8%)	Unadjusted OR (95% CI)	P-value
Sex	Male 41 (65.0) Female 22 (35.0)	Male 18 (56.3) Female 14 (43.7)	0.5 (0.2–1.3) Reference	0.139
Median Age	53 years (IQR 45–60)	49 years (range 43–58)	0.9 (0.9–1.0)	0.033
Origin	European 55 (87.3) Other 8 (12.7)	European 29 (90.6) Other 3 (9.4)	Reference 0.5 (0.1–2.5)	0.426
Type of transmission	Sexual 29 (59.2) Other 20 (40.8) Missing 14	Sexual 15 (55.6) Other 12 (44.4) Missing 5	Reference 1.4 (0.4–4.4)	0.568
CDC stage	A 26 (45.6) B 16 (28.1) C 15 (26.3) Missing 6	A 17 (56.7) B 6 (20.0) C 7 (23.3) Missing 2	Reference 0.3 (0.1–1.2) 0.5 (0.1–1.7)	0.193
Psychoactive treatment	Yes 11 (21.2) No 41 (78.8) Missing 11	Yes 6 (21.4) No 22 (78.6) Missing 4	1.0 (0.3–3.9) Reference	0.958
Heroin replacement therapy	Yes 7 (13.2) No 46 (86.8) Missing 10	Yes 4 (14.3) No 24 (85.7) Missing 4	1.2 (0.2–6.1) Reference	0.806
Median time since HIV+ diagnosis	12 years (IQR 6–22)	12 years (IQR 8–23)	1.0 (1.0–1.1)	0.565
Median nadir of CD4+	158 cell/mL (IQR 61–315)	202 cell/mL (IQR 80–378)	1.0 (1.0–1.0)	0.372

PE6/12

Expanding access to HIV tests in 13 cities in Indonesia: an interrupted time series investigating effect of HIV policy intervention using six years population data

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Purpose: To control the growing HIV epidemic in Indonesia, the Strategic Use of Antiretroviral (SUFA) was launched in 2013. Since an evaluation of SUFA's impact on the rate HIV testing and detection has not been performed, we performed a study to assess the impact on these outcomes.
Method: Monthly data were collected from persons 15 years of age or older from 13 cities. The pre-SUFA data collection period was defined as 26 Dec

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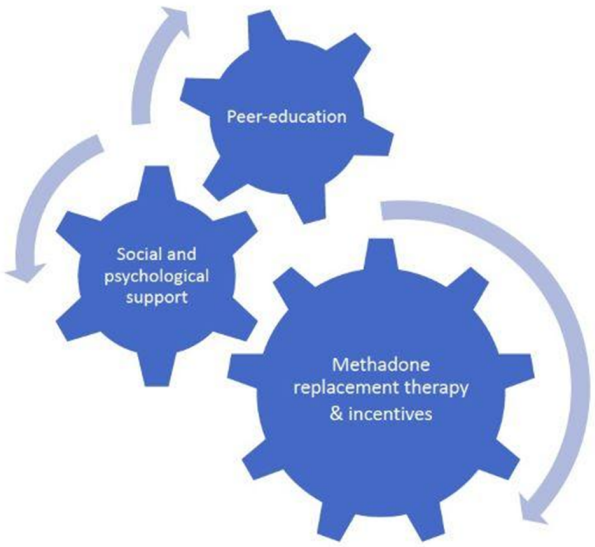
2010–25 Dec 2013 and post-SUFA as 26 Dec 2013–25 Dec 2016. An Interrupted time-series analysis was performed using a multilevel negative binomial regression model to assess the number and rate of HIV tests and detected cases. Rates of HIV cases were assessed with and without adjustment for the number of HIV tests performed.
Results: Pre-SUFA there was a median (IQR) of 44 (22–70) HIV cases detected/month from 448 (200–910) HIV tests performed. Post-SUFA there were 50 (27–79.5) HIV cases detected/month from 1546 (676.5–2394.5) HIV tests performed. Post-SUFA there was an immediate increase in the rate of HIV tests performed (41%; 95% CI 1.25–1.59; p<0.001) and an immediate reduction in the rate of HIV cases detected (23%; 95% CI 0.69–0.86; p<0.001) even after adjusting for the number of tests performed. The time trends for rates of HIV tests performed and detected cases also differed significantly between periods.
Conclusion: SUFA effectively increased the rate of HIV testing which likely contributed to the reduced rate of detected HIV cases. Future evaluation is important to explore strategies to find additional areas of the population containing PLHIV.

PE6/13

Link HIV-infected injection drug users after the imprisonment to continuum of HIV care program in Taiwan

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Purpose: Injection drug users (IDUs) is criminalized in Taiwan. In 2019, 28,680 people were found guilty of drug crime, and there are 1899 people (6.6%) living with HIV (PLHIV) in detention centers. However, the key challenge is 2nd 90% which is the worst among IDU (58% vs. 92% in men who have sex with men) in Taiwan. Once HIV-infected inmates are released from prison, there is a breaking point in the treatment cascade as the patients are less likely to return to HIV designated hospital. The aim of the program is to improve continuum of HIV care among IDUs.
Method: Taoyuan General Hospital staff is taking care of 550 HIV IDU patients in 3 prisons, and the program was implemented from August 2017 till December 2018. We provided comprehensive awareness and educational programme before release from prison aiming at providing (1) Social and psychological support with planning life after imprisonment (stable job search, housing); (2) Peer-education about importance of continued HIV treatment (3) Methadone replacement therapy (4) Removal of possible barriers to return to outpatient clinic (pre-arranged return visit date, reminding card with location, incentive (transportation/meal coupon)). (figure 1)



Link care in HIV-infected injection drug users

Results: From August 2017 till December 2018, forty-three inmates were enrolled (32 males and 11 females), and 36 patients (83.7%) remain on stable linkage to the continuum of HIV care program in Taoyuan General Hospital, and 36 patients (83.7%) are taking anti-retroviral regimens (ARV) with full suppressed HIV viral loads (< 50 copies/mL)by December 2018. Two patients died and 5 patients were lost to follow-up by end of observation period.
Conclusion: After the implementation of linkage to continuum of HIV care among this most challenging population, more HIV-infected IDU patients increased adherence to their treatment and also achieved suppressed HIV viral loads.

PE6/14

HIV continuum of care by sex and mode of transmission in Spain, 2016: use of different sources of information

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Purpose: Our aim was to calculate the HIV Continuum of Care (CoC) by sex and mode of transmission in Spain, 2016.
Method: Stage 1: People living with VIH (PLHIV) and stage 2: PLHIV diagnosed were estimated using mathematical models based on surveillance data (*New HIV diagnoses and AIDS cases Information Systems). Stage 3:* Diagnosed PLHIV on ART and stage 4: PLHIV on ART with viral load suppressed (VLSUP) were calculated using both cohort data - *multicenter cohort of HIV-infected adults of the Spanish HIV/AIDS Research Network (CoRIS)* and cross-sectional data - *one-day cross-sectional hospitals survey.*
The four stages were estimated stratifying by sex and mode of transmission.
Results: The overall HIV prevalence was 0.37%, 0.62% in men and 0.13% in women. Table 1 summarizes the estimates for the four stages of the HIV Continuum of Care by sex and mode of transmission.
The global percentage of PLHIV with viral load suppressed varied from 69.0% using cohort data to 72.8% using cross-sectional data in Spain. These percentages varied from 69.6% to 71.3% for men and from 65.7% to 76.4% for women using cohort or cross-sectional data, respectively. Likewise, these figures ranged between 68.7% and 70.7% for men who had sex with men (MSM); 66.8% and 84.9% for persons who inject drugs (PWID) and between 64.9% and 69.9% for heterosexuals using cohort or cross-sectional data, respectively.
Conclusion: Spain is very close to achieve the global UNAIDS goal (73% of PLVIH virally suppressed). In our complex epidemic, there is a need to assess gaps in the different subpopulations for guiding specific prevention strategies. The use of different data sources lets us a better approach to the current situation of HIV infection in Spain.

Estimates for the four stages of the HIV Continuum of Care by sex and mode of transmission in Spain, 2016

			On ART		VLSUP	
	PLHIV (number)	Diagnosed PLHIV	Cross-sectional data	Cohort data	Cross-sectional data	Cohort data
Global	146,500	86.2%	93.4%	92.5%	90.4%	86.5%
Sex						
Male	119,937	86.2%	92.4%	92.5%	89.6%	87.3%
Female	26,559	86.3%	96.0%	92.2%	92.3%	82.6%
Mode of transmission						
MSM	58,936	83.5%	92.0%	92.9%	92.0%	88.6%
PWID	20,278	97.6%	93.5%	86.4%	93.0%	79.2%
Heterosexuals	30,404	82.9%	94.9%	93.3%	88.8%	83.9%

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PE6/15

Temporal trends in time from HIV diagnosis to viral load suppression in CoRIS

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Purpose: Our aim was to analyze trends in time from HIV diagnosis to Viral Load Suppression (VS) in the Cohort of the AIDS Research Network (CoRIS).
Methods: We analyzed treatment-naïve adults with HIV infection recruited in CoRIS from 2004 to 2017 who achieved VS (two consecutive Viral Load measurements<50 cop/mL) during follow-up. We categorized the year of HIV diagnosis in periods corresponding to ART initiation guidelines recommendations (< 2004;2004–08;2009–12;2013–14;2015–17). We calculated medians and interquartile ranges (IQR) to describe the time intervals from HIV diagnosis to VS and subintervals of interest (table).
Results: From 2004 to 2017, 14,458 persons were enrolled in CoRIS. We excluded 2,438 who never initiated ART and 2,050 who not achieved VS (992 had no or just one Viral Load measurement after ART initiation, 496 were lost to follow-up before achieving VS, 95 died and 467 never achieved VS). The final analysis included 9,970 (69%) persons who achieved VS during follow-up. They were predominantly male (84%), and 61% were from Spain. Median age at HIV diagnosis was 36 (IQR: 30–43). Transmission mechanism was heterosexual in 30% and sex between men in 59%. Median time from HIV diagnosis to VS (and subintervals) decreased over time (table 1). From 2004–08 to 2015–17, time (median days [IQR]) from enrolment in CoRIS to ART initiation decreased from 108(20–741) to 23(6–53), respectively. Likewise, considering the same periods, time from HIV diagnosis to VS decreased from 621(261–1363) to 161(99–249), respectively.
Conclusions: Time from HIV diagnosis to VS in CoRIS declined sharply from 2004 to 2017; mainly due to a decrease in time from enrollment in CoRIS to ART initiation. Efforts to speed up the linkage to care an rapid initiation of ART after HIV diagnosis should be made to furtherly decrease the time from HIV diagnosis to VS.

Table 1. Median (IQR) time (days) from HIV diagnosis to VS and subintervals of interest

	<2004	2004–08	2009–12	2013–14	2015–17
HIV diagnosis to Enrolment	3318 (1271–5439)	36 (12–100)	29 (10–73)	22 (7–48)	21 (8–40)
Enrolment to ART initiation	62 (14–580)	108 (20–741)	91 (17–476)	38 (12–144)	23 (6–53)
ART initiation to VS	143 (85–272)	149 (88–250)	147 (89–238)	127 (71–209)	81 (38–152)
HIV diagnosis to VS	3871 (2200–6160)	621 (261–1363)	456 (231–954)	272 (170–495)	161 (99–249)
HIV Seroconversion to VS	3996 (2601–5937)	966 (424–1662)	702 (409–1137)	476 (267–715)	301 (177–483)

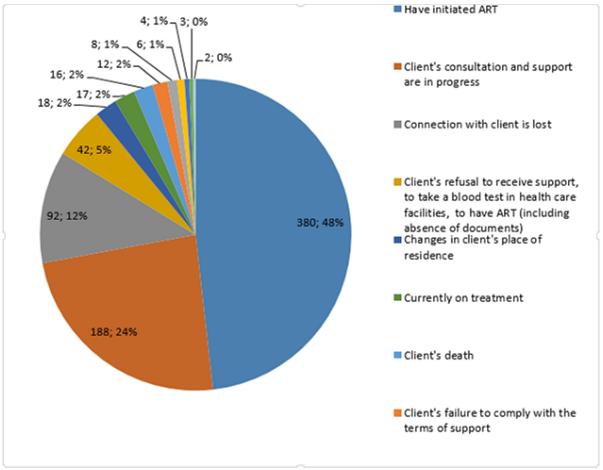
PE6/16

Navigation of HIV positive clients. Reasons of gaps in HIV cascade among PWID

O Pashchuk[1]

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Purpose: To reach an ambitious treatment target 90–90–90 to help end the AIDS epidemic.
Method: Directly assisted self-testing is a combination of self-testing and testing performed by outreach worker. The last one describes in detail the testing procedure, monitor compliance with the key requirements for the test (temperature regime, correct volume of blood and buffer, time to wait for the test result etc.) and helps the clients to conduct tests correctly. In the end of procedure, the social worker fixates the test result in the form of testing records, thus the Alliance gather the information about the number of testing and detection rate. In case of the positive result, social worker accompanies such clients to the health care facilities to get the confirmation test, link them to care and start the ART. For this purpose in 2018 Alliance started the component of Navigation of HIV positive clients. Main features of Navigation: Easy cases - client is encouraged to start treatment; Duration - up to 3 weeks for the first stage of cascade; One-time rewards for social workers for linkage to care and start of ART
Results: Among all PWID involved in Navigation in 2018: 48% have initiated ART, 24% were in progress, 12% connection with client was lost, 5% refused to receive support, 11% - other reasons of lost to follow up. The results are to be compared with the 1 half of 2019.
Conclusion: Due to Navigation 72% of PWID initiated ART, in 19% of cases we still can affect, in 8% of cases we can't affect.



[Reasons of gaps in cascade]

PE6/17

Tracing the patterns of HIV-1 transmission among individuals with different time to diagnosis in Greece

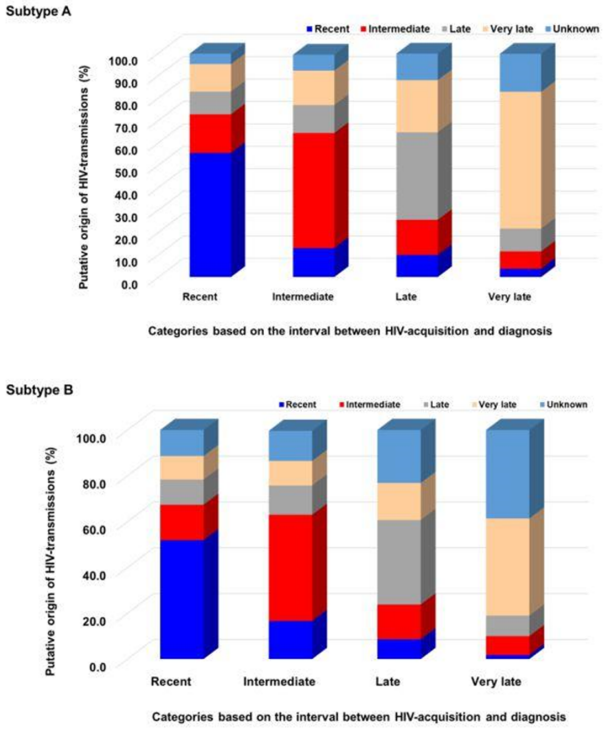
E-G Kostaki[1], S Limnaios[1], G Adamis[2], G Xylomenos[2], M Chini[3], N Mangafas[3], M Lazanas[3], S Patrinos[4], GS Metallidis[5], O Tsachouridou[5], V Papastamopoulos[6], D Chatzidimitriou[7], E Kakalou[6], D Kavatha[8], A Papadopoulos[8], K Protopapas[8], M Psichogiou[9], D Basoulis[9], D Pilalas[10], D Paraskeva[11], G Chrysos[11], V Paparizos[12], S Kourkounti[12], H Sambatakou[13], NV Sipsas[14], M Lada[15], E Barbounakis[16], E Kantzilaki[16], P Panagopoulos[17], E Maltezos[17], S Drimis[11], G Magiorkinis[1], L Skoura[7], V Sypsa[1], A Hatzakis[1] and D Paraskevis[1]

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Purpose: To investigate the contribution of late and recent diagnosis to subsequent HIV transmission in Greece.
Method: Our analysis included 3,127 sequences of subtypes A1 and B, collected from people living with HIV (PLHIV) between 1999 and 2015 in Greece. HIV acquisition dates were estimated by molecular clock analysis. Individuals were categorized into four quartiles according to the time interval between HIV acquisition and diagnosis (median, IQR, in years): recent (0.49, 0.32–0.72), intermediate (1.40, 1.16–1.65), late (2.64, 2.25–3.16) and very late (5.97, 4.68–7.98); the four categories in this analysis were not based on CD4 count at diagnosis. The HIV dispersal patterns between PLHIV with different diagnosis status were estimated by a modified statistical phylogeography method.
Results: For the recently diagnosed group, 55.4% and 51.9% of subtypes A1 and B transmissions, respectively, originated from individuals of the same group. Late diagnosed individuals were infected at 39.1% and 36.9% within each group and at 23.3% and 16% from those with very late status, for subtypes A1 and B, respectively. For both subtypes, PLHIV were a significant source of transmission mostly to the neighboring groups (i.e. intermediate to recent, recent and late to intermediate). The recently diagnosed PLHIV were a major source of HIV transmissions only to the intermediate category. The largest number of transmissions were found to originate from the very late presenters.



HIV-1 dispersal patterns among different groups divided according to the time interval

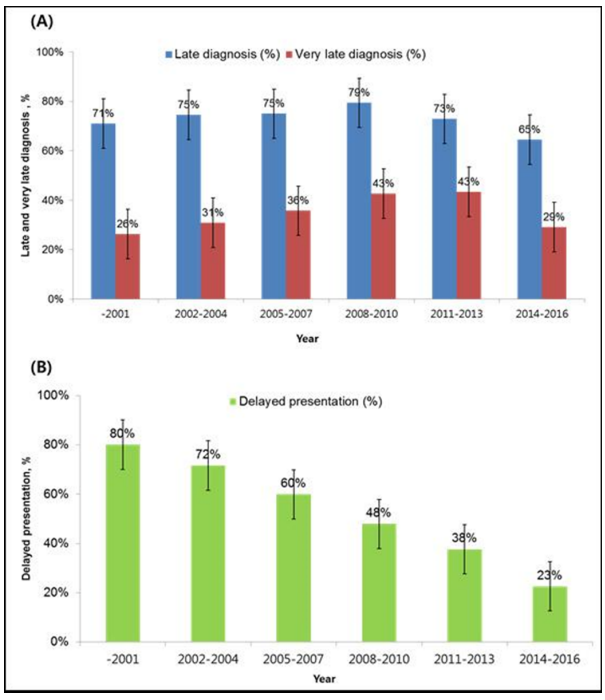
Conclusions: We provide evidence that a large proportion of infections took place among PLHIV with a recent diagnosis, suggesting that for this group most transmissions occur close to their HIV acquisition dates. Very late diagnosed individuals are sources of HIV transmissions across different categories. Given the contribution of all groups to subsequent transmission, additional effort is needed to improve diagnosis rates across different categories and to initiate treatment rapidly.

PE6/18

Late diagnosis and delayed presentation in Korean HIV/AIDS cohort

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Purpose: Late diagnosis and delayed presentation are problems in the control of HIV epidemics. We aimed to quantify the degree of late diagnosis and delayed presentation in Korean HIV/AIDS Cohort.
Method: The Korea HIV/AIDS cohort is a multi-center, prospective study consisting of 15 university hospitals nationwide with ongoing enrollment of HIV-infected adult patients older than 18 years. We analyzed 1,369 HIV individuals enrolled in Korea HIV/AIDS cohort between December 2006 and December 2016. Late diagnosis (CD4 count<350 cells/mm^3 or AIDS-defining condition (ADC) within 3 months of diagnosis), very late diagnosis (CD4 count<250 cells/mm^3 or ADC within 3 months of diagnosis), delayed presentation (≥3 months from diagnosis to treatment) and late treatment (CD4 count<350 cells/mm^3 or ADC within 3 months of treatment) were measured.
Results: Mean age of patients was 38.3 (SD 12.4). Male was 79.8%. Mean CD4 + count at diagnosis and at anti-retroviral therapy (ART) were 272.0 (SD 205.9) and 193.2 (SD 159.3), respectively. Proportion of late and very late diagnosis were peak in 2008–2010 (79% and 43%, respectively) (Figure). And, decreasing linear trend of late diagnosis was observed after 2010 (Figure). Trend of late treatment is very similar to late diagnosis. Decreasing linear trend of delayed presentation from 2001 to 2016 (80% to 23%) was observed (Figure).
Conclusion: Late and very late diagnosis is very common in Korea. Recent improvement of late diagnosis and continuous improvement of rapid linkage to ART is present. Still we have to give an effort to increasing early HIV diagnosis and rapid linkage to ART.



Trend of late diagnosis, very late diagnosis and delayed presentation in Korean HIV/AIDS Cohort

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PE6/19

Interruption of HIV care: understanding the predictors and outcomes in the Belgian national HIV cohort

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Purpose: We aimed to study HIV care interruption (HCI) in Belgium and its predictors and outcomes.
Method: We analyzed data of adult patients with at least 2 HIV care records in the Belgian HIV cohort between 01/01/2007 and 31/12/2016. HCI was defined as one year without HIV care record. HCI rate was analyzed using Poisson regression, return to HIV care with a cumulative incidence function with death as competing risk, and factors associated with gap in care during HCI by cause-specific hazard models.
Results: We included 16066 patients accounting for 78625 person-years of follow-up. Rate of HCI was 5.3/100 person-years (95% CI: 5.1–5.4/100). The incidence of return to HIV care after HCI was estimated at 77.5 % (95% CI: 75.7–79.2%) (Figure 1). Of those returned, 43.7% had a VL<200 copies/mL suggesting care abroad or suboptimal care in Belgium without HIV follow-up record during HCI. The 56.3% returned without controlled VL were considered as having experienced a gap in HIV care.
After adjustment, HCI was strongly associated with never on ART and moderately with lower age, IDU, non-Belgian nationalities and shorter time since HIV diagnosis. Lower rate of HCI was moderately associated with female gender, being a man having sex with men, high blood pressure, low nadir CD4. Return after a gap in HIV care was associated with younger age, female gender, Belgian nationality and longer time since HIV diagnosis (Tables).
Conclusion: Maintenance in care for HIV as a chronic condition will increasingly be necessary in the context of a growing HIV population. This study highlights the need to examine return to care and viral status at return, to better understand HCI. The rate of real gap during HCI was estimated at 2.3/100 person-years. Identified predictors could help healthcare workers to target patients at higher risk of HCI for awareness and support.

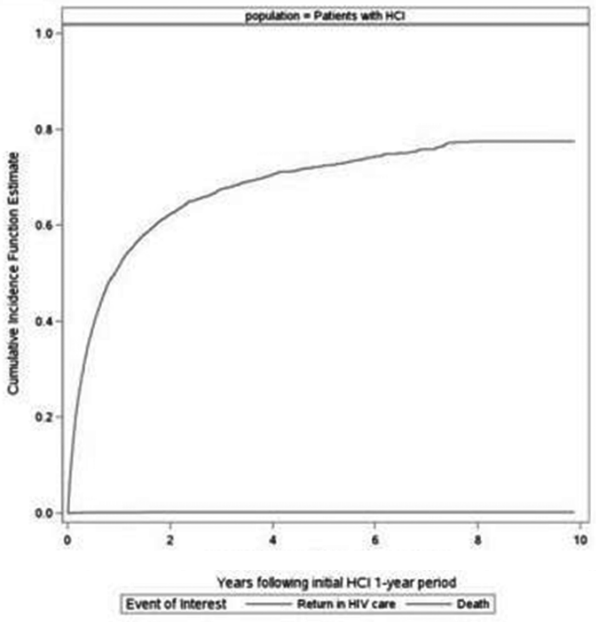


Figure 1. Cumulative incidence for return to HIV care and death after the initial one-year HCI

Rate ratios for HCI and for return after a gap in HIV care by demographic characteristic, adjusted for variables significant at univariate analysis

Characteristic	Value	Adjusted RR for HCI	Adjusted HR for return after gap among patients with a HCI
Gender (ref: Men)	Women	**0.8 (0.7–0.8)**	**1.2 (1.1–1.4)**
Age (ref: ≥ 50 years)	18–24 years	**1.9 (1.6–2.2)**	**2.3 (1.8–2.9)**
	25–39 years	**1.5 (1.4–1.7)**	**1.9 (1.6–2.2)**
	40–49 years	**1.2 (1.1–1.3)**	**1.5 (1.2–1.8)**
Mode of HIV acquisition (ref: Heterosexual)	MSM	**0.7 (0.6–0.8)**	1.0 (0.8–1.1)
	IDU	**1.6 (1.3–1.9)**	1.1 (0.8–1.5)
	MTCT	0.9 (0.7–1.3)	1.2 (0.7–1.8)
Nationality (ref: Belgian)	Sub-Saharan Africa	**1.5 (1.4–1.6)**	**0.7 (0.6–0.8)**
	Europe	**1.7 (1.6–1.9)**	**0.4 (0.4–0.5)**

Rate ratios for HCI and for return after a gap in HIV care by clinical characteristic, adjusted for variables significant at univariate analysis

Characteristic	Value	Adjusted RR for HCI	Adjusted HR for return after gap among patients with a HCI
ART (ref: Ever)	Never	**6.6 (6.0–7.2)**	1.1 (0.9–1.2)
Time since HIV diagnosis (ref: >10 years)	< 1 year	**1.9 (1.7–2.1)**	**0.7 (0.6–0.9)**
	1 to 3 years	**1.2 (1.1–1.4)**	0.9 (0.8–1.1)
	>3 to 10 years	**1.1 (1.0–1.2)**	1.0 (0.8–1.1)
Nadir CD4 (ref: >=350)	<350	**0.8 (0.8–0.9)**	0.9 (0.8–1.0)
Systolic BP (ref: Normal)	High	**0.8 (0.8–0.9)**	1.0 (0.8–1.1)
Obesity (ref: BMI<30)	Obese (BMI>=30)	1.1 (1–1.2)	1.1 (0.9–1.3)

PE6/20

The HIV continuum of care: current situation and advances. A systematic review

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Purpose: The continuum of care (CoC) model has been used to illustrate the progress of HIV care with a view to end the epidemic. However, modelling studies predict that reaching the 4-stage cross-sectional UNAIDS targets does not guarantee HIV elimination. This study aims to review the used CoC methods and illuminate gaps in the CoC analyses not captured so far, especially in terms of time analysis which stand as critical factors for an effective response to the epidemic.
Method: A PubMed and EMBASE databases search resulted in 1,667 papers, of which 382 were considered relevant. Abstract reading led to the rejecting of 200, mainly because CoC definitions were not provided.
Results: Included studies (182) reported results on 1–6 CoC stages, i.e. people living with HIV, diagnosed, linked, retained, treated and virally suppressed. Sixty-five studies estimated the undiagnosed fraction, either nationwide (35) or in subgroups/cohorts (30). Only 52 provided the number of diagnosed individuals from surveillance/national data, whereas 34 and 63 used data from cohorts or HIV (+) surveys, respectively. In 91 studies, linkage was determined by a medical test/consultation, while in 28 studies it was based on self-report. In 48 studies retention was determined from medical records, in 8 was self-reported, and in 2 was based on other information. In half of the studies, viral suppression was defined as a viral load<200 copies/mL. Thirty-three studies provided time-based information on the CoC (e.g. time spent at specific stages) or attrition rates (Table 1).
Conclusion: This study summarizes methods applied in HIV CoC studies worldwide. Our results indicate that only a few studies provide additional

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information beyond the standard, cross-sectional CoC. To accurately evaluate progress towards HIV elimination, an updated CoC model that will include longitudinal components is warranted in order to highlight gaps in the time-response to the HIV epidemic.

Table 1. Details of the 33 studies which included additional time-based information or attrition rates*.

Type of information	N (%)
Time between diagnosis, linkage, ART or suppression	15 (45.5)
Time between infection and diagnosis**	1 (3.0)
Time between infection and VL suppression**	1 (3.0)
Observed*** time from diagnosis to linkage	2 (6.1)
Cumulative time spent in each stage	4 (12.1)
Mortality/LTFU rates	4 (12.1)
% loss from previous stage	1 (3.0)
Other	5 (15.2)

* Four studies also use graphs to visualize the additional information ** Infection date has been estimated in these studies ***These studies did not use time-to-event analysis techniques

PE6/21

The contribution of a partnership with a civil society organization (SCO) to early HIV diagnosis and UNAIDS goals

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Purpose: Portugal has just reached the 90–90–90 UNAIDS goals but still shows a high proportion of late diagnosis, higher than similar EU countries. The MSM had the fastest growing relative to the new HIV diagnoses in the last years. So, it's important to evaluate the contribution of particular approaches of early diagnosis and linkage to care in this population, namely those established in partnership with SCO, looking at their benefits and potential for replication in other settings. The aim of this study is to compare the MSM new diagnosed cases admitted through a SCO referral with the total of new diagnosed cases in MSM and with all new diagnosed cases in Portugal, according to demographics and stage of infection and evaluate the potential benefits of this referral system.
Method: We study the MSM population admitted to our center by Checkpoint LX referral (MSM LX) with a new HIV diagnosis between 2014–2018 (n=192). We analyze some demographics and stage of HIV infection (CD4 cell count, late diagnosis/advanced disease) comparing these results with those obtained in a) the new HIV MSM diagnosed cases (MSM PT) and b) all new diagnosed cases (ALL PT). The statistical analysis was done using $\chi 2$ and t-test.

Results:

	MSM LX (2014–18) n=192	MSM PT (2014–17) n=1469	p	ALL PT (2014–17) n=4097	p
Age (mean)	30	33	<0.0001	40	<0.0001
Migrant (n/%)	74 (38.5)	416 (28.3)	<0.0001	1484 (36.2)	0.029
CD4/mm3 (mean)	486	447	0.036	386	<0.0001
CD4<350/mm3 (n/%)	60 (31.2)	559 (38.0)	**0.035**	2043 (49.8)	**<0.0001**
CD4<200/mm3 (n/%)	18 (9.3)	297 (20.2)	**0.0002**	1254 (30.6)	**<0.0001**

Results: demographics and stage of infection

Conclusion: 1) The HIV (+) MSM admitted through CheckpointLX referral were significantly younger, had a higher proportion of migrants and significantly less late diagnosis and advanced disease; 2) These data reinforce that, at least in the MSM population, this methodology is a useful tool, should be applied in other regions and by other SCO in Portugal and can be useful in other key populations. 3) This methodology not only contributed to reach the 2020 but also can help to reach 2030 UNAIDS goals.

PE6/22

HIV cascade of care in Turkey: data from the HIV-TR cohort

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Purpose: To predict the estimated number of people living with HIV (PLHIV) and to develop the cascade of care for HIV in Turkey between 2011 and 2016.
Method: The number of PLHIV and the number of undiagnosed infections were calculated by the Incidence Method of the European Center for Disease Control (ECDC). The HIV-TR cohort is the largest cohort in Turkey including centers from all regions. Data obtained between 2011 and 2016 and data reported by the Turkish Ministry of Health (MoH) for the same time period were used for the calculations and the results were compared for agreement. Data obtained from the HIV-TR cohort between 2010 and 2016 were used for the development of the cascade of care. Virologic suppression was defined as HIV RNA<50 copies/mL at 48 weeks of antiretroviral therapy (ART).

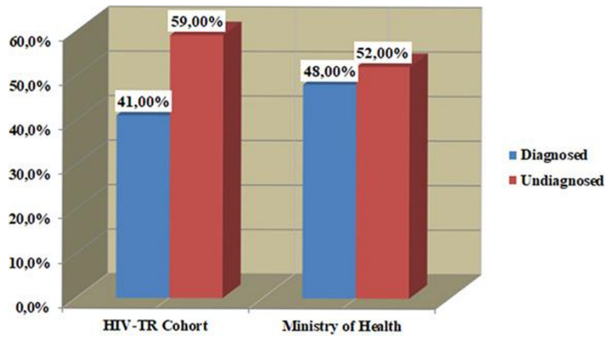


Figure 1. The percentages of diagnosed and undiagnosed patients for two datasets

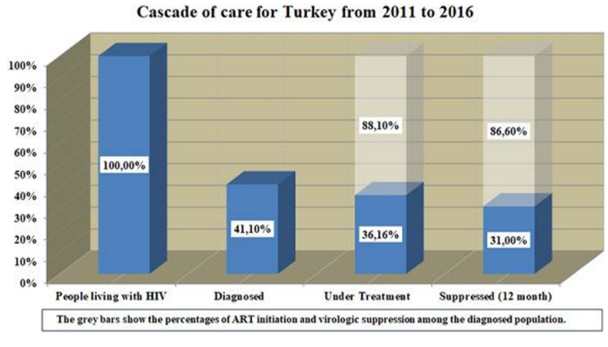


Figure 2. The cascade of care for Turkey from 2011 to 2016

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Results: The HIV-TR cohort includes 3242 registered cases between 2011 and 2016, and the total number of reported cases for the same time range in the MoH dataset is 10227. The predicted numbers of diagnosed and undiagnosed for both datasets are shown in Figure 1. The predicted rate of undiagnosed infection was 59% and 52% according to the HIV-TR cohort and the MoH data, respectively. The annual and overall cascade of care for the HIV-TR cohort is shown in Figure 2. ART initiation and virologic suppression increased during this period, exceeding the 90–90–90 goals in 2015 and 2016. HIV-TR cohort data and the MoH data seemed to be concordant in all calculations.
Conclusion: The largest gap in the HIV cascade of care for Turkey is in the diagnosis step of the cascade. Once diagnosed, ART initiation and virologic suppression are high and above the targeted rates.

PE6/23

Cascade analysis of anonymous voluntary HIV counseling and testing among HIV-infected patients in Taiwan

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Purpose: To evaluate the implication and performance of anonymous voluntary HIV counseling and testing (VCT) cascade among HIV(+) Taiwanese.
Method: We conducted a questionnaire among 430 participants diagnosed from 2015 to 2018 at three HIV/AIDS referrals in Taiwan. We designed a continuum of 5 stages targeting at regular access to VCT, called anonymous VCT cascade, from at high risk population (stage 1), through hearing of (stage 2), be willing to (stage 3), ever access to VCT (stage 4), and finally to regular access to VCT (stage 5). Each participants was further grouped: never receive VCT, unable to receive VCT regularly, and regularly receive VCT. 4 domains of reasons using the 5-point scale: perceived risk for HIV, fear of testing positive due to discrimination and stigma, and structural barriers to VCT, were used to measure the causes of unwilling to receive VCT, unable to receive VCT, and unable to receive VCT regularly. Finally, each participant was grouped based on the status of HIV stage on diagnosis: non-late presentation (LP) and LP.
Results: In multivariable analysis, regularly receive VCT (vs. never receive VCT) remains a protective factor of LP on diagnosis ($p<0.05$). The overall frequency of participants in each stage of cascade was 100%, 90%, 73.9%, 57.1%, and 28.7%, respectively, with the greatest loss from stage 4 to stage 5 (unable to receive VCT regularly, 49.7%). The performance of each stage in cascade remains unchanged (*P* for trend>0.05) across the study. Fear of testing positive due to discrimination and stigma were the two main reasons of participants unable to receive VCT regularly.
Conclusion: Although the study prove the role of regular VCT on the early diagnosis of HIV, further strategies to lessen the fear of negative relationship and social consequences of HIV is needed to update the VCT in Taiwan.

PE6/24

Late presentation of HIV in Armenia

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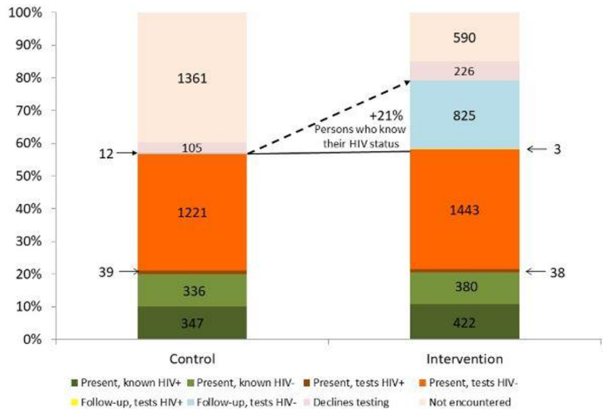
Purpose: Early diagnosis of HIV infection has become critical for medical and public health purposes. The aim of this study was to investigate the issue of late presentation in Armenia.
Method: Study includes adult Armenian citizens (aged≥15 years) newly diagnosed with HIV from 2013–2017 case surveillance national database. Late presenter (LP) is defined as a person diagnosed with HIV with a CD4 cell count<350 cells/mm3 or an AIDS defining illness regardless of the CD4 cell count in the six months after HIV diagnosis. All analyses were performed using IBM SPSS software.
Results: Of the 1502 newly diagnosed HIV-infected individuals, 1352 (90%) had either a CD4 cell count or an AIDS defining illness diagnosis available. A total of 796 (58.9% CI: 56.1–61.5) of the 1392 studied cases over these 5 years were LPs. In latter 5 years the level has remained the same but the highest proportion of LP was in 2015- 62.7% (CI: 57.1–68.7). Males had an increased risk of late presentation compared with females, with odds ratio (OR) of 1.85 (95% CI, 1.46–2.3).
Those, who probably contracted HIV abroad, mainly outbound labour migrants, had an increased risk of late presentation compared with those, who were probably infected in Armenia, with an OR of 1.82 (95% CI, 1.45–2.2): outbound migrants make up 62.1% of LPs (95% CI: 58.5–65.1). LPs were more likely to die - OR: 13.34 (95% CI: 7.7–23.2). Depending on mode of transmission the highest proportion of LP was among PWID - 73.9% (CI: 66.4–80.6) and the lowest was among MSM - 35.6% (CI: 23.2–48.1).
Conclusion: LP is a challenge for Armenia. The study findings show that in latter 5 years it maintains a high level.
Scaling-up HIV testing services coverage at community level, targeted to outbound labour migrants could mitigate this problem.

PE6/25

Oral self-testing for individuals absent or refusing testing during home-based HIV testing – a cluster-randomized trial in Lesotho (HOSENG trial)

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Purpose: In sub-Saharan Africa, home-based HIV testing is validated and accepted, but coverage remains low due to absent household members (HM). This cluster-randomized trial measured the effect of secondary distribution of oral HIV self-tests (HIVST) on coverage during home-based testing.
Method: Clusters were defined as villages in catchment area of 20 health facilities in Lesotho. In intervention clusters, HIVST were left for HM who were absent or declined testing. The primary outcome was HIV testing coverage among HM (age ³12) within 120 days after home-based testing, defined as a confirmed HIV test result, known HIV+, or recent HIV- result. Secondary outcomes included effect modification by sex and age (≤24, >24). Analyses were by intention-to-treat. Intervention effects were estimated with random effects logistic regression models. Trial registration: NCT03598686.
Results: 3106 consenting households with 7,846 HM aged≥12 were enrolled (intervention: 57 clusters, 1628 households, 4192 HM; control: 49, 1478, 3654). 2413 (58%) intervention and 2070 (57%) control HM were present. Of those with unconfirmed status, 1278/1382 (92%) intervention HM and 1118/1224 (91%) control accepted testing.
In intervention arm, 1889 HM were absent/refused testing, 1447 (77%) were left HIVST of which 826 (57%) were returned. In control arm, 1695 HM were absent/refused testing of which 12 (0.7%) tested at the facility.
HIV testing coverage was 3372/4188 (81%) in the intervention versus 2187/3654 (60%) in control arm (odds ratio 2.9 [95% confidence interval 2.5–3.5];



Testing coverage by Intervention arm

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p<0.001). The intervention effect was greater in males (74% vs 44%; 4.2 [3.3–5.2]) than females (86% vs 73%; 2.4 [1.9–3.0], p interaction<0.001) and in adolescents (75% vs 38%; 5.6 [4.4–7.1]) than adults (84% vs 71%; 2.2 [1.8–2.7], p interaction<0.001).
Conclusion: In the HOSENG trial, secondary distribution of HIVST achieved an increased HIV testing coverage of>20%. The intervention was particularly successful among males and adolescents.

PE6/26

Acceptability of rapid tests for migrants during the medical consultation at the migration point

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Purpose: High prevalence of HIV and hepatitis B and C among migrants from certain countries justifies existing targeted screening recommendations from health authorities. Therefore, the STRADA study implemented the use of rapid tests, offered to migrants during the medical consultation at the OFII. A study of acceptability aimed at measuring the obstacles impeding screening so as to identify levers on which to act for a better acceptance rate.
Method: The acceptability study is performed in the 20 centers of the OFII in France. A 3-minutes online form is filled by the health practitioners at the end of every service period.
The reasons for not offering or refusing the screening tests are analyzed and sorted into different categories, and the acceptability rate is calculated by comparing the number of patients who accepted screening to the number of screening propositions.
Results: The results over two months show the proposition and acceptability rates are respectively 83.3% and 48.7% of the patients who attended the consultation.
Impeded communication is reported in 59.2% of the cases, of which 93.6% are related to language barriers. Organizational issues and lack of time are mentioned in 26.6% of the cases.
Among the reasons for refusing screening, a previous screening is cited in 41.7% of the cases. 16% of the patients do not want screening, or do not see any relevance, and 12.7% feel either not at risk or not concerned.
Conclusion: To resorb language and organization-related barriers, several solutions have been proposed: telephone interpreting services, adapting the conducting of medical consultations, calling less patients and hiring medical personnel specifically to offer screening.

PE6/27

Evaluation of the "test and treat" strategy in an high-income setting: data from a multicenter Italian cohort

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Purpose: We aim to evaluate Test and treat (T&T) strategies in a multicenter cohort of HIV-1 positive patients in Italy.
Method: We recognized 3 groups among patients diagnosed in 2018: the "one-day treatment" (1DT) group, in which patients started ARV on the same day of the first blood sample; the "fast treatment" (FT) group, including patients that started ARV within 7 days, and "standard of care" (SOC) group in which therapy was started after 7 days. We followed the patients evaluating retention in care and virological outcome.
Results: We enrolled 196 patients from 9 Italian clinical centers: 120 patients started a triple therapy with tenofovir/emtricitabine plus an integrase inhibitor (83 with dolutegravir, 21 with elvitegravir and 16 with raltegravir), 32 with abacavir/lamivudine/dolutegravir, 17 with tenofovir/emtricitabine plus boosted darunavir, 11 with tenofovir/emtricitabine plus rilpivirine. Other patients' characteristics at baseline are in Table 1. Median times from HIV diagnosis to the first visit and ARV initiation were 6 days (IQR 1–12) and 14 (IQR 8–29), respectively. Median time between the first visit and ARV initiation was 7 days (IQR 1–15). At ARV initiation, genotypic resistance test was available in 36.6% of patients. Regarding the above described classification, 44 (22.4%) pts belonged in the 1DT group, 53 (27.0%) in the FT group and 99 (50.5%) in the SOC group. At 12 months the overall rate of retention in care was 81.1%, with no significant differences between groups (p=0.103). We found a significantly lower rate of virological suppression in FT group compared with the other groups, both at 6 (p=0.033) and 12 months (p=0.017). Finally, we observed a higher rate of discontinuation of the first-line ARV in 1DT group (log-Rank p=0.023).

Table 1. Patients' characteristics at baseline (N 196)

Variables	
Age (years), Median (IQR)	39.3 (32.2–49.1)
Female, n (%)	32 (16.5)
Risk factor for HIV infection, n (%):	
Heterosexual	71 (36.2)
MSM	79 (40.3)
Others/Unknown	46 (23.5)
Anti-HCV antibodies positive, n (%)	12 (6.3)
AIDS event at HIV infection diagnosis, n (%)	38 (19.4)
CD4 + cell count (cell/μL), Median (IQR)	270 (108–496)
Zenith HIV-RNA>500.000 copies/mL, n (%)	48 (24.7)

Conclusion: In our cohort, we did not observe an advantage in using a one-day treatment approach compared to other strategies of ARV initiation.

PE6/28

Pill box return as a predictor of adherence to antiretroviral therapy in PLHIV: a prospective cohort study

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Purpose: Adherence to antiretroviral therapy (ART) remains a challenge in developed and developing countries. Perceived and experienced stigma are associated with concealment of medication and disposal of the pillbox to avoid disclosure of status. We aimed to determine the association between pillbox return and treatment outcome among HIV-infected adults.
Method: We included consenting HIV-infected adults ³18 years enrolled in the Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) between 01/2013 to 11/2018 with ³ 3 months on ART and ³6 months of follow-up. Failed pillbox return was defined as failure to bring the pillbox in<95% of visits. Lost to Follow-up (LTFU) was defined as not seen in the clinic ³60 days from the last scheduled visit. Virological failure was defined as a viral load ³1000 c/mL 6 months after starting ART and immunological failure as 50% drop in CD4 count from peak value or return to Pre-ART baseline CD4 count. Logistic regression was used to assess the association of failed pillbox return with LTFU, immunological and virologic failure.
Results: Of 4,507 patients enrolled in KIULARCO, 2,414 adults were included (Figure 1). Median age at enrolment was 38.4 years (IQR 31.7–46.0), 1,643 (68.1%) were female and median CD4 cell count was 249/mm^3 (IQR 115 - 438) (Table 1). During a median follow-up of 28.2 months (IQR 13.3–47.2) and

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28,950 visits with pillbox return assessed, 78% (1883/2414) had a failed pill box return. In the multivariate regression, failed pill box return was associated with LTFU (OR=1.42 [95% CI 1.10, 1.84] and immunological failure (OR=1.78 [95% CI 1.37–2.31]). Association with virologic failure (OR=1.02 [95% CI 0.68, 1.54]) was insignificant (Table 2).

Conclusion: Failed pillbox return was associated with LTFU and immunological failure. Pillbox return might be used as a predictor of treatment outcome. Specific adherence interventions could be designed based on this prediction.

Figure 1: Study participant's flowchart

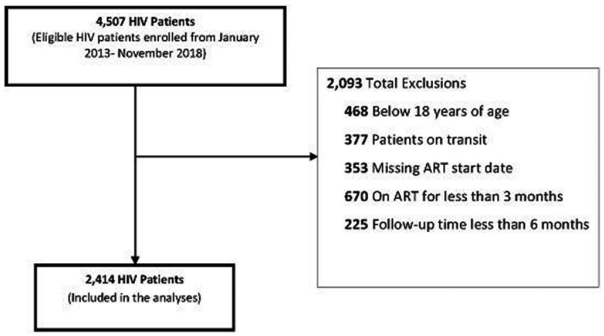


Table 1. Baseline characteristics of study participants

Age (years), median (IQR)	38.4 (31.7–46.0)
Gender, Female (%)	1643 (68.1%)
Marital Status, Married (%)	1472 (61.0%)
Disclosed HIV Status, Yes (%)	1846 (79.0%)
Baseline CD4 count (cells/μl), median (IQR)	249 (115–438)

Table 2. Association between Failed Pill Box return and lost to follow up, Virological and Immunological failure

Characteristics	Univariate OR (95% CI), P-value	Multivariate OR (95% CI), P-value
Lost to follow-up		
No	Reference	Reference
Yes	1.44 (1.12 - 1.84), 0.004	1.42 (1.10 - 1.84), 0.007
Virological failure		
No	Reference	Reference
Yes	1.10 (0.74 - 1.63), 0.63	1.02 (0.68 - 1.54), 0.92
Immunological failure		
No	Reference	Reference
Yes	1.71 (1.31 - 1.21), <0.001	1.78 (1.37 - 1.31), <0.001

PE6/29

Potentially missed opportunity to diagnose HIV with standard testing algorithm among adult patients with ongoing mononucleosis-like illness

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Purpose: To evaluate the dynamic of HIV prevalence and the potency of standard testing approach among adult patients hospitalized in Infectious Diseases Hospital (IDH) with ongoing mononucleosis-like illness (MLI). MLI is well known indicator condition for HIV testing. Republic of Belarus is an upper middle income Eastern European country with concentrated slow-steady growing HIV epidemic. Minsk is the capital city with country-unique IDH for adults. Until now the governmental health-care settings use the third-generation immunoassay (HIV-Ab ELISA or rapid test) as the first HIV test for everyone except for pregnant women and blood or organ donors.

Method: The HIV prevalence among consecutive adult patients with MLI in 2010 and 2013–2017 was compared and tested with 95% CI, using the exact binomial method. HIV positivity meant HIV-Ab and/or PCR RNA HIV positive results. PCR RNA HIV was used in HIV-Ab negative patients according to clinical suspicion about acute HIV-infection and was not considered to be standard approach.

Results: Testing rate with HIV-Ab test was as high as 95.6% (IQR 94.95–96.51%) during all periods. In 2010 nobody was diagnosed as HIV+, but since 2013 HIV prevalence was ranged from 1.0 to 8.61%. 46 patients were tested as HIV+ with prevalence 6.82% for five years [95% CI 5.04–8.99 p=0.03] (Table). Among them 9 were HIV negative with 3rd generation HIV-Ab test and were diagnosed using HIV RNA (19.57% [95% CI 9.36–33.92 p<0.0001]). Of those testing HIV positive 76 % were male, 4% identified themselves as homo- or bi-sexual and 51% were injecting drug users.

Conclusion: HIV prevalence is high among hospitalized adult patients with MLI. Almost each fifth positive testing result might be missed according to approved national testing algorithm unless it was physicians' competence. The 4th generation immunoassays should be implemented at least for testing patients with MLI.

HIV testing results 2010, 2013–2017 in Minsk IDH

year	N admitted	N tested	Test rate (%)	N test HIV positive	Prevalence (95% CI)	N missed by 3rd gen test
2010	119	115	96.6	0	0.0 (0–3.05)	0
2013	100	95	95.0	1	1.0 (0.03–5.45)	0
2014	151	151	100.0	13	8.6 (4.66–14.27)* *p<0.05	1
2015	136	129	94.9	9	6.6 (3.07–12.19)	1
2016	158	150	94.9	12	7.6 (3.98–12.88)	3
2017	129	124	96.1	11	8.5 (4.34–14.75)	4
Total 2013–2017	674	649		46	6.8 (5.04–8.99)* *p<0.05	9

PE6/30

HIV Continuum of Care Cascade in Cluj County, Romania. Comparative situation of the years 2016, 2017, 2018

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Purpose: The continuum of care is a conceptual framework that enables countries to monitor the effectiveness of key areas of HIV response. At the end of 2017 cascade of care in Romania showed that 92% of patients were on ART, and 68% of them had viral suppression

The aim of this study was to evaluate the continuum of care for the people living with HIV in Cluj county between 2016–2018.

Method: This was a retrospective analyse of the electronic database.

Inclusion criteria: people diagnosed with HIV from Cluj County, on ART for at least 6 months. We included demographic data - e.g. age, sex, route of transmission, viral load. We compared the data from the years 2016, 2017 and 2018. P value less than 0.05 was considered statistically significant.

Results: At the end of 2018, 322 patients were linked to care. 88% (283) were on ART and 252 (89%) were viral suppressed. 214 were male, M/F ratio was 1.98. The median age was 32 years. Route of transmission: heterosexual 46.28%, MSM 37.80%, national cohort 8.83% and unknown 3.53%. In 2016, 254 patients were linked to care; of those 222 (87%) were on ART and 185 (83%) were viral suppressed. In 2017, 288 were linked to care, 264 (91%) were on ART and 208 (78%) were viral suppressed. There was a significant increase in the viral suppressed people, from 78% in 2017 to 89% in 2018. (p=0.001). No significant difference for cascade of care in women with heterosexual transmission route was noticed (p=0.20). In MSM people, there was a significant increase in viral suppressed people in 2018 compared to 2016 (p=0.02).

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Conclusion: The significant increase of virally suppressed peoples suggests that enhance linkage to care and universal initiation of ART regardless CD4 cells count, are effective measures to fulfill UNAIDS targets.

PE6/31

People living with HIV lost to follow up in the Paris region area and actions carried out by HIV care centers

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Purpose: Several studies have identified individual factors of PLWHIV loss to follow up (LTFU) but few studies investigated factors related to HIV care centers.
Method: A regional study has been set up in the Paris region in France. The rate of LTFU and actions carried out were collected by clinical study technicians and referring physicians.
Results: Out of 45 centers, 43 responded to the survey, representing 45,612 PLWHIV in care in 2016. In median the rate of LTFU was of 7.1%, IQR [1.3%-23.8%]. This rate was not correlated with the size of the center. The median number of physicians and nurses in therapeutic education involved in HIV care was 2.0, IQR [1–6] and 0.8, IQR [0–3] respectively. A therapeutic education consultation was absent in 35% of the centers, more often in small centers (< 550 PLWHIV). While 65% of centers have an emergency consultation, only 19% have a consultation on Saturday morning. Only 51% of centers offered a day hospitalization for all patients annually, most often in large centers (≥1000 PLWHIV). In 16% of the centers, appointments could only be made via an appointment booking platform and not via the service secretariat and 79% send a systematic SMS before appointment. A systematic phone call of patients not come was carried out in 37.2% of the centers. Free access to antiretrovirals for patients without health insurance coverage was possible in 98% of centers. Access to a health mediator was not possible in 57% of centers and 51% of centers had no or limited access to professional interpreter. A list of patients is transmitted regularly to physician in two-thirds of centers.
Conclusion: The LTFU is still too common in France. Control tools are unevenly accessible. Further work is needed to analyze the effect of these inequalities on the rate of LTFU.

PE6/32

Far from 90–90–90 goals in Latin America

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Purpose: One year away from 90–90–90 WHO goals, a final 52% of viral suppression among people living with HIV (PLWH) in Latin America (LA) was reported by UNAIDS in 2017, based upon estimations and information provided by governments. The objective of our study was to measure rates of retention in ART and virological suppression (VS) in LA by independent data collection from HIV Care Centers.
Method: We collected data from 34 HIV centers on charge of 62,375 out of 499,020 patients under control in 8 LA countries. Patients admitted to care in 2016 were followed up and one-year outcomes were registered in grouped sex and age stratified sheets. The continuum of care was built starting from UNAIDS PLWH estimations, the number of patients under control following an elicitation procedure (1st 90 includes diagnosed and linked) and the results of follow up for retention and suppression. Sensitivity analysis was carried out according to the expected PLWH under control in each country.
Results: From 7,820 patients admitted to care in 2016, 252 died in the first year (3.2%) and 224 transferred out were censored for analysis. 85.4% of patients were retained in ART at one year (77.3% to 93.2%) and 90.0% of them achieved VS below 1,000 copies/mL (61.0% to 96.3%). The final 90–90–90 rate ranged from below 40% in Venezuela, Guatemala and Peru to 57.9% in Argentina with an average of 46.9% for the 8 countries.

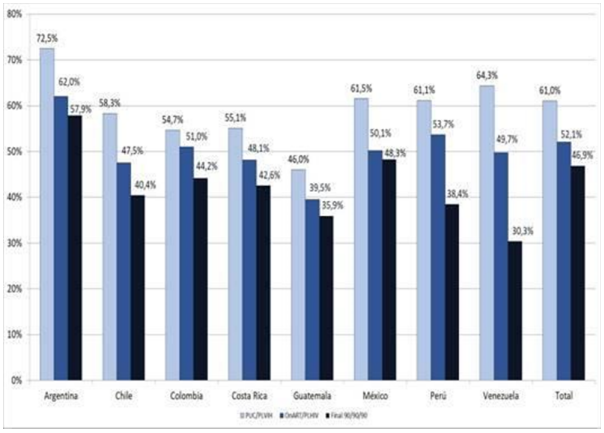


Figure 1

Conclusion: Our independent data collection shows that rates of retention in ART and VS in LA are close to the goals. Nevertheless, we are far to achieve the final 90–90–90 in LA being the main gap insufficient testing and linkage to care. Our results are valuable to focus and intensify the treatment as prevention efforts.

PE6/33

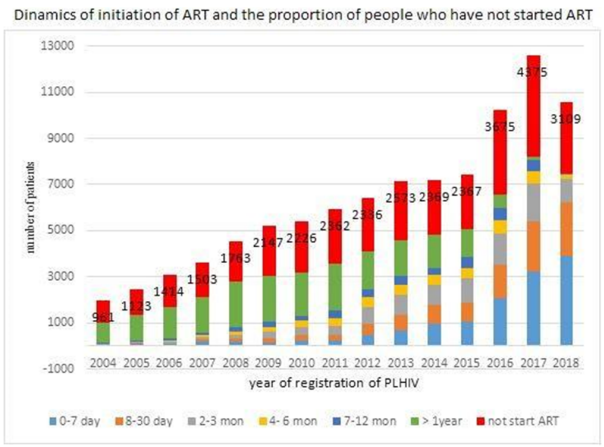
Barriers to involving patients in ART as a challenge to the national health system in Ukraine

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Purpose: Estimated number of people living with HIV in Ukraine is 244 000 persons. About 100 000 patients in Ukraine received ART now. National targets for 2020 year are to include 196,000 patients in ART. maximum engagement in treatment is an urgent challenge. For the last 14 years.
Method: An analysis of the data of the electronic health information system, which includes data on over 144000 HIV patients.
Results: Over the decade, patient enrollment for treatment has increased significantly over the year, from 245 per year in 2004, to about 5,000 in 2009–2012, and to about 15,000 in recent years. For the period from 2004 to 2018 years, more than 34 thousand PLHIV were registered but did not start ART by the end of 2018. The proportion of people who do not start treatment remains almost the same throughout all years, regardless of the number of patients who started ART.
Conclusion: To influence the HIV epidemic in Ukraine, the urgent need is to include the maximum number of patients in ART and reduce the proportion of patients, who did not start ART. Social and psychological support to the PLHIV prior to the start of ART is an important issue. Clarifying the causes of barriers to involving patients in ART and development of SOP and action plan are the next major steps for the national health system.

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Dynamics of ART and the proportion of people who have not started ART

PE6/34

Index testing and intensified case finding for efficiency in HIV testing in Rwanda

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Purpose: As Rwanda inches closer to the UNAIDS HIV first 90, finding the remaining positives may be difficult using passive methods. Therefore, Rwanda initiated the implementation of Active HIV Case Finding (ACF) through index testing with partner notification services (PNS) and family testing.
Methods: ACF is implemented as part of Case Surveillance (CS) system in all 23 sites of Kigali city. Three index testing strategies are used to actively find new cases of PLHIV including client referral, provider testing and contact referral. The cases identified through ACF are linked to care and followed up longitudinally in CS. CS system captures core demographic, epidemiological and service delivery variables.
Results: Between October and June 2019, 2598 index cases were registered. Of them, 1792, 624, 156 and 26 Index cases were registered from Voluntary counseling and testing, provider initiated testing, antenatal clinic and maternity respectively. From the total index cases, 2316(89.1%) provided partner's information for the last 12 months with an index case to partner ratio of 1.5 (3844 elicited partners, mean=1.5, median=1). Of those, 3344 (86.9%) partners were successfully contacted; 37% were reached through client referral, 32% by provider and 31% by contract referral.
Of all partners contacted, 2833 (84.7%) came to the health facility for HIV testing and 118(4.2%) were already aware of their HIV+ status. Of 2715 who previously self-reported testing negative or never tested, 2442(89.9%) were tested for HIV. Of those 2442, 218(8.9%) tested HIV+ and 203(93.1%) of those were linked to treatment.
Conclusion: All three index-testing approaches provided important contributions to epidemic control .The high level of partner testing through active case finding, partner positivity rate and near universal linkage of positive partners to treatment highlight the substantial impact that active case finding can have on Rwanda's pathway towards HIV epidemic control.

Clinical trials of vaccines

PE8/1

Seroprevalence of vaccine preventable viral diseases and vaccine response among HIV positive patients

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Purpose: Vaccination is very important to limit the increased risk of severe infectious diseases in HIV-infected patients . On the other hand, vaccine response may be diminished due to impaired immune functions. The purpose of the study was determination of serostatus against the common viral infections and vaccine needs of the newly diagnosed HIV-positive adult patients.
Method: All the newly diagnosed HIV-positive patients were included the study. The vaccination history was obtained from each patient. All patients underwent serological testing by ELISA and immune status of them against hepatitis B, hepatitis A, measles, mumps, rubella, varicella were determined initially.
Results: Seventy four male and 18 female patients with a mean age of 43.4 years (20–78 yrs) old were evaluated. Almost all of them could not remember the vaccination history. Nearly Seronegativity rates were 52% for hepatitis B, 16.3% for hepatitis A, 1.1 % for measles, 3.30% for mumps, 1.1% for rubella, 1.1 for varicella. Hepatitis B co-infection was detected in 8.7 of the patients. All the seronegative patients responded to hepatitis B (standard doses) and hepatitis A vaccines independently from CD4 + T cells count. Vaccination for measles, mumps, rubella vaccine was planned with patients based on the CD4 + cells count.
Conclusion: More than half number of HIV positive adults lacked immunity against common vaccine preventable infections. Initial evaluation and personalized vaccination plans might be helpful to improve the vaccination among HIV positive patients.

PE8/2

Could we recommend the current herpes zoster vaccine for patients living with HIV (PLHIV)?

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Purpose: Most live attenuated vaccines (LAV) are recommended in PLHIV with undetectable HIV- RNA and CD4>200/mm3. The incidence of herpes zoster (HZ) with severe postherpetic neuralgia remains higher in PLHIV. As they are getting older and better with a similar quality of life to the general population, we should offer them all the preventions like prevention against the risk of zoster and its morbidity. The LAV against zoster virus is safe and efficient to reduce incidence and morbidity of HZ. But it is still not recommended for PLHIV while LAV against varicella virus is recommended in case of negative serology.
Method: Indications and injections of HZ vaccine were explained to the requesting PLHIV, aged 65 to 74 years (as recommended for the French general population), with CD4>200/mm3 and HIV- RNA<20 copies/mL in our center. Here we report clinical data collected from NADIS medical records since February 2017.
Results: Fourteen PLHIV received the HZ vaccine. The median age was 69 years (66–74), HIV-RNA was<20 copies/mL and the median CD4 was 517 / mm3 (306–990). Nine PLHIV received the vaccine between 65 and 69 years old and 5 between 70 and 74 years old. Four had an history of HZ disease a median time before HZ vaccine of 19.5 years (15–22). During a median follow-up of 13 months (3–21), no side effect related to the vaccine was reported and no HZ event happened.
Conclusion: PLHIV are aging better with a safe immuno-virological status but they are at higher risk of HZ. Before to obtain the recombinant adjuvanted subunit vaccine, we could vaccinate them against HZ disease with the LAV in light of our data and a recent study by *Benson et al.* about 395 younger PLHIV.

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Co-morbidities, ageing

PE9/1

Detectable subclinical myocardial abnormalities in people living with HIV: insights from cardiac magnetic resonance imaging (MRI)

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Introduction: People living with HIV (PLWH) experience significant comorbidities as they age, with increased rates of cardiovascular disease (CVD), including acute myocardial infarction (MI), heart failure (HF) and sudden cardiac death (SCD).
Cardiac MRI is used for investigating young patients as there is no radiation exposure, good reproducibility of results and accurate comparative data during follow-up testing. It can be used to assess ischaemia, left (LV) and right ventricular function, structural heart disease and fibrosis/scar such as in MI, HF and SCD.
Methods: The study analysed 42 PLWH from cardiology clinic (37 men, mean age 55.7 ± 11.07 year (y) and HIV duration of 16.2 ± 9.27 years) and 39 healthy volunteers (39 men, mean age 46.1 ± 7.8) were recruited.
All subjects underwent cardiac MRI with T1, T2 mapping, fourteen PLWH also underwent adenosine stress with myocardial perfusion mapping.
Results: Compared to healthy volunteers, PLWH had significantly decreased ejection fraction, increased LV mass, but no difference in native T1, a marker of diffuse fibrosis . T2, a more specific marker of myocardial oedema, was elevated in PLWH (Table 1). Sixteen PLWH (41%) showed late gadolinium enhancement (LGE)(8 ischaemic and 8 non-ischaemic pattern). Only 7 (18%) PLWH were classified as having normal test results.

Table 1. Comparison of cardiac MRI parameters in PLWH and healthy controls

	LVEF(%)	T1	T2	ECV	LGE	LV Mass	LVM Idx
PLWH							
(n)	41	35	32	7	21(16)	40	40
Mean	60.0	1019.9	48.0	0.3		155.6	80.0
SD +/-	15.4	56.9	3.2	0.1		47.6	23.8
Control							
(n)	31	39	39	26	36(0)	31	31
Mean	64.7	1001.1	45.9	27.7		118.9	59.7
SD +/-	5.3	40.9	3.2	3.0		34.1	13.0
Statistics							
t Test	−2.36	1.96	3.01	1.20		3.63	4.28
p Value	<0.05	0.053	<0.01	0.241		<0.01	<0.01

LVEF: left ventricular ejection fraction; ECV: myocardial extracellular volume; LVM Idx: left ventricular mass index

Conclusion: In PLWH, the elevated LV mass may be associated with long-standing hypertension, common within this patient population. The high myocardial T2 may be due to chronic low grade cardiac inflammation. Focal areas of non-ischaemic scarring were present and may relate to previous myocarditis and provide a link to the increased SCD seen in PLWH.
This study identifies a number of cardiac abnormalities associated with chronic HIV infection and prolonged ART. It illustrates the benefit of cardiac MRI in providing additional structural information which may require early medical intervention.

PE9/2

Hypertension and ECG alterations in HIV positive patients in DREAM centres in Mozambique

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Purpose: Prevalence of hypertension in Mozambique raised from 33.1% in 2005 to 38.9% in 2015. Cardiology services in Mozambique are still scarce. HIV patients are known to have higher risk of hypertension and subsequent cardiac impairment.
DREAM program, run by Community of Sant'Egidio, is a program for HIV treatment established in Mozambique in 2002. Global Health Telemedicine (GHT) is an ONG supporting DREAM health centres with specialist teleconsultation.
Purpose of the analysis is to evaluate blood pressure and basic ECG features in a cohort of African HIV+ patients.
Methods: Both routine or on demand ECG of HIV+ patients in ART attending 7 DREAM facilities in Mozambique in 2018 were enrolled. ECG were analysed by European cardiologist affiliated to GHT. Age, sex, blood pressure (BP) and heart rate (HR) were recorded.
Results: 711 ECG were executed in 2018. 395/711(55.6%) were in female patients. Mean age, BP mix, BP max and HR were respectively: 48(±12) years, 96(±16)mmHg (n=621), 158(±27)mmHg(n=621) and 75(±14)bpm (n=601). 507/621(81.6%) patients had elevated BP measurements (one systolic or diastolic BP measurement>140 mmHg or BP>90 mmHg) and 35/601(5.8%) had tachycardia (HR>100 bpm).
296/711(41.6%) ECG were reported to have any alteration, 17%/711(24.6%) reported ventricular hypertrophy. 26/258(10.1%) patients with abnormal ECG had no sign (no hypertension nor tachycardia).
Male patients had higher rates of elevated BP (86.3% vs 77.9%, OR 1.7[1.16–2.73]), of abnormal ECG (47.2% vs 37.2%, OR 1.5[1.11–2.03]), and ventricular hypertrophy (30.4% vs 20.0%, OR 1.7[1.23–2.46]).
Elevated BP measurements (systolic BP>140 mmHg or diastolic BP<90 mmHg) were associated with older age (41 vs 50 years, p>0.000), abnormal ECG (OR 2.3 [1.47–3.65]) and ventricular hypertrophy (OR 5.0[2.51–10.31]).
Conclusion: Special attention should be paid to cardiologic aspects in HIV patients in Mozambique. Despite not wide spread, ECG could represent a useful tool to early detect cardiologic diseases needing appropriate therapy.

PE9/3

Cardiovascular events are declining in men with HIV aged 50 years or older in Austria

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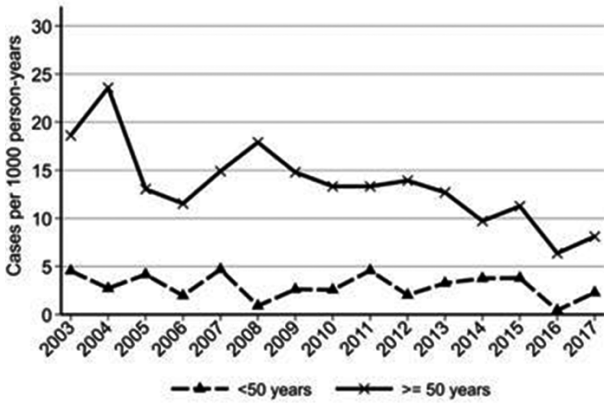
Purpose: To evaluate whether the rate of cardiovascular events changed in recent years in men with HIV in Austria.
Method: We calculated the incidence rate of a first cardiovascular event per 1000 person-years (PY) for men in the Austrian HIV Cohort study. A first cardiovascular event was defined either as acute myocardial infarction (AMI) or invasive cardiovascular procedures (ICP) (stenting, bypass grafting or endarterectomy) or stroke. In absence of a cardiovascular event, patients were censored at date of last visit plus 6 months or death. Observation period lasted from 1st January 2003 until end of 2017. Use of antiretroviral, co-medications and viral load were also collected.
Results: Overall 6026 men accumulated 49857 years of follow-up. The median age increased from 40 to 46 years between 2003 and 2017, 1947 (55%) passed the age of 50 during the observation period, so that median age

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remained stable in men below 50 years of age and in those 50 years or older (39 and 57 years, respectively). We observed 597 cardiovascular events in 257 men (244 AMI, 192 ICP and 161 strokes). The incidence rate of their first cardiovascular events declined from 7.0 (95% CI 3.9–11.6) events per 1000 PY to 4.6 (95% CI 2.7–7.4) in 2017. In men aged 50 years or older declined from 18.6 (95% CI 7.5–38.4) in 2003 to 8.1 (95% CI 4.2–14.2) in 2017 (p-value for trend≤0.004), respectively (Figure), whereas all factors, regarding risk of cardiovascular events, improved substantially (Table).
Limitations: Smoking was not included due to incomplete data.
Conclusion: The decline in cardiovascular events in men aged 50 or older is associated with factors, generally seen as beneficial. However, the observational design of our study precludes conclusions on causality of any particular effect.

Drugs and a viral load above 200 copies in men aged≥50 years (P-value for trend across all years from 2003–2017)

	2003	2008	2013	2017	P-value
Acetylsalicylic acid	14.6%	18.6%	20.6%	19.4%	0.007
ACE inhibitors/AT antagonists	17.9%	24.3%	34.9%	34.9%	<0.001
Beta blocker	8.3%	13.1%	18.9%	17.8%	0.001
Statin	12.6%	27.0%	36.0%	36.4%	<0.001
Insulin	2.7%	3.2%	3.7%	3.4%	0.304
Oral antidiabetics	6.0%	6.7%	6.5%	6.7%	0.566
Abacavir use	28.2%	37.1%	24.2%	27.5%	0.067
PI use	36.5%	47.8%	43.1%	16.4%	0.273
≥1 viral load>200 copies/mL	45.8%	22.5%	11.4%	8.0%	<0.001



First cardiovascular events in men with HIV

PE9/4

Prevalence of HIV-associated neurocognitive disorder (HAND) in Turkey and assessment of Addenbrooke's Cognitive Examination Revised (ACE-R) test as a screening tool

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Purpose: We aimed to determine the prevalence and associated factors for HAND among HIV-infected patients in Turkey. In addition, ACE-R and three questions (3Qs, EACS Guidelines) were also assessed as potential screening tools for HAND.
Method: HIV-infected patients were enrolled consecutively from two different teaching hospitals between March 2018 and September 2018. Patients underwent the 2 screening tools, a neuropsychological (NP) test battery covering 7 cognitive domains and an assessment of activities of daily living. HAND was diagnosed according to the Frascati's criteria and applying Global Deficit Score (GDS) approach. A ROC curve analysis was performed to compare the predictive accuracy of ACE-R to the NP test battery. Several factors were evaluated for association with HAND using a multivariate logistic regression analysis.
Results: The study population included 162 participants (median age: 43.5 years, 94% male, median education: 13 years, median nadir CD4: 295 cells/mL). Plasma HIV-RNA was<200 copies/mL in 158 subjects (97.5%). The median time on ART was 3 years (IQR 1.5–6.6). HAND prevalence was 45.7% (asymptomatic neurocognitive impairment (ANI)=37.7%; mild neurocognitive disorder (MND)=7.4%; HIV-associated dementia (HAD)=0.6%) according to the Frascati criteria, and 31.5% (ANI=25.9%; MND=4.9%; HAD=0.6%) using the GDS. Memory (learning, recall) (27.2%), attention/working memory (24.7%) and planning/executive (20.4%) were the most frequently impaired domains. In ROC analysis, the ACE-R showed an area under the curve of 0.74 at a cut off score of 89 (Figure 1). Sensitivity, specificity and correct classification rate of screening tests for HAND diagnosis were as follows: ACE-R (62.2%, 67%, 64.8%) and 3Qs (10.8%, 88.6%, 53%). In multivariate analysis, only education level (aOR: 0.84; 95% CI: 0.76–0.92; p=< 0.001) was an independent risk factor for HAND.
Conclusion: Despite a very well controlled population, HAND is a prevalent comorbidity in HIV-infected persons in Turkey. The sensitivity of ACE-R and 3Qs as screening tools are lower than desired.

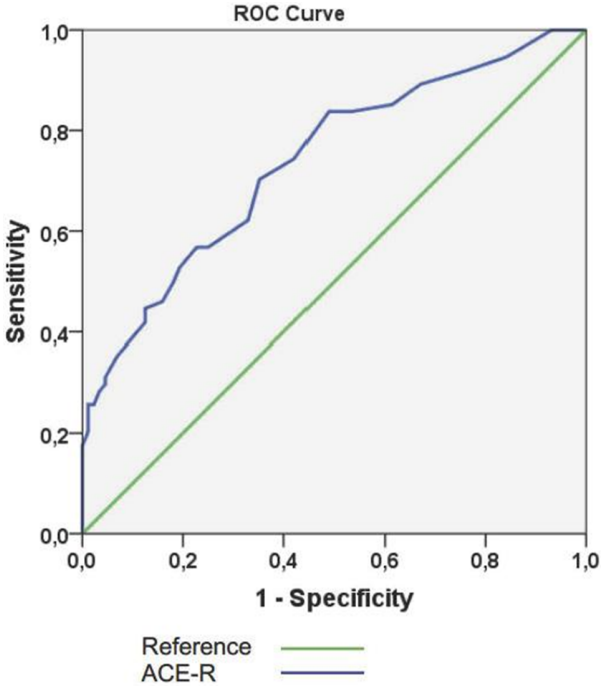


Figure 1. Receiver Operator Curves for Addenbrooke's Cognitive Examination Revised (ACE-R) test

PE9/5

Pilot study assessing the Rotterdam Healthy Aging Score in a cohort of HIV-positive adults

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Purpose: A standard measure of healthy aging would enable identification of factors predictive of health and facilitate evaluation of interventions. The Rotterdam Healthy Aging Score (HAS) is a validated multidimensional index constructed from five health domains (mental health, cognitive function, physical function, social support and quality of life). We describe the HAS distribution among a cohort of HIV-positive adults.
Methods: A prospective pilot study of 100 adults attending a tertiary HIV clinic, aged≥40 on cART with suppressed HIV RNA. Participants completed

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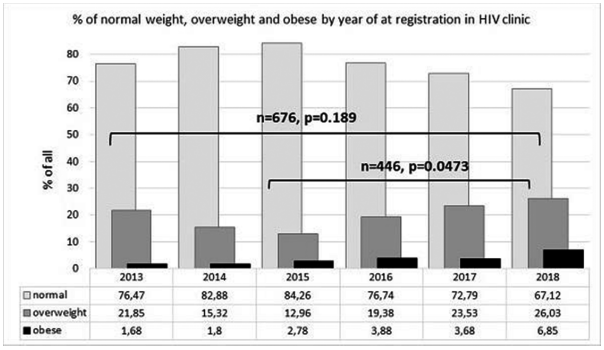
questionnaires to calculate the HAS (range 0–14). Demographics, HAS and domain scores were compared by age and sex using the Kruskal-Wallis Rank-Sum or Fisher's Exact test.
Results: Median (IQR) age was 56 (50, 62), 81 (81%) male, and 50 (51.5%) born in Canada. Participants aged≥61 were more often Caucasian (75%) compared to those 40–50 (47%) and 51–60 (59%, p=0.056). Women were more often black (53%) compared to men (9%, p<0.001). Participants≥61 had longer HIV duration (25y, p=0.001) and lower CD4 nadir (152 cells/mm^3, p=0.05) compared to 40–50 (16y, 267 cells/mm^3) or 51–60 (22y, 190 cells/mm^3). Median (IQR) CD4 was 574 (417, 790) cells/mm^3. Median (IQR) HAS was 12 (10.13) and 38 (38.4%) achieved a score>12 (considered healthy aging). HAS did not vary by age group (p=0.72) or sex (p=0.49). Younger participants were more likely to have low mental health scores (27% for age 40–50 and 27% for age 51–60) compared to those≥61 (6%, p=0.04). Women were more likely to have low pain scores
(i.e. experience greater pain, 16%) compared to men (1%, p=0.02).
Conclusions: HAS scores ranged from 4–14 in this cohort of older treated HIV adults with 38% attaining the "healthy" range. The HAS requires further study for its ability to discriminate health outcomes and determine health domains that dominate poor scores.

PE9/6

Obesity and HIV – the overlapping epidemics

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Background: Obesity is a leading cause of death among preventable diseases worldwide. The rates among adults are increasing. Here we investigate the prevalence of obesity among newly diagnosed HIV-positive patients.
Methods: We retrospectively analyzed ARV naive patients newly registered at the HIV Out-Patient Clinic in Warsaw between 1st Jan 2015 and 31st Dec 2018. The inclusion criteria were: BMI measured at first visit in the clinic, having two visits in three months, having at least one CD4 and VL measurement and starting ARV during follow-up. Data were exported from prospectively designed electronic database.
Results: 676 patients fulfilled the inclusion criteria: 637(94.2%) were men, 544(80.7%) MSM, median: age 32.4 (IQR: 27.1–37.8), BMI 22.5(20.4–24.7), CD4 count 369(232–506) cells/ul, HIV RNA 4.6 (4.0–5.1) log copies/mL. 280 (41.7%) patients started PI based and 302(44.9%) InSTI based regimen. As for NRTIs 363 (70.1) patients started TDF, 119 (17.7%) TAF and 92 (13.7%) ABC. Of all patients 521 (70.1%) were classified as normal weight (BMI<25), 133 (19.7%) as overweigh (BMI 25–30) and 22 (3.2%) as obese (BMI>30). The proportion of overweight and obese (OOB) patients increased over calendar time, with a significant trend for 2015–2018 (Figure).



Figure

Obesity, but not overweight was associated with longer time to HIV<50 copies/mL (p=0.027) OOB were associated with higher levels of triglycerides (p<0.001), LDL (p=0.003) and total cholesterol (p<0.001). We did not find OOB to be associated with other baseline characteristics, choice of ARV regimen, time to starting ARV or switching ARV.
Conclusions: In a single center experience the proportion of OOB among newly registered patients increased over time. This was also reflected in lipid abnormalities, but did not affect ARV choice. The finding on association between OOBP and time to HIV RNA<50 needs to be further investigated in a prospectively planned study including pharmacokinetic assessment of ARV.

PE9/7

Exhaled nitric oxide levels are higher in people living with HIV compared to uninfected controls suggesting increased eosinophilic pulmonary inflammation

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Objective: HIV infection is associated with an excess risk of chronic pulmonary diseases, including asthma and COPD. Exhaled nitric oxide (eNO) is a marker of eosinophilic pulmonary inflammation and is often increased in people with asthma. We assessed eNO levels in people living with HIV (PLWH) and matched uninfected controls and studied whether HIV status is independently associated with eNO.
Methods: eNO was quantified in breath by NIOX Vero® and pulmonary function was assessed by spirometry in 432 PLWH from the Copenhagen Comorbidity in HIV infection (COCOMO) Study and in 1623 age- and sex-matched uninfected controls from the Copenhagen General Population Study. Elevated eNO was defined as>25 parts per billion (ppb). Linear and logistic regression analyses were used to study associations between eNO and HIV status adjusting for potential confounders.
Results: Mean (SD) age of PLWH was 50.7 (11.3) and 97.4% received cART. PLWH had higher absolute eNO than uninfected controls (mean±SD) 21.0 ± 16.0 versus 15.7 ± 12.4 ppb, p<0.001 (Fig 1). Also, PLWH had a higher prevalence of elevated eNO than uninfected controls (25.2% versus 11.0%, p<0.001), (odds ratio (OR): 2.74 [95% CI: 2.10–3.58], p<0.001). This association was stronger after adjusting for age, sex, height, smoking status, blood eosinophils and S-IgE (adjusted OR (aOR): 3.86 [95% CI: 2.72–5.47], p<0.001) (Table 1). Self-reported asthma and wheezing were also associated with elevated eNO (aOR: 2.55 [95% CI: 1.56–4.17], p<0.001 and aOR: 1.46 [95% CI: 1.03–2.08], p=0.034, respectively) whereas airflow limitation (FEV_1/FVC< lower limit of normal) was not (aOR: 0.95 [95% CI: 0.61–1.42], p=0.836). Current smoking was negatively associated with elevated eNO (aOR: 0.18 [95% CI: 0.10–0.32], p<0.001).
Conclusion: HIV status was an independent predictor of elevated eNO suggesting increased eosinophilic pulmonary inflammation. Elevated eNO was associated with wheezing but not with airflow limitation and may contribute to the greater burden of respiratory symptoms in PLWH.

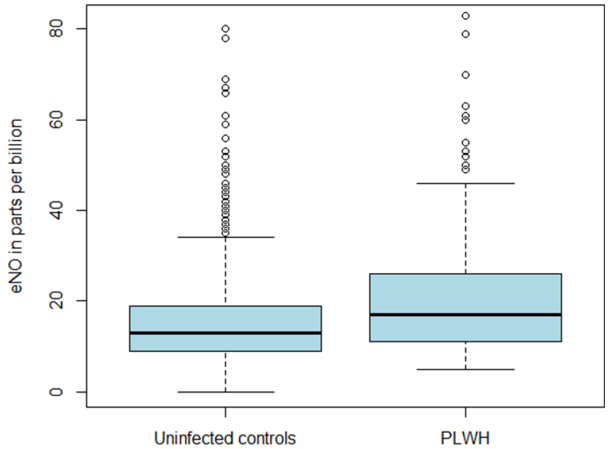


Figure 1. Exhaled nitric oxide (eNO) levels in People living with HIV (PLWH) and Uninfected controls

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Table 1. Uni- and multivariate logistic regression analysis for factors associated with elevated eNO

	OR [95% CI]	p-value	aOR [95% CI]	p-value
HIV yes vs no	2.74 [2.10–3.58]	<0.001	3.86 [2.72–5.47]	<0.001
Smoking status (Ref: Never)				
Current smoker	0.25 [0.15–0.42]	<0.001	0.18 [0.10–0.32]	<0.001
Former smoker	0.96 [0.74–1.25]	0.786	0.82 [0.60–1.12]	0.211
Self-reported outcomes				
Asthma yes vs no	2.31 [1.51–3.54]	<0.001	2.55 [1.56–4.17]	<0.001
Wheezing yes vs no	1.18 [0.87–1.59]	0.287	1.46 [1.03–2.08]	0.034
Airflow limitation				
FEV1/FVC < LLN yes vs no	0.79 [0.52–1.18]	0.241	0.95 [0.61–1.42]	0.836

PE9/8

Comparison of changes in bone microarchitecture with abacavir–lamivudine versus tenofovir disoproxil fumarate–emtricitabine in adults living with HIV

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[1]VA North Texas Health Care System, Dallas, USA [2]University of Texas Southwestern Medical Center, Medicine, Dallas, USA tates

Background: Antiretroviral therapy with tenofovir disoproxil fumarate-emtricitabine (TDF/FTC) is associated with greater decreases in bone mineral density (BMD) than abacavir-lamivudine (ABC/3TC). Trabecular bone score (TBS) is a novel measurement of bone microarchitecture from Dual-energy X-ray Absorptiometry (DXA) scan images that improves fracture prediction independent of BMD. We hereby compared changes in TBS with initiation of ABC/3TC or TDF/FTC in first-line regimens, and analyzed predictors of TBS change.
Methods: We utilized BMD data collected in a multi-center randomized trial (ASSERT) of ABC/3TC vs. TDF/FTC. TBS scores were calculated from weeks 0, 24 and 48 lumbar spine (LS) DXA images captured with Hologic® densitometer. Mixed effects repeated measures models were used to compare between arms changes in TBS from baseline to week 48, controlling for baseline values, age, BMI, race and sex.
Results: A total of 158 subjects were enrolled in the study (75 TDF, 83 ABC). Baseline mean TBS scores were 1.32 vs. 1.33. Age and BMI were predictors of BMD ($p<0.05$) but not TBS. In adjusted analyses, there was a greater BMD decline in the TDF than ABC group at weeks 24 (−2.6% vs. −1.7%) and week 48 (−2.2% vs. −1.4%). TBS declined significantly over 48 weeks in both groups. However, decline in TBS was not significantly greater in the TDF group at week 24 (−1.4% vs. −1.8%) or week 48 (−2.3% vs. −1.5%; model $p=0.3$) (figure 1). Higher baseline TBS was predictive of greater TBS decline in the TDF group but not the ABC group ($p<0.01$). In the combined arms, changes in TBS were correlated with changes in BMD at weeks 24 ($r=0.18$; $p=0.03$) and 48 ($r=0.41$; $p<0.01$).
Conclusions: First-line ART containing either TDF/FTC or ABC/3TC led to significant decline in TBS. TBS use could potentially increase the accuracy of fracture risk assessment with newer antiretrovirals.

PE9/9

Limitations of FRAX equation for predicting low bone mineral density or bone loss progression among people living with HIV: the role of secondary causes of osteoporosis

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Purpose: We assessed the usefulness of the Fracture Risk Assessment (FRAX) tool to identify HIV-infected patients with low bone mineral density (BMD) and bone loss progression. We further evaluated the effect of secondary causes of osteoporosis and HIV-related factors on FRAX results.
Method: Longitudinal study of 217 consecutive patients (mean, 45.8 years, women 24%) included after dual X-ray absorptiometry (DXA) scan. Low BMD and osteoporosis were defined as a femoral neck or spine T-score<2 and<2.5, respectively. The risk of major osteoporotic and hip fracture was calculated by FRAX equation, considering HIV as a secondary cause of osteoporosis, without/with femoral neck BMD data. The threshold for high-risk of fracture was defined as>3% for hip and>10% for lumbar spine.
Results: A low femoral neck and spine BMD was observed in 56% and 64% of patients, respectively. FRAX without BMD data did not identify any patient aged<75 at high risk of fracture. The inclusion of BMD data increased the estimated fracture risk (up to + 221% in individuals with osteoporosis), though only two patients reached the current high-risk threshold for fracture. Moreover, the estimated fracture risk decreased in the oldest patients (−33%) and in individuals with normal BMD (−93%) after including BMD data. Conversely, FRAX results increased significantly with the inclusion of BMD data among individuals with classical and HIV-related secondary causes of osteoporosis (Figure 1). Notably, patients with lower BMD and higher FRAX score at baseline had less bone decline in a consecutive DXA scan (rho=0.21, p=0.008).
Conclusion: FRAX equation without BMD data does not identify HIV-infected patients with low BMD, delaying DXA assessment. After including femoral neck BMD, most patients remain below the current high-risk threshold for fracture. Different secondary factors, classical and HIV-related, affect fracture risk estimation by FRAX in this population.

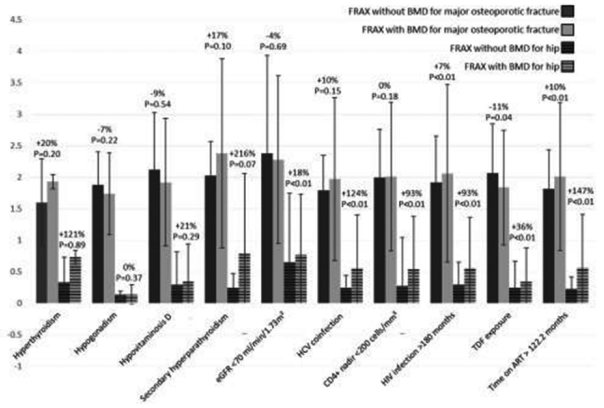


Figure 1. Estimated fracture risk by FRAX computed without and with bone mineral density (BMD)

PE9/10

Elevated body mass index during pregnancy and gestational weight gain in HIV-infected women in Cape Town, South Africa: association with adverse birth outcomes

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Background: In pregnancy, HIV infection has been shown to be associated with adverse birth outcomes, in part, via weight-loss related mechanisms. However, with the majority of HIV-infected people using ART, obesity in these women is becoming more prevalent. There is limited data regarding the impact of co-morbid HIV infection and obesity on birth outcomes in this population.
Aim: To examine whether adverse birth outcomes are associated with maternal body mass index (BMI) and gestational weight gain (GWG) among HIV-infected women.
Methods: In an urban South African community, 1058 consecutive HIV-infected pregnant women attending primary health care services were assessed at their first antenatal visit, with a subset enrolled in a longitudinal

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study assessed three times during pregnancy. All women had birth outcome data from medical records and study questionnaires. In analysis, the associations between BMI, GWG, maternal factors and adverse birth outcomes were assessed with logistic regression models.
Results: Overall, HIV-infected women had a median BMI of 30 kg/m^2 (IQR, 26–35) at their first antenatal visit. Increased BMI was positively associated with age, haemoglobin, parity and gestational age at first antenatal visit. In adjusted models, increased BMI was associated with a range of adverse outcomes, including 8% increase in high birthweight (aOR 1.08, 95% CI 1.02–1.15), 5% increase in large size for gestational age (aOR 1.05, 95% CI 1.02–1.08), 5% decrease in low birthweight (aOR 0.95, 95% CI 0.91–0.99) and 5% decrease in small size for gestational age (aOR 0.95, 95% CI 0.92–0.98). Associations involving GWG were in similar directions but did not achieve statistical significance consistently.
Conclusion: High BMI during pregnancy is prevalent in this setting and appears associated with increased risk of adverse birth outcomes in HIV-infected women. Weight management interventions targeting women of child-bearing age are needed to promote healthy pregnancies and reduce adverse birth outcomes.

PE9/11

Facilitating primary care non-antiretroviral drug prescribing in people living with HIV: the Think ARV project

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Purpose: Comorbidities affecting people with HIV (PWH) often results in general practitioners (GPs) prescribing non-ART drugs to PWH on cART. Partial knowledge on interactions between cART and non-ART drugs, and limited pharmacy support for prescribers in the community results in an increased risk of medication related problems (MRPs). To address this, we developed an evaluated a pharmacy intervention to support safe-prescribing of non-ART drugs by GPs.
Method: The "Think ARV" intervention was co-designed by HIV physicians, pharmacists and GPs. It was developed to facilitate local GPs' access to real-time specialist prescribing advice, reflecting preferences for enhanced telephone and email access identified in a previous project. The intervention consisted of a bespoke sticker containing details of a new dedicated mobile phone staffed by pharmacists during working hours, and an email address for non-urgent advice. Data on cART, non-ART drugs, nature of query, intervention and method of communication were collected 6 months before implementation and 6 months thereafter. Severity of the DDIs were categorised according to www.hiv-druginteractions.orgrating system.
Results: Over 12 months, 122 queries were recorded, with a significant increase from 26 pre-intervention to 96($p<0.001$; CI (1.6–1.8). Table 1 summarises the types of queries received; most common was potential DDIs. More contraindicated DDIs were identified post-intervention compared to pre-intervention (7 vs 3), and a higher number of DDIs required dose adjustments and/or additional monitoring during the second period (18 vs 5). Although only 6 out of 15 service evaluations were returned, all reported a high level of satisfaction with the accessibility, timeliness and quality of the advice received.
Conclusion: The Think ARV intervention provided a simple and effective way of improving communication and support between GPs and pharmacists to prevent MRPs in PWH. Plans to implement this intervention in secondary care services and community pharmacies are ongoing.

Types of medicine-related problems (MRPs)

MRPs type	Pre-intervention (n=26)	Post-intervention (n=96)	Total (n=122)
Drug-drug interactions	20	92	112
Drug history	3	1	4
Vaccine advice	2	2	4
Adverse effects of cART	1	0	1
Adherence of cART	0	1	1

PE9/12

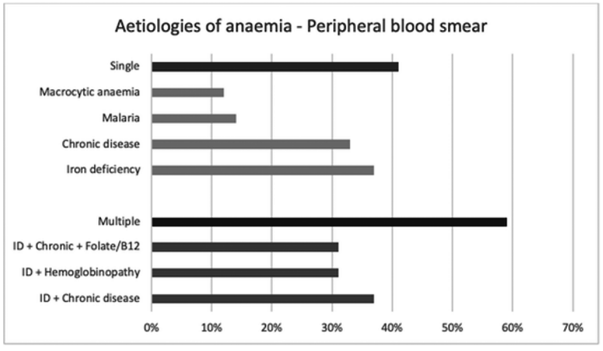
Characterization of moderate and severe anemia by PEripheral blood smear in HIV infected patients in the Kilombero and Ulanga antiretroviral cohort

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Purpose: Anaemia is the most common hematological complication among people living with HIV (PLHIV) and is associated with mortality and disease progression. In resource-limited settings, identification of the etiology of anaemia has been inadequately studied due to the lack of diagnostic tools and financial constraints.
Method: In this cross-sectional study of PLHIV≥18 years of age enrolled in the Kilombero and Ulanga Antiretroviral cohort (KIULARCO) in Ifakara, rural Tanzania we analyze the prevalence of different anaemia etiologies by peripheral blood smear and blood analyzer in patients with moderate (Hb 7–9.9 g/dl) and severe (Hb<7 g/dl) anaemia at baseline or follow-up visits since 01/2019. Here we report on preliminary findings of the first 105 enrolled patients. Aetiologies of anaemia based on blood smear and interpretation by blood analyzer results were compared.
Preliminary results: During the first 6 months, moderate and severe anaemia was present in 76/105 (74%) and 29/105 (28%) PLHIV, respectively. Median age was 41 years (IQR 18–74); 96/105 (91.5%) were female, and 102/105 (97%) were on antiretroviral therapy. Of these, 62/79 (80%) were virally suppressed (HIV RNA<40 c/mL); 18/105 (17%) had a CD4 cell count<200/mm^3. Multiple concurrent anaemia etiologies were more prevalent than single etiologies (62/105.59% vs 43/105.41%). Single etiologies were predominantly iron deficiency (16/43.37%) and chronic disease (16/37.33%), followed by malaria (6/43.14%) and possible non-megaloblastic macrocytic anaemia (5/43.12%). Peripheral blood smear results indicated multiple anaemia etiologies in 30/49 (61%) of patients with microcytosis and hypochromia by blood analyzer results and suggested an iron deficiency component in 5/15 (33%) of

Aetiologies of anaemia based on blood smear results compared with blood analyser.

Blood smear + Blood analyser (by haematology)	Micro/ Hypo N, 49	Normo/ Normo N, 15	Normo/ Hypo N, 26	Macro/ Normo N, 6	Micro/ Normo N, 5
Single aetiology	19 (39%)	9 (60%)	10 (38%)	4 (67%)	1 (20%)
Multiple aetiology	30 (61%)	6 (40%)	16 (62%)	2 (33%)	4 (80%)
Iron deficiency component	42 (86%)	5 (33%)	18 (69%)	0 (0%)	2 (40%)
Chronic disease component	6 (12%)	8 (53%)	5 (19%)	5 (83%)	1 (20%)



Aetiologies of anaemia in HIV - peripheral blood smear.

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cases with normocytosis and normochromia (Figure 1). Comparison of interpretation of etiologies by hematologist compared to clinician is shown in Table 1.

Conclusion: Multifactorial causes of anaemia were more common than single disorders. The most prevalent reason in this rural sub-Saharan African setting was deficiency alone or in combination with hemoglobinopathy, vitamin B12/folate deficiency and chronic disease anaemia.

PE9/13

HIV infection and smoking: PET imaging reveals early pulmonary perfusion abnormalities

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Rationale: Studies suggest that the development of COPD is accelerated amongst people living with HIV. Although prior investigation has established an association between chronic HIV infection and the development of COPD independent of smoking, the cause for this enhanced susceptibility remains unclear. Multimodal functional imaging may detect early physiological abnormalities in the distribution of pulmonary perfusion in these susceptible individuals.

Methods: We used low dose computed tomography (LDCT) and positron emission tomography (PET) in 46 subjects. We collected anthropometrics, lung function and smoking history for all subjects. Global and regional perfusion in each subject were analyzed using nitrogen-13 (^{13}NN) PET scans. We tested for a difference in the total spatial heterogeneity of perfusion (CV^2_{Qtotal}) and the heterogeneity caused by its components ($CV^2_{Qtotal} = CV^2_{Qvgrad}$ (vertical gradient) + CV^2_{Qzgrad} (axial gradient) + CV^2_{Qr} (residual heterogeneity)) between clinical groups, based on HIV infection and smoking.

Results: Of the 23 subjects with documented HIV infection, 12 were current smokers. There were no significant differences in demographic parameters between subjects living with and without HIV. Compared to controls, nonsmokers living with HIV had a significantly greater CV^2_{Qr}/ CV^2_{Qtotal} (0.36 vs 0.48, p=0.05) and reduced CV^2_{Qvgrad}/ CV^2_{Qtotal} (0.46 vs 0.65, p=0.038). Current smokers, independent of HIV status, had a significantly reduced CV^2_{Qvgrad}/ CV^2_{Qtotal} compared to nonsmokers (0.36 vs 0.6, p=0.002). Amongst smokers, there was a trend towards an attenuated slope of vertical perfusion gradient in smokers living with HIV.

Conclusions: In subjects living with well-controlled HIV and minimal radiographic emphysema, both HIV infection and smoking are associated with an increased perfusion heterogeneity and a reduction in the vertical gradient of perfusion. These data indicate the onset of subclinical pulmonary perfusion abnormalities prior to the development of significant lung disease in these susceptible individuals.

PE9/14

Bariatric surgery in HIV obese patients: first results of the French ObéVIH ongoing study

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Purpose: Bariatric surgery (BS) is the key treatment for morbid obesity and associated comorbidities. Few data exist in HIV obese patients particularly for sleeve gastrectomy.

Method: ObeVIH is a prospective cohort study of HIV obese patients with BMI>35 kg/m^2 with comorbidity or>40 kg/m^2 and plasma HIV viral load<50 copies/mL (pVL) who underwent single port sleeve gastrectomy. They were matched 1:1 with obese non HIV-infected subjects. The primary objective is to study subcutaneous and visceral adipose tissue. We reported here preliminary outcomes on clinical safety, evolution of body weight, comorbidities and HIV status.

Results: ObeVIH enrolled 20 patients: 15 women, median age of 49.5 years (range: 30–57), Sub-Saharan Africa origin (n=13), median ART duration: 13 years (3–21), duration of viral suppression: 3 years (1–10). ART included INI (13), NNRTI (8) and PI (2). All except one had comorbidities: sleep apnea (16), osteoarticular disorders (17), diabetes (2), dyslipidemia (6) and hypertension (6). At baseline, median weight was 113 kg (88–160), BMI of 39.9 kg/m^2 (36–52) and CD4 count of 835/mm^3 (326–1522).

Surgery was performed within an ambulatory setting for 5 patients. Seven patients experienced grade 1 adverse effects (fatigue, nausea). The median weight loss was 10 kg (6–13.5) at M1, 18.4 (12–26) at M3 and 27 (13–37) at M6. Median BMI was 38 kg/m^2 (32–49) at M1, 32.3 (25–45) at M3 and 29.3 (24.5–42) at M6.

No change in ARV was performed. The pVL remain undetectable at M1 for all, one had 83 copies/mL at M3 and 3 patients had a detectable VL (only one>200 copies/mL) at M6, without resistance. No change in CD4 count occurred during the follow-up. All comorbidities have been improved or cured in the first 6 months.

Conclusion: BS had good results in weight loss, no impact on HIV infection and improved comorbidities.

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PE9/16

Plasma cotinine cut-off for distinguishing smokers from non-smokers among people living with HIV (PLWH)

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Purpose: Cotinine is the main specific metabolite of nicotine and a biomarker of tobacco smoking. Plasma cotinine (P-cotinine) cut-off for distinguishing smokers from non-smokers has been defined to be 14 ng/mL (80 nmol/L) in the general population. Despite different metabolism rate, there is no standard cut-off among PLWH. We aimed to determine the best P-cotinine cut-off for smoking status in a large population of PLWH.
Method: We included 988 PLWH aged 30–70 years from the Copenhagen Co-morbidity in HIV Infection (COCOMO) Study. Information about smoking habits was collected using a detailed and structured questionnaire. P-cotinine was measured using liquid chromatography/tandem mass spectrometry (LC-MS/MS). We used area under the receiver operating characteristic curve (AUROC) and Youden Index (J) to define the best P-cotinine cut-off.
Results: Median (IQR) age was 50 (43–58) years, 971 (98%) received cART, 926 (94%) had undetectable viral replication. The number of current, former and never smokers were 300 (30%), 350 (35%) and 338 (34%), respectively, and 87 (9.4%) used nicotine-substitution or E-cigarette. P-cotinine level was highest among current smokers and among former-smokers with nicotine substitution (Figure 1). Highest value for *J* (0.896) was at P-cotinine cut-off 19 ng/mL (108 nmol/L; AUROC=0.978, P<0.001, 95% CI=0.968–0.989) (Figure 2). The sensitivity, specificity, PPV and NPV for cotinine cut-off 19 ng/mL among PLWH without nicotine-substitution or E-cigarette were 95%, 94%, 87% and 98%, respectively.
Conclusion: In a large population of well-treated PLWH, we found the best P-cotinine cut-off to differentiate current-smokers from non-smokers to be 19 ng/mL. This cut-off is marginally higher than that used in the general population possibly due to different smoking behavior or nicotine metabolism rate among PLWH. Cotinine level cannot separate former-smokers with nicotine-substitution or E-cigarette from current-smokers. This cut-off can be helpful in future studies, especially when there is no data on self-reported smoking.

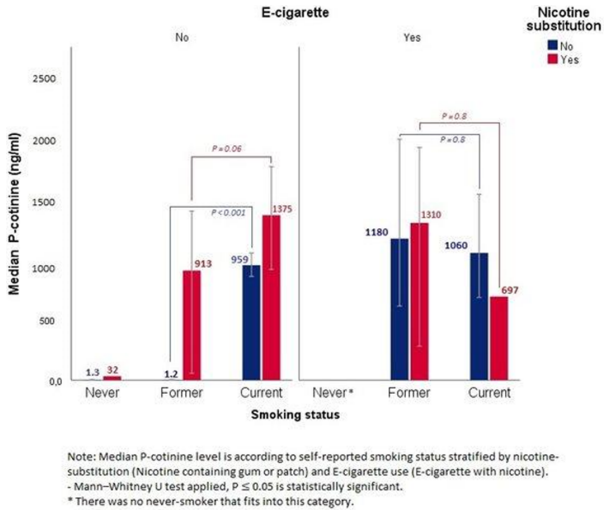


Figure 1. Median P-cotinine level among people living with HIV

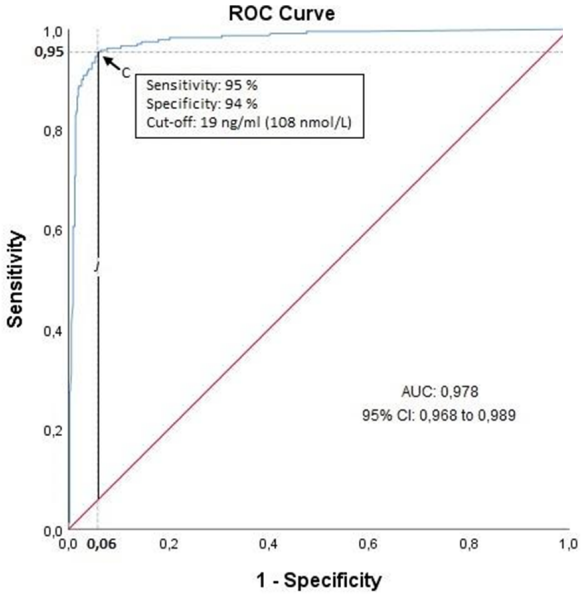


Figure 2. Receiver Operating Characteristic (ROC) curve for the best P-cotinine

PE9/17

An analysis of HIV and co-morbidity profiles for adults accessing health care in Khayelitsha, South Africa

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Purpose: To explore the HIV co-morbidities profile of patients accessing public health care at Khayelitsha.
Method: A longitudinal dataset for all individuals who accessed public health facilities at Khayelitsha from January 2016-December 2017 was obtained from the Western Cape Provincial Health Data Centre. Descriptive and inferential statistics explored demographics, HIV cases, and co-morbidities, and pairwise associations between co-morbidities using Pearson's product-moment correlation.
Results: Of 181 620 individuals (median age 37 years, IQR:30–48) seeking health, 131 933(72.6%) were females and 49 521(27.4%) were males. Of 88 316 people living with HIV (PLHIV), 63 016 (71.4%) were female and 25 219 (28.6%) male. Males seeking health care were 1.15 (CI=1.11–1.16) times more likely to have HIV than females. Median age (IQR) of HIV ascertainment differed in females 35 (30–43) and males 40 (34–47), p<0.001. Tuberculosis (31.4%), Hypertension (14%), Mental health conditions (5.3%), Diabetes (4.1%), Cancers (1.81%), and Chronic kidney disease (CKD) (1.7%) were the top 6 co-morbidities identified, with correlations between hypertension and diabetes (r=0.24), hypertension and CKD (r=0.13), and diabetes and CKD (r=0.13); all p<0.001 in PLHIV. Whilst co-morbidity clustering varied with age, median ages of ascertainment of co-morbidities were younger in PLHIV than HIV negative individuals except for tuberculosis

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Table 1. Median age (Interquartile range) of ascertainment of each co-morbidity in HIV- and HIV+ individuals

Co-morbidity	HIV- Median Age (IQR)	HIV+ Median Age (IQR)	P value
HIV	38(28–55)	37(31–44)	<0.001
Diabetes	57(48–65)	48(40–56)	<0.001
Hypertension	55(46–64)	46(39–54)	<0.001
Tuberculosis	37(28–53)	39(33–46)	<0.001
Chronic Kidney Disease	66(58–74)	50(42–58)	<0.001
Cervical Cancer	57(45–65)	42(36–48)	<0.001
Chronic Obstructive Pulmonary Disease	53(36–64)	43(35–51)	<0.001
Mental Health Condition	42(29–57)	39(32–48)	<0.001

Significant differences were also found between median ages of ascertainment for co-morbidities in females and males with HIV.

Conclusion: As HIV-related mortalities decline and life expectancy increases, PLHIV face increasing burden of chronic co-morbidities. This burden, in addition to existing tuberculosis, in PLHIV seeking care in South Africa is rising. Differences between female and male demographics also reflect to some extent contraceptive and maternal care access by women in good health. The emerging burden of chronic HIV co-morbidities requires in-depth studies to inform adequate planning for all-encompassing health care delivery.

PE9/18

Femoral arteries better indicator than carotid arteries of cardiovascular risk in HIV/AIDS patients

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Purpose: The aim of this study was to compare the prevalence of atherosclerotic plaques and subclinical atherosclerosis in the carotid and femoral arteries in HIV/AIDS patients on cART.

Method: In this cross-sectional study were included 135 HIV/AIDS patients on cART for at least 24 months. Measurements of intima media thickness (IMT) and assessment of the plaque presence was performed by a single radiologist using a linear array probe (10 MHz and 42 mm) in the supine position. The mean carotid-IMT (cIMT) and femoral-IMT (fIMT) were defined as the mean of IMT in both right and left sides of the common carotid artery and common femoral artery, respectively. Atherosclerotic plaque was defined as a focal structure with IMT≥1.5 mm. Subclinical atherosclerosis was defined by IMT≥0.9 mm or≥1 plaque. All p-values less than 0.05 were considered significant.

Results: Subclinical atherosclerosis were present in the carotid and femoral arteries in 73 (54.1%) and 92 (68.2%) patients, respectively. The cIMT and fIMT were 1.09 mm (0.75–1.26 mm) and 1.46 mm (0.80–1.60 mm), resceptively. The mean fIMT was significantly higher than mean cIMT ($p<0.001$). The prevalence of subclinical atherosclerosis in femoral arteries was statistically higher in femoral than in carotid artery ($p=0.001$). Atherosclerotic plaques were present in the carotid and femoral arteries in 30 (22.2%) and 44 (32.6%) patients, respectively. The prevalence of atherosclerotic plaques was statistically significantly higher in femoral arteries than in carotid arteries ($p=0.004$).

Conclusion: In accordance to our knowledge, we showed for the first time, that neither intima media thickness nor plaque formations located in the carotid arteries can reflect generalized atherosclerosis in HIV/AIDS patients. Thus femoral arteries should be also examined in order to estimate subclinical atherosclerosis in this patient population.

PE9/19

Cardiovascular risk assessment in PLWH over 50: agreement between cardiovascular risk predictors and Coronary Artery Calcium CT Scoring (CACS)

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Purpose: Conventional algorithms validated in the general population to predict the 10-year risk of developing cardiovascular disease (CVD) may underestimate risk in PLWH. We assessed the agreement between CV risk predictors (QRISK2–2017, Framingham and D:A:D) with Coronary Artery Calcium CT Scores (CACS) in a cohort of PLWH seen in the "Over50 clinic" at Chelsea and Westminster Hospital.

Method: Cross-sectional study of PLWH over the age of 50 without prior CVD that performed a CACS between 2009–2018. CACS was calculated using the Agatston method and reported as a centile by comparing with age and gender-matched controls. QRISK2–2017, Framingham and full D:A:D scores were stratified into 'low' (< 10%),'intermediate' (10–20%) and 'high' (> 20%) risk categories. Agreement between risk scores and CACS was assessed using weighted Cohen's Kappa test.

Results: A total of 744 patients performed CACS during the study period (92.9% male, mean age 56 ± 5 years); 5 patients were excluded due to missing data. Level of agreement amongst CVR predictors was moderate to fair whereas CACS showed poor agreement with all CVR scores (Kappa values reported in Table 1). Overall, CACS allowed re-stratification of risk in 54.6–58.8% of patients. Within patients with significant coronary calcification (CACS>50th centile), 15.6% were identified as low risk with QRISK2, 12.6% with Framingham and 16.1% with D:A:D and therefore would not have been eligible for CVD prevention. Age, polypharmacy and years of exposure to D-Drugs were significantly associated with raised CACS.

Conclusion: Our results indicate that CV risk predictors alone may fail to identify PLWH at high-risk of developing CVD and who would benefit from more aggressive prevention strategies. Incorporation of CACS can re-stratify CVD risk predictions and inform clinicians, allowing for more appropriately tailored preventative strategies.

Table 1. Agreement between CACS and CV risk scores

Cardiovascular Risk		QRISK-2017	Framingham	DAD
	Agreement	44.5%	41.1%	45.3%
CACS	Kappa	0.05 (poor)	0.07 (poor)	0.06 (poor)
	95% CI	0–0.67	0–0.08	0–0.08

PE9/20

Safety and tolerance of denosumab in HIV patients

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Purpose: Osteoporosis (OP) is about three times more frequent in HIV patients than the general population. Denosumab is a human monoclonal antibody that acts selectively against the activating receptor ligand of Nuclear Factor Kappa B (RANK-L). Among the side effects described are infections. Our objective is to analyse the safety and tolerance data of denosumab in HIV patients.

Method: Retrospective longitudinal observational study. We included all HIV patients with OP diagnosed by bone densitometry and treated with denosumab from August 2014 to the present. We recorded sociodemographic data, and variables related to HIV Infection and OP.

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Results: We included 14 patients (8 women and 6 men) with a mean of 57.71 (54–64) years old, a mean of 20.96 (SD 9.45) years of HIV infection and 15.52 (SD 9.91) years of ART. The immunological situation at the onset of denosumab was heterogeneous with a median of CD4 549 cel/mcl (240–1091) and a median viral load of 19 (19–52) copies/mL.
Reviewing the ART: 10 patients (71.42%) have been on protease inhibitors for a mean time of 166.7 (SD 30.38) months and 11 (78.57%) were treated with TDF for a mean of 50.9 (SD 42.58) months.
The mean of follow-up with denosumab was 24.07 (± 13.56) months. Three types of adverse events were reported: two upper respiratory tract infections, one rash and one death in a patient with lung carcinoma who died of pneumonia. There were neither new fractures nor mandibular osteonecrosis after the onset of denosumab. The treatment was withdrawn in two patients: the first one due to a rash and the second one temporarily after performing the dental procedure.
Conclusion: Treatment with denosumab is safe and well tolerated in HIV patients in our sample. We need more studies to confirm the safety of denosumab in our patients.

PE9/21

Lower incidence of liver steatosis in patients treated with lamivudine plus dolutegravir dual therapy

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Purpose: We aimed to assess the prevalence of liver steatosis and its possible correlation with the therapeutic history of this population.
Method: A screening program with abdomen ultrasound (US) on HIV-positive patients at our clinical center by the same operator. Detection and grading of hepatic steatosis were based on the assessment of liver echogenicity; those with a history of chronic hepatitis (viral or alcoholic) were excluded. We compared parameters through non-parametric tests and linear regression, as appropriate.
Results: A total of 60 patients were analyzed 60 pts: 45 (75%) were males, with a median age of 50.5 years, a median of 13.1 years from HIV diagnosis and a median time from ARV initiation of 10.8 years. Full patients' characteristics are shown in table 1. Median hepatic right lobe length was 15 cm while median spleen diameter was 10.5 cm; 14 pts (23.3%) had mild steatosis, 12 (20%) a moderate one while 3 pts (5%) presented severe steatosis. Being on a 2-drug regimen with 3TC+DTG was inversely associated with any grade of hepatic steatosis vs other regimens (p=0.042). In patients with low-grade steatosis, a higher fib-4 value was predicted by years of suboptimal ARV (per 1 year more, +0.6, 95% CI 0.1–1.2, p=0.032), while it was negatively predicted by time of exposure to DTG (per one month more, −0.02, 95% CI −0.03 to −0.01, p=0.035); in patients with more severe steatosis, a higher fib-4 was exclusively predicted by a longer time of suboptimal therapy (+0.3, 95% CI 0.1–0.6, p=0.039).
Conclusion: Although NAFLD remains a common finding in HIV-infected patients receiving ART, those on DTG + 3TC seemed less likely to develop this condition, thus suggesting a safer metabolic profile of the 2-drug regimen when compared to standard cART.

Patients' characteristics at baseline (N=60)

Risk factors for HIV, n (%) a) MSM b) Heterosexual c) IDUs	a) 26 (44%) b) 31 (52%) c) 2 (3.4)
CDC stage C, n (%)	6 (30%)
Years since HIV diagnosis, median (IQR)	13 (6;20)
Time on cART (yrs), median (IQR)	10 (5.8; 18.4)
Nadir CD4 + cell count (cells/mm3), median (IQR)	17 (47; 275)
Zenith viral load (log10 copies/mL), median (IQR)	5 % (4.26; 5.70)
Current ARV regimen, n (%) a) 2NRTI+ bPI b) 2NRTI + NNRTI c) 2NRTI + INI d) 3TC + DTG e) Other 2 drugs regimen f) Other	a) 4 (6.7) b) 8 (13.4) c) 22 (36.7) d) 14 (23.3) e) 10 (16.6) f) 2 (3.3)
Fib-4 value, median (IQR)	0.99 (0.78; 1.39)
Body Mass Index, median (IQR)	22.9 (20.8; 25.9)
Right hepatic lobe length (cm), median (IQR)	15 (14; 16.3)

PE9/22

Correlations between computerised and standard cognitive testing in persons with HIV and controls

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Purpose: Whilst computerised cognitive batteries offer shorter and potentially more accurate assessments of cognitive function, few studies have compared results of computerised and standard/traditional 'pen-and-paper' cognitive assessments. We investigated the correlation between cognitive function and agreement between classifications of cognitive impairment (CI) when measured via computerised and standard testing in people with HIV (PWH) and lifestyle-similar HIV-negative controls.
Method: PWH (≥18 years) and matched HIV-negative controls (≥50 years) enrolled in the POPPY study underwent both computerised (CogState, 6 domains) and standard (5 domains) cognitive batteries. Raw scores from both were converted into demographically-adjusted T-scores and used to define CI according to Frascati, global deficit score (GDS) and multivariate normative comparison (MNC) criteria. The correlation between the global T-scores in PWH and controls, separately, was assessed using the Spearman's rank correlation and their difference using the z-test after Fisher's transformation. The agreement between classifications of CI obtained from different batteries was assessed using the Cohen's κ.
Results: In 316 PWH (median age: 61 years, 89% male, 92% white, 97% with HIV-RNA≤50 copies/mL) and 110 controls (median age: 57 years, 68% male, 95% white), global T-scores were poorer in PWH than controls when measured with both the computerised (difference=-2.2, p<0.001) and the standard battery (difference=-2.0, p=0.004). The correlation between global T-scores was 0.53 (0.45–0.60) in PWH and 0.47 (0.31–0.60) in controls (p=0.48). The prevalence of CI in PWH was higher when assessed with the computerised battery and the agreement between the same classification of CI obtained from different batteries was fair in PWH and slight in HIV-negative controls, regardless of the criteria considered (Table).
Conclusion: We observed a moderate correlation in overall cognitive function assessed via computerised and standard batteries, which was similar in PWH and lifestyle-similar controls. Classifications of CI only showed fair agreement, indicating substantial intra-individual variation.

Prevalence and agreement (Cohen's κ) between classifications of CI obtained from computerised and standard cognitive batteries

	PWH (n=316)			HIV-negative (n=110)		
	Computerised n with CI (%)	Standard n with CI (%)	Cohen's κ (95% conf.int.)	Computerised n with CI (%)	Standard n with CI (%)	Cohen's κ (95% conf.int.)
Frascati	93 (29.5%)	72 (22.8%)	0.28 (0.16–0.39)	18 (16.4%)	17 (15.5%)	0.08 (−0.13–0.29)
GDS	102 (32.3%)	94 (29.7%)	0.32 (0.21–0.43)	20 (18.2%)	32 (29.1%)	0.21 (0.01–0.40)
MNC	38 (12.0%)	14 (4.4%)	0.30 (0.13–0.47)	11 (10.0%)	2 (1.8%)	0.13 (−0.13–0.38)

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PE9/23

Whole body MRI detects high prevalence of incidental findings in older HIV-1-infected patients participating in a randomised, controlled trial of maraviroc and/or metformin for non-alcoholic fatty liver disease

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Purpose: MAVMET is a randomised controlled 48-week trial of maraviroc and/or metformin for non-alcoholic fatty liver disease in HIV-1-infected participants aged≥35 years. The primary endpoint is the change over 48 weeks in the percentage of liver fat assessed by the magnetic resonance proton density imaging fat fraction. The change in visceral and organ adiposity are exploratory endpoints requiring whole body MRI(WB-MRI). All research WB-MRI scans undergo clinical review and are formally reported for incidental or unexpected adverse findings as per trial protocol.
Method: All scans were performed on a 3.0T Philips Ingenia system (Best, Netherlands). mDixon FatQuant sequences were used at 5 anatomical stations for coverage from the maxillary sinuses to the mid-thigh. Additional anatomical axial and coronal single-shot T2-weighted images were also obtained of the abdomen and pelvis.
Results: Baseline WB-MRI from 76/77 participants were included. Of these, 70(92%) were male; the median(IQR)[range] age was 53 years(48, 57)[35, 70] and median(IQR)[range] time on antiretroviral therapy was 12 years(7, 18)[1, 27]. All WB-MRI were reported within 2 weeks. Thirty-nine percent had≥1 incidental finding (Table 1); in 87% there was a single incidental finding. The most common incidental finding was of gallstones or gallbladder polyps in 7 participants; in 1 of these participants, atazanavir was changed to darunavir, after discussion with the referring clinician and participant. Three participants were fast tracked for further radiological and/or specialist review to exclude malignancy; no malignancies were diagnosed at baseline.
Conclusions: The prevalence of incidental findings on WB-MRI was much higher than expected. This emphasises, first, the importance of ensuring a rapid-reporting system for trials with imaging endpoints, in particular where whole body scans are performed. Second, that there may be a role for WB-MRI screening in an ageing population of HIV-infected patients especially as the sensitivity/specificity of WB-MRI continues to improve.

Table 1. Baseline incidental findings on WB-MRI

Organ System	Findings	Fast track to exclude malignancy, and subsequent diagnosis
Respiratory tract	Sinus abnormality (n=5); left upper paratracheal fatty tissue (n=1)	
Skin and soft tissues	Sebaceous cyst (n=1); inguinal lymph nodes (n=1)	
Musculoskeletal	lipoma (n=2)	
Bone and joint	Traumatic injury right humeral head (n=1)	
Upper GI tract	Distal oesophagus nodularity (n=1)*; splenomegaly (n=3); irregular hepatic contour (n=1); atrophic left lobe of liver (n=1)**; gallstones or gallbladder polyps (n=7); pancreas cyst (n=2); epigastric hernia (n=1); hepatic haemangiomas (n=1)	*hiatus hernia diagnosed at endoscopy **Atypical hepatic configuration, likely congenital diagnosed on further imaging
Renal tract	Bladder diverticulum (n=1); renal cysts (n=2); dilated left renal collecting system (n=1)	
Gynaecological	Bulky uterus (n=2); Bartholin's cyst (n=1); discrete breast mass (n=1)***	***biopsy confirmed benign fibroadenoma

PE9/24

An analysis of potential drug-drug interactions in an aging HIV cohort

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Purpose: The advent of antiretroviral drugs has transformed the treatment of HIV and has led to an increase in life expectancy of patients with HIV. Patients are therefore more likely to acquire comorbidities which require pharmacological management. This increased pill burden is likely to lead to an increase in potential drug-drug interactions (PDDIs) between medicines.
Method: The files of HIV patients aged over 50 (n=128) at Cork University Hospital (CUH) were examined to obtain demographic data, ART regimens and co-medications. Interactions were then screened for using the University of Liverpool interaction database and stratified according to severity and statistical analysis conducted using SPSS.
Results: 72.3% (94/128) of patients took at least one co-medication with 49.2% (63/128) of patients having at least one PDDI. A total of 23 category yellow, 81 category orange and 6 category red interactions were detected. Statins and Colecalciferol were found to contribute the most to PDDIs, leading to 19.1% and 17.3% of all PDDIs respectively. Cobicistat (29.4%) and integrase inhibitors (32.2%) were found to be the ART agents which lead to the highest numbers of PDDIs. A correlation was found to exist between the total number of PDDIs and the number of co-medications which they took ($R=0.621$, $p=<0.0001$) and between an increasing number of PDDIs and a decreased CD4 count ($R=-0.207$ $p=0.019$) while age and gender were found not influence on the number of PDDIs to a statistically significant degree.
Conclusion: Owing to the complexity of the pharmacological interactions taking place and the necessity to prescribe for co-morbid conditions, it is almost inevitable that some of these medications will interact. It is therefore advisable to utilise an interaction checker database as well as careful, consistent clinical monitoring to optimise patient outcome.

PE9/25

A standardized comparison of cardiovascular risk factor prevalence between people living with HIV and general population in Spain

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Purpose: The prevalence of traditional cardiovascular (CV) risk factors has been found higher in people living with HIV (PLWH), as compared to general population. However the role of age and sex distribution of HIV patients is rarely taken into account. We aim to compare the general Spanish population prevalence of CV risk factors with that of Spanish PLWH, after standardizing for referent age and sex population distributions.
Method: We used 5,680 PLWH with complete data from the VACH Spanish cohort and the general population DARIOS cohort, a pooled analysis of 11 population surveys from 10 Spanish communities (n=28,342) (http://darios.

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imim.es/). The prevalence of diabetes, blood pressure, body mass index (BMI), total and high-density (HDL) cholesterol, and smoking was compared in the age group 35 to 74 years. Prevalence rates were standardized by the direct method by sex and 10-year age groups with the European standard populations. All participants signed their informed consent.

Results: In Darios and VACH, the proportion of males was 46.5% and 80.4 % (p-value<0.001), respectively and mean age 53.5 (11.1) and 42.5 (7.4) (p-value<0.001), respectively. Standardized BMI and lipid profile are significantly better in PLWH except low HDL and triglycerides which are significantly higher in PLWH. Blood pressure profile is better in male PLWH male but similar between HIV and general female populations. Only female PLWH are heavier smokers than their general population counterparts (Table).

Conclusion: After appropriate standardization to correct the effect of age and sex differences between PLWH and the general population, we found that the prevalence of traditional CV risk factors are similar. However, PLWH have a higher frequency of diabetes, lower HDL levels and higher levels of triglycerides in both sexes, more female smokers, and higher total cholesterol/HDL cholesterol ratio in females

Comparison of cardiovascular risk factor standardized prevalence between MALE PLWH and general population

	General population (N=13,193)	Male PLWH (N=4,566)	p-value
Body mass index	28.1 (28–28.1)	24.3 (24.2–24.5)	<0.001
Diabetes (%)	15.4% (14.8%–16.0%)	21.1% (19.6%–22.6%)	<0.001
Hypertension (%)	29.0% (28.2%–29.7%)	23.7% (22.2%–25.2%)	<0.001
Total cholesterol (mg/dL)	214.2 (213.6–214.9)	189.1 (187–191.1)	<0.001
LDL cholesterol (mg/dL)	139 (138.4–139.6)	114 (112.2–115.8)	<0.001
HDL cholesterol (mg/dL)	48.5 (48.3–48.6)	44.7 (44–45.4)	<0.001
Cholesterol/HDL ratio	4.6 (4.6–4.6)	4.6 (4.5–4.6)	0.331
Triglycerides (mg/dL)	141.1 (139.5–142.7)	172.3 (167.3–177.3)	<0.001
Smoking (%)	33.6% (32.8%–34.4%)	34.2% (32.7%–35.7%)	0.488

Comparison of cardiovascular risk factor standardized prevalence between FEMALE PLWH and general population

	General population (N=15,149)	Female PLWH (N=1,114)	p-value
Body mass index	27.5 (27.4–27.6)	24.3 (23.9–24.8)	<0.001
Diabetes	10.6% (10.1%–11.1%)	19.5% (16.4%–22.7%)	<0.001
Hypertension	27.4% (26.7%–28.0%)	25.9% (22.6%–29.2%)	0.392
Total cholesterol mg/dL	213.9 (213.3–214.5)	198.1 (193.2–203)	<0.001
LDL cholesterol mg/dL	135.8 (135.2–136.3)	120.4 (116.3–124.5)	<0.001
HDL cholesterol mg/dL	57.2 (57–57.4)	51.9 (50.4–53.3)	<0.001
Cholesterol/HDL ratio	3.9 (3.9–3.9)	4.1 (4.0–4.2)	0.001
Triglycerides mg/dL	107.4 (106.5–108.4)	153.6 (146–161.3)	<0.001
Smoking	21.2% (20.6%–21.9%)	28.4% (25.8%–31.0%)	<0.001

PE9/26

Subclinical atherosclerosis burden by ultrasound in carotid and femoral territories in HIV subjects: relationships with HIV and non-HIV related factors

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Purpose: The study aims to describe the prevalence of subclinical atherosclerosis in different vascular territories and analyze the (HIV and non-HIV) factors associated with an increased risk of presenting the disease in a cohort of HIV-1 infected subjects

Method: Cross-sectional (with partial retrospective data collection) analysis of the prevalence of atherosclerotic plaques in four vascular territories. Bilateral carotid and femoral regions were explored by US to determine the number of plaques and areas affected. Patients must be chronically infected with HIV-1 with no history of CVD at the time of HIV diagnosis. In this interim analysis, we seek for correlation (univariate analysis) of HIV and non-HIV related factors with the presence of atheromatous plaques

Results: 388 patients were included at the time of this analysis. Baseline characteristics are shown in table 1. A total of 166 subjects (47.2%) had atherosclerotic plaques in at least one vascular site. Subclinical disease was more frequent in the femoral vascular site (38.1%) than in the carotid arteries (18.3%).

In the univariate analysis presence of atherosclerotic plaques correlated positively with age, time with HIV, current CD8 (count and percentage), Stage 3 CDC (versus stage 1), Time on ARV treatment and CVR score (Regicor and D: A:D equations). Odds ratios (95% CI) are shown in table 2.

Conclusion: We have seen a high prevalence of subclinical atherosclerosis in our cohort of HIV-1 infected patients. Among HIV related factors, time with HIV, time on ART, advanced HIV disease, and immune activation have been correlated with the presence of atherosclerotic plaques. Vascular ultrasound may be a promising method to improve the early detection of cardiovascular disease risk in HIV patients.

Table 1. Baseline characteristics

Variable	N (388)
Age, median years (Q1,Q3)	50.3 (40.8, 55.7)
Male gender	83.5%
Time since HIV diagnosis, median months (Q1, Q3)	125.5 (61.6, 229.4)
Time on ARV treatment, median years (Q1, Q3)	8.8 (4.2, 11.0)
Stage 3 CDC	24.2%
Current CD4 count (cells/μL), mean (SD)	758 (337)
Current CD4/CD8 ratio, mean (SD)	0.9 (0.5)

Table 2. Factors correlated with the presence of atherosclerotic plaques

Variable	OR	95% CI
Age (years)	1.128	1.097–1.161
Time from HIV diagnosis (months)	1.009	1.007–1.012
Current CD8 count (cells/μL)	1.001	1.000–1.001
Current CD8 (%)	1.023	1.004–1.043
Stage 3 CDC (vs. stage 1)	2.522	1.430–4.450
Time on ARV treatment (years)	1.177	1.133–1.244
REGICOR CVR score	1.628	1.410–1.879
DAD equation: High CVR (vs. Low)	8.230	1.632–41.497

PE9/27

Subcutaneous adipose tissue modifications induced by a switch to dual raltegravir-maraviroc therapy in controlled HIV-infected patients: a sub-study of the ANRS-ROCnRAL157 clinical trial

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Objectives: Integrase inhibitors including raltegravir have been associated with weight/fat gain. The mechanisms involved remain unknown. The ROCnRAL study enrolled suppressed HIV-infected patients with central fat accumulation switched to maraviroc/raltegravir. Herein, we analyzed the

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effects of this switch on metabolic modifications and subcutaneous abdominal adipose tissue(scAT) transcriptome.
Material and methods: In 8 patients, paired scAT samples, withdrawn by needle aspiration at inclusion and the end of the study, were available. We extracted total mRNA and examined the transcriptomic profile using Illumina microarrays, as well as scAT adipocyte size.
Results: All patients were male, aged 55 + /-3y (mean+/-SD), BMI=26.1 kg/m^2, Waist circumference=94.6 cm, HOMA-IR=2.4. After a mean follow-up of 25 weeks, BMI increased to 26.4 kg/m^2 (p=0.01), HOMA-IR to 6.7 (p=0.05) and adipocyte size to 113 microns (p=0.09). In the 16 paired samples, we identified 16094 variants: 458 genes were up-regulated with an FDR of 10.6–1.1 while 244 genes were down-regulated with an FDR of 0.66–0.9. We further examined the functional changes that characterized this transcriptomic profile using KEGG data base. The most enriched function (19.4%) was ubiquitin-mediated proteolysis. Functions related to apoptosis were also enriched. Moreover, the main impoverished functions (29.7%) were related to ribosomes, followed by functions related to cell adhesion, grouping genes involved into immune cell recognition (27%), and functions involved into immune-related diseases (10.8%) suggesting a major reduction of scAT immune function/activation. While IL25, IL7R, CD247, CD3D and CD58 gene expression was decreased, that of IL10 and IL18 was increased.
Conclusion: In eight controlled HIV-infected patients with central fat accumulation switching to raltegravir/maraviroc resulted in major modification of adipocyte size and transcriptomic pattern. Overall, function related to protein degradation and apoptosis were increased and to protein synthesis decreased. Immune-related genes were mainly decreased. Further investigation is required to examine the link between these modifications and raltegravir-associated weight/fat gain.

PE9/28

Results of 10 year experience of a specialist clinic for people living with HIV over 50 at Chelsea and Westminster Hospital

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Purpose: Life expectancy of people living with HIV (PLWH) has increased since the introduction of combination antiretroviral therapy (cART). PLWH are more likely to be on polypharmacy and might develop comorbidities more frequently that people without HIV, according to cohort study data. In order to establish a holistic approach and to improve quality of care, a multidisciplinary clinic for PLWH over the age of 50 was established in 2009 at Chelsea and Westminster Hospital. We herein describe our service evaluation after 10 years of activity.
Method: We performed a retrospective cross-sectional analysis of clinical records from patients attending the Over 50 clinic between January 2009 and December 2018. We aimed at estimating the prevalence of major non-infectious comorbidities, polypharmacy [≥5 medications] and multi-morbidity [≥2 non-HIV related comorbidities].
Results: 744 among patients who attended the clinic during this period were considered: 92.9% were male; mean age 56 ± 5 years, 87.2% were MSM; 97.7% were on cART and 96.1% had undetectable HIV-RNA at the time of evaluation. Patients referred by HIV specialists or general practitioners attended the clinic. The most common comorbidities diagnosed were dyslipidaemia (50.1%), hypertension (21.5%), mental-health disorders (depression and/or anxiety disorders, 15.7%), osteoporosis (12.2%), obesity (11.9%), chronic kidney disease (7.5%), hypogonadism (6.9%) and diabetes (5.8%). Low vitamin D levels were found in 428/690 (62%) patients (184/428, 43% deficiency [< 40 mmol/L] and 244/428 57% insufficiency [40–70 mmol/L]. 31/614 (5%) patients presented an abnormal PSA. The overall prevalence of polypharmacy and multi-morbidity was 46.6% and 69.3%, respectively.
Conclusion: Results of our audit indicate a high prevalence of polypharmacy and multi-morbidity in PLWH over 50 years of age. Over 50 care pathways for PLWH should be widespread in order to improve comorbidities prevention, diagnosis and management. Also collaboration with general practitioners could substantially improve the clinical outcome.

PE9/29

Discordance in diagnosis of osteoporosis in HIV-infected patients: prevalence, characteristics, and impact on FRAX equation

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Purpose: We examined the prevalence and characteristics of people living with HIV (PLHIV) with spine-hip bone mineral density (BMD) measurement discordance.
Method: Cross-sectional study of consecutive PLHIV included after whole-body dual X-ray absorptiometry (DXA) scan. BMD categories of osteoporosis, osteopenia, and normal bone mass were defined as T-scores≤-2.5, - 2.5 to 1.0, and>-1.0, respectively. Discordance was defined as different BMD categories at lumbar spine (LS) and femoral neck (FN): major discordance in the case of osteoporosis versus normal BMD, and minor discordance in the case of osteoporosis versus osteopenia, or osteopenia versus normal BMD.
Results: Of a total of 208 PLHIV (mean 46 years, women 23%), 91 (44%) presented BMD discordance (major discordance, 2%; minor discordance, 42%); similar values were observed in individuals aged under and over 50. Discordance due to lower LS-BMD was more frequent, and 81% (30/37) of individuals with LS osteoporosis had discordance. Conversely, of 10 cases of FN osteoporosis, 43% were missed from measurements at the LS. Individuals with BMD discordance had distinctive characteristics: PLHIV with lower FN-BMD had a significantly higher prevalence of smoking (p=0.01), lipodystrophy (p=0.03) and HCV coinfection (p=0.04), and longer duration of HIV infection (p=0.04) and antiretroviral therapy (p=0.01) than individuals with lower LS-BMD. Moreover, the risk of major osteoporotic and hip fracture was significantly higher in PLHIV with lower FN-BMD versus lower LS-BMD (+36%, p=0.04, and + 135%, p<0.01, respectively) (Figure 1).
Conclusion: BMD measurement discordance was observed in 44% of PLHIV, largely due to lower LS-BMD. BMD measurement at a single site underestimates the prevalence of osteoporosis, as over 80% of cases of LS osteoporosis were not reflected by FN-BMD. HIV-related factors contribute to lower FN-BMD and in part, to discordance. Fracture risk estimation by FRAX was higher for PLHIV with discordant results.

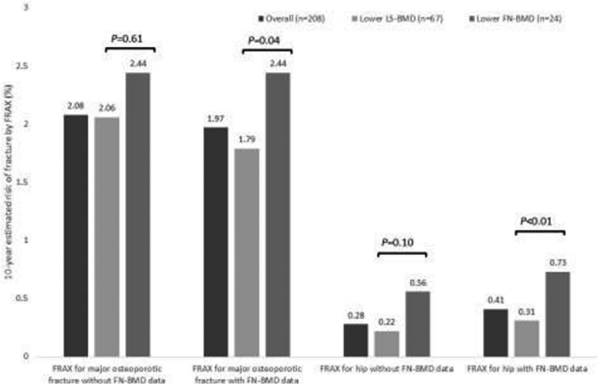


Figure 1. Fracture risk in discordant individuals according to the site of lower bone mineral density

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PE9/30

CD4/CD8 ratio is a better indicator of acute phase inflammation than absolute CD4 count during virally-suppressed HIV infection

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Purpose: Life expectancy of treated HIV infection approaches that of the general population. Persistent increased mortality and non-AIDS comorbidity is driven by residual immune activation/ inflammation. Absolute CD4 count (CD4 count) and CD4/CD8 ratio (CD4/CD8) both correlate with poorer clinical outcomes in prospective cohorts. We sought to identify which parameter best correlates with biomarkers of acute phase immune activation.
Method: We enrolled 83 consenting ART-treated HIV-positive participants with viral load suppression and diverse CD4 count and CD4/CD8 responses from a tertiary care HIV site in Toronto, Canada. In a cross-sectional study, blood plasma and peripheral blood mononuclear cells were isolated and stored for batched measurement of soluble immune activation markers by ELISA (CRP, TNF, IFNγ, sCD14, D-Dimer, I-FABP, MCP-1, VCAM, ICAM), and co-expression of HLA-DR and CD38 on CD8 T cells (CD8 activation). Multiple log-linear regression models adjusted for age, sex, duration of ART, and recent infection/ vaccination were used to estimate the association of each outcome with: (1) CD4 count, and (2) CD4/CD8.
Results: CD4 count and CD4/CD8 were strongly correlated (0.76, $p<0.0001$). A 0.1 increase in CD4/CD8 was associated with a 3% decrease in plasma TNF ($p<0.01$) and a 5% decrease in plasma CRP ($p=0.05$). Higher CD4 count (per 100 cells/mm^3) was associated with a 2% decrease in sCD14 ($p=0.02$) while no association was observed with plasma TNF or CRP levels. Neither CD4 count nor CD4/CD8 were associated with CD8 activation.
Conclusion: CD4/CD8 and CD4 count are strongly linked, but CD4/CD8 correlates more strongly with two soluble markers of acute phase immune activation (TNF, CRP). CD4 count was more strongly associated with a marker of a distinct immune activation pathway (sCD14; TLR4 activation by LPS). Novel therapies to reduce non-AIDS comorbidity by targeting residual immune activation pathways warrant exploration in the context of persistently low CD4/CD8.

PE9/31

Immune activation and chronic inflammation: is there an additional effect of HIV in a geriatric population?

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Purpose: it is known that aging is intrinsically associated with hyper-inflammation and immune system deterioration, the relative impact of chronic HIV infection on such inflammatory and immune activation has not yet been studied on a aging HIV-infected population. The objectives were to assess blood markers of immune activation and inflammation, using ultrasensitive techniques (Luminex & Simoa), in HIV-infected patients≥75 years with no or 1 comorbidity, in comparison with age adjusted HIV-uninfected individuals aged≥75 years (control group), to identify whether biomarkers were associated with comorbidities.
Method: 28 inflammatory and immune biomarkers were performed in a centralized laboratory. Wilcoxon nonparametric tests were used to compare the levels of each biomarkers between control and HIV+ groups; logistic regression to identify biomarkers associated to comorbidity in the HIV+ group and principal component analysis (PCA) to determine clusters associated with a group or a comorbidity.
Results: 111 HIV+ subjects of whom 39 without comorbidity (median age 81 years (IQR 78–84), median HIV duration and ART of 18.2 (12–23) and 15.9 (9–19) years, respectively, were included from the Dat'AIDS cohort and compared to a control group of 63 HIV-negative subjects (median age of 83.4 years (IQR 78–89)). In the HIV+ group, 4 biomarkers were associated with comorbidity: MCP-1 OR(CI95%) 0.78(0.68–0.91), NFL 1.42(1.08–1.87), Neopterin 1.99(1.33–2.97) and sCD14 1.01(1.00–1.02). Six biomarkers (IL-1B, IL-7, IL-18, Neopterin, sCD14 and FABP) were significantly higher in the HIV+ group compared to the control group, 11 biomarkers (MPO, IL-1RA, TNFR1, IFN gamma, MCP-1, TNF-R2, IL-22, usCRP, fibrinogen IL-6 and NFL) were lower. Despite those differences, PCA analysis did reveal no clustering.
Conclusion: No specific inflammatory or immune profile has been identified in HIV+ group according to comorbidity status. In this selected geriatric HIV population, HIV infection does not seem to have an additional impact on age-related inflammation and immune disorder.

PE9/32

Trends in cardiovascular risk factors and estimated 10-year cardiovascular risk score in a spanish cohort of PLWH: 2010–2018

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Purpose: The aim of this study was to describe cardiovascular risks factors changes during the years 2010–2018 in a cohort of PLWH
Method: Since 2010, adult HIV-infected patients attended in our hospital (Hospital Universitario Son Espases, Palma de Mallorca, Spain) have underwent cardiovascular risk estimation using the Regicor and Framingham risk scores at least annually. Additional cardiovascular risk factors including creatinine clearance, urine proteins, weight, body mass index, and smoking were also prospectively collected using proprietary software (eVIHa).
Results: At the end of 2018, 2030 patients were actively followed up in our centre. Mean age was 48 years and 76.6% were males. Almost all were receiving antiretroviral treatment, being over 90% with HIV viral load<50 copies/ul.

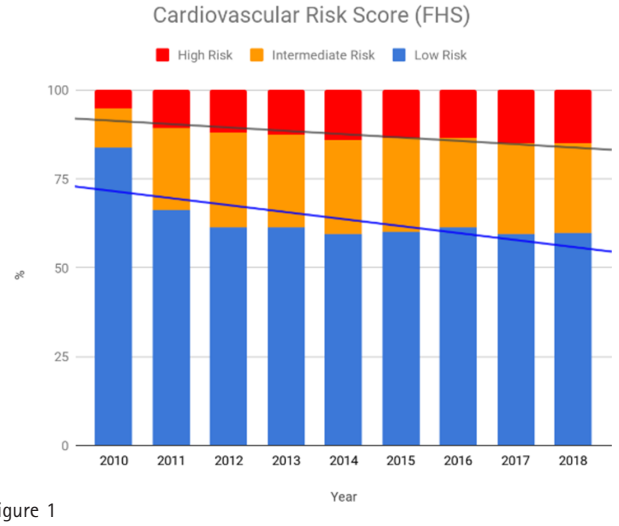


Figure 1

Despite a modest reduction in smoking prevalence, 10-Year Cardiovascular risk estimated in our cohort tended to worsen over the years with 15% of the patients being classified as high risk and 25% as intermediate. Prevalence of

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Cadiovascular risk factors and FRS: 2010–2018

	2010	2011	2012	2013	2014	2015	2016	2017	2018
n	1676	1715	1746	1807	1834	1852	1904	1952	2030
Sex (% male)	73.72	73.93	75.09	75.43	75.47	75.96	76.37	76.49	76.60
Receiving HAART (%)	88.72	89.74	89.63	90.20	92.20	93.79	95.54	97.39	97.54
Patients without comorbidities (%)	73.32	68.22	65.68	63.85	61.48	60.31	57.39	56.63	56.62
Smoking (%)	63.84	61.85	60.62	59.79	59.95	60.96	60.61	58.51	55.89
BMI>30 kg/m^2 (%)	8.47	10.44	11	11.27	11.07	11.46	12.13	13.20	14.20
ClCr<60 mL/min (%)	2.35	2.36	2.40	1.66	2.75	2.78	3.62	3.64	3.87
FRS 10–20% (%)	10.95	22.98	26.61	25.86	26.58	26.34	25.19	25.44	25.02
FRS>20% (%)	5.31	10.70	12.07	12.68	13.99	13.47	13.51	15.14	15.15

obesity, decreased creatinine clearance and comorbidities presented all a steady increase.
Conclusion: Estimated cardiovascular risk increased during follow up despite lower smoking prevalence. Moreover, the prevalence of additional risk factors such as obesity increased and should be also considered

PE9/33

Prevalence of depression and associated psychosocial factors among HIV positive patients attending ART clinic at Gulu Regional Referral Hospital

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Purpose: Mental health is a major problem in Uganda contributing 13% to the national disease burden. Depression is one of the commonest psychiatric complications of HIV/AIDS and is associated with poor HIV-related outcomes including poor ART adherence, treatment failure, HIV progression and death. Despite how common depression is among HIV positive patients; it is commonly missed. Prompt diagnosis and treatment of this comorbidity is critically important in HIV/AIDS management.
Aim: To determine the prevalence of depression and associated psychosocial factors among HIV positive patients attending the ART clinic at Gulu Regional Referral Hospital.
Methods: In this cross sectional study, 385 HIV positive patients attending ART clinic at Gulu Regional Referral Hospital were enrolled between February and May 2016. Data was collected using the Beck Depression Inventory (BDI) questionnaire. Descriptive and analytical statistics were performed using data base software computer package SPSS 16.0.
Results: The prevalence of depression was 17.1% (66/385). Of the total enrolled, 3.6% (14/385) had been diagnosed and started on treatment for depression. Without the depression screening questionnaire, 13.5% (52/385) of patients with depression would have been missed. For those who screened positive for depression, demographics are summarized in (Table 1)
Symptoms associated with depression included; experience pessimism, loss of pleasure, guilty feeling, self-criticalness, suicidal thoughts, irritability, concentration difficulty, loss of interest in sex, changes in sleep pattern, changes in appetite ($p<0.05$) (Table 2)
Conclusions: We demonstrated that depression is common amongst HIV positive patients, but is commonly missed. Associated symptoms included; experience pessimism, loss of pleasure, guilty feeling, self-criticalness, suicidal thoughts, irritability, concentration difficulty, loss of interest in sex, changes in sleep pattern, changes in appetite. HIV positive patients should routinely be screened for depression using validated depression screening tools for prompt referral.

Table 1. Socio-demographic characteristics of HIV positive patients who screened positive for depression. (n=66).

Characteristics	CATEGORY	FREQUENCY	PERCENTAGE
Age	12–19 20–29 30–39 40–49 50–54	5 25 19 10 7	7.6 37.9 28.8 15.1 10.6
Sex	Male Female	12 54	18.2 81.8
Marital status	Married/ cohabiting Divorced/ separated Single Widowed Not applicable	31 17 6 10 2	47.0 25.8 9.1 15.2 3.0
Occupation	House wife Peasant farmer Student/pupil Business Teacher	9 26 5 24 2	13.6 39.4 7.6 36.4 3.0
Religion	Catholic Protestant Muslim Born again	41 16 4 5	62.1 24.2 6.1 7.6
Education level	Primary Secondary Tertiary None	29 24 5 8	43.9 36.4 7.6 12.1
Number of Children	0–5 6–10	54 12	81.8 18.2
Tribe	Acholi Langi Muganda Lugbara Samya Munyankole Mugishu	55 6 1 1 1 1 1	83.3 9.1 1.5 1.5 1.5 1.5 1.5

Table 2. Profile of symptoms and psychosocial factors amongst HIV positive patients (n=385).

Symptom	Frequency	Percentage	p-value	Odds ratio
Experience Pessimism	85	22.1%	0.023	5.297
Loss of pleasure	121	31.4%	0.032	4.397
Self-criticalness	121	31.4%	0.003	7.776
Suicidal thoughts	57	14.8%	0.025	6.287
Irritability	108	28.1%	0.011	5.817
Concentration difficulty	69	17.9%	0.022	5.110
Los of interest in sex	203	52.7%	0.019	10.427
Changes in sleep pattern	115	29.9%	0.025	4.191
Changes in appetite	116	30.1%	0.002	8.037

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PE9/34

Potentially inappropriate medications in older adults with HIV in the region of Madrid, Spain

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Objective: Age-related comorbidities, physiological changes, and care by multiple providers predispose older (≥ 65 years) people living with HIV (O-PLWH) to inappropriate prescribing. We assessed the prevalence of potentially inappropriate medication (PIM) among O-PLWH in the region of Madrid.
Methods: We analyzed the dispensation registry of community and hospital pharmacies from the Madrid Regional Health Service (SERMAS) between January 1 and June 30, 2017, looking specifically at PIMs according to the 2019 Beers Criteria (J Am Geriatr Soc 2019; 67: 674–694). The SERMAS registry permits access to demographics and all prescription drugs (antiretrovirals [ARVs] and non-antiretroviral medications [co-medications]). Co-medications were classified according to the Anatomical Therapeutic Chemical (ATC) Classification System.
Results: During the study period, 6,636,451 different individuals received medications. Among them, 22,945 were receiving ARVs, of those 1,292 were O-PLWH. Overall, 1,135 (87.8%) O-PLWH were taking at least one co-medication and polypharmacy (≥ 5 co-medications) was observed in 852 (65.9%). A PIM was identified in 482 (37.3%) O-PLWH. Factors independently associated with PIM were polypharmacy (aOR 7.08 [95% CI: 5.16–9.72]) and female sex (aOR 1.75 [95% CI: 1.30–2.35]). The distribution of PIMs according to ATC drug classes were nervous system drugs (N=369 [28.6%]), musculoskeletal system drugs (N=140 [10.8%]), gastrointestinal and metabolism drugs (N=72 [5.6%]), cardiovascular drugs (N=61 [4.7%]), respiratory system drugs (N=13 [1.0%]), antineoplastic and immunomodulating drugs (N=10 [0.8%]), and systemic anti-infectives (N=2 [0.2%]). Five drugs accounted for 84.8% of the 482 O-PLWH with PIMs: lorazepam (38.2%), ibuprofen (18.0%), diazepam (10.2%), metoclopramide (9.9%), and zolpidem (8.5%).
Conclusions: The results of this population-based study show that prescription of PIMs is highly prevalent in O-PLWH. Consistent with data in uninfected elderly, the most frequently observed PIMs were benzodiazepines and NSAIDs (Eur J Clin Pharmacol 2018; 74:679–700). Targeted interventions are warranted to reduce inappropriate prescribing and polypharmacy in this vulnerable population.

PE9/35

Impact of the reproductive/hormonal status on weight, fat and insulin resistance in HIV-infected women switching from a PI regimen to dual raltegravir-etravirine therapy: results from the ANRS163-ETRAL trial at 48 and 96 weeks

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Objectives: The ANRS-163 ETRAL trial has previously shown the viral efficiency of dual raltegravir/etravirine therapy in 165 PI-controlled ageing individuals followed up to 96w (Katlama, JAC, 2019). While lipid and bone parameters improved, patients gained weight, trunk and limb fat and increased insulin resistance (HOMA-IR). We evaluated whether these modifications were dependent upon sex and the reproductive/menopausal status.
Methods: We recorded the menopausal status of the 48 women. Fat mass and bone mineral density were evaluated by DEXA at D0/W48/W96. In 40 women, the anti-Müllerian hormone (AMH Gen II ELISA) level evaluated ovarian reserve. Baseline values and percent changes from baseline were compared between groups using Mann-Whitney and Kruskall-Wallis tests.
Results: BMI, total, trunk and limb fat mass similarly increased in men (n=117) and women (n=48) and lipid parameters improved similarly (increased HDL, decreased triglycerides) at W48/W96. HOMA-IR, similar at baseline, increased in men at W48 and W96 and in women only at W48.
Twelve women (30%, 46y) had reproductive activity with ovarian reserve (group 1, AMH>0.06 ng/mL), 6 (15%, 47y) were premenopausal (group 2, no ovarian reserve, AMH<0.02 ng/mL) and 22 (55%, 54y) post-menopausal (group 3). At inclusion, BMI and fat repartition were similar in the 3 groups. At W48 and W96, BMI, total and trunk fat increased in groups 2/3 but not in group 1. Moreover, HOMA-IR tended to improve in group 1 but worsened in groups 2/3. The evolution of limb fat and bone parameters was not different between the three groups.
Conclusion: Women with reproductive activity and ovarian reserve were protected from raltegravir/etravirine-induced weight gain and associated insulin resistance while pre/post-menopausal women increased weight, fat and insulin resistance as did men. A role for the estrogen/androgen status should be considered in the impact of antiretroviral drugs on weight gain.

This study was granted by ANRS/MSD:

Table: Comparison of BMI, total fat and HOMA-IR according to sex and to reproductive/menopausal status in the ANRS163-ETRAL study

		n	Baseline	% change at W48	% change at W96	BL vs W48	BL vs W96
BMI kg/m²	Men	117	24.1(22.5-25.7)	1.5(-1.3-5.3)	2.8(0-6.5)	0.000	0.000
	Women	48	24.9(22.5-29.2)	1.6(-1.9-4.6)	1.8(-1.8-6.8)	0.043	0.010
	P-value		0.094	0.758	0.510		
Total fat kg	Men	71	16.7(11.9-22)	1.8(-2.7-21.6)	11.8(0-22.5)	0.001	0.000
	Women	22	25.7(17-38.1)	6.4(0.6-18.1)	6.8(-2.5-21.9)	0.025	0.023
	P-value		0.000	0.539	0.492		
HOMA-IR	Men	110	1.7(1.2-2.4)	1.6(-17.2-43.6)	15.2(-12.8-59.4)	0.017	0.000
	Women	46	1.9(1.2-3.2)	13.7(-28.7-80.9)	3.5(-25.4-32.4)	0.025	0.731
	P-value		0.450	0.442	0.074		
BMI kg/m²	Reproductive activity	12	27.7(23.6-34.1)	-1(-4.6-1.6)	-1(-5.5-2.6)	0.333	0.594
	Premenopausal/Postmenopausal	28	24.9(22.5-27.7)	2.7(0-9.2)	2.3(0-6.9)	0.009	0.005
	P-value		0.302	0.018	0.074		
Total fat kg	Reproductive activity	5	36.5(30.6-39.3)	0.6(-6-1.5)	-2.6(-8.9--2.1)	0.893	0.500
	Premenopausal/Postmenopausal	12	23.9(17-36.3)	16.6(4.5-22.2)	17.3(2.8-28.2)	0.008	0.012
	P-value		0.343	0.020	0.035		
HOMA-IR	Reproductive activity	12	3(1.8-4)	-42.6(-61--0.1)	-40.2(-54.4--1.6)	0.239	0.084
	Premenopausal/Postmenopausal	27	1.7(1-2.8)	40.8(-8.6-87.7)	16.8(-6.2-50.3)	0.002	0.022
	P-value		0.051	0.003	0.004		

Comparison of BMI, total fat and HOMA-IR according to sex and to reproductive/menopausal status

PE9/36

Non-communicable disease screening and prevention in adolescents and youth living with HIV in the context of rapid urbanization in South Africa

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Purpose: Non-communicable diseases (NCDs) are projected to become the leading cause of death in sub-Saharan Africa by 2030. HIV-positive individuals face elevated risk of NCDs, due to HIV-infection and complications of long-term anti-retroviral therapy (ART). Most risk factors for adult disease start during adolescence. We set out to investigate the integration of NCD risk screening and prevention in management of adolescents and youth living with HIV (AYLHIV) receiving ART.
Method: We reviewed medical records of 491 AYLHIV across nine primary care facilities in Cape Town from November 2018- March 2019. We collected information on HIV management and care, existent NCDs, NCD risk and any documented NCD-related health promotion.
Results: The median participant age was 20 years (IQR: 14- 23) and the median duration on ART was three years (IQR: 1.1–8.9). The majority were virally suppressed (52%) and on first line ART regimens (78%).For those with a reported co-morbidity, there was documented history of substance use (3%), mental disorders (4%) and chronic respiratory diseases (4%). At least 13% had a documented and treated HIV opportunistic infection or ART-related condition. Of those with documented anthropometrics (62%), 48% were overweight or obese. Only 59% had a documented blood pressure measurement. For 6% with documented family history: it was either tuberculosis (71%), diabetes (14%), alcoholism or high blood pressure (7%). Nineteen percent had a documented health promoting intervention, ranging

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Cross-sectional characteristics of 491 Adolescents and Youth living with HIV receiving ART in primary care

Characteristic		Data collected (N=491)	Median (IQR) or Frequency (%)
Current ART regimen:	Age at folder review		20 (14–23)
	Age at ART initiation	473 (96%)	18 (6 - 21)
	CD4 count in cells/mm^3	395 (80%)	489 (355—690)
	Viral suppression: vL<20 copies/mL	369 (75%)	256 (52%)
	First line: Abacavir+ Lamivudine+ Efavirenz (ABC, 3TC, EFV)		84 (17%)
	Tenofovir+ Emtricitabine+ Efavirenz (TDF, FTC, EFV)		298 (61%)
	Second line: Abacavir+ Lamivudine+ Lopinavir/ritonavir (ABC, 3TC, LPV/r)		39 (8%)
	Zidovudine+ Lamivudine+ Lopinavir/ ritonavir (AZT, 3TC, LPV/r)		29 (6%)
	Other regimens		40 (8%)

from alcohol or substance abuse (17%); healthy weight or diet (13%) and mental health counselling (14%).

Conclusion: Our results highlight NCD risk in AYLHIV among those measured and recorded. The true prevalence of these risk factors is uncertain and would be important focus for further investigation. Poor documentation of NCD risk-factors for the majority of participants demonstrates a missed opportunity for detecting comorbidity and NCD risk in primary care; and for early intervention in AYLHIV.

Physical Assessments Measured and Recorded for 491 Adolescents and Youth living with HIV on ART in Primary Health Care

Characteristic		Median (IQR) or Frequency (%)
Body Mass Index in kg/m^2 : n=305 (62%)	Underweight (BMI<18.5 kg/m^2)	30 (10%)
	Normal weight (BMI 18.5- 25 kg/m$^{2)}$	129 (42%)
	Overweight (BMI 25- 30 kg/m^2)	80 (26%)
	Obese (BMI>30 kg/m $^{2)}$	66 (22%)
Blood Pressure in mmHg: Systolic and Diastolic Blood Pressure (SBP, DBP) n=289 (59%)	Normal: SBP<130 & DBP<85	210 (73%)
	High normal: SBP 130–139 or DBP 85–89	41 (14%)
	Mild hypertension: SBP 140–159 or DBP 90- 99	35 (12%)
	Moderate hypertension: SBP 160–179 or DBP 100- 109	3 (1%)
Heart rate in beats per minute: n=224 (46%)		82 (74—94)

PE9/37

Age- and sex-related differences in concomitant diseases and use of co-medication in patients with treated HIV-infection in Germany

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Demographic ageing of HIV-infected populations poses new challenges to physicians. Advancing age is associated with (multiple) chronic diseases and need for co-medication.

BESIDE was a cross-sectional study evaluating the prevalence of concomitant diseases and co-medication including OTC in PLWH on ART from 2016–2017. Regional distribution of study sites (n=20), consecutive recruitment and age-stratified sampling ensured a representative sample of the PLWH population in Germany.

453 PLWH were enrolled: female 22%, median age 46 years (y), median time living with HIV 9y, CDC C 15%, median CD4 count 650 cells/μL.

Among the top comorbidities, Vitamin D deficiency (29% overall) and depressive episodes (28% overall) were reported across age groups. The third differed: In younger PLWH, acute respiratory infections (< 30y, 11%) and gastro-esophageal reflux disease (30–39y, 8%) were most prevalent, while older PLWH increasingly reported hypertension (40–49y, 12%; >60y, 41%).

Women more often (f/m, Δ >5%) suffered from nutritional anemias (11%/4%), other nutritional deficiencies (39%/28%), bone density/structure disorders (9%/1%) and thyroid gland disorders (10%/4%). Conversely, metabolic disorders (10%/21%), sexually transmissible infections (2%/9%), polyneuropathies/peripheral nervous system disorders (1%/7%) and dorsopathies (2%/8%) were more common in men.

Most common drugs used across all ages were vitamin supplements (32% overall). Followed by anti-inflammatory/antirheumatic agents (16%), except>60y where antithrombotic agents were more frequent (30%). Additionally, younger patients received vaccines (< 30y, 9%) and used psychoactive drugs (30–39y, 10%; 40–49y, 12%), whereas in older patients renin-angiotensin system agents (50–59y, 21%; >60y, 30%) ranked higher.

Women more commonly used (f/m, Δ >5%) antianemia preparations (14%/6%), vitamins (38%/30%) and mineral supplements (10%/5%); men used antithrombotic agents (4%/11%), renin-angiotensin system agents (7%/14%) and lipid modifiers (6%/12%).

Although prevalence of concomitant diseases and use of co-medication among PLWH in Germany are high across gender and all ages, the disease and drug patterns change in an age- and sex-related manner.

PE9/38

Kidney transplantation in HIV-positive patients in Israel including the first case of HIV-positive living donor to HIV-positive recipient with a 7-year follow-up

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Purpose: Since the introduction of effective cART, the comparable patient and graft outcomes between HIV-negative and HIV-positive kidney recipients were demonstrated in several studies and the use of HIV-positive donors for HIV-infected recipients is increasing worldwide. However, there is a concern regarding the safety of kidney donation from an HIV-infected person, given the risk of renal disease associated with HIV infection. We report our experience in kidney transplantation to the HIV-infected patients, including the first case of a kidney transplantation from HIV-positive living donor to HIV-positive recipient with a 7 years follow-up.

Method: Tel Aviv Sourasky Medical Center is the Israeli national referral hospital for HIV-positive patients considered for organ transplant. We reviewed the data from our kidney transplant program and collected the cases of HIV-positive recipients, including the long-term follow-up.

Results: Since 2012, five kidney transplantations in the HIV-positive individuals were performed in our center (4 cases of living donor kidneys and 1 - deceased donor kidney). A long-term post-transplant follow-up of 12 to 88 months showed good results with stable graft function, as well as satisfactory immune status and well controlled HIV viral load in all kidney recipients. In one of these cases, living donor kidney transplant was performed in July 2012 between a couple, both HIV-positive, infected with the same viral strain. Both donor and recipient were on effective ART with efficiently suppressed viral replication and satisfactory pre-transplantation immune status. The 7-years follow-up shows stable renal function and immune status in both donor and recipient.

Conclusion: To the best of our knowledge, this is the earliest case of HIV-positive-to-positive living donor kidney transplantation reported. The present successful case confirms our belief that an HIV-infected person meeting the

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living-donor criteria may be safely considered for kidney donation when properly selected and adequately treated by a multidisciplinary team.

PE9/39

Vitamin D deficiency and frailty phenotype in HIV-infected men

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Purpose: Frailty is a geriatric syndrome that increases vulnerability to stressors due to dysregulation in multiple physiological systems. More HIV-infected experience frailty with the introduction of highly active antiretroviral therapy (HAART). Vitamin D deficiency may interfere with immune restoration following HAART and accelerate onset of frailty in HIV-infected populations. We examined the association between vitamin D and frailty among HIV-infected men from the Multicenter AIDS Cohort Study.
Method: Levels of 25-hydroxyvitamin D (25[OH]D) and 1,25-dihydroxyvitamin D (1,25$[OH]_2$D) were measured in serum from 625 HIV-infected men, collected 2 years post-HAART between 1999–2008. Vitamin D deficiency was defined as 25[OH]D<20 ng/mL. 1,25$[OH]_2$D was analyzed as tertiles. Frailty was assessed at 6-month intervals between 1994–2018 using the Fried frailty phenotypic criteria with those meeting≥3 of 5 criteria considered frail and 1–2 criteria prefrail. Discrete-time multistate models examined factors associated with transitioning from non-frail to prefail or frail, adjusting for baseline and time-updated covariates.
Results: HIV-infected men had a median of 24 frailty measures (IQR:18–32) and median follow-up of 14.9 years (11.8–18.6). At baseline, vitamin D deficiency prevalence was 41%, 60% of men were non-frail, 27% prefrail, and 5% frail. Vitamin D deficiency had no effect on the probability of becoming prefrail/frail. However, non-frail men with 1,25$[OH]_2$D values in the smallest tertile had 2.74 (95% CI: 1.10–6.84) times the risk of becoming frail compared to the highest tertile. There was an elevated risk of becoming prefrail/frail with older age, depression, diabetes, AIDS diagnosis, and low kidney function. CD4≥200cells/mm^3 conferred protection against becoming frail (RRR for 25[OH]D: 0.13, 95% CI: 0.04–0.46; RRR for 1,25$[OH]_2$D: 0.14, 95% CI: 0.04–0.48), while BMI (25–29.9 kg/m^2), college education, and HIV RNA<50 copies/mL decreased the risk of becoming prefrail.
Conclusion: The active metabolite, 1,25$[OH]_2$D, captured an increased risk of becoming frail among non-frail men. Risk factors contributed to varying degrees to increase or decrease the risk of becoming frail, consistent with prior work.

PE9/40

The UCSD performance-based skills assessment is associated to cognitive performance in HIV positive population with very good immunological condition

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Purpose: Explore everyday functioning (EF) and its association with cognition in HIV+ subjects.
Method: Cross-sectional single cohort study enrolling 85 HIV+ outpatients and 23 age-and-education matched healthy controls (HC). Each patient underwent a comprehensive neuropsychological assessment (NPA). Global performance was measured by transforming raw scores at each task into standardized Z-scores and averaging to calculate a composite total score. IADL scale and the UCSD Performance-Based Skills Assessment-Brief Version (UPSA-B; assessing financial and communication skills) were administered.
Results: HIV+ patients were 77.6% male with a median age of 54 yrs (IQR 48–60). Median time from HIV diagnosis and first ART was 13 (IQR 4–23) and 12 (IQR 4–20) yrs, respectively. Overall 6% of patients were HCV co-infected, 28% with past AIDS-defining events and 93% showed HIV-RNA<50 copies/mL. Median adherence to ART was 95% (IQR 85–100) on a 0–100 VAS scale.All patients were cognitive asymptomatic and, on NPA, the total mean Z-score was 0.36 (SD 0.63). While IADL score was at ceiling, the mean UPSA-B total score was significantly worse in HIV+ group when compared to HC [mean 82.1 (SD 9.3) vs 89.2 (SD 6.2); p<0.001]. At communication subtest HIV+ group and HC were significantly different (p=0.002), while no difference emerged at financial score (p=0.096).
In HIV+ patients, a better performance at UPSA-B total score was independently associated to higher total cognitive z-score (β 7.76; 95% CI 4.9/10.5; p<0.001), after adjusting for education (p=0.438) and adherence (p=0.106); in the same regression model, also the performance at UPSA-B communication (β 5.04; 95% CI 2.71/7.38 p=< 0.001) and financial (β 2.77; 95% CI 1.31/4.23 p=< 0.001) skills were associated to higher total cognitive z-score.
Conclusion: UPSA-B seemed to better discriminate EF impairment than IADL in HIV+ patients and it was associated with cognitive functions, also in the absence of symptomatic cognitive impairment.

PE9/41

Alcohol, smoking and the association with HIV virological non-suppression among people living with HIV on ART

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Purpose: Evidence on the association between increased alcohol intake and viral non-suppression in people living with HIV (PLWH) is mixed, with limited data from large European studies. We investigated this association in an unselected outpatient population in the UK.
Method: Antiretrovirals Sexual Transmission Risk and Attitudes (ASTRA) was a multi-centre cross-sectional self-completed questionnaire study in PLWH attending eight HIV clinics in the UK between February 2011 and December 2012. Evidence of hazardous drinking was based upon a self-reported CAGE score (>=2) or estimated weekly consumption (>20 units of alcohol). Current smoking status was also collected. HIV viral load at recruitment was obtained from the clinics. Logistic regression was used to assess the association of alcohol use and smoking, with virological non-suppression (VL>50c/mL), adjusted for socio-demographic factors (age, gender/sexual orientation, ethnicity, education), in those who were currently on ART and started >=6 months previously.
Results: 3258 HIV-diagnosed individuals (2248 MSM; 373 heterosexual men; 637 women) completed a questionnaire (response rate 64%). Alcohol consumption was available for 2584 (81.3%), of which 566 (17.7%) had a CAGE score >=2 and 325 (10.1%) drank>20 units per week. 31.5% (n=1213) were current smokers.
On multivariable analysis, among 2459 individuals on ART who started>6 months previously, the adjusted ORs [95% CI] of virological non-suppression were: 1.52 [1.09, 2.13] for Cage score >=2, 1.23 [0.77, 1.96] for>20 units per week and 1.67 [1.22, 2.27] for current smoking.
Conclusion: Elevated alcohol intake and currently smoking were both found in this study to be associated with having a detectable HIV viral load in PLWH currently on ART. Active screening, advice and referral to smoking cessation and alcohol services should be integrated into HIV outpatient clinics, while clinicians should be alert to the potential for increased risk of non-adherence and viral rebound.

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Odds Ratio of Alcohol Use and Cigarette Smoking in ASTRA Cohort separated by Demographic, Lifestyle Factors and Treatment

	Patient Cohort n (%)	High Risk Alcohol Use (CAGE score>2 or>20 units/week)			Current Smoker		
		n (%)	OR	95% Confidence Interval (p)	N (%)	OR	95% Confidence Interval (p)
MSM	2248/3258 (69.0%)	554/706 (78.1%)	1.00	–	829/1011 (82.0%)	1.00	–
Heterosexual Male	373/3258 (11.5%)	87/706 (12.3%)	0.96	[0.74, 1.24] (0.702)	115/1011 (11.4%)	0.79	[0.62, 1.00] (0.046)
Female	637/3258 (19.6%)	68/706 (9.6%)	0.37	[0.28, 0.49] (<0.001)	67/1011 (6.6%)	0.21	[0.16, 0.27] (<0.001)
On ART	2771/3202 (86.5%)	583/699 (83.0%)	0.70	[0.55, 0.87] (0.002)	837/1005 (83.3%)	0.68	[0.55, 0.84] (<0.001)
Current Smoker	1011/3213 (31.5%)	283/704 (40.0%)	1.63	[1.37, 1.94] (<0.001)	1011/1011 (100.0%)	1.00	–
Recreational Drugs Use (Past 3 months)	1242/3258 (38.1%)	346/706 (49.0%)	1.76	[1.47, 2.06] (p<0.001)	601/1011 (59.4%)	3.59	[3.05, 4.21] (<0.001)
University or Higher Qualifications	1317/3172 (41.5%)	307/700 (43.9%)	1.12	[0.64, 1.32] (0.192)	332/985 (33.7%)	0.61	[0.52, 0.72] (<0.001)

Odds Ratio of having an undetectable Viral Load separated by lifestyle factors in patients treated with ART for>6 months

		Unadjusted Odds ratio of Detectable Viral Load		Adjusted Odds ratio of Detectable Viral Load (Age, Gender and Ethnicity)		Adjusted Odds ratio of Detectable Viral Load (Age, Gender, Ethnicity, Hardship and Education)	
Risk Factor	N (%)	OR	95% Confidence Interval (p)	aOR	95% Confidence Interval (p)	aOR	95% Confidence Interval (p)
20 + Units/wk	229/2450 (9.35%)	1.12	[0.72, 1.75] (0.615)	1.32	[0.83, 2.08] (0.234)	1.23	[0.77, 1.96] (0.386)
CAGE Score>2	426/2454 (17.36%)	1.52	[1.10, 2.08] (0.011)	1.54	[1.11, 2.13] (0.009)	1.52	[1.09, 2.13] (0.015)
High Risk Alcohol Use (>20 units or CAGE>2)	518/2454 (21.11%)	1.43	[1.04, 1.92] (0.025)	1.52	[1.10, 2.08] (0.010)	1.45	[1.05, 2.00] (0.023)
Recreational Drugs (Past 3 months)	912/2459 (37.09%)	0.96	[0.72, 1.27] (0.759)	1.04	[0.76, 1.45] (0.794)	1.01	[0.72, 1.39] (0.963)
Injected Drugs (Past 3 months)	53/2459 (2.16%)	2.27	[1.12, 4.55] (0.023)	2.27	[1.11, 4.55] (0.025)	2.17	[1.04, 4.55] (0.038)
Current Smoker	733/2568 (29.97%)	1.69	[1.28, 2.22] (<0.001)	1.82	[1.33, 2.44] (<0.001)	1.67	[1.22, 2.27] (0.001)

PE9/42

Decreasing incidence of diabetes mellitus in HIV-positive Taiwanese patients on combination antiretroviral therapy from 2004 to 2011

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Purpose: Increasing trends of metabolic complications, including type 2 DM, have threatened the long-term successful management of HIV infection. We aimed to examine the trend of DM in HIV-positive Taiwanese adults who initiated ART in 2004–2011.

Method: Between 2004 and 2011, 1,416 antiretroviral-naïve patients without DM initiated ART at a university hospital. The trends of DM were compared between patients initiating cART in 2004–2007 (n=582) who were followed until 31 May, 2015 and those initiating cART in 2008–2011 (n=834) who were followed until 31 May, 2019. Incident DM was defined as fasting glucose≧126 mg/dl or HbA_1C≧6.5%. Cox proportional hazards models were used to assess the relationship between DM and exposure to cART after adjustment for age, gender, and CD4 count and plasma HIV viral load at baseline.

Results: DM was diagnosed in 56 patients, resulting in an incidence rate of 4.43 per 1,000 PYFU, which has decreased from 5.05 per 1,000 PYFU in the 2004–2007 cohort to 3.35 per 1,000 PYFU in the 2008–2011 cohort (p=0.05). Incident DM was associated with older age (aHR, 1.089; 95% CI, 1.045–1.135) and exposure to protease inhibitor (aHR, 3.859; 95% CI, 1.007–14.793). The incident rate of DM increased with cumulative exposure duration to protease inhibitor-containing regimens: < 12 months, 1.7‰; 12–24 months, 2.2‰; 24–36 months, 8‰; and ≧36 months, 5.8‰; and that increased with exposure duration to zidovudine/lamivudine: < 12 months, 2.7‰; 12–24 months, 3.6‰; 24–36 months, 4.8‰; ≧36 months, 4.8‰)]. In contrast, the rate of DM remained stable with cumulative exposure to tenofovir-containing regimens.

Conclusion: We found that the incidence of DM has decreased from 5.05 per 1000 PYFU in the 2004–2007 cohort to 3.35 per 1000 PYFU in the 2008–2011 cohort. The risk of DM increased with older age and culmulative exposure to protease inhibitor-containing regimens in Taiwan.

PE9/43

Incidental findings in PLWH over 50 undergoing coronary artery calcium scoring (CACS) for cardiovascular risk assessment

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Background: Cardiovascular risk assessment of people living with HIV (PLWH)≧50 years using coronary artery calcium scores (CACS) has added benefits and costs of detecting extra-cardiac abnormalities. Data is limited on the prevalence or progression of incidental lung findings detected on Cardiac CT in PLWH. The objective of this study was to analyse the prevalence and progression of non-coronary incidental findings in patients undergoing CACS.
Methods: Longitudinal observational study of PLWH≧50 years undergoing Cardiac CT for CACS determination between 2009 and 2018. We report incidental extra-cardiac findings and follow-up required. A univariate logistic regression analysis was used to identify factors associated with incidental findings.
Results: 744 patients were included (92% male, mean age 56 ± 5 years, 84% white British, 87% MSM). The mean CD4 was 660 ± 258 cells/μL; 97% were on antiretroviral therapy (ART) with a suppressed viral load (VL) in 94%. Median years living with HIV was 16 years (IQR 12), median CD4:CD8 was 0.8 (IQR 0.6) and median CACS centile was 25–50th. 42% were active smokers.

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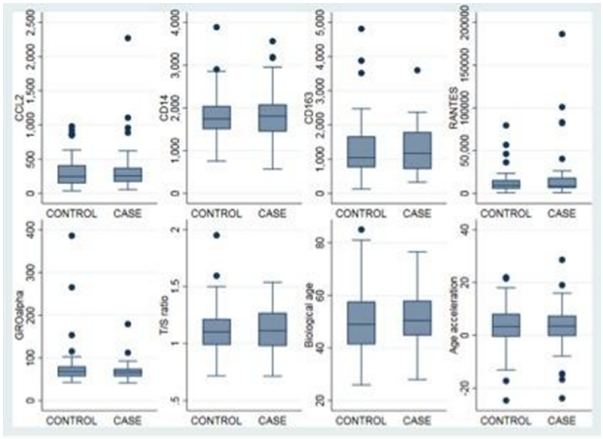
30% of patients had an incidental finding and 85% were newly diagnosed. 94% were incidental lung findings, most commonly pulmonary nodules, followed by atelectasis, and emphysema. 27.8% required follow-up or onward referral; 58% were stable or resolved at follow-up. 2 lung malignancies were detected. CD4:CD8 ratio≤0.5 was found to be associated with the presence of an incidental finding (p=0.007).
Conclusions: Our study indicates PLWH on ART with a suppressed VL have a similar the prevalence of incidental findings as HIV-negative populations on Cardiac CT. Having an impaired immune function despite a suppressed VL in this study was associated with incidental lung findings. CACS in risk stratification for cardiovascular disease has added value of identifying clinically significant lung abnormalities.

PE9/44

Aging biomarkers, inflammatory cytokines and development of cardiovascular ischemic events or diabetes in HIV-infected persons

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Purpose: Novel biomarkers of aging could help identify persons at risk for Non-AIDS co-morbidities. To investigate if leukocyte telomere length (LTL), age acceleration, and soluble inflammatory cytokines related to occurrence of cardiovascular events or diabetes in treated HIV-infected persons.
Method: Case-control study nested in the Spanish cohort of HIV-infected patients (CoRIS). Cases were participants with cardio-metabolic events [myocardial infarction (MI), stroke, sudden death, or diabetes (DM)] after starting ART and with available samples at inclusion. Controls without cardio metabolic event were matched 1:1 for sex, age, tobacco use, pre-ART CD4 cell count and viral load, and sample time-point. LTL was analysed in whole blood by qPCR (T/S ratio). Age acceleration (biological age minus chronological age) was analysed with DNA methylation changes by next generation sequencing using the Weidner aging formula. Cytokines (CCL2, sCD14, sCD163, RANTES, GROα) were measured using specific ELISA kits. Conditional logistic regression explored the association between cytokines, telomere length and age acceleration with cardio-metabolic events.
Results: 188 participants [94 cases (44 MI/sudden death, 24 stroke and 120 DM) and 94 controls]. 84% were male, median (IQR) age 46 (40,56), 53% current smokers, 21.8% had CD4 count≤200 cells/mm3 and median (IQR) viral load 27,819 cp/mL (145–100,000). LTL and age acceleration were similar in cases and controls: median LTL (T/S ratio) of 1.11 (0.98–1.24) and age acceleration of 3.41 years (−0.45–8.03). There were no significant associations between LTL, age acceleration and soluble cytokines with cardio metabolic events (Figure). LTL was significantly correlated with sCD14 (−0.2325; p=0.01), chronological age (−0.3849; p<0.001), and biological age (−0.1916; p=0.0249). Monocyte activation markers were correlated with chronological age (sCD14 0.2095; p=0.007 and sCD163 0.1709; p=0.02).
Conclusion: In this cohort we found no associations between telomere length, age acceleration and inflammatory cytokines and myocardial infarction, stroke or diabetes after ART initiation.



Association between Telomere length, inflammatory cytokines and cardio metabolic events

PE9/45

Falls but not frailty are common in people living with HIV using an mHealth platform: issues of ageing within the EmERGE cohort

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Mobile technology platforms represent a method of streamlining long-term HIV care, yet they may fail to address broader health issues such as age-related conditions.
Purpose: To estimate the prevalence of frailty and falls among stable individuals with HIV engaged with remote healthcare, delivered via a novel smartphone application.
Method: Cross-sectional, questionnaire-based sub-study of EmERGE participants. Frailty was assessed using the FRAIL scale, a five-item self-report screening tool. Present criteria were summed (range 0–5) and catergorized: 0=robust, 1–2=pre-frail, ≥3 frail. Falls and their frequency were assessed and dichotomised to faller/non-faller and single/recurrent falls.
Results: 944 individuals participated across five European study sites. Mean age was 44.6 years (SD 9.9), with 33% aged>50. 92% were male, 79% were of Caucasian ethnicity. Full frailty data were available for 891/944 (94%). Three quarters were robust (74%, 663/891); 25% (219/891) pre-frail; and 9 frail (1%). Of the frailty criteria, fatigue was most frequently reported (13%) followed by unintentional weight loss (12%), problems with walking (6%) and stairs (5%). Only 2 participants reported>4 comorbidities. Demographic data were available for 6/9 frail individuals: 83.3% were aged>50; all were male. 120/940 (13%) participants had fallen in the last year. Fallers experienced a median of 2 falls (IQR 1–3), with 59% (68/116) falling recurrently (≥2falls). Fallers were on average 3.1 years older than non-fallers (95% CI 1.2–5.1), with a greater proportion aged>50 (44% vs 31%, p=0.005). Falls were more common in frail (5 vs 1%) and pre-frail individuals (43 vs 22%).
Conclusion: Ageing issues were relatively uncommon in this cohort. Frailty was rare, with pre-frailty seen in 25%. Falls occurred and often recurred, and were related to frailty status and older age. Opportunities to explore ageing concerns with patients should be retained within mHealth delivered care and comprehensive geriatric assessment considered if identified.

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PE9/46

A standardized comparison of cardiovascular risk factor treatment in people living with HIV and general population

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Purpose: Cardiovascular (CV) risk factor prevalence is often found different in people living with HIV (PLWH) as compared to general population. However the treatment rates of risk factors is rarely addressed taking into account the age and sex distribution of PLWH. In this project we compare the general Spanish population treatment rates of main non-life style CV risk factors with that of Spanish PLWH, after standardizing for referent age and sex population distributions

Method: We used 5,680 PLWH with complete data from the VACH Spanish cohort and the general population DARIOS cohort, a pooled analysis of 11 population surveys from 10 Spanish communities (n=28,342) (http://darios.imim.es/). The treatment of diabetes, hypertension and cholesterol was compared in the age group 35 to 74 years. Prevalence and treatment rates were standardized by the direct method by sex and 10-year age groups with the European standard populations. All participants signed their informed consent.

Results: In DARIOS and VACH, the proportion of males was 46.5% and 80.4 % (p-value<0.001), respectively and mean age 53.5 (11.1) and 42.5 (7.4) (p-value<0.001), respectively. Standardized diabetes, hypertension and dyslipidemia treatments were significantly poorer among HIV patients than in general population (Table).

Conclusion: After the appropriate standardization to correct the effect of age and sex, we found striking differences in the control of risk factors between the general population and PLWH. The proportion of PLWH on pharmacological treatment for diabetes, hypertension, and dyslipidemia are significantly lower than in the general population. It is very important to improve the pharmacological control of CV risk factors in PLHW that matches at least that of the general population.

Comparison of cardiovascular risk factor treatment in FEMALE PLWH and general population

	General population (DARIOS cohort, N=15,149)	Female PLWH (VACH cohort, N=1,114)	p-value
Diabetes	10.6% (10.1%–11.1%)	19.5% (16.4%–22.7%)	<0.001
Treated diabetes	34.4 (31.5–37.2)	13.1 (8.4–17.8)	<0.001
Hypertension	27.4% (26.7%–28.0%)	25.9% (22.6%–29.2%)	0.392
Treated hypertension	62.7% (60.7%–64.7%)	22.9% (17.2%–28.6%)	<0.001
LDL cholesterol mg/dL	135.8 (135.2–136.3)	120.4 (116.3–124.5)	<0.001
Treated dyslipidaemia	14.0% (13.5%–14.6%)	8.1% (5.9%–10.3%)	<0.001

Comparison of cardiovascular risk factor treatment in MALE PLWH and general population

	General population (DARIOS Cohort, N=13,193)	Male PLWH (VACH Cohort, n=4,566)	p-value
Diabetes	15.4% (14.8%–16.0%)	21.1% (19.6%–22.6%)	<0.001
Treated diabetes	40% (37.1%–42.9%)	17.0% (14.3%–19.7%)	<0.001
Hypertension	29.0% (28.2%–29.7%)	23.7% (22.2%–25.2%)	<0.001
Treated hypertension	59.3% (57.5%–61.1%)	26.2% (23.2%–29.3%)	<0.001
LDL cholesterol	139 (138.4–139.6)	114 (112.2–115.8)	<0.001
Treated dyslipidemia	15.1% (14.5%–15.7%)	8.5% (7.4%–9.5%)	<0.001

PE9/48

Perceptions of ageing and desire for ageing information amongst users of the EmERGE mHealth platform

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In the era of well-treated HIV, attention is turning towards how successful ageing can be achieved for all. Integral to this success is personal well-being which can be influenced by perceptions of ones' ageing.

Purpose: To describe perceptions of ageing among individuals living with stable HIV engaged with remote healthcare delivered via a novel smartphone application ('app').

Method: All EmERGE participants were eligible for this ageing sub-study. Two questions drawn from the US Health and Retirement Study assessed: 1) satisfaction with ageing, rated on a Likert scale (strongly disagree to strongly agree), 2) 'What age do you feel?'. Lastly, participant opinion on inclusion of information on ageing issues within the 'app' was sought.

Results: 944 individuals participated across five European study sites. Mean age was 44.6 (SD=9.9), with 32.6% aged>50. 91.5% were male and 79.4% were Caucasian. 99% responded to the statement 'So far I am satisfied with the way that I am ageing?' with the majority either somewhat or strongly in agreement (68.8%) and 14.7% either somewhat or strongly disagreed, as shown in table 1. Satisfaction did not vary by age, except for greater dissatisfaction in over 60s. The overall mean age felt (n=916) was 39.4 (SD=10.8), with mean difference from actual age of −5.2 years. 10.4% felt their age, with most (69.5%) feeling younger (by a median of 7 years, IQR 4–11) and 20.2% feeling older (by 3 years, IQR 1–7). The proportion feeling younger increased with increasing age group (p<0.001). 793/930 (85.3%) agreed to some degree that information on ageing with HIV should be included in the 'app', 42.2% strongly agreed.

Conclusion: The majority of 'app' users were satisfied with how they were ageing and felt younger than their chronological age, yet 85% would like accessible information regarding ageing with HIV built-in to the 'app'.

Ageing variable	N	%
Satisfied with ageing (n=937)		
Strongly disagree	63	6.7
Somewhat disagree	75	8.0
Slightly disagree	76	8.1
Slightly agree	78	8.3
Somewhat agree	331	35.3
Strongly agree	314	33.5
Inclusion of ageing information in 'app' (n=930)		
Strongly disagree	58	6.2
Somewhat disagree	38	4.1
Slightly disagree	41	4.4
Slightly agree	164	17.6
Somewhat agree	237	25.5
Strongly agree	392	42.2

Table 1. Perceptions of ageing and desire for within 'app' ageing information in EmERGE participants

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PE9/49

Switching to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in adults aged>65 or older: week 48 results from a phase 3b, open-label trial

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Purpose: As the age of people living with HIV increases, studies are needed to assess the safety and efficacy of antiretroviral therapy in this population. B/F/TAF is a small single-tablet regimen with few drug-drug interactions and a high barrier to resistance. In this ongoing 96 week study, we evaluated the efficacy and safety of switching participants≥65 years to B/F/TAF.
Method: Virologically suppressed (HIV-1 RNA<50 copies/mL) participants≥65 years old currently receiving either E/C/F/TAF or a TDF-based regimen were switched to B/F/TAF. The primary endpoint was HIV-1 RNA<50 copies/mL at Week(W) 24 as defined by Food and Drug Administration Snapshot algorithm. Here we report efficacy and safety outcomes at W48.
Results: 86 participants were enrolled at sites across 5 European countries, median age was 68 years (IQR 66, 71), 13% were female, and 99% were White; At W48, HIV RNA<50 copies/mL was 87% (75/86); 11 (13%) had no virologic data in window (3 discontinued study drug due to AE but had last available HIV-1 RNA<50 copies/mL; 4 had no data within the window but had HIV-1 RNA<50 copies/mL after the W48 window, and 4 had missing data). Using the missing=excluded analysis, W48 HIV RNA<50 copies/mL was 100%. There were no virologic failures. No Grade 3–4 study drug-related adverse events (AEs) were observed. Three AEs led to premature study drug discontinuation; one (abdominal discomfort, grade 2) was considered study drug-related (Table). Median changes from baseline in lipid parameters were: total fasting cholesterol (−16 mg/dL), LDL (−5 mg/dL), HDL (−1 mg/dL), triglycerides (−26 mg/dL) and total cholesterol:HDL (−0.2).
Conclusion: Through W48, high rates of virologic suppression were maintained in older participants who switched to B/F/TAF. The safety and efficacy data support the switch to B/F/TAF in virologically suppressed HIV-infected individuals aged≥65 years.

Adverse Event	B/F/TAF (N=86), % (n)
Any Grade 3–4 Study Drug-Related AEs 0	0
Grade 3 or 4 Laboratory Abnormalities	6% (5)
Any Study Drug-Related Serious AE	0
AEs Leading to Study Drug Discontinuation	3.5% (3)*

* 1) abdominal discomfort (grade2, drug-related), 2) alcohol withdrawal, 3) benzodiazepine withdrawal

Adverse Events

PE9/50

Safety and efficacy of switching from tenofovir disoproxil fumarate to tenofovir alafenamide in people with HIV aged 50 years and older

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Purpose: To compare safety and efficacy of switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) in people with HIV (PWH) aged≥50 years.
Method: We pooled data from five phase 3 randomized controlled trials evaluating switching from TDF to TAF-containing antiretroviral regimens. Virologic suppression was defined as proportion of participants with HIV RNA<50 copies/mL at 48 weeks (W) using the Snapshot algorithm. Renal and bone impact were assessed at W96 by eGFR (Cockcroft-Gault), β2M:Cr and RBP:Cr ratio, and bone mineral density (BMD) by DXA.
Results: Pooled analyses included 1,408 PWH aged≥50y (768 TAF, 640 TDF). Median age was 54y; 86% male, 20.6% black, 14.9% Hispanic or Latino/Latina. Baseline medical conditions included hyperlipidemia (48.8%), hypertension (38.7%), diabetes (8.4%), and cardiovascular disease (5.9%). Virologic suppression was maintained in 94.1% of participants taking TAF and 93.5% taking TDF (p=0.86). Study drug-related adverse events occurred in 16.2% of participants taking TAF and 12.3% of participants taking TDF, leading to discontinuation in 0.5% and 2.2% respectively. Median eGFR increased in participants on TAF and decreased in those on TDF (Table 1). Markers of proximal renal tubular dysfunction (β2M:Cr and RBP:Cr) decreased in participants taking TAF and increased in those taking TDF (Table 1). There were 2 cases of Fanconi syndrome in participants taking TDF and none in those taking TAF. Participants taking TAF had improvements in hip and spine BMD, while those taking TDF remained stable or worsened (Table 2). The frequency of osteoporosis decreased in participants taking TAF and increased in those taking TDF (Table 2)
Conclusion: In PWH aged≥50, switching to TAF from TDF maintained virologic suppression and was associated with improved markers of renal function and improved BMD compared to TDF. These findings suggest that TAF is a safe and effective option for aging PWH.

Table 1. Renal outcomes

	TAF	TDF	p value*
eGFR (median change, IQR)	5.1 (-1.6, 12.5)	-0.2 (-7.2, 7.2)	<0.001
RBP:Cr (median % change, IQR)	-10.2 (-48.7, 35.2)	82.9 (12.1, 220.1)	<0.001
β2M:Cr (median % change, IQR)	-34.1 (-76.7, 12.5)	78.1 (-26.4, 279.7)	<0.001

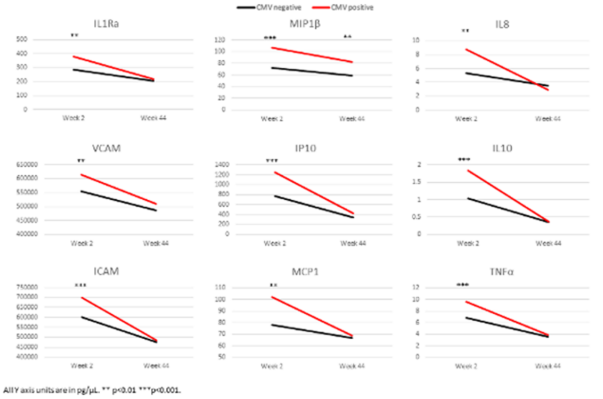
* p value is from the Wilcoxon rank sum test

Table 2. Bone outcomes

	TAF	TDF	p value
Spine BMD (median % change, IQR)	2.1 (-0.3, 4.6)	0.07 (-2.2, 2.7)	<0.001*
Hip BMD (median % change, IQR)	1.5 (-0.2, 3.1)	-0.7 (-2.5 ,0.9)	<0.001*
% With spine osteoporosis (baseline→week 96)	8.3 → 6	4.8 → 5.9	<0.001†
% With hip osteoporosis (baseline→week 96)	1.4 → 1.2	0.8 → 1.4	0.005†

* p value is from the Wilcoxon rank sum test
† p value is from rank analysis of covariance for clinical status change (normal, osteopenia or osteoporosis), adjusting for baseline clinical status.

Figure 1. Nine Inflammatory Biomarkers Raised in Patients with CMV Viraemia at ART Initiation and their Trajectory over 42 Weeks



All Y axis units are in pg/μL. ** p<0.01 ***p<0.001.

[Tables]

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PE9/51

HIV testing in patients diagnosed with community acquired pneumonia or primary lung cancer from 2014 to 2018 in a tertiary reference hospital in Northern Spain

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Purpose: HIV testing is reinforced in patients diagnosed with community acquired pneumonia (CAP) or primary lung cancer (PLC). The aim of this study is to evaluate the frequency for HIV testing on patients admitted with CAP or PLC to a tertiary hospital.
Method: The authors present a retrospective observational study from January 2014 to December 2018, evaluating HIV testing in patients diagnosed with CAP or PLC. Patients were included by CIE-10 diagnostic codes in clinical records, and HIV testing was assessed by crosschecking databases.
Results: A total of 7745 patients were diagnosed with CAP and 3524 with PLC, with a total of 11269 opportunities for HIV testing. Patients were mostly males (62.9%) and with similar ages in both groups: 68.69 and 66.0 years-old in CAP and PLC.HIV was tested in 1197 patients (10.62%), detecting a higher request rate in patients with CAP (11.26%) than PLC (9.22%) (difference of 2.04%, p<0.01). HIV was also more often tested in male patients (OR 1.21, IC95% 1.06–1.37), independently from diagnosis. In the CAP subgroup, HIV was more frequently tested when patients were admitted to the ICU (21.13%) or to an Infectious Diseases unit (ID) (34.29%), rather than Internal Medicine (IM) (12.16%) or Pneumology (8.38%).
From the 1175 samples processed for HIV test, 39 (3.32%) presented a positive result. Positive HIV tests proportion was similar in both diagnosis (CAP 3.75% vs PLC 2.17%, p=0.18) and gender (males 3.03% vs females 3.99%, p=0.40). Only 13 positive tests were new diagnosis of HIV, representing 1.09% of the total HIV tests requested in this study.
Conclusion: HIV testing in patients with CAP or PLC in this cohort is very low, with some HIV diagnostic opportunities lost. Nevertheless, studies are needed to evaluate the rentability of specific HIV diagnostic protocols in CAP or PLC patients.

PE9/52

Menopause in aging women living with HIV: changes in bone mineral density and trabecular bone score

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Objective: HIV infection and tenofovir-disoproxil fumarate (TDF)-containing antiretroviral regimens alone or in association with boosted protease inhibitors are associated with impaired bone quality and quantity and high fracture risk. The aim of the study was to describe pattern of bone quantity (lumbar bone mineral density (BMD)) and bone quality (trabecular bone score (TBS)) changes across menopause in WLWH undergoing ART with or without TDF.
Methods: We conducted a longitudinal retrospective study including WLWH attending Modena HIV Metabolic Clinic from 2012 to 2019. The observation period was divided into reproductive, transitional, early and late menopause according to STRAW criteria. Lumbar BMD and TBS derived from DEXA evaluation. GEE models were built to predict changes in BMD and TBS across menopause and TDF or TDF+PI/r/c containing ART regimens.
Results: We included 185 (mean age=49.3 years) ART-experienced women observed for a median of 6.08 years. 134 observations were assessed in the "Reproductive Period", 180 in the "Menopause Transition", 185 in the "Early Menopause" and 20 in the "Late Menopause", for a total of 519 DEXA observations. At baseline, median duration of HIV infection was 244 months, median CD4 cell count was 635 cells/uL. Across menopause, LDL, CRP, vitamin D and PTH significantly increased, while ASMI, FFMI, lumbar BMD, TBS score and FRAX® score worsened (p<0.001). In GEE models, independent predictors of BMD and TBS changes were time from menopause and calcium concentration; waist circumference was positively correlated with BMD and negatively correlated with TBS. TDF and PI/c/r were not predictors of BMD and TBS changes.
Conclusions: BMD and TBS remained stable in the pre-menopause period. Bone loss was more rapid in the early than late menopausal period, captured both with BMD and TBS. Current TDF or PI/c/r exposure was not independently associated with neither BMD nor TBS lowering in menopause.

PE9/53

Higher anti-CMV IgG concentrations are not associated with longitudinal brain injury in virally suppressed people with HIV

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Introduction: People with HIV (PWH) have a higher CMV seroprevalence than HIV-negative individuals. Higher CMV IgG concentrations have been associated with poorer cognitive function in cross-sectional studies of PWH. We compared the longitudinal relationships between CMV, cognitive function and neuroimaging biomarkers in PWH and demographically-matched HIV-negative controls.
Methods: CMV-seropositive, virally-suppressed PWH and HIV-negative controls from the COBRA study were included. The relationship between anti-CMV IgG and high avidity anti-CMV IgG titres with cognitive function (standardised T-scores measured with a six-domain battery) and MRI biomarkers (volumetric, diffusion and a machine-learning derived prediction of apparent 'brain age'), measured at baseline and after two years, were determined using rank regression adjusted for potential confounders.
Results: 130 PWH and 61 HIV-negative controls were included. Across the whole cohort cross-sectionally, higher anti-CMV IgG titres were associated with poorer global cognitive function and in the domains of processing speed, executive and motor function. This was only observed in PWH (largest effect size motor function: $rho_{adj} = -0.25$, p<0.01) although there were no statistically significant interactions between HIV-status and anti-CMV IgG titres.
Relationships between anti-CMV IgG titres and neuroimaging biomarkers were generally weak across the cohort ($rho_{adj} < 0.15$ for all, table 1) aside from an association with increased brain-predicted age (brain-PAD) in PWH ($rho_{adj} = 0.24$, p<0.01; HIV-status interaction p=0.02).
Relationships between baseline anti-CMV IgG titres, and *longitudinal* cognitive function and neuroimaging biomarkers were weak ($rho_{adj} < 0.15$ for all) with some associations being in the opposite direction to those found cross-sectionally (executive function and brain-PAD).
Conclusions: Higher anti-CMV IgG titres were not associated with short-term progressive brain injury in virally suppressed PWH. These findings and the lack of associations in HIV-negative controls suggest that the cross-sectional associations in PWH may represent type 1 errors or that CMV-associated brain injury is a static phenomenon in virally suppressed PWH.

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Table 1. Rank regression of total anti-CMV IgG with neuroimaging biomarkers across the whole cohort (n=191)

	Cross-sectional			Longitudinal		
Neuroimaging biomarker	rho adj (95% CI)	p	HIV-interaction p	rho adj (95% CI)	p	HIV-interaction p
Grey matter volume	−0.02 (−0.11, 0.08)	0.70	0.88	0.09 (−0.03, 0.22)	0.13	0.99
White matter volume	−0.01 (−0.10, 0.08)	0.84	0.14	0.00 (−0.12, 0.11)	0.94	0.05
Cortical thickness - Left	−0.09 (−0.22, 0.05)	0.20	0.35	0.03 (−0.09, 0.15)	0.65	0.47
Cortical thickness - Right	−0.11 (−0.25, 0.02)	0.11	0.33	0.06 (−0.06, 0.17)	0.34	0.86
Whole brain FA	−0.07 (−0.19, 0.05)	0.25	0.14	0.00 (−0.12, 0.13)	0.95	0.43
Whole brain MD	0.10 (−0.01, 0.22)	0.08	0.28	0.03 (−0.09, 0.14)	0.67	0.67
Brain-PAD score	0.16 (0.03, 0.30)	0.02	0.03	−0.11 (−0.23, 0.02)	0.10	0.05

PE9/55

Higher Prevalence of CKD in HIV+ individuals compared to the general population

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Purpose: Whether prevalence of Chronic kidney disease (CKD) is increased in people living with HIV (PLWH) compared to the general population, independent from commonly known risk factors for CKD, remains open. We investigated the risk for CKD in PLWH and HIV-negative controls.
Method: We compared HIV+ outpatients from the HIV Heart (HIVH) study and participants from the population-based Heinz Nixdorf Recall study (HNR) in a cross-sectional setting. Both studies were recruited from the German Ruhr area since 2000 and were matched in a 2:1 ratio based on age and sex. eGFR was calculated using the MDRD-equation, defining eGFR<60 mL/min as CKD. Odds ratios (ORs) and corresponding 95% confidence intervals (CI) were calculated in conditional logistic regression in a non-adjusted model and a multivariate model adjusted for BMI, Diabetes status, smoking status, systolic blood pressure, and use of hypertensive medication at baseline.
Results: Baseline characteristics of HIVH- (N=437) and HNR-participants (N=874) are shown in Table 1. The mean eGFR was 78(±17)/ 70(±16) and 85 (±19)/ 80(±19) mL/min/1.73 m^2 in male and female HIVH and HNR-participants, respectively. CKD was more common in HIVH-participants than HNR-participants (male: 10 vs. 3%; female: 26 vs. 7%). HIVH-participants were more often active smokers (male: 49% vs. 29%; female: 47 vs. 31%) and had higher SBP (male: 138 vs. 134mmHG; female: 143 vs. 124mmHG). Risk for CKD at baseline (male: OR=3.34; 95%-CI=2.04–5.47; female: OR=6.11; 95%-CI=2.0–18.73) was higher in HIVH-participants than HNR-participants. When adjusting for further CKD risk factors, the risk remains greater for HIVH-participants compared to HNR (male: OR=4.96; 95%-CI=2.69–9.15; female: OR=7.44; 95%-CI=1.57–35.22).
Conclusion: In PLWH, risk for CKD was higher independent of CKD risk factors, which may indicate that factors related to HIV and antiretroviral therapy have an impact on the rate of CKD. However, some CKD risk factors have potential for improvements in HIV care.

PE9/56

Effect of CMV viraemia on endothelial dysfunction over 42 weeks in Malawian adults initiating ART with advanced immune suppression

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Purpose: Advanced immune suppression in HIV is still common in low-income Sub-Saharan Africa. We characterised the effect of CMV viraemia on endothelial dysfunction over 42 weeks of ART in late presenters.
Method: We recruited Malawian adults with CD4<100 cells/ul two weeks after starting ART (enrolment) in the REALITY trial (NCT01825031). CMV PCR and 22 inflammatory biomarkers were assessed at enrolment and 42 weeks later, along with carotid femoral pulse wave velocity (cfPWV). Logistic regression assessed predictors for CMV viraemia and cfPWV.
Results: 61(32%) of 193 participants were CMV PCR+ at enrolment; 28(15%) had viral load>1000 copies/mL. Despite not receiving CMV specific treatment, 60(98%) participants became undetectable after 42 weeks' ART.
At enrolment CMV viraemia showed significant positive correlation with IL1Ra, VCAM, ICAM, MIP1β, IP10, MCP1, IL8, IL10, TNFα (all ranksum p<0.001); VCAM (p=0.04) and MIP1β (p=0.01) remained significantly associated when adjusted for CD4 count (median 25 versus 45 cells/μL, p=0.02) and %activated CD8 T-cells (83% versus 71%, p=0.0003). At week 42, MIP1β remained significantly higher in those CMV PCR+ at enrolment (p=0.005. Figure 1).

Baseline characteristics among 1482 participants from the HIVH and the HNR study

Characteristics	HNR male N=874 (88.46 %)	HIVH male N=437 (88.46 %)	P-value	HNR female N=114 (11.54 %)	HIVH female N=57 (11.54 %)	P - value
CKD2 (GFR<60) @ Baseline, N (%)	30 (3.43 %)	45 (10.3 %)	<0.001	8 (7.02 %)	15 (26.32 %)	<0.001
Age [years]	54.58 ± 6.55		1.00	51.33 ± 6.26		1.00
Baseline eGFR3 [mL/min/1.73 m^2]	85.48 ± 19.25	78.03 ± 16.5	<0.001	80.42 ± 18.66	69.5 ± 16.2	<0.001
Active smoker	255 (29.18 %)	214 (48.97 %)	<0.001	35 (30.7 %)	27 (47.37 %)	0.064
Diabetes at baseline	65 (7.44 %)	37 (8.47 %)	0.512	8 (7.02 %)	6 (10.53 %)	0.430
Systolic blood pressure [mmHg]	134.39 ± 18.73	137.6 ± 21.68	0.006	123.66 ± 24.79	142.84 ± 29.31	<0.001
Diastolic blood pressure [mmHg]	84.32 ± 10.65	85.11 ± 12.37	0.226	79.43 ± 12.88	88.37 ± 13.32	<0.001
Use of antihypertensive medication at baseline	253 (28.95 %)	103 (23.57 %)	0.039	22 (19.3 %)	15 (26.32 %)	0.294
BMI [kg/m^2]	27.92 ± 3.93	24.61 ± 3.8	<0.001	26.36 ± 5.14	24.55 ± 4.44	0.024

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There was no difference in cfPWV between those CMV PCR+ and PCR- at enrolment [median cfPWV 7.3 m/s and 7.2, p=0.15 respectively]. There was a trend towards higher cfPWV for those with enrolment CMV viral load below compared to above 1000 copies/mL at both enrolment [median 7.7 m/s and 7.2, p=0.06] and 42 weeks [7.5 m/s and 6.6 m/s, p=0.05]. However, this association did not persist when adjusted for age, blood pressure and haemoglobin (enrolment p=0.34 and week 42 p=0.13 respectively).
Conclusion: CMV viraemia was common but did not explain endothelial dysfunction at ART initiation. However, CMV viraemia at presentation was associated with persistent inflammation at 42 weeks. Whether treating CMV viraemia at presentation reduces long-term endothelial dysfunction on ART in this cohort remains unknown.

PE9/57

High prevalence of neurocognitive impairment in adults with perinatally acquired HIV infection

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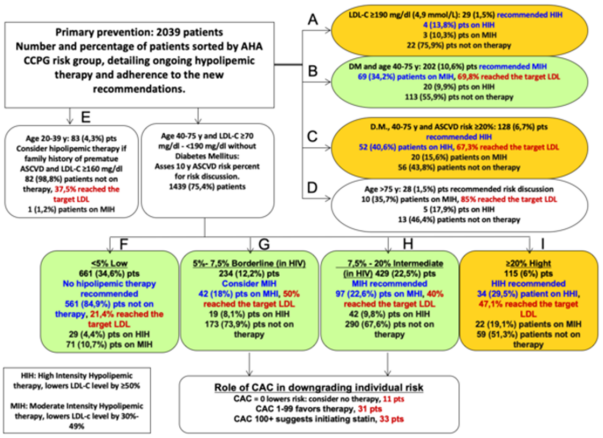
Purpose: To analyze the prevalence of neurocognitive impairment (NCI), affected neurocognitive domains and damaged brain areas in HIV-adults with perinatally acquired HIV (PHIV).
Method: Observational, cross-sectional study. Inclusion criteria: >18 years; perinatally acquired HIV; informed consent. NCI was diagnosed using Frascati criteria. 7 neurocognitive domains were analyzed: attention and working memory, processing speed, long-term memory, learning, executive functions, verbal fluency and motor functioning. Damaged brain areas were studied with Magnetic Resonance Imaging (MRI). We used a 3T clinical Magnet (Philips Achieva) employing a predefined protocol that included standard brain images (T2, FLAIR, SWI) as well as, diffusion tensor imaging (DTI) and isotropic T1 weighted images for tractography and volume calculations processed with commercially available software.
Results: 11/15 (73%) patients of our HIV-cohort with PHIV were included. Mean age was 23.9 ± 3.5 years, 72.7% males and 6(54.54%) had a previous AIDS diagnosis: 3 HIV-encephalopathy, 2 Burkitt's lymphoma and 1 HIV-myelopathy. At basal, all participants were receiving ART, 6 (54.54%) maintained HIV viral load undetectable and mean: CD4 + 864.6 ± 353.03 cells./μL. NCI prevalence was 54.6% (IC: 95% 23.4–83.3). The most impaired cognitive domains were: long-term memory (54.5%), verbal fluency (54.5%) and processing speed (45.5%). 9 patients accepted to be voluntarily evaluated with MRI. 1 patient showed morphologic changes suggesting global atrophy and white matter changes probably secondary to HIV encephalopathy. All patients showed abnormalities in the DTI study, specifically in the inferior longitudinal fasciculus (n=7), inferior frontoccipital fasciculus (n=4), corticospinal tracts (n=4), corpus callosum (n=6), cingulum (n=2), and uncinate fasciculus (n=1).
Conclusion: We found a high prevalence of NCI in adults with PHIV. The most impaired cognitive domains were: long-term memory, verbal fluency and processing speed. These patients showed abnormalities in the inferior longitudinal fasciculus and alterations in white matter microstructure probably related to past disease severity. Neuropsychological outcome of these population is unknown.

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Modeling 2018 AHA cholesterol guidelines in HIV

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Purpose: The objective was to assess statin use in people living with HIV (PLWH) in relation to the 2018 AHA Cholesterol Clinical Practice Guideline (CCPG) recommendations and related LDL targets. Data were analyzed vis-a-vis the recent AHA scientific statement on prevention and management of CVD in people living with HIV.
Method: Cross sectional study of PLWH followed at the Modena HIV Metabolic Clinic (MHMC) in 2017–2018. Mutually exclusive groups were built according to CCPG treatment algorithms recommending high and moderate intensity hypolipemic therapy (HIH or MIH).
Results: We included 2123 patients (74% men, mean age 53.5 years). Mean LDL-c and 10-year risk of CV events were 114 ± 33 mg/dl and 8.1 ± 0.9%. Figure 1 shows the distribution of risk among 2039 primary prevention PLWH. CCPG recommends HIH in groups A, C, I. HIH was prescribed in 13.8%, 40.6% and 29.5% of patients in those categories. Among the treated patients, 0%, 67.3% and 47.1% reached an LDL<100 mg/dl.
CCPG recommends MIH in groups B, G, H. MIH was prescribed in 34.2%, 18% and 22.6% of patients in those categories. Among the treated patients, 69.8%, 50% and 40% reached an LDL<100 mg/dl.
In 114 secondary prevention PLWH aged<75 years (6% of our cohort), HIH was prescribed in 34 patients (29%) and MIH in 25 patients (21.9%). Among these patients, only 26.5% reached the LDL-C target<70 mg/dL.
Conclusion: In real life statins are largely under-prescribed. The recommended LDL target was reached most often in patients with diabetes mellitus type 2. AHA-PLWH statement failed in identifying recommendations that may clarify statin prescription needing in PLWH.
The recent AHA statement on CV disease in PLWV is ambiguous with regards to treatment indications and LDL goals leaving a therapeutic gap that needs to be filled to improve patients' outcome.



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PE9/59

A multi-disciplinary Neuro-HIV Platform in managing patients with neurocognitive impairment

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Purpose: Neurocognitive impairment (NCI) represents a potential health burden for people with HIV (PWH). A multidisciplinary platform was developed to optimise the care of PWH.
Method: The Platform was developed at Lausanne University Hospital and accepts referrals from practitioners throughout Switzerland. Once a month, patients are seen by a neurologist, neuropsychologist, psychiatrist and an infectious diseases physician and undergo cerebral MRI and lumbar puncture. NCI is graded according to Frascati criteria and by neuropsychological test z-scores. Following this multidisciplinary assessment, treatment recommendations are made to the referring practitioner and follow-up visits at the Platform are planned as required.
Results: Between 2011 and 2019, 185 patients were seen at the Platform over 218 visits. 158 patients were seen once, 27 more than once. The median age of the 185 patients was 48 (IQR: 42,55), 59% men, mean nadir CD4 count 214 cells/mL (SD: 14). NCI was identified in 135 patients (73%): 35 (19%) with HIV-associated NCI. Non-HIV NCI were identified among 100 (54%) patients, including psychiatric and structural neurological sequelae. Among these, 18 patients (18%) were identified as having previously undiagnosed depression. Among the 27 patients who have been seen at the Platform several times, the neuropsychological diagnosis was stable for 17 patients, improved for two patients, worsened for one patient and fluctuated for 7 patients.
Conclusion: The Neuro-HIV Platform provides a unique multidisciplinary single day clinic to PWH suspected of having NCI. By reviewing neurological, neuropsychological, psychiatric and HIV-related components in each patient, it has been possible to identify reversible causes of NCI which might otherwise be missed in patients followed up in a single-specialty setting.

PE9/60

Archi-Prevaleat project. A national register of color-Doppler ultrasonography of the epi-aortic vessels in patients living with HIV

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Background: The introduction of effective antiretroviral (ARV) regimens has reduced mortality in patients with HIV, but has determined higher incidence of comorbidities like cardiovascular disease (CVD). Measurement of carotid Intima Media Thickness (IMT) with color-Doppler ultrasonography is a non-invasive, sensitive technique for identifying and quantifying atherosclerotic lesions. IMT measurement is especially important because is predictive of future CV events.
Aim: PREVALEAT (PREmature VAscular LEsions and Antiretroviral Therapy) is a multicenter, longitudinal cohort study involving several Italian centers, aimed to the evaluation of CV risk in HIV-infected patients since 1998. Our aim is to generate a National Register of color-Doppler ultrasonography (Archi-Prevaleat) to evaluate the characteristics of vascular lesions in HIV patients.
Material and methods: The project involves, at present,9 Italian centers in which the ultrasonographic examination is performed by specifically trained physicians during a Continuing Medical Education stage. The Register is made by an on-line platform aimed at collecting data regarding patients routinely submitted to the examination. We have enrolled until now 159 patients who performed color-Doppler ultrasonography whose data are summarized in Table 1.IMT of common and internal carotid for both left and right sides is registered. IMT of>1 mm is considered pathological. Atherosclerotic plaques, if present, are described.
Results: The tendency is to perform the investigation in older patients, in males and subjects with an history of AIDS. The prevalence of IMT>1 has been 22.6% at left carotid bulb,13.6% at right carotid bulb, 12.6 % at left common carotid and 11.7% at right common carotid (Fig.A).
Conclusions: The preliminary data of our Register show an unexpectedly high prevalence of pathological IMT even if the investigation is performed in patients at higher risk. This will prompt extend the investigation to all patients and will help to prevent CVD, that may have a negative impact on long-term prognosis.

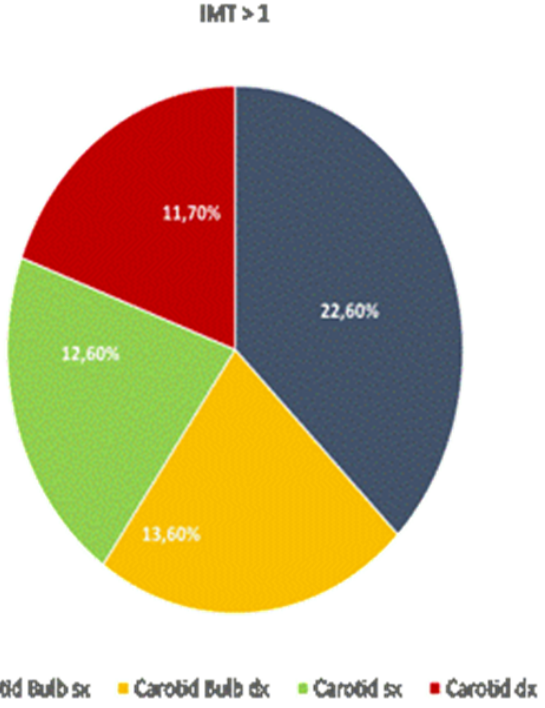
Table 1

Sex Male, n (%)	77 (78.6)	• IVDU	9 (9,18)	• NNRTI	22 (22,45)	Charlson comorbidity score>4, n (%)	19 (20,21)
Age, median [IQR]	57 [51–64]	Smoke, n (%)	47 (47,9)	• PI	3 (3,06)	Cardiovascular event, n (%)	53(54,08)
Years of HIV positivity,median [IQR]	20 [13–25]	Alcohol, n (%)	6 (6,12)	• NRTI	1 (1,02)	Type of cardiovascular event n (%)	
Years of ART, median [IQR]	17,5 [10–22]	HCV n (%)	18 (18,37)	• Other	16 (16,33	• Ischemic	16 (16,35%)
Nadir CD4 + , median [IQR]	262,5 [12–563]	HBsAg positivity, n (%)	HBsAg positivity, n (%)	STR, n (%)	50 (51,02)	• Nonischemic	29 (29,59%)
Zenith HIV-RNA, median [IQR]	55000 [7000–225000]	Anti-HBc positivity, n (%)	30 (30,61)	Drug use	6(6,12)	• None	53 (54,08%)
Ethnicity Caucasic, n (%)	83 (84,69)	AIDS, n (%)	25 (25,51)	Framingham level (available for 85 patients), n (%)		IL-6>10 pg/mL, n (%)	13 (13,98)
Risk, n (%)		Acute Retroviral Syndrome, n (%)	7 (7,14)	• <10	31 (36,47)	Lpa>300 mg/mL, n (%)	37(37,76)
• Heterosexual	47 (47,9)	Current therapy, n (%)		• 10—20	26 (30,59)	NT-proBNP>100 pg/mL, n (%)	13 (13,27)
• MSM	37 (37,7)	• INI	56 (57,14)	• >20	28 (32,94)	hPCR>0,9 mg/mL, n (%)	14 (14,28)

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Archiprevaleat data

Numbers of patients	159
% of patients>50 years old	83/76 (52.5%)
Male/Female	124/35
Risk factors for HIV infection	MSM 53 (33.3%) PWID 17 (10.6%) HETERO 62 (38.9%) OTHER 27 (16.9%)
CVD	11 (6.9%)
PI based regimens	53 (33.3%)
% of IMT>1 at Carotid bulb sx	33/146 (22.6%)
% of IMT>1 at Carotid bulb dx	20/146 (13.6%)
% of IMT>1 at Carotid sx	14/111(12.6%)
% of IMT>1 at Carotid dx	13/111(11.7%)



IMT

PE9/61

Preliminary results of a diagnostic-therapeutic work-up to early detect cardiovascular disease in HIV positive patients

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Purpose: To detect CVD in a population of HIV positive patients from a single tertiary care Hospital applying a new diagnostic-therapeutic work-up.
Methods: This is a cross-sectional study conducted at the time of the visit. HIV-infected patients in ART aged≥40 years old underwent a comprehensive cardiological evaluation (Figure 1) which included ECG, transthoracic echocardiogram (TTE) and, when indicated, advanced cardiovascular imaging modalities such as Cardiac MRI, Cardiac CT, stress Echocardiography and coronary angiogram. We collected data about age, sex, viro-immunological history and co-infection. hsCRP, Lp(a), IL-6, NT-pro BNP were tested. Framingham score (FS) was calculated. Logistic multivariate analysis was performed to identify any possible predictive factor for CVD.
Results: Since January 2018 we have enrolled 142 HIV positive patients. We focused on 98 who had no prior history of CVD and were asymptomatic. Clinical and demographics characteristics are summarized in Table 1. CVD was diagnosed in 45 patients out of 98 (overall prevalence 45.2%):29 (29.5%) had a non-ischemic heart disease, whereas 16 (16.3%) presented a coronary artery disease (CAD). All patients with CVD were treated with medical therapy. Four out of 16 patients with CAD were diagnosed with critical CAD and underwent coronary revascularization (3 percutaneous, 1 surgical). 1 had a silent myocardial infarction with no evidence of myocardial viability. At multivariate analysis only FS>20 was associated with higher risk of CVD (p=0.06). Nevertheless, 8 (21.5%) patients with FS<10 had a CVD . Levels of hCRP, Lp(a), IL-6 and NT-pro BNP were not significantly associated with CVD.
Conclusions: CVD is increasingly common in HIV positive patients. According to our experience FS may underestimate the real cardiovascular risk burden in HIV asymptomatic positive patients. A diagnostic-therapeutic work-up may be useful to unmask CVD in patients with no prior history of cardiovascular accident.

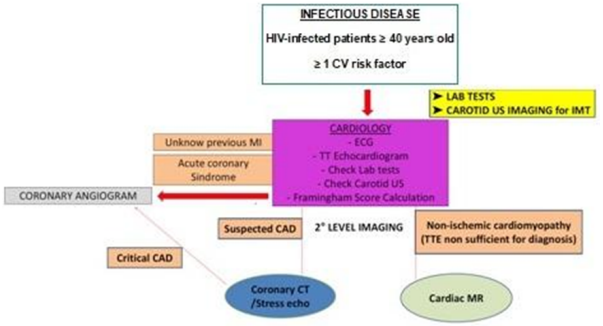


Figure 1. Diagnostic work-up

PE9/62

Bone mineral density changes in young African women on tenofovir disoproxil fumarate antiretroviral therapy and non-hormonal contraception

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Purpose: There are limited prospective data on bone mineral density (BMD) changes in HIV infected young women in low income countries initiating tenofovir disoproxil fumarate (TDF) containing antiretroviral therapy (ART). The NIH funded BONE: CARE study (R01AI118332) enrolled HIV infected depot medroxyprogesterone acetate (DMPA), or non-hormonal contraceptive users initiating TDF based ART, as well as an HIV, DMPA unexposed control group. We compare longitudinal data on BMD changes 2 years post TDF initiation among infected non-hormonal users compared to un-infected controls.
Method: Women were recruited from HIV care centers and general health facilities in and around Kampala, Uganda and classified into 4 groups: A) HIV+/DMPA+/TDF+; B) HIV+/DMPA+/TDF-; C) HIV+/DMPA-/TDF+; and D) HIV-/-DMPA-/TDF-. All HIV-infected women were ART-naïve at baseline. BMD assessments of lumbar spine (LS), total hip (TH) and femoral neck (FN) were conducted using dual energy x-ray absorptiometry at semi-annual intervals. We used repeated measures analyses to compare the rate of change, calculated as the percent change in BMD per year between HIV-infected and uninfected women during the initial 2 years of ART initiation adjusting for age, parity, education, and baseline BMD.
Results: Between March 2015 and October 2017, we screened 549 women. Of the 529 women enrolled, 176 were non-hormonal contraceptive users; 109 HIV-infected and 69 uninfected. The median age was 25. There was greater adjusted BMD percent decline among HIV-infected women than controls at the LS and NF compared to HIV-uninfected women (p=0.01, and 0.004 respectively) but not at the TH (p=0.716), figure. Prior use of DMPA≥2 years

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pre-ART initiation was not significantly associated with greater BMD loss among infected women.

Differences in bone mineral density among 2 years post TDF initiation among infected non-hormonal users compared to un-infected controls

Body site	Crude % difference in mean BMD change (95% CI)	P-value	Adjusted % difference in mean BMD change (95% CI)	p-value
Lumbar spine	-0.75 (−1.25 to −0.27)	0.002	-0.90 (−1.46 to −0.36)	0.001
Total hip	0.086 (−0.35 to 0.53)	0.703	-0.09 (−0.58 to 0.40)	0.716
Femur neck	-0.73 (−1.38 to −0.09)	0.026	-1.04 (−1.75 to −0.33)	0.004

Adjusted for age, BMI, education and baseline BMD

Conclusion: HIV-infected non-hormonal users experienced significantly greater BMD loss at the LS and TH. Data from DMPA users in this cohort will establish the additional effect of DMPA use on BMD among women on TDF.

PE9/63

Examination of HIV-infected patients regarding weight gain while using integrase inhibitors in Japan

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Purpose: The purpose of this study was to confirm the change in weight of HIV-infected patients using integrase inhibitors (doltegravir, raltegravir) over time, and to examine the change in weight.
Method: We targeted HIV infected patients going to hospital from January 2014 to January 2018 in our university hospital. A triple drug regimen using one integrase inhibitor as the key drug and two reverse transcriptase inhibitors as the backbone was targeted for HIV patients who continued to take medication for 2 years. HIV-infected patients using integrase inhibitors were 25 doltegravir and 22 raltegravir. These patients aren't naive. All have been treated as switch regimen cases. We analyzed using Wilcoxon's rank sum test.
Results: All genders were male, with a median overall age of 46 (32 to 74). BMI was 24.11 (17.69–33.34), the average number of CD4 positive cells was 549 (326–1223), and HIV-RNA level was less than 20 copies/mL or undetected. In the dolutegravir-treated group, body weight at one year after the previous value increased by an average of 1.9 kg, and after two years, body weight increased by an average of 3.02 kg ($p<0.001$). In the raltegravir group, the body weight one year after the previous value decreased by an average of 0.004 kg, and after two years, the body weight increased by an average of 0.03 kg and did not change significantly throughout the two years ($p=0.566$).
Conclusion: After two years of follow-up and comparison of the body weight of the two integrase inhibitors, it was found that the weight gain of doltegravir tends to be higher than that of raltegravir. Further accumulation of cases is considered necessary and will be studied.

PE9/64

The relationship between diabetes and depressive symptoms in men with or at risk for HIV

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Purpose: To compare the prevalence of comorbid diabetes and depressive symptoms between men with and at risk for HIV and to determine the associations between glycemic control and depressive symptoms.
Method: We conducted a cross-sectional analysis in HIV+ and HIV- men in the Multicenter AIDS Cohort Study (MACS). The exposure of interest was glycemic status, categorized as normal for fasting blood glucose (FBG) <100 mg/dL, prediabetes for FBG 100–125 mg/dL, and type 2 diabetes (T2D) (defined by self-report, diabetes medication use, or FBG≥126 mg/dL for≥2 consecutive visits). T2D was further categorized as controlled (HbA1C<7.5%) or uncontrolled (HbA1C≥7.5%). The primary outcome, elevated depressive symptoms, was defined as a Center for Epidemiologic Studies Depression Score≥16. A modified Poisson regression model with robust variance was used and adjusted for covariates including HIV-serostatus, body mass index, and depression treatment.
Results: The study included 920 HIV+ men and 840 HIV- men. HIV+ men had greater prevalence of depressive symptoms (28.5% vs 20.1% among HIV- men, $p<0.001$) but a similar prevalence of diabetes (12.83% vs.11.31%, $p=0.330$). The concomitant prevalence of diabetes and elevated depressive symptoms did not differ by HIV-serostatus ($p=0.516$). Compared to normal glycemic status, the adjusted prevalence ratios of elevated depressive symptoms were 1.06 (95% CI 0.82, 1.37) in men with prediabetes, 1.21 (95% CI 0.89, 1.65) in men with controlled T2D, and 1.55 (95% CI 1.06, 2.28) in men with uncontrolled T2D (Table 1). The associations between glycemic status and elevated depressive symptoms did not differ by HIV-serostatus ($p=0.32$).
Conclusion: Uncontrolled T2D was independently associated with depressive symptoms, regardless of HIV-serostatus. Longitudinal studies are needed to examine whether the relationship between glycemic status and incident elevated depressive symptoms differs by HIV-serostatus.

PE9/65

Predictors of sarcopenia and its impact on components of the frailty phenotype in an Asian population living with HIV

G Lui[1], M-C Chan[2], J Woo[1], O Tsang[2] and T Kwok[1]

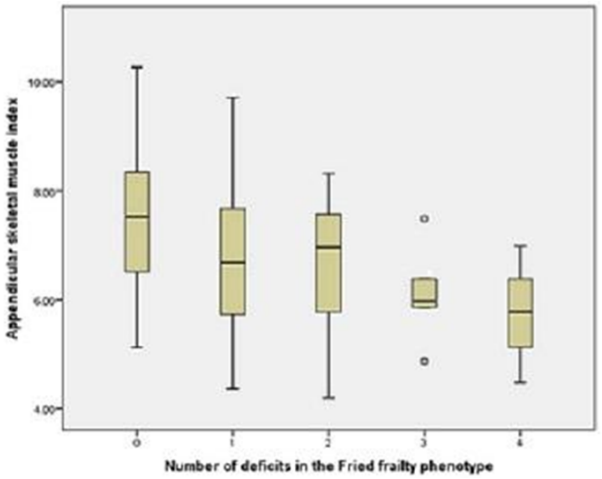
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Purpose: We aim to study the prevalence and predictors of sarcopenia in people living with HIV (PLWH) in Asia. The impact of sarcopenia on the components of frailty phenotype is explored.
Method: We performed a prospective observational cohort study in Hong Kong involving PLWH aged≥18 years (N=251). Sarcopenia was defined by appendicular skeletal muscle index (ASMI=lean mass of extremities/height^2) <7.0 kg/m^2 in men and<5.4 kg/m^2 in women according to the Asian Working Group for Sarcopenia, as measured by DEXA. The Fried frailty phenotype (unintentional weight loss, exhaustion, low physical activity, and diminished gait speed and grip strength) was assessed in a subgroup of this cohort (N=142). Comparisons between groups were performed with Chi square test, Mann Whitney U tests and one-way ANOVA as appropriate. Multivariable binary logistic regression model was performed to determine predictors of sarcopenia.
Results: Mean±SD age was 52 ± 13 years, 209 (83.3%) were male, and 233 (92.8%) were Chinese. The duration of HIV diagnosis was 7 (IQR 1–13)years, 27 (10.8%) had hepatitis B.
In this cohort, 105 (41.8%) had sarcopenia. Sarcopenia was independently associated with Chinese ethnicity (adjusted odds ratio [aOR 6.2 [95% CI 1.0–39.1]), hepatitis B (aOR 4.9 [1.6–15.7]), body weight (aOR 0.87 [0.84–0.91]), and exposure to stavudine (aOR 2.4 [1.1–5.4]), adjusted for confounders (Table).
Among the five components of frailty phenotype, sarcopenia was associated with weak hand grip (39.4% vs. 13.7%, $p=0.001$), low physical activity (24.2% vs. 10.7%, $p=0.032$), and weight loss (21.9% vs. 8.2%, $p=0.024$). A significant reduction of ASMI was observed with increasing number of deficits in the frailty phenotype ($p=0.001$) (Figure).
Conclusion: In an Asian cohort of PLWH, sarcopenia was present in 42%, and was associated with Chinese ethnicity, hepatitis B, low body weight and exposure to stavudine. Sarcopenia was associated with several components of the frailty phenotype.

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Variables associated with sarcopenia in univariate analysis

Variables	Sarcopenia N=105	No sarcopenia N=146	p
Chinese	103 (98.1%)	130 (89.0%)	0.006
Hepatitis B	17 (16.2%)	10 (6.8%)	0.018
Hepatitis C	10 (9.5%)	3 (2.1%)	0.008
History of AIDS	42 (40.0%)	41 (28.1%)	0.048
CD4 count, cells/mm3	423 [250–670]	533 [359–731]	0.007
CD4:CD8 ratio	0.54 [0.31–0.81]	0.70 [0.43–0.95]	0.016
HIV RNA, copies/mL	40 [40–68]	40 [20–40]	0.002
Body weight, kg	58.1 ± 8.0	71.4 ± 13.8	<0.001
Exposure to stavudine	26 (24.8%)	20 (13.7%)	0.025



Appendicular skeletal muscle mass according to number of deficits in the Fried frailty phenotype

PE9/66

Failure to restore CD4 cell count with combination antiretroviral therapy is associated with increased systemic inflammation

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Purpose: Systemic immune activation is thought to drive non-AIDS comorbidity despite suppressive antiretroviral therapy (ART). Immunologic non-responders (INR) do not restore blood CD4 T cells to>350/mm^3. We sought to characterize the inflammatory profile of INRs, including the level of T cell activation and inflammation-associated soluble markers linked to non-AIDS comorbidity. We hypothesized that co-expression of HLA-DR and CD38 on CD8 T cells (CD8 activation) would be elevated in INRs.
Method: 101 consenting adults were enrolled in a cross-sectional study at HIV care sites in Toronto, Canada. Virally-suppressed HIV-positive participants were categorized as INR (N=36), or CD4 restorers ("CR"; >350/mm^3; N=47). An HIV-negative group was included (N=18) Peripheral blood mononuclear cells and blood plasma were cryopreserved before measurement of T cell activation by flow cytometry (co-expression of HLA-DR and CD38) and soluble immune activation-related markers by ELISA (CRP, TNF, IFNg, sCD14, D-Dimer, I-FABP, MCP-1, VCAM, ICAM). Multiple log-linear regression models were used to estimate the association between INR phenotype and markers after adjusting for age, sex, duration of ART, and recent infection/vaccination.
Results: HIV-positive individuals had median [IQR] infection 16 [9, 26] years, and ART duration 12 [6, 21] years, with no difference between groups. In adjusted log-linear regression models, INRs had 35% higher CD8 activation (p=0.02), 54% higher CD4 presentation of HLA-DR (p<0.001), and 20% higher plasma VCAM (p<0.01) compared to CRs. HIV-positive individuals had higher median [IQR] CD8 (2.96 [1.88, 4.46]) compared to HIV-negatives (1.82 [1.17, 2.81], p<0.01). INR phenotype was not associated with CRP, TNF, IFNg, sCD14, D-Dimer, I-FABP, MCP-1, ICAM or CD8%DR + .
Conclusion: INRs, compared to CRs (and controls), had higher disease-associated CD8 activation that could be assessed as a target of intervention to improve outcomes. VCAM (marking endothelial activation) and CD4 activation were elevated amongst INRs and require exploration as prognostic indicators.

PE9/67

High prevalence of left ventricular systolic dysfunction assessed by speckle tracking in asymptomatic HIV patients

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Purpose: Advancements in the care of people living with HIV (PLWHIV), have shifted care from a cohort of young otherwise healthy individuals to an aging population with comorbidities. Immune dysregulation, inflammation and exposure to HAART have been associated with cardiomyopathy and peripheral vascular disease, aside from traditional risk factors. Diagnosis at preclinical stages could enable prompt and effective therapeutic interventions.
Method: We investigated the association between global longitudinal strain (GLS), assessed by 2-D speckle tracking and

a) patient history,
b) demographic and clinical baseline characteristics,
c) carotid intima-media thickness (IMT) and presence of carotid atheromatic plaque(s), measured by ultrasonography,
d) temperature difference along each carotid artery (CΔT), measured by microwave radiometry and
e) basic blood panel measurements, including high-sensitivity troponin-T (hsTnT) and NT-proBNP in virally suppressed HIV monoinfected individuals without history of cardiovascular disease.

Results: We prospectively enrolled forty PLWHIV. Baseline characteristics appear in table. Subclinical left ventricular systolic dysfunction, defined as a value of GLS>-18.7%, was prevalent in 14/40 (35%) patients. GLS was associated with age (Pearson co-efficient, r=0.410, p=0.013), history of hyperlipidemia (r=0.370, p=0.026), BMI (r=0.462, p=0.005), waist circumference (r=0.471, p=0.007) and right bulb IMT (r=0.390, p=0.036). hs-TnT levels were associated with age (r=0.513, p=0.001), current CD4 count (r=-0.357, p=0.025), serum creatinine (r=0.338, p=0.035) and the presence of carotid plaque (r=0.374, p=0.038). NT-proBNP levels were associated with history of diabetes (r=0.336, p=0.048) and serum creatinine (r=0.548, p=0.001). CΔT was associated with length of TAF exposure (r=-0.402, p=0.014), but not with TDF or tenofovir, ABC exposure (r=0.39, p=0.017), 3TC (r=0.481, p=0.003), d4T (r=0.360, p=0.029), NNRTI (r=0.374, p=0.023) and NVP (r=0.342, p=0.038).
Conclusion: Our results indicate that apart from age, a dysmetabolic component, may be implicated in the pathogenesis of premature systolic myocardial dysfunction. It appears that TAF might have a protective effect on the stability of carotid plaque.

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Baseline characteristics of study cohort

Variable	% or Value ± SD
Age, years	51.6 ± 12.6
Male gender, %	92.5
Hypertension, %	30.0
Diabetes, %	15.0
Dyslipidemia, %	42.5
Chronic kidney disease, %	7.5
Body mass index (BMI), kg/m^2	26.3 ± 4.9
Troponin-T, pg/mL	7.2 ± 6.2
NT-proBNP, pg/mL	51 ± 75

PE9/68

Polypharmacy and drug-drug interactions - prevalence in a Portuguese HIV Metabolic Clinic

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Introduction: With the advent of more effective and tolerable antiretroviral drugs, HIV patients are living longer. Ageing translates in an increasing rate of comorbidities, requiring chronic treatment. Therefore, polypharmacy has become a challenge in the mainstay treatment of this population.
Objective: Evaluate the frequency of polypharmacy and potential drug-drug interactions (DDI) in patients attending our HIV metabolic clinic.
Methods: Retrospective study with review of clinical records of patients that attended the HIV metabolic clinic between June 2018 and June 2019. Polypharmacy was defined by use of≥5 medications not including antiretrovirals (ARV). Interactions were assessed using according to University of Liverpool database. Statistical analysis was performed using IBM SPSS25®
Results: Two hundred and ten patients attended the consultation. Seventy-eight percent (n=164) were male. Mean age was 53 yo (min. 23 max 82) and 45.2% (n=95) were 55 yo or older. The main concomitant medications were statins in 45.4% of the patients, anti-hypertensive in 36.4% and colecalciferol in 38.6%.
Polypharmacy was found in 24.9% and was more prevalent in patients>55 yo (p=0.00), with lower CD4 + nadir (p<0.05) and with longer TARV exposure (p<0.05).
DDI were present in 34.3% of the patients. The antiretroviral classes implied in DDI were protease inhibitors (39.5%), non-nucleoside analogues (31.5%), integrase inhibitors (23.7%) and nucleoside analogues (5.3%). Two patients had concomitant medications that were contraindicated and in one patient the medication could potentially decrease ARV exposure.
Associating antiretroviral drugs, the pill burden in the polypharmacy group was 7.7 pills versus 3.5 pills in non-polypharmacy group (p=0.00).
Conclusion: We found a polypharmacy prevalence of 24.9% mainly in older with lower CD4 + and longer TARV exposure. The DDI frequency was 34.3%. Facing these results, we emphasize the importance of previous checking of potential interactions whenever a new drug is added.

PE9/69

Bone density alterations in the HIV-infected patient - epidemiologic characterization of a Portuguese cohort

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Background: Over 36 million people are infected with HIV making it one of the world's most serious public health problems. Today, the average life expectancy of HIV-infected patients is on the rise thanks to combined antiretroviral therapy. Therefore, long-term comorbidities, such as decreasing bone density, became a major concern.
Purpose: Characterization of the HIV-infected population of Centro Hospitalar e Universitário do Porto, analysing the prevalence of osteoporosis and its risk factors.
Method: A retrospective observational study was carried out in a population of 302 HIV patients who attended the non-infectious comorbidities in the HIV+ patient appointments of our centre between 2016 and 2018. Data concerning sociodemographic characteristics, bone densitometry results and osteoporosis risk factors were collected from the patients records. A descriptive analysis was performed using IBM® SPSS® Statistics 25.0.
Results: Overall, only 196 patients had undergone bone densitometry and were analysed. Seventy-three percent were males and the median age was 55 years old. The majority (62.2%) had low bone mineral density (T-Score<-1) and 24% had osteoporosis. Sixty-one per cent had taken tenofovir disoproxil fumarate for, at least, two years and a quarter had taken a protease inhibitor for two years.
More than half (54.6%) had vitamin D deficiency, 34.2% smoked, 20.9% had more than 3 units of alcohol per day (1 unit=8 g of alcohol), 19.4% took opioids, 18.4% were diabetic, 11.2% were on antidepressants and 9.2 % had chronic liver disease.
Conclusion: This is the first study ever to demonstrate the high prevalence of osteoporosis and associated risk factors in the Portuguese population infected with HIV. We confirmed that low mineral bone density is far more prevalent on the HIV-infected patients compared with the rest of the Portuguese population. Osteoporosis risk factors were also more frequent on HIV-infected according to Portuguese available data.

PE9/70

Cigarette smoking disproportionately impairs nitric oxide signaling in pulmonary artery endothelial cells in HIV: role of viral and host factors

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Purpose: The objective of this study is to determine whether cigarette smoking (CS) disproportionately impairs the pulmonary artery endothelial cell (PAEC) function and increases the risk of HIV-PAH. Studies have shown that the circulating HIV-1 viral accessory protein, Negative factor (Nef), binds to the host C-X-C motif chemokine receptor 4 (CXCR4) on endothelial and other cells. We *hypothesized* that CS increases CXCR4-Nef interaction, which results in the downstream impairment of endothelial nitric oxide synthase (NOS3) dependent vasodilation and the development of HIV-PAH.
Methods: Smokers and non-smokers with and without HIV-1 infection were recruited at the University of Alabama at Birmingham HIV 1917 clinic. All HIV positive patients were on ART and had low blood viral load. Plasma levels of endothelial cell function markers were measured. To determine the role of CS in Nef-CXCR4 interaction and NOS3 dysfunction, human PAECs (HPAECs) were treated with recombinant Nef protein in the presence or absence of cigarette smoke extract (CSE), and CXCR4 binding to Nef, NOS3 expression and function was assessed. It was also determined whether the pharmacological inhibition of CXCR4 by AMD3100 attenuated Nef signaling.
Results: HIV positive smokers had significantly lower plasma levels of endothelial markers, nitrite/nitrate (stable metabolic products of nitric oxide), cGMP, and prostacyclin compared to HIV positive non-smokers or HIV negative smokers. Exposure to 2% of CSE increased CXCR4 protein levels in HPAEC and increased CXCR4-Nef interaction when these cells were treated with recombinant Nef. CSE and Nef also reduced plasma membrane expression of NOS3, cellular nitrite/nitrate and cGMP levels. Treatment of cells with AMD3100 abrogated effect of Nef on cells.
Conclusion: The data suggests that CS dependent Nef/CXCR4 signaling is an important driver of endothelial dysfunction in HIV and CXCR4 inhibition can be a potential therapeutic target for HIV-PAH.

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PE9/71

Frailty phenotype in older virologically suppressed PLWHIV is strongly correlated with specific comorbidities and tobacco use

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Purpose: People living with HIV (PLWHIV) are mostly virologically suppressed and efficiently followed up, growing older and accumulating health problems related to ageing. This ageing state is characterised by a decreased capacity to manage adverse outcomes (disease, hospitalization, disability, falls) which defines the frailty phenotype.
Our aim was to assess factors related to frailty according to Fried phenotype in a French cohort of elder PLWHIV (≧50 years old).
Method: This cross-sectional multicenter study was carried out between November 2012 and April 2014 in 12 HIV-dedicated Hospital Units. We evaluated demographic factors, HIV-related parameters, as well as general health parameters (BMI for Body Mass Index, associated comorbidities, pain scale, social deprivation). Phenotype of Frailty according to Fried is based on the assessment of 5 criteria: shrinking (unintentional weight loss), weakness (grip strength), poor endurance (exhaustion), slowness (walking speed) and physical activity. Frailty phenotype corresponded at the presence of at least 3 criteria of the above mentioned.
Results: Our study involved 509 PLWHIV, 72.8% were male, of a mean age of 58.4 ± 7 years, mostly (87.9%) virologically suppressed. Mean duration of infection since HIV diagnosis was 18.3 ± 7.4 years. Prevalence of frailty concerned 8.2% between them. Multivariate analysis of variables selected at $p<0.20$ in the univariate model confirmed associations of frailty state with BMI, pain scale, psychiatric and rheumatologic history, falls, while revealing associations with cancer history, tobacco use and CD4 T cell nadir count less than 200/mm3.
Conclusion: Our study strongly suggests that comorbidities are the main factors that convey the embrittlement state of older virologically suppressed PLWHIV. This state precedes polypathology or disabilities and undermines ones capacity to fight against physical or mental assaults. Efficient medical follow-up focusing on preventing comorbidities especially in individuals with cancer history, could delay frailty as well as its associated adverse outcomes.

PE9/72

HIV-FUNCFRAIL study: differences between women and men aging with HIV

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Purpose: To evaluate differences between women and men aging with HIV.
Methods: Prospective cohort study. Patients from the "HIV-FUNCFRAIL: Multicenter spanish cohort to study frailty and physical function in 50 years or older HIV-infected patients" were included and stratified by sex. We recorded sociodemographic data, comorbidities, variables related to HIV infection, frailty, physical function, VACS index and pain as a quality of life measurement.
Results: We evaluated 563 PLWH who were 50 years old or over, of which 145 (25.8%) were women. Median age was 56.2 (IQR=6.9) years. Median current CD4 + T-cell count was 711 (IQR=461) in women and 655 (IQR=421) in men (p=0.0002). Median CD4/CD8 ratio was 0.9 women to 0.7 men (p=0.0001). There were differences in comorbidity between women and men regarding ischaemic heart disease, non-AIDS malignancy in the past, depression and osteoarticular pathology. Mean number of comorbidities was 2.9 (SD 1.9) in women and 2.6 (SD 1.8) in men (p=0.025) in men. Polypharmacy was significantly higher among women [28.7% vs 19.4% p=0.026] and particularly the use of neuroleptics, painkillers and opioids. Pain was more prevalent in women than in men [54.9% vs 34.7% (p=0.013)]. No differences were found regarding frailty, physical function (SPPB, gait speed), falls and cognitive impairment (MOCA-test). The mean VACS risk of 5-year all-cause mortality was 11.8 (SD 10.1) in women and 9.9 (SD 9.4) in men (p=0.003).
Conclusion: In our cohort, older women represented one in four of the total patients. Despite the fact that women have better immunological recovery measured by CD4 T-cell count and CD4/CD8 ratio, they have more comorbidities and polypharmacy than men, their risk of 5-year all-cause mortality was higher than in men and, their quality of life measured by the presence of pain was worse.

PE9/73

Prevalence, risk factors and outcomes of cardiovascular, metabolic and chronic kidney diseases in HIV-infected vs. uninfected adults in sub-Saharan Africa: a systematic review and meta-analysis

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Background: Sub-Saharan Africa (SSA) has the highest burden of HIV in the world; more than 25.5 million Africans are living with HIV in the region, including nearly 15 million on antiretroviral therapy (ART). Expanding use of ART has led to a notable decline in HIV-associated morbidity and death in SSA. Nonetheless, people living with HIV (PWH) in SSA are at substantially increased risk for both cardiovascular and metabolic disease (CVMD) and chronic kidney diseases (CKD).
Methods: We searched electronic databases (Ovid MEDLINE and EMBASE) from 1985 to July 2018. We included studies that reported prevalence estimates for any CVMD and CKD in SSA and information on HIV status and treatment status.
Results: A total of 89 studies involving 263,262 participants were included in the meta-analysis. Prevalence estimates were reported in 41 studies on hypertension (HTN), 29 on type 2 diabetes mellitus (T2DM), 14 on metabolic syndrome (MS), 9 on cardiovascular disease (CVD) and 22 on CKD. The reported

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prevalence estimates varied greatly within countries, between countries and within regions: HTN (5.2% to 45.0%), T2DM (0.9% to 28.1%,), MS (2.1% to 20.4%) and CKD (0.6% to 53.3%). There was no significant difference in the prevalence of HTN and T2DM between HIV-infected and -uninfected participants. The prevalence of MS (OR=1.66, 95% CI 1.01 to 2.72, 2 studies) and CKD (OR=2.30, 95% CI 1.12 to 4.72, 6 studies) were higher in HIV-infected participants than HIV-uninfected participants.
Conclusions: The burden of CVMD and CKD among PWH in SSA is high, although there are wide variation within and across countries and regions. A better understanding of the complex interplay of genetic, environmental and HIV-factors in the pathogenesis of these comorbidities is essential. Furthermore, rigorous implementation science to determine optimal screening, prevention and treatment strategies in PWH in SSA is also critical.

PE9/74

People living with HIV are more likely to be screened for cardiovascular disease risk factors than other members of the general population in Botswana – a community based study

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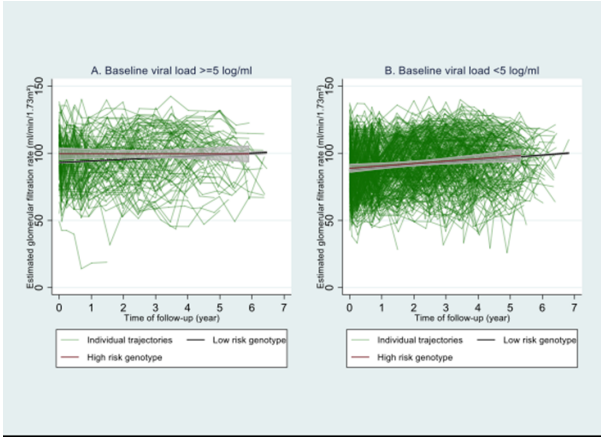
Purpose: People living with HIV (PLWH) are more likely to experience cardiovascular diseases compared to the general population. We aimed to assess whether PLWH were more likely to be screened for cardiovascular disease risk factors (CVDRF) compared to those without HIV.
Method: A population-based, cross-sectional study was conducted among individuals aged 16 to 64 years across 22 communities in Botswana between February and August 2017 as part of a larger community-based HIV prevention trial. Participants were asked if they were screened for and counselled about CVDRF (history of hypertension, blood glucose and cholesterol measurements, weight check and weight control, tobacco smoking and cessation, alcohol use and physical activity) in the last 3 years. HIV testing was offered to those with unknown HIV status. Multivariate logistic regression analysis controlling for age and sex, was used to assess the relationship between CVDRF screening and HIV status.
Results: Among 3981 participants enrolled, 2547(64%) were female, and 1196(30%) were PLWH (93% already on ART). PLWH were more likely to report previous screening for diabetes (25% vs 19%, p<0.001), elevated cholesterol (17% vs 12%, p<0.001) and to have had their weight checked (76% vs 55%, p<0.001) than participants without HIV. PLWH were also more likely to have received counselling on salt intake (42% vs 32%, p<0.001), smoking cessation (66% vs 46%, p<0.001), weight control (38% vs 29%, p<0.001), physical activity (46% vs 34%, p<0.001) and alcohol consumption (35% vs 23%, p<0.001) than those without HIV. Overall, HIV positive status was significantly associated with screening and counselling for CVDRF (AOR 1.84, 95% CI: 1.46 - 2.32).
Conclusion: PLWH were almost two times more likely to have been previously screened for CVDRF indicating a need for scale up of integrated management and prevention of CVD in those without HIV.

PE9/75

APOL1 high risk genotype has an adverse impact on kidney function in African HIV-infected patients with high viral load

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Purpose: To determine the impact of *APOL1*high-risk genotype (HR) on kidney function in African HIV+ patients starting a second line antiretroviral treatment (ART).
Method: Patients from Africa were randomized to receive one of three second line combinations (randomized phase 3 trial ANRS 12169). In this sub-study, we genotyped the *APOL1*G1 and G2 risk alleles through Taqman and defined HR by the carriage of two risk alleles (G1/G1, G1/G2 or G2/G2) vs. low-risk genotype (LR: G0/G0, G0/G1 or G0/G2). The kidney function was assessed by the CKD-EPI estimated glomerular filtration rate (eGFR). Logistic regression and mixed linear models were implemented to test the association of *APOL1*HR with rapid eGFR decline (>5 mL/min/1.73 m²/year) and eGFR evolution over time, respectively.
Results: 370 patients (71% female) from Cameroon (294), Burkina Faso (47) and Senegal (29) were included. 27(7.3%) patients had hypertension and 11 (3.0%) had an eGFR<60 mL/min/1.73 m² at baseline. Median (interquartile-range) baseline characteristics were 38.4 (33.2–46.3) yo, 176(78–288) CD4 T-cells/µl, 4.5 (4.1–5.1) log(viral load)/mL and 95.7 (80.9–111.2) mL/min/1.73 m² for eGFR. 12 patients (3.2%) were *APOL1*HR. Patients were on the second line ART for 57.9 (46.7–64.7) months. During follow-up, eGFR increased of 2 (95% confidence interval [CI], 1.7 to 2.3) mL/min/1.73 m² per year. Patients with baseline high viral load (≥5 log/mL) and *APOL1*HR had higher risk of rapid decline in eGFR (adjusted OR=24.9[1.5;419.5]) and tend to have a lower improvement in eGFR over time (adjusted β=-3.2[−6.8;0.4]mL/min/1.73 m²/year) than patients with baseline low viral load and *APOL1*LR (figure).
Conclusion: Compared to previous reports, the *APOL1*HR prevalence was low in our cohort (Estrella, 2015; Ekulu, 2019). In patients with baseline high viral load, those with APOL1 HR exhibit a suboptimal improvement in kidney function on second line ART.



Individual and predicted longitudinal estimated glomerular filtration rate (eGFR) by APOL1 high-risk

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PE9/76

Comparison of 2 frailty scores in PLWHIV aged 50 and over: SOF index and FRIED phenotype

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Purpose: The overall life expectancy of people living with HIV (PLWHIV) is increasing mainly due to access to highly active antiretroviral treatment and multidisciplinary care. The prevalence of frailty among PLWHIV is frequent and begin earlier compared to the general population. The measurement of frailty in PLWHIV is currently recommended but the best identification tool remain to be defined. The objective of this study was to compare the frailty criteria according to the FRIED phenotype and the SOF index (Study of Osteoporotic fractures) in PLWHIV.
Method: This multicentre, cross-sectional study included 509 PLWHIV aged 50 and over treated in 12 French hospitals. Demographic data, comorbidities, HIV data, geriatric parameters, Fried phenotype fragility markers and the SOF index were collected.
Results: Among the 509 PLWHIV (73% male, mean age 58.4 ± 7 years), according to the Fried phenotype 58.8% were pre-fragile and 8.2% were fragile; according to the SOF index, 37.1% were pre-fragile and 11.2% were fragile. The SOF index was weakly correlated to Fried's phenotype, with a Kappa score=0.267 ± 0.042 for patients classified as "fragile and pre-fragile" versus "robust" patients. In multivariate analysis, the presence of Fried's phenotype fragility markers was associated with the risk of depression, falls and a history of cancer. Frailty according to the SOF index was significantly associated with precariousness, incapacity for activities of daily living, risk of depression and falls.
Conclusion: In PLWHIV over fifty years old the SOF index and Fried's phenotype are low correlated scores. The use of Fried's phenotype identify more pre-fragile and fragile patients and therefore to be potentially more useful in identifying fragility in this population. Prospective studies assessing frailty and the risk of adverse change in morbidity and mortality are crucial in order to define relevant screening tools for this population.

PE9/77

Annexin V, Annexin A1 and cardiovascular risk in HIVpopulation

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Background: Whereas HIV-related mortality has decreased, rate of CVD death has increased(1). The endothelium plays a pivotal role in the pathogenesis of atherosclerosis. Several studies suggest that endothelial dysfunction is an independent predictor of adverse events in CVD patients(2). Annexins are one of the classes of proteins regulated by Ca2 + levels, characterized by a unique architecture that allows them to regulate different cellular events such as membrane morphology and organization, cytoskeletal activity.
The presence of extracellular annexins, such as Annexin A1 (AnxA1) and Annexin V (AnxV), is particularly evident in inflammation, a condition in which the annexins play an anti-inflammatory role. In addition, low AnxV levels are related to a greater atherosclerotic and thrombotic risk in systemic diseases. The aim of this study is to evaluate the relation between plasmatic AnxV and AnxA1 and cardiovascular risk scores in patients with HIV infection in viro-immunological stability.
Methods: We enrolled 222 HIV-positive outpatients in cART at the Infectious Diseases Clinics of Chieti and Roma. Demographic and anamnestic data were collected, blood and immunological parameters were measured and AnxA1 and V1 were analyzed. Framingham and DAD5 as CVD Risk scores were calculated.
Results: Levels of AnxA1 was 16.74 + /-19.02 ng/mL and AnxV was 1.4 + /-1.9 ng/mL; DAD5 was 2.27 + /- 2.54 and Framingham was 8.52 + /-6.5 . We found a negative association between DAD5 score and AnxV1 (r=-0.17 e p=0.008) and AnxA1(r=-0.17 e p=0.01). Furthermore, we observed a negative correlation between AnxA1 and Framingham score (r=-0.13 e p=0.05).
Conclusions: Annexins levels were significantly correlated with high risk CVD. Our work demonstrqte a correlation between the inflammatory annexins and the results obtained from the cardiovascular risk scores in HIV population . This work highlight how inflammation participates in the pathogenesis of cardiovascular damage and circulating levels of Annexins will be useful in improving cardiovascular risk calculation.

PE9/78

Could we consider the intima-media thickness (c-IMT)>1 mm as a risk factor for cardiovascular diseases in HIV+ subjects chronically treated with antiretrovirals?

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Background: HIV patients have a higher risk to develop cardiovascular diseases, which may be related to chronic inflammation and associated endothelial dysfunction. The relationship between carotid intima-media thickness (cIMT) and cardiovascular risk has not been fully explored in HIV patients on antiretroviral therapy (cART).
Methods: A cross-sectional study on 130 HIV+ on cART was performed to evaluate the relationship between cIMT and several parameters: epidemiological, immunological (CD4 nadir, CD4/CD8 ratio), virological (HIV-RNA), metabolic (total cholesterol, HDL, LDL, triglycerides) and clinical (time from HIV diagnosis, time on treatment, hypertension, diabetes or dyslipidemia).Mean value of the bilateral cIMT was considered for the quantitative analysis, whereas the greatest value for the qualitative analysis (cut-off 1 mm) . Cardiovascular risk was assessed using ASCVD risk calculator.
Results: Data of our population are resumed in Tables 1 and 2. Among 130 patients, 56 (43.1%) had cIMT>1 mm. These patients are older, have a longer history of infection and treatment, with lower CD4 nadir (p<0.0001) than patients with IMT<1 mm.
Age, time from diagnosis, time on cART were positively correlated with cIMT (respectively r=0.4555, r=0.3495 and r=0.3453) whereas CD4 nadir was correlated negatively (r=0.2854).
The multivariate logistic regression analysis revealed that age was the only independent risk factor of cIMT [OR=1.092 (C.I.1.037–1.151) p=0.0009]. ASCVD risk value>7.5% was found in 20 (35.7%) patients with cIMT>1 mm (p=0.011).
Conclusions: cIMT>1 mm was observed in a high percentage (43.1%) of HIV patients on cART; surprisingly age was the only independent risk factor associated with. In this setting, historical and actual immunological and virological parameters do not seem to play a role. Finally a cIMT>1 mm could be considered an alert of high estimated cardiovascular risk.

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Table 1. Epidemiological, clinical, virological data

Variables	N=130
Median (IQR) Age (years)	47.50 (40–53.35)
Median (IQR) Years of Infection (years)	9 (5–19)
Median (IQR) Time on Treatment (years)	7.5 (4–18)
Media ± DS (Zenit HIV -RNA (log copies/mL)	5.0 ± 0.7
Median (IQR) Nadir CD4 (cell/μL)	259 (119.50–375)
Median (IQR) CD8 (cell/μL)	765.50 (579.25–1112.75)
Median (IQR) CD4/CD8 (ratio)	0.91(0.57–1.1)
Median (IQR) right cIMT (mm)	0.80 (0.60–1.10)
Median (IQR) left cIMT (mm)	0.80 (0.60–1.03)

Table 2. Comparison between data collected in subjects with IMT more than or below 1 mm (univariate analysis)

		cIMT<1 mm: 74 (56.9%)	cIMT>1 mm: 56 (43.1%)	p
Sex	Male	61 (82%)	48 (85.7%)	ns
Risk Factors	MSM	47 (63.5%)	27 (48%)	ns
	IVDU	6 (8%)	6 (10.7%)	ns
Age	Years	43 (35–50)	52 (47–57.5)	<0.0001
Time from HIV Diagnosis	Years	7 (3.75–12)	16 (8.25–21)	<0.0001
Time on cART	Years	6 (3–10)	14 (7.25–19)	<0.0001
HIV-RNA VL<50	cases (%)	67 (90.5%)	48 (85.7%)	ns
Nadir CD4	cells/μl	321 (168.5–425)	146.5 (73–306)	0.01
ASCVD risk value>7.5%	cases (%)	11 (16%)	20 (35.7%)	0.011

PE9/79

Immune reconstitution inflammatory syndrome (IRIS) in HIV-infected hospitalized patients with advanced disease

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Purpose: The purpose of this study is to describe clinical characteristics of HIV-infected hospitalised patients who develope IRIS between January 2009 and December 2018 in a tertiary Public Health System hospital of Madrid (Spain).
Method: Retrospective single-centre study of HIV patients treated with HAART.
Results: During the study period, 678 hospital admissions of 313 HIV patients were registered. Of them, 141 patients (45%) had detectable viral load, most of whom (60%) were not receiving ART at baseline. 48 patients (34%) did not know HIV diagnosis before admission (of which 70% was diagnosed with advanced disease stage). 75% were men, median age was 45 years old (IQR 39–51) and the most probable way of HIV acquisition was IDU (33%), heterosexuals (24%), and homosexuals (22%). 35.7% was HCV co-infected. Nadir and baseline CD4 + T-cell count were 70/mm3 (IQR 23–167) and 107/mm3 (IQR 26–320), respectively. IRIS occurred in 22 patients (15.6%). IRIS was related to Mycobcaterium (27%), cytomegalovirus (27%), *Pneumocystis jiroveci* (13.6%), progressive multifocal leukoencephalopathy (9%), Castleman's disease (9%), Kaposi sarcoma (4.5%), histoplasmosis (4.5%), and leishmaniasis (4.5%). Baseline CD4 + T-cell count was 11 /mm3 (5–35) and pre-ART VL was 5.71 log10.copies/mL (SD 0.73). CD4 + T-cell count was 77/mm3 (38–121) and VL was 3.1 log10 copies/mL when IRIS was diagnosed, 15 days after ART was initiated (12–21). Rapid decline in HIV viral load (2.72 log) resulted significant (95% CI 2.4–3.1; p<0.00001), unlike for increase in CD4 + T cell count (p=0.973). 13% stopped ART, 13% changed ART and 74% continue the same regimen (100% of INSTI group, 75% of NNRTI and 50% of bPI). Cumulative mortality prevalence was 21% across last ten years, without associated risk factors.
Conclusion: IRIS occurred early in patients with very low CD4 T-cell count and rapid decline of HIV viral load after ART was initiated during hospitalization.

PE9/80

Low Body Mass Index (BMI) in ART naïve HIV-positive subjects and risk of virological failure and drug discontinuation: data from the ICONA Foundation Cohort

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A condition of low BMI — defined as a value<18.5 — affects 5% of HIV+ population and is associated with increased mortality.
Objectives: Assess the proportion of patients naïve to antiretroviral treatment (ART) with low BMI at treatment start; describe their demographic and clinical features; evaluate immunological, virological, clinical and therapeutic outcomes.
Methods: Naïve subjects who started any ART in 2008–2018 within the ICONA cohort and with a measure of BMI available before ART were included. Descriptive statistics and non-parametric (Chi-square and Kruskal-Wallis)

Table 1. Main characteristics of patients by baseline BMI group (Chi-square and Kruskal-Wallis as appropriate).

Characteristics	0-18.4 N= 315	18.5-24.9 N= 3926	24.9-29.9 N= 1374	29.9+ N= 306	Unknown N= 2635	p-value*
Female Gender, n(%)						
	141 (44.8%)	753 (19.2%)	206 (15.0%)	75 (24.5%)	523 (19.8%)	<.001
Mode of HIV Transmission, n(%)						
IDU	33 (10.5%)	296 (7.5%)	110 (8.0%)	19 (6.2%)	151 (5.7%)	<.001
Homosexual contacts	101 (32.1%)	2029 (51.7%)	645 (46.9%)	107 (35.0%)	1114 (42.3%)	
Heterosexual contacts	159 (50.5%)	1416 (36.1%)	553 (40.2%)	166 (54.2%)	1059 (40.2%)	
Other/Unknown	22 (7.0%)	185 (4.7%)	66 (4.8%)	14 (4.6%)	311 (11.8%)	
Nationality, n(%)						
Not Italian	94 (29.8%)	949 (24.2%)	309 (22.5%)	65 (21.2%)	788 (29.9%)	0.019
AIDS diagnosis, n(%)						
Yes	42 (13.3%)	194 (4.9%)	54 (3.9%)	10 (3.3%)	196 (7.4%)	<.001
Age, years						
Median (IQR)	35 (28, 42)	37 (30, 44)	39 (33, 47)	40 (35, 50)	38 (31, 45)	<.001
CD4 count, cells/mmc						
Median (IQR)	218 (47, 400)	344 (204, 480)	370 (240, 507)	399 (242, 545)	314 (149, 481)	<.001
CD8 count, cells/mmc						
Median (IQR)	752 (474, 1083)	888 (620, 1257)	945 (660, 1320)	997 (748, 1420)	888 (588, 1279)	<.001
Viral load, log10 copies/mL						
Median (IQR)	4.97 (4.25, 5.53)	4.65 (4.02, 5.22)	4.58 (3.90, 5.11)	4.51 (3.76, 5.03)	4.66 (3.93, 5.23)	<.001
Diabetes, n(%)						
Yes	2 (0.6%)	49 (1.2%)	48 (3.5%)	19 (6.2%)	48 (1.8%)	<.001
Smoking, n(%)						
No	158 (50.2%)	1929 (49.1%)	701 (51.0%)	174 (56.9%)	689 (26.1%)	<.001
Yes	133 (42.2%)	1610 (41.0%)	504 (36.7%)	103 (33.7%)	574 (21.8%)	
Unknown	24 (7.6%)	387 (9.9%)	169 (12.3%)	29 (9.5%)	1372 (52.1%)	
Total cholesterol, mg/dL						
Median (IQR)	152 (128, 178)	160 (135, 184)	166 (142, 193)	167 (143, 190)	156 (134, 182)	<.001
HDL cholesterol, mg/dL						
Median (IQR)	39 (31, 51)	40 (32, 48)	38 (31, 46)	37 (31, 46)	38 (31, 48)	<0.001
Education, n(%)						
Primary school	31 (9.8%)	216 (5.5%)	75 (5.5%)	23 (7.5%)	81 (3.1%)	<0.001
Secondary school	69 (21.9%)	745 (19.0%)	272 (19.8%)	57 (18.6%)	291 (11.0%)	
College	103 (32.7%)	1352 (34.4%)	450 (32.8%)	96 (31.4%)	570 (21.6%)	
University	28 (8.9%)	587 (15.0%)	173 (12.6%)	21 (6.9%)	235 (8.9%)	
Other/Unknown	84 (26.7%)	1026 (26.1%)	404 (29.4%)	109 (35.6%)	1458 (55.3%)	
Employment, n(%)						
Unemployed	74 (26.7%)	559 (16.2%)	179 (14.9%)	41 (16.0%)	244 (15.2%)	<.001
Employed	116 (41.9%)	1766 (51.2%)	587 (49.0%)	136 (52.9%)	761 (47.5%)	
Self-employed	35 (12.6%)	553 (16.0%)	235 (19.6%)	37 (14.4%)	258 (16.1%)	
Occasional	8 (2.9%)	160 (4.6%)	38 (3.2%)	9 (3.5%)	48 (3.0%)	
Student	16 (5.8%)	169 (4.9%)	28 (2.3%)	4 (1.6%)	58 (3.6%)	
Retired	9 (3.2%)	76 (2.2%)	57 (4.8%)	14 (5.4%)	60 (3.7%)	
Invalid	0 (0.0%)	7 (0.2%)	4 (0.3%)	1 (0.4%)	4 (0.2%)	
Housewife	14 (5.1%)	77 (2.2%)	26 (2.2%)	10 (3.9%)	37 (2.3%)	
Other/unknown	5 (1.8%)	85 (2.5%)	44 (3.7%)	5 (1.9%)	131 (8.2%)	

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tests were used; KM probability curves and multivariable Cox regression models for virological failure, treatment discontinuation and clinical events were used. Mean changes in CD4 and CD8 cell count from fitting a linear mixed model after ART start were estimated.
Results: 5,921 subjects were included: 315 individuals (5.3%) showed a BMI below 18.5. Subgroups stratified according to BMI resulted different in terms of demographic, clinical and social features (Table 1).
In the unadjusted analysis, baseline BMI class was associated with a significantly different risk of virological failure and treatment discontinuation with a worse trend for the group with BMI<18.5, while no correlations with clinical events were observed (Figure 1). The difference in risk of virological failure and treatment discontinuation was attenuated after controlling for key confounding factors (mainly age and CD4 count). CD4 count and CD4/CD8 ratio trend over time had no correlation with BMI, while CD8 count showed a steeper slope of decrease during ART in low and in obese BMI classes.
Conclusion: BMI<18.5 is uncommon in ART naïve subjects but is related to virological failure and treatment discontinuation, although age and pre-ART CD4 count played the pivotal role. Low BMI is an indicator of vulnerability and might be considered as a predictor of treatment failure.

Figure 1. Kaplan-Meier estimates for virological failure (A), drug discontinuation (B), AIDS and severe non-AIDS clinical events, including death (C).

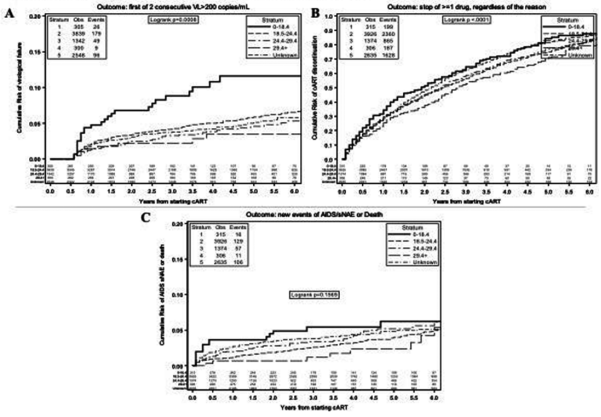


Figure 1. KM estimates for virological failure, drug discontinuation and clinical events

PE9/81

Sistatin C, KIM1 and NGAL as biological markers for detecting early kidney injury in HIV positive patients

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Purpose: HIV positive people are at increased risk for kidney damage because of the disease itself, comorbidities and drugs used. Proteinuria and eGFR are not enough for early diagnosis. In this study our aim is to investigate the role of Cystatin C, Kidney Injury Molecule-1 (KIM1) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) in early kidney damage.
Method: Sample size was calculated and 88 HIV positive patients who admitted to Infectious Diseases Outpatient Clinic and were willing to participate the study were enrolled. 81 control patients were selected among healthy volunteers. Patient demographics, underlying conditions, treatments were recorded. Cystatin C, Kidney Injury Molecule-1 (KIM1) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) was studied by ELİSA from serum and urine samples.
Results: Mean age was 38.5 ± 12.6 and 67.5% (n=114) was male totally. There was no difference between ages of patient and control groups (p>0.05) but more women were included in the control group (13.6% vs 51.3%, p<0.001). There was a correlation between eGFR and urine NGAL (p<0.001). Mean Cystatin C, Kidney Injury Molecule-1 (KIM1) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) levels of patient and control groups are shown in table 1. eGFR, serum Cystatin C, serum and urine NGAL, and serum KIM-1 was significantly lower in the patient group.
Conclusion: Serum levels of Cystatin C, NGAL, KIM-1 and urine NGAL were found lower in HIV positive patients and these biochemical markers are candidates for the diagnosis of early kidney damage in this patient population.

Mean Cystatin C, Kidney Injury Molecule-1 (KIM1) and Neutrophil Gelatinase-Associated Lipocalin (NGAL) levels of patient and control groups

	Patient (n=88)		Control (n=81)		
	Mean	Standart deviation	Mean	Standart deviation	p value
eGFR	107.9081	23.48673	122.9820	24.39907	<0.001
Serum_Sistatin_C	36.53	52.038	54.23	52.174	0.03
NGAL_serum	835.24003	1525.303625	1300.08744	1455.311707	0.045
NGAL_urine	111.02	72.591	242.95	62.283	<0.001
KIM1_serum	3.94591	5.802521	6.11611	5.890953	0.017
KIM1_urine	0.58628	0.286272	0.55826	0.202525	0.467

PE9/82

Long-term AIDS survivors: comorbidities and polypharmacy a new challenge

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Purpose: There are many people living with HIV (PLWIV) diagnosed in the 80s and early 90s when there was no efficacious antiretroviral treatment (ART) who are still alive. They have also survived the era of lipodystrophy and other adverse events and are getting older. The objective of our study is to characterize the comorbidities and their treatment in PLWHIV of our cohort who were diagnosed before 1997.
Method: Single-centre observational, retrospective, non-interventional study carried out in a third level hospital in Spain. Our cohort included PLWIH diagnosed before 31 December 1996 visited in the outpatient clinics at least once from January 1, 2017 to December 31, 2018. Baseline sociodemographic, clinical characteristics, ART, comorbidities and concomitant medication were analyzed using STATA 14.
Results: We included 374 patients with a mean age of 54 ± 6.14 years old of which 262 (70.05%) were men. The mean time of follow up was 27.56 (±3.28) years. The main risk factor of transmission was the use of intravenous drugs (55.6%). 39 of them (10.5%) where diagnosed of HIV and AIDS at the same time. The most frequent comorbidities were: lipodystrophy 70 (77.54%), HCV coinfection 216 (57.75%), dyslipidaemia 178 (47.59%) and hypertension 93 (24.87). Only 30 patients (8.02%) didn't have any comorbidity. 161 (43%) had 3 or more comorbidities and 114 (30.48%) had two comorbidities. The mean Charlson Comorbidity index was 3.3 (SD 2.9) and VACS index was 23.9 (SD 15.4). The mean of treatments per patient was 4.1 (±3) (23% of our patients≥5 drugs). Nervous system drugs are the most frequently prescribed (35.29%) followed by alimentary tract and metabolism (21.95%) and cardiovascular system (18.78%) drugs.
Conclusion: The long-term AIDS survivors have a high prevalence of comorbidities and polypharmacy. The right management of comorbidities is a challenge to improve their quality of life and their survival.

Comorbidities (n, %)

Diabetes mellitus	70 (17.72)
Hypertension	93 (24.87)
Dyslipidaemia	178 (47.59)
HCV coinfection	216 (57.75)
Hepatic steatosis	86 (23)
Lipodystrophy	70 (77.54)
Non AIDS malignancy	49 (13.1)
Osteopenia/osteoporosis	76 (20.32)
COPD	48 (12.83)
Ischaemic heart disease	18 (4.81)

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Polypharmacy.Co-medication (n, %)

Nervous system	468 (35.29)
Alimentary tract and metabolism	291 (21.95)
Cardiovascular system	249 (18.78)
Blood and blood forming organs	62 (4.68)
Genitourinary system and sex hormones	21 (2.41)
Antiinfectives for sistemic use	27 (2.04)
Músculo-skeletal system	41 (3.09)
Respiratory system	85 (6.41)
Antiparasitic products	14 (1.06)
Sensory organs	14 (1.06)

PE9/83

Risk Factors associated to immune reconstitution inflammatory syndrome (IRIS) in HIV-infected hospitalized patients with advanced disease

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Purpose: The purpose of this study is to determine risk factors associated to IRIS in HIV-infected hospitalised patients between January 2009 and December 2018
Method: Retrospective single-centre study of HIV patients treated with HAART.
Results: During the study period, 678 hospital admissions of 313 HIV patients were registered. Of them, 141 patients (45%) had detectable viral load, most of whom (60%) were not receiving ART at baseline. IRIS occurred in 22 patients (15.6%). There were no differences by sex (12.5% of male Vs 12.9% of women, (p=0.954). Known HIV infection duration was inferior in patients with IRIS (median difference of 10 years, 95% CI 5.5–15.1). 21% showed HCV-coinfection, vs 46% of patients without IRIS (p=0.033). 95% suffered from an AIDS-disease as cause of admission; IRIS was developed in 22% of patients with AIDS cause of hospitalization and 0.5% of non-AIDS reasons (p<0.0001). 54% did not know HIV status (6% in patients without IRIS; p<0.0001). Rapid decline in HIV viral load (2.72 log) resulted significant (95% CI 2.4–3.1; p<0.00001), unlike for increase in CD4 + T cell count (p=0.973). 42% were taking NNRTI, 10% PI and 47% INSTI (p=0.023). Inside NNRTI family efavirenz was most associated to IRIS (p=0.061). There were no differences between lopinavir, atazanavir and darunavir. Dolutegravir was most related to IRIS in INSTI group (75%; raltegravir 25%; p=0.017). Factors associated to IRIS in multivariate analysis were: undetectable viral load before admission: aOR 0.035 (95% CI from - 0.065 to - 0.005; p=0.021). AIDS cause of hospitalization: aOR 14.7 (95% CI 10.9–18.5; p<0.0001). Unknown HIV infection: aOR 13.2 (95% CI 7.3–19.1; p<0.0001).
Conclusion: Detectable viral load, AIDS cause of admission and unknown HIV infection were associated to IRIS in our cohort. Efavirenz and dolutegravir could be most related drugs to IRIS but further investigations are needed.

PE9/84

Sleep disorders and depression through efavirenz to dolutegravir transition in Brazil: what really changed after all

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Purpose: Sleep and Depression usually walk together in HIV patients' life, related to their own condition or as consequence of Antiretroviral therapy (ART). These disturbances were common in Efavirenz therapy and recently questionable in integrase era. Inadequate sleep contributes to a poor quality of life. Otherwise anxiety and depression are psychological factors that affect sleep quality.
Method: The Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale adapted to Brazil (ESS-Br) and Patient Health Questionnaire-9 (PHQ-9) were applied to evaluate ART correlation to sleep disturbances and depression.
Results: This was a cross-sectional study of 92 HIV positive out-patients who were taking regularly ART (Efavirenz/EFZ=21, Dolutegravir/DTG=66 and Atazanavir/r/ATV=5) in the clinic pharmacy at Unichristus University/Ceara/Brazil.
Results: Based on the sleep quality assessment, 67% in EFZ, 70% in DTG and 80% in ATV of the patients had PSQI>5 that was defined as sleep disturbances, without difference between EFZ and DTG (p=0.79). This scale is based on seven "component" scores: subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbances (C5), use of sleeping medication (C6), and daytime dysfunction (C7). Study results for each component was: C1 (EFZ=1.3, DTG=1.1, ATV=1), C2 (EFZ=1.3, DTG=1.2, ATV=1.2), C3 (EFZ=1.2, DTG=0.9, ATV=1.2), C4 (EFZ=0.6, DTG=0.5, ATV=0.2), C5 (EFZ=1.3, DTG=1.3, ATV=2.2), C6 (EFZ=1.1, DTG=0.8, ATV=1.2), C7 (EFZ=1, DTG=0.9, ATV=1.4), and global score (EFZ=7.9, DTG=6.7, ATV=8.4). Evaluating daily sleepiness (ESS-Br) was identified risk in 23.8% in EFZ, 20.3% in DTG and 20% in ATV, without difference between EFZ and DTG (p=1). PHQ-9 Management Summary for Depression severity was: Minimal or none (EFZ=38%, DTG=40.6%, ATV=0%), Mild (EFZ=23.8%, DTG=25%, ATV=80%), Moderate (EFZ=9.5%, DTG=7.8%, ATV=20%), Moderately severe (EFZ=9.5%, DTG=20.3%, ATV=0%) and Severe (EFZ=14.3%, DTG=6.2%, ATV=0%).
Conclusion: Sleep disorders and depression are a major problem both for EFZ and DTG groups. Nothing changed after all.

PE9/85

Patterns of inflammation and comorbidity in Human Immunodeficiency Virus (HIV) infection: a clustering analysis from the CARDAMONE study

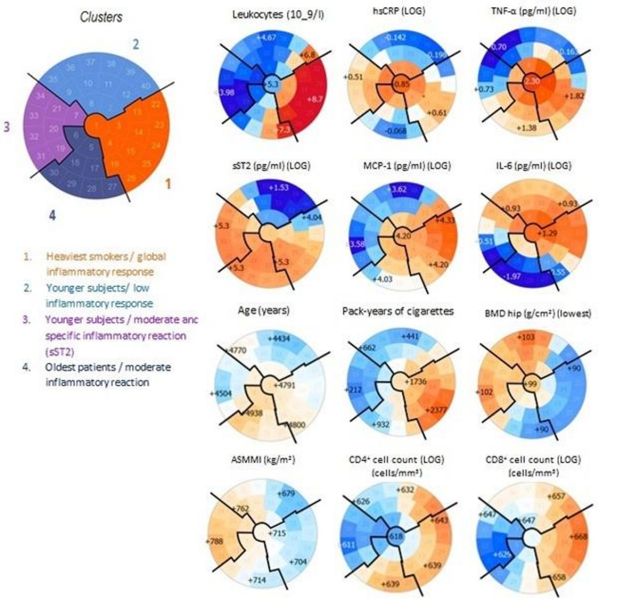
S Zebachi[1], S Hüe[2,3], L Boyer[4,5], S Gallien[2,3], M Surenaud[2,3], J-L Lopez Zaragoza[2,3], J-D Lelièvre[2,3] and É Audureau[1]

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Purpose: Since the advent of ART, the occurrence of AIDS-related events has decreased in HIV-infected individuals. Associated with increasing life expectancy, a raise in the incidence of comorbidities (cardiovascular diseases and metabolic complications) has been reported in this population. While the role of key inflammatory markers such as IL-6, TNF-α and sST2 has been discussed, less is known regarding their complex interactions with age and other risk factors. We aim to better characterize and understand the associations between chronic inflammation and the occurrence of comorbidities in HIV-infected individuals through machine-learning methods.
Method: Data were drawn from the CARDAMONE study, including 241 HIV-1-infected participants under ART with comprehensive clinical, biological and functional phenotyping. To identify specific patients' profiles with similar inflammation patterns and their association with comorbidity occurrence, unsupervised clustering analyses were performed using Self-Organizing Map (SOM) artificial neural network approach, allowing two-dimensional mapping of patients and grouping those with similar inflammation features in clusters. Other clinic-biological characteristics and comorbidities prevalences were analysed as illustrative features.
Results: 4 clusters were identified:
(1) gathered the heaviest smokers developing an elevated global inflammatory response (IR) (MCP-1, hsCRP, IL-6, IL1-β, TNF-α, sST2),
(2) comprised younger subjects, mainly women, with globally low IR,
(3) included younger subjects with a moderate and highly specific IR (sST2, hsCRP) despite the lowest smoking frequency but with the lowest CD4 and CD8 values,

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(4) grouped the oldest patients with a moderate IR.
Conclusion: Clustering analysis identified contrasted inflammation profiles with distinct associations with age, smoking and HIV-related endpoints. We find, as already shown in the literature, a cluster composed of smokers with a high degree of inflammation and a cluster of older people developing a different type of inflammation. The novelty here is the identification of a cluster of relatively young subjects, non-smokers, but developing a particular inflammatory profile.



Maps (SOMs) with proposed boundaries defining clusters - Inflammatory profiles

PE9/86

Cognitive impairment in patients with HIV in a Mexican hospital

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Purpose: To describe the clinical characteristics of patients with HIV and cognitive impairment.
Method: We conducted a pilot study in 104 patients with VIH that were seen in outpatient care at Infectious Diseases Hospital in LA Raza National Medical Center during March to December 2018. We studied 21 patients with Montreal Cognitive Assessment (MOCA) test equal or inferior than 26 points. Brain magnetic resonance, lumbar puncture and neurologic evaluation were performed.
Results: We found 12 (57.14%) female patients and 9 (42.8%) males. Most of the patients were being treated with protease inhibitors (71.42%) plus nucleoside analogue reverse transcriptase inhibitor (61.90%) by the time of the study. Two of 15 patients with undetectable serum HIV load reported detectable HIV viral load in (CSF), which represents 13% of the serum undetectable patients. We divided patients into two groups, one with undetectable HIV viral load in CSF [15 patients (71.42%)] and the second one with detectable viral load in CSF [6 patients (28.57%)]. In regard to HIV duration, the first group had an average of 22.66 years with HIV, the second one with 21.73 years. Amongst CD4/CD8 relation, this was higher in the first group with a value of 0.90, versus 0.74 in the second group. The most prevalent abnormalities on magnetic resonance were small vessel disease (62.5%), followed by hippocampal atrophy (56.25%). At evaluation by neurologist the most prevalent impairment was dysmetria in 6 patients.
Conclusion: The prevalence of detectable CSF HIV load in patients with undetectable serum HIV load was higher than reported by international studies, which could be related to viral scape and cognitive impairment.

In other series the most sensible brain abnormality for HIV cognitive impairment was brain atrophy unproportioned to age. In this study more than half of the patients presented hippocampal atrophy.

PE9/87

Clinical management of ageing people living with HIV in Europe: The view of the care providers

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Purpose: Although guidelines for the management of HIV infection include recommendations for aging people living with HIV (PLWH), clinical practice of European HIV care providers may vary. We aimed at investigating the clinical management of ageing PLWH from the perspective of the care provider.
Method: We performed a study using a 3-phase Delphi methodology by involving a panel of clinicians with expertise in HIV infection clinical management. The first phase involved 10 clinicians to identify HIV comorbidities of interest. The second and third phases recruited clinicians virtually via a web-based questionnaire that included 137 questions focussed on 11 comorbidities (e.g. cardiovascular disease, pulmonary disease, etc). Results were analysed thematically and consensus (or not) among European physicians reported.
Results: Ninety-seven and 85 responses were collected in phase 2 and 3, respectively. While we observed general agreement in the relevance of assessing cardiovascular risk, smoking and allergy history, lipids, renal parameters, bone health via FRAX calculation or BMD scan, depression and anxiety and sexual health screening, there was disagreement in determining the best marker for diagnosis of impaired glucose tolerance (fasting glucose versus HbA1c) and responders did not seem to evaluate frailty or menopause in their clinical practice.
Conclusion: High levels of agreement were found among clinical care providers across Europe and with the European AIDS Conference Society (EACS) guidelines regarding key items of clinical management of comorbidities in ageing PLWH. However, we identified some important gaps, such as the lack of standardisation or implementation of the assessment of frailty or menopause, which are emerging as important factors to optimise ageing PLWH clinical care. Further studies are warranted to confirm whether intensified screening translates into HIV morbidity advances.

PE9/88

Real-word characterization of the Portuguese population living with HIV who initiated Raltegravir based-regimen in the last three years - REALITY Study

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Purpose: Over the last years, RAL has proven to be an effective and well tolerated drug, with few drug-drug interactions. As real-world data are missing about the Portuguese HIV-infected population who initiated RAL-based regimens, this study aimed to characterize patients who initiated RAL in the last 3 years.
Method: Non-interventional, retrospective study conducted in 11 Portuguese centers. Data was collected from hospital medical records from patients who initiated RAL in the last 3 years. Baseline was defined as the time of initiation of RAL.
Results: A total of 302 patients were recruited between 17 Jul 2018–02 Apr 2019 with 34.1% being naïve and 65.9% experienced with a mean duration of 4.2 years on previous ART. The proportion of patients with CD4 + T counts>500 cells/mm3 was 24.8% (diagnosis), 46.7% (baseline) and 67.5% (last measurement). RNA HIV was detectable for 99.2%, 48.8% and 4.0% at each time point, respectively. The mean duration of RAL was 25.3 months.More than half of the patients was<50 years old and had non-AIDS related comorbidities at baseline (53.3%, 161/302). The median number of non-AIDS related comorbidities was 2 and the most reported comorbidities at baseline were: hypercholesterolemia (44.1%) arterial hypertension (42.2%) and diabetes *mellitus* (17.4%) Depression and renal failure were also present in more than 10% of the study population (17.4% and 11.8%, respectively). Other comorbidities were also reported at baseline and included mostly anxiety (n=12), bronchitis (n=6), malignancy (n=6) and obesity (n=6).
Fifty patients (16.6%, 50/302) reported 3 or more comorbidities at baseline.
Conclusion: At last measurement, more than 90% of the patients presented sustained virologic suppression. Data from the REALITY study showed that more than half of the Portuguese HIV-infected population at the time of initiation of a RAL based regimen presented non-AIDS related comorbidities.

PE9/89

Long-term lipid-lowering-therapy in HIV is clinically effective

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ASCVD-outcomes of statins in HIV have not been studied in conjunction with other health outcomes and those of other cardiovascular preventive medications (CVPM), particularly non-statin (NS) lipid-lowering therapy (LLT). We analyzed the clinical impact of CVPM use in all HIV-infected US-veterans after their first undetectable HIV-viral load on HAART from 1995–2011, examining LLT (statins, fibrates, fish-oil, ezetemibe, and nicain), antihypertensives (AHT), and cardiac Aspirin (ASA) in relation to mortality, cardio- or cerebrovascular (ASCVD) events, severe infections, and cancer. We applied marginal structural models for each outcome controlling for all exposure levels within each CVPM class. Exposure models for all antiretrovirals (ARVs), and CVPMs were based on weekly-updated VA-pharmacy out-and inpatient data. We used: demographics, calendar year, hospital-size, follow-up frequency, HCV-status, smoking, drug-use, 1-year HAART/ARV possession rates, past-year HIV-VL and CD4-averages, liver and kidney function, hemoglobin, BMI, blood-pressure, and 1-year cholesterol averages (total and HDL) to build individual propensity scores for each exposure level and outcome. We defined long-term exposure as≥11/12 months, recent exposure as<11 months exposure in the past year, and remote exposure as last use>1-year ago. Non-death clinical events were defined by ICD-9-codes, except for acute CVD events that also used PTCA procedure codes and evidence of neuroimaging for new cerebrovascular insults.
We followed 23,267 patients (97% male, 46% black) for median 5.2 years (IQR:2.5–9.2). Median age was 53 years (IQR:46–60). 42% were ever exposed to LLT. The tables contain the hazard ratios for clinical outcomes. Mortality findings were similar when restricting the analysis to≥2006 (not shown).
Our analysis confirms a substantial mortality benefit for HIV patients taking long-term LLT. The statin effect is likely driven by reduced infection and cancer risk while NS-LLT only exerts a protective effect on ASCVD risk. In contrast, neither AHT nor ASA seemed to confer clinical benefits.

Table 1

Long-Term Exposures	Patient years	Death	New CVD Event	Acute CVD Event	Infection	Cancer
	140,130	*n=4,622*	*n=3,783*	*n=1,368*	*n=6,618*	*n=3,469*
Statins only	7,752	0.51 (0.37–0.70) p<0.0001	1.04 (0.83–1.30) p=0.11	0.95 (0.62–1.47) p=0.55	0.62 (0.51–0.76) p=0.0007	0.63 (0.46–0.84) p=0.005
Non-Statin LLT only	2,493	0.29 (0.17–0.51) p<0.0001	0.86 (0.45–1.64) p=0.69	0.16 (0.06–0.46) p=0.003	0.78 (0.52–1.16) p=0.32	0.70 (0.45–1.08) p=0.17
Combined LLT	6,150	0.35 (0.23–0.53) p<0.0001	1.28 (0.98–1.68) p=0.37	1.17 (0.64–2.16) p=0.42	0.61 (0.46–0.79) p=0.01	0.82 (0.58–1.16) p=0.37
Mono AHT	19,910	1.39 (1.21–1.60) p<0.0001	1.68 (1.45–1.96) p<0.0001	2.33 (1.76–3.08) p<0.0001	1.14 (1.02–1.28) p=0.02	1.01 (0.87–1.17) p=0.97
Dual AHT	11,351	1.24 (0.98–1.57) p=0.11	1.36 (1.08–1.72) p=0.02	1.76 (1.16–2.68) p=0.01	1.13 (0.96–1.34) p=0.22	0.93 (0.73–1.19) 0.54
Cardiac ASA	4,472	* joint with recent use (see Table 2)	2.62 (1.81–3.79) p<0.0001	3.43 (1.76–6.67) p<0.0001	0.99 (0.76–1.31) p=0.90	1.54 (1.09–2.19) p=0.02

Table 2. (Hazard Ratios (95% Confidence interval), multiplicity-corrected p-values)

Recent/Remote Exposures	Patient Years	Death	New ASCVD event	Acute ASCVD event	Severe Infection	Cancer
Recent LLT	23,701	0.65 (0.57–0.74) p<0.0001	1.57 (1.40–1.77) p<0.0001	1.89 (1.55–2.29) p<0.0001	0.76 (0.68–0.85) p<0.0001	0.89 (0.77–1.04) p=0.22
Remote LLT	9,044	1.04 (0.87–1.24) p=0.70	0.89 (0.71–1.10) p=0.37	0.85 (0.58–1.24) p=0.45	0.78 (0.66–0.93) p=0.01	0.72 (0.58–0.90) p=0.007
Recent AHT	28,438	2.17 (1.96–2.40) p<0.0001	2.36 (2.10–2.64) p<0.0001	3.15 (2.54–3.91) p<0.0001	1.26 (1.16–1.37) p<0.0001	1.05 (0.92–1.20) p=0.52
Remote AHT	15,157	1.23 (1.07–1.42) p=0.01	1.10 (0.90–1.35) p=0.40	0.83 (0.58–1.20) p=0.42	1.11 (0.98–1.25) p=0.20	0.92 (0.79–1.09) p=0.43
Recent ASA	15,437	1.58* (1.40–1.77) p<0.0001	4.94 (4.41–5.53) p<0.0001	8.09 (6.79–9.63) p<0.0001	1.48 (1.32–1.66) p<0.0001	1.08 (0.91–1.28) p=0.42
Remote ASA	16,691	1.19 (1.05–1.36) p=0.01	1.20 (1.02–1.42) p=0.06	1.22 (0.91–1.65) p=0.33	1.13 (1.00–1.27) p=0.11	0.97 (0.83–1.13) p=0.75

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Gender issues

PE10/1

Patient, clinical and virus genetic characteristics of female migrants from Eastern, Central and Western Africa enrolled in the SHCS

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Purpose: We aim at identifying patient, clinical and virus genetic characteristics of female migrants in Switzerland; a group with a high HIV prevalence known to be vulnerable and important.
Method: Our study population consisted of female Swiss HIV Cohort Study (SHCS) participants of black ethnicity coming from Eastern, Central or Western Africa. The study population was compared to a control population of white female SHCS participants infected with HIV subtype B, matched by median SHCS registration year. Both, study and control population, were infected with HIV through heterosexual contacts and had at least one sequence in the SHCS resistance data base. A phylogenetic tree including one sequence per SHCS participant and blasted Los Alamos background sequences was built.
Results: Compared to our control population, our study population had a comparable number of median follow-up visits per year, a higher median ability to work 100% and fewer reported psychiatric problems (Table). Adherence to antiretroviral treatment (ART) was considerably poorer ($p<0.001$) and in line with this, the mean log10 RNA values after the first initiation of ART was significantly higher for the study population compared to the control population. First CD4 cell counts were lower for our study population ($p<0.001$), and fewer participants were diagnosed during primary infection ($p<0.001$). Our study population was infected with a wide range of HIV-subtypes, greatly differing for the respective regions of patient origin, and less than half had a SHCS participant as the closest neighbor on the phylogeny.
Conclusion: Awareness and accessibility to HIV-testing should be raised in the population of female migrants from Eastern, Western and Central Africa to capture infections early. However, the phylogenetic clustering with Los Alamos sequences along with the subtypes detected in the study population indicates that the contribution to the ongoing HIV epidemic originating from these migrant women is rather low.

Variable	Controls	All migrants	p (all migrants vs controls	Western Africa	Eastern Africa	Central Africa
Total	638	726	-	139	254	333
Patient characteristics						
Median birth year	1966	1973	< 0.001	1975	1972	1973
Median registration year	2005	2005	0.962	2006	2003	2005
Median diagnosis year	2004	2003	0.099	2004	2002	2004
Psychiatric problems	42.9%	31.3%	< 0.001	33.1%	31.1%	30.6%
Ability to work 100%	69.2%	85.5%	< 0.001	90.2%	82.3%	86%
Imperfect adherence	16.6%	29.3%	< 0.001	34.4%	28.1%	28%
Clinical characteristics						
Median number follow-up per year	3.5	3.8	0.24	3.8	3.9	3.8
Mean first CD4 measurement	408	304	< 0.001	302	295	311
Mean CD4 nadir	229	207	0.012	206	205	209
Mean first log viral load	4.35	4.33	0.759	4.25	4.34	4.36
Documented primary infection	7.1%	1.9%	< 0.001	2.2%	1.6%	2.1%
Opportunistic infection	45%	41.5%	0.208	35.3%	42.1%	43.5%
Mean log10 RNA after ART start	0.62	0.91	0.003	0.9	0.94	0.89
Genetic characteristics						
Three most frequent subtypes	B (100%)	02_AG (26.97%) C (22.13%) A (19.36)	-	02_AG (54.68%) G (12.23%) Recomb (10.79%)	C (57.94%) A (24.6%) D (5.95%)	02_AG (34.64%) A (20.18%) Recomb (10.54%)
Closest neighbor on phylogeny enrolled in SHCS	78.2%	47.3%	< 0.001	45.3%	46.8%	48.5%

Patient, clinical and virus genetic characteristics of study and stratified control population. P-value

PE10/2

Menopause impacts drug use and mental health in women with HIV in Switzerland

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Purpose: We aimed to assess age at menopause and factors associated with early menopause in HIV-positive women, and to explore its impact on HIV viral load, behaviour changes and mental health disorders.
Methods: We performed a retrospective analysis of HIV-positive women followed in the Swiss HIV Cohort Study (SHCS) with documented menopause between 01/2010 and 12/2018. We investigated age at onset of menopause according to different sociodemographic variables and fitted logistic regression models with the respective indicator variable for the behavioural characteristic, and used interrupted time series analysis (ITS) to identify time dependent peri- and postmenopausal trends.

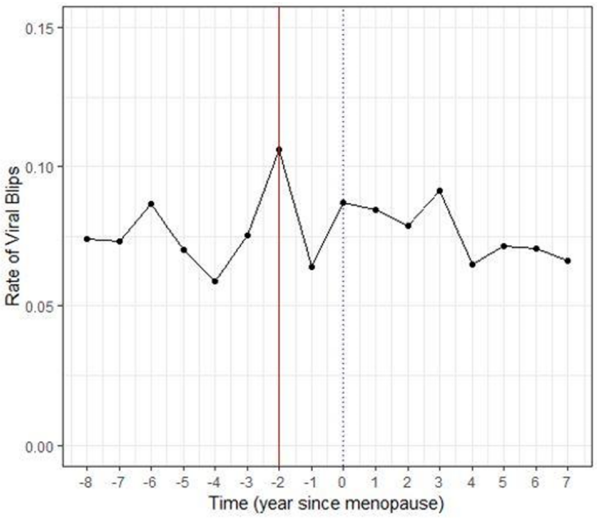


Figure 1. Rate of viral blips per year

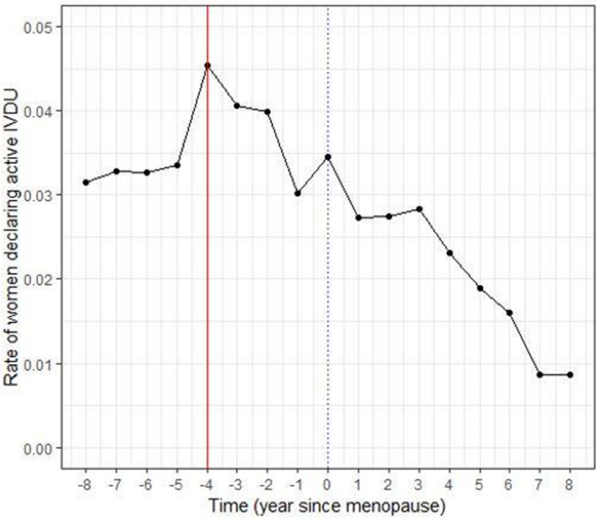


Figure 2. Rate of women declaring active intravenous drug use

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Results: Between 2010 and 2018, 1130 women within the SHCS experienced menopause and the percentage of postmenopausal women tripled from 11.5% (n=274) in 2010 to 36.1% (n=961) in 2018.
Median age at menopause was 50, early menopause (< 45) occurred in 115 (10.2%) and premature menopause (<40 y) in 23 (2%) patients. Early menopause was associated with black ethnicity (52.2% versus 21.6%, p<0.001), but not with HIV acquisition mode, CDC stage, viral suppression, CD4, HCV, smoking or active drug use.
We identified a number of trends in the 2–5 year timeframe prior to menopause; both, viral blips (OR 1.69 [95% CI 1.13, 2.55], p=0.01) and intravenous drug use (OR 1.65 [95% CI 1.02, 2.67], p=0.04), (Figure 1 and 2) increased. Odds of needing psychiatric care increased until 1 year after menopause (OR 1.04 [95% CI 1.00, 1.09], p=0.07), and decreased afterwards (OR 0.95 [95% CI 0.90, 1.00], p=0.05).
Conclusion: The median age of HIV-positive women at menopause is around 2 years earlier than reported for HIV-negative women in Switzerland. Of note, most relevant behavioural changes occured in the years before menopause with relevant increases in viral blips, intravenous drug use and mental health disorders requiring psychiatric care.

PE10/3

Gender-specific analysis of a German cohort of HIV-infected patients on Raltegravir-based therapy shows distinctive baseline co-morbidity profiles of women versus men but no impact on treatment outcomes

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HIV-infected women are facing specific needs in the context of antiretroviral therapy. For a better understanding, we performed a gender-specific post-hoc analysis for patients on Raltegravir (RAL)-based therapies in the German real-life cohort WIP.
The WIP study was a prospective, observational, multicenter cohort study in routine clinical care with data collection between 2010 and 2014. Safety and efficacy outcomes of RAL-based antiretroviral therapy in a population enriched for aging patients (274, 61% ≥50 years) were documented. Detailed methods are described elsewhere (Naumann et al., J STD AIDS 2016).
The cohort included 69 (15%) female and 382 (85%) male HIV-infected patients. Mean age was 51 years in both groups. At RAL initiation women and men were 13% vs. 23% therapy-naïve, 49% vs. 51% pretreated with virologic suppression and 33% vs. 23% without virologic suppression. At baseline, female patients suffered more frequently from depression (23% vs. 16%) as well as chronic hepatitis C virus infection (20% vs. 9%) and male patients more often from cardiovascular diseases including hypertension (15% vs. 20%) as well as lipid abnormalities such as hypercholesterolemia (6% vs. 11%) and hypertriglyceridemia (1% vs. 6%). Concomitant medications at baseline were consistent with these comorbidity profiles. No gender-specific differences in RAL-based therapy were observed in women versus men: RAL was combined with PI in 17% vs. 16%, with NRTI in 64% vs. 64% and with others in 19% vs. 20%. Regarding treatment outcomes, virologic response rates were comparable between women and men (Table 1).

Table 1. Therapeutic outcomes at week 48

	Women			Men		
	VL<50 c/mL N (%)	VL≥50 c/mL N (%)	early DC N (%)	VL<50 c/mL N (%)	VL≥50 c/mL N (%)	early DC N (%)
Therapy-naive	7 (78%)	0 (0%)	2 (22%)	65 (75%)	10 (12%)	12 (14%)
Pretreated - suppressed	29 (85%)	2 (6%)	3 (9%)	156 (81%)	10 (5%)	27 (14%)
Pretreated - failing	15 (65%)	4 (17%)	4 (17%)	57 (65%)	16 (18%)	15 (17%)
Pretreated - ART interruption	1 (33%)	2 (67%)	0 (0%)	7 (50%)	3 (21%)	4 (29%)
Total	52 (75%)	8 (12%)	9 (13%)	285 (75%)	39 (10%)	58 (15%)

In this German real-life cohort, characterization of female versus male patients demonstrated divergent co-morbidity profiles and minor differences in utilization patterns of RAL-based therapy. Nevertheless, in both women and men similar and high response rates comparable to clinical trial results could be observed.

PE10/4

Menopausal symptoms, sleep disorders and anxiety/depression among premenopausal and postmenopausal HIV-infected women: a multicenter cohort study in Spain

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Purpose: To assess menopausal symptoms, sleep disorders and depression/anxiety among premenopausal and postmenopausal HIV-infected women aged 45–60 years from the cohort of Spanish HIV/AIDS Research Network (CoRIS).
Method: Menopause was defined as 12 consecutive months without menstruation. Menopause Rating Scale was used to evaluate menopausal symptoms (Psychological, Somatic and Urogenital subscales), 3-items Jenkins Sleep Scale for sleep disorders and the 4-item Patient Health Questionnaire-4 for anxiety/depression. Multivariable logistic regression models were used to evaluate the impact of menopause in the different outcomes.
Results: Of 251 women included, 137 (55%) were postmenopausal. Median age at menopause was 48 years (IQR: 45–50). 66% of postmenopausal and 54% of premenopausal had any menopausal symptoms. The most frequent symptoms were: muscular discomfort (66% vs 62%, postmenopausal and premenopausal, respectively), physical/mental exhaustion (63% vs 52%), sleep problems (58% vs 52%) and depression (51% vs 42%). Prevalence for psychological symptoms was 64% vs 50%; for somatic 61% vs 50% and for urogenital 61% vs 48%, among menopausal and premenopausal women, respectively. In multivariable analysis, postmenopausal women had a two-fold increased risk of suffering from urogenital symptoms than premenopausal (table 1).
Prevalence of moderate-to-severe anxiety/depression was 22% vs 16% among post and premenopausal women, respectively. The corresponding prevalences for sleep disorders were 67% vs 52%. Only sleep disorders were significantly associated with menopausal status in multivariable analysis (table 1).
Overall, 19% of the women had moderate to severe anxiety and/or depression and 60% had sleep disorders. When considering menopausal and premenopausal women, these percentages were 22% vs 16% for anxiety/depression and 67% vs 52% for sleep disorders, respectively.
Conclusion: HIV-infected women showed a high prevalence of menopausal symptoms, anxiety/depression and sleep disorders. Urogenital symptoms sleep disorders were more frequent in postmenopausal women. There were no significant differences in the presence of somatic or psychological symptoms, nor anxiety/depression.

Adjusted OR for the association between postmenopausal status and the presence of menopausal symptoms, anxiety/depression and sleep disorders

	MRS			Anxiety/depression	Sleep disorders
	Psychological OR (95% CI)	Somatic OR (95% CI)	Urogenital OR (95% CI)	OR (95% CI)	OR (95% CI)
Menopause - Yes	1.58 (0.93–2.69)	1.49 (0.78–2.84)	2.40 (1.61–3.57)	0.98 (0.51–1.86)	1.88 (1.19–2.97)

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Table 1. Annual health review in 2018

	Assessment conducted		Assessment conducted		
Cardiovascular		Bone health		Reproductive	Assessment conducted
BMI (kg/m^2)	87 (95%)	FRAX score calculated	14 (15%)	Menstruation/menopause discussed	68 (74%)
Total cholesterol (mmol/l)	88 (96%)	DEXA scan performed	14 (15%)	Smear performed	55/80 (69%)****
BP (mm/Hg)	86 (93%)	Emotional Health		Breast screening***	12/37 (32%)
10-year CV risk (QRisk3)	32 (35%)	Informal assessment**	42 (45%)	Contraception use discussed	72/92 (78%)
Smoking	89 (97%)	Formal mental health assessment	7 (8%)	Liver-ALT	89 (97%)
Renal health		Sleep quality assessment**	3 (3%)	HbA1C	8 (9%)
Renal profile - bloods	88(96%)			Medication Review	84 (91%)
Urinalysis*	79(85%)	*Only performed among those with proteinuria on urinalysis **Patient asked informally by clinician during visit (e.g. "how are you feeling, emotion-wise?")		***Restricted to>50 years ****n/a for n=12	

PE10/5

An evaluation of the care given to older women attending an HIV clinic in London

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Purpose: Although HIV-related outcomes are regularly assessed, the wider health needs of women living with HIV (WLHIV) are often overlooked. We evaluated the cardiovascular, renal and bone health of women living with HIV aged 40–55 in a central London HIV unit and whether their reproductive and emotional needs were being assessed in clinical care.

Method: An audit was conducted of a random sample of 1 in 6 WLWH under follow-up in 2018 aged 40–55. Data collected included demographics, presence of co-morbidities and adherence to British HIV Association (BHIVA) standards of care.

Results: 92 women (median age 48 years; 78% black African; median 14 years since diagnosis) were included. 79(86%) had VL<40 cps/mL and the median (IQR) nadir and current CD4 counts were 195 (110–256) and 589 (424–758).

42 (46%) did not attend at least one appointment during 2018. 11 (12%) had a period of non-attendance of>1 year in the past 5 years.

Menstrual status was discussed in 76% women and contraception in 78%. Emotional well-being was only assessed in 56% of patients and mainly consisted of informal enquiry.

48% of the cohort had a BMI>30. HbA1C was measured in 9%. Cardiovascular assessments were performed on 35% despite 98% having necessary data for evaluation. FRAX scores were calculated on 15% despite 53% being on Truvada.

Conclusion: This cohort of women is very distinct as their rates of smoking, alcohol and recreational drug use are extremely low; they also had low cardiovascular risk scores when calculated. However they have a high prevalence of co-morbidities and unmet health needs and are at high risk of disengagement. Evaluation of emotional well-being was low despite evidence of higher prevalence of depression and anxiety in WLWHIV. This study highlights the need for more tailored, women-focused assessment frameworks to be incorporated into clinical care.

PE10/6

Anti-Mullerian hormone a plausible indicator of cardiometabolic risk in HIV-infected women

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Purpose: The definition of a biological aging-profile is of major importance for risk stratification in women living with HIV (WLHIV). Follicle Stimulating (FSH), Luteinizing (LH) and Estradiol (E2) hormones have been classically related to menopause, but recently Anti-Müllerian Hormone (AMH) has emerged as a novel indicator. Lower AMH associates with cardiovascular risk markers and represents a possible modulator of cardiovascular system. We compared AMH levels in WLHIV with those reported in non-HIV population for

Table 2. Presence of co-morbidities and high risk indicators

	Median (IQR) or N (%)	High risk		Median (IQR) or N (%)	High risk
Cardiovascular			Renal health		
BMI (kg/m^2)	29.7 (25.0–34.5)	>30: 42/87 (48%)	CKD stage (CKD EPI) Normal>60 (CKD1 and 2) 30–60<30	85 (97%) 2 (2%) 1 (1%)	n/a
Total cholesterol (mmol/l)	4.9 (4.1, 5.4)	>4.5; 8/88 (9%)	Urinalysis - proteinuria present uPCR (n=20)*	42/79 (53%) 1 (1, 19)	n/a
Receive Lipid lowering agents	6 (7%)		Bone health		
Systolic BP (mm/Hg)	125 (116–135)	>140; 13/86 (15%)	DEXA scan Normal Osteopenia Osteoporosis	7/14 (50%) 5/14 (11%) 2/14 (4%)	n/a
Diastolic BP (mm/Hg)	81 (73, 86)	>90; 14/86 (16%)	Reproductive		
Receiving anti-hypertensives	10 (11%)	n/a	Menstrual status Regular Irregular Last period>1 year Last period>2 years Hysterectomy Hormonal contraception Not asked	31/68 (46%) 11/68 (16%) 2/68 (3%) 16/68 (24%) 3/68 (4%) 5/68 (7%) 24/92 (26%)	n/a
10-year CV risk (QRisk3)	2.25% (1.3%, 3.2%)	>10%; 5 (6%)	Contraception type Condom IUD IUS Implant POP None Not asked	10/72 (14%) 1/72 (1%) 12/72 (18%) 2/72 (3%) 3/72 (4%) 43/72 (60%) 20/92 (22%)	n/a
Smoking Current/Ex Never	8/89 (9%) 81/89 (91%)	n/a	Recreational drug use Recreational drug use not recorded Excess alcohol use Alcohol use not recorded	1/86 (1%) 8/92 (9%) 2/73 (3%) 19/92 (21%)	n/a

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the same age. Also we have investigated the impact of AMH levels in markers of cardiovascular risk.
Methods: A panel of cardiovascular biomarkers was compared between groups of women with the same age and accordingly the appropriateness of AMH levels to their age. Plasma protein cysteinylation levels were quantified as a novel aging marker associated with cardiometabolic diseases.
Results: Our study included 269 WLHIV and 35% had AMH levels below the 10th percentile expected for their age. A total of 106 women were aged 25–44 years old (yo), 63% caucasian. In this group nine had undetectable AMH; 66 were in low AMH group (below median expected values for their age) and 31 in high AMH group. FSH ($p<0.01$) LH ($p<0.01$) were lower and E2 ($p<0.05$) higher in high and low AMH groups in comparison to undetectable AMH group. However, the classical hormone profile was not different between low and high AMH groups. Moreover, high AMH group had lower total cholesterol ($p<0.05$), lower plasma protein cysteinylation ($p<0.01$) and higher eGFR ($p<0.05$) than women with undetectable AMH. No differences were found for triglycerides or HDL-c.
Conclusions: WLHIV have lower AMH levels than expected for their age. AMH might have a better predictive value on cardiovascular risk assessment than female hormone classic profile.

PE10/7

Differences in sexual health among HIV infected and uninfected women of child-bearing age

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Purpose: Female sexual dysfunction (FSD) is a highly prevalent sexual health problem affecting more than 40% of women associated with poor quality of life. Prevalence and factors associated with FSD in HIV positive women are poorly known. The aim of this pilot study is to describe the prevalence of FSD and Generalized anxiety disorder (GAD) in a cohort of childbearing HIV positive women compared to a similar aged HIV uninfected.
Method: 43 women in child-bearing age were enrolled in the study: 22 clinically stable, receiving effective ART, HIV women and 21 healthy women (HW) attending a screening program. FSD and GAD evaluations were assessed with self-administered respectively Female Sexual Function Index (FSFI) exploring desire, arousal, lubrication, orgasm, pain and satisfaction and GAD Test. An FSFI score £ 26.55 is classified as FSD and Z index 58.7 is classified with moderate/severe anxiety symptoms. Clinical parameters were recorded. Non-parametric tests were used for statistical analysis.
Results: Characteristics of HIV women and HW are listed in table 1. 48% of HIV women showed FSD compared to 18% of HW ($p=0.02$). Considering the domains of FSFI, differences in sexual desire, arousal and pain were found (respectively $p=0.001$, $p=0.02$, $p=0.04$). No associations between FSD and nationality, smoking status, working status, to have HIV partner, past pregnancy was found.

Characteristics of HIV women and HW

	HIV	HW	p
Age, median (min-max)	38 (29–49)	33(23–49)	NS
CDC stage A, B, C n (%)	17(77%),2(9%), 3(13%)	—–	
CD4 cell/m nadir, median, (min-max)	239 (3–695)	—–	
CD4 cell/m at the enrollment, median, (min-max)	798 (11–1118)	915(482–1732)	NS
CD8 cell/m at the enrollment, median, (min-max)	895(303–808)	491(303–808)	<0.0001
CD4/CD8 ratio	0.92(0.16–2)	1.8 (1–2.59)	<0.0001
YLWH median, (min-max)	7(1–29)	—–	
Comorbidities n (%)	9 (40%)	8(38%)	NS

No correlations between FSFI and the years of virological suppression, HIV-RNA Zenith, CD4 + T-cell nadir and CD4 + /CD8 + ratio were found. Regarding anxiety, a GAD was found only in the HIV group (20% vs 0%, $p=0.05$).
Conclusion: Our study showed that despite a good immunovirological response, high prevalence of FSD was found in HIV young women on stable ART. A dipper attention to these aspects should be paid in order to increase the quality of care in HIV+ women. A larger study with a multivariate analysis is urgently needed.

HIV and marginalised groups

PE11/1

Sexual behaviors and seroprevalence of HIV, HBV, and HCV among hill tribe youths of Northern Thailand

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Purpose: To examine sexual behaviors and assess the seroprevalence of HIV, HBV, and HCV among hill tribe youths.
Method: A cross-sectional study was conducted tThe participants were recruited from 60 randomly selected hill tribe villages in Chiang Rai Province, Thailand. A validated questionnaire and 5 mL blood specimen were used to collect data. Data were collected by a self-reporting method. Rapid immunochromatographic tests were used to detect anti-HBs, HBsAg, anti-HCV, and anti-HIV-1 and -2. Chi-square and Fisher'sexact test were used to detect the associations between variables at analpha of 0.05.
Results: A total of 1,325 participants were recruited forthe analysis.The majoritywere females (60.5%), aged 15–17 years (58.9%), and 72.5% graduated high school. A total of 14.5% smoked, 22.4% drank alcohol, 14.2% were tattooed, and 61.4% had their ears pierced.Among the 30.3%who had sexual experience, 42% experienced one-night stands, 26.9% had sexual contact with a prostitute within one year prior to the study, 18.9% used alcohol prior to having sexual intercourse, and 15.7% had been tested for HIV/AIDS previously. Among males, 11.5% were males who have sex with males (MSM), and 4.6% were bisexual. Among females, 83.0% were females who have sex with males, and 5.0% were females who have sex female. Different sexesand tribes were found to havesignificantlydifferent risk behaviors and sexual behaviors. Amongthe836 obtained blood samples, none werepositive for anti-HIV-I and -II, 6.4% were positive for anti-HBsAg, 1.9% were positive for HBsAg, and 0.2% were positive for anti-HCV.
Conclusion: Hill tribe youths in Thailand are at risk of HIV, HBV, and HCV infections according to their risk behaviors and sexual behaviors,which differ between sexes and tribes. Effective behavioral interventions should be promoted among hill tribe youths to minimize the risk for these diseases in the future.

PE11/2

Rapid HIV tests and linkage of people who inject drugs (PWID) to health facilities for antiretroviral therapy (ART) in Nigeria

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Purpose: The National HIV/AIDS and Reproductive Health Survey 2012 shows low uptake of HIV testing in Nigeria especially among the key population. In Nigeria, People who inject drugs (PWID) face discrimination, criminalization that prevent them from accessing health care and inclusion in the society.
HIV prevalence among PWID in Nigeria was 3.4% in 2017. Women who inject drugs are particularly affected with prevalence of 13.9% compared to 2.6% among men. Female sex workers who inject drugs face highest HIV prevalence (43%). It is thought that 9% of new HIV infections in Nigeria every year are among people who inject drugs according to 2017 The Joint United Nations Programme on HIV/AIDS (UNAIDS) statistics.
Method: The study was conducted among PWID living in Atikankan area of Ado-Ekiti. This area is a slum characterized by the presence of homeless

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shelters, drug peddlers trading openly, commercial sex workers, runaway teenage girls being used as sex slaves in exchange for drug and little cash.
78 PWID's were examined consisting of 67 males and 11 females between the ages of 15–47 years. They were provided with HIV testing services between October - December 2018, utilizing multiple HIV test kits for screening and confirmation to improve quality. Positive clients were counseled and referred to health centers for free Antiretroviral Treatment.
Results: 2.34% were confirmed to be HIV positive and were successfully referred for ART. There was low turnout of PWID's to events promoting HIV prevention, testing and treatment.
Conclusion: Participants reported that fear of being handed to police as a major reason for not seeking HIV testing and services. PWID's and other key populations need adequate access to HIV/AIDS prevention, treatment and support services.
Screening via rapid HIV tests need to target Key Populations if the 90–90–90 target of the UNAIDS is to be achieved.

PE11/3

The blind spot: high HIV burden among slum-dwelling school-age girls in Kampala, Uganda

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Background: Adult and youthful slum dwellers have been documented to have a higher prevalence of HIV compared to the general population. However, there is paucity of information on the extent of this infection among slum-dwelling school age (5–14 years) children in Uganda. This study explored the burden of HIV among slum-dwelling school-age children (SDSAC) of Namuwongo, Kampala, Uganda.
Methods: We analyzed data derived from HIV counselling and testing records of school-age children that tested at Kisugu HCIII between 2011 and 2016. A total of 555 anonymised records were analyzed for; residence, HIV, religious, and sex status. Using STATA version 13; bi-variate analysis was conducted to obtain joint distribution and the two-sample test of proportions test; to elicit associations and their significance.
Results: The overall study population burden of HIV was 2%, with girls (2.6%) more affected than boys (0.9%). SDSAC had a higher HIV burden (3.3%) compared to non-slum dwellers (1.2%). HIV was more prevalent among slum-dwelling girls (5.2%) compared to their non-slum dwelling counterparts (0.9%). A positive HIV result was associated with being a slum dwelling girl [95% CI: (0.3%-8.3%), p=0.013] and belonging to the 10–14 year age group [95% CI: (0.002–0.065), p=0.015].
Conclusions: There is a high burden of HIV among slum-dwelling school-age girls in Kampala. SDSAC should be included among the blind spot population and we recommend expansion of school age friendly preventive, promotive and therapeutic HIV services to these areas.

PE11/4

Research of behavioral models of transgender people leading to high rates of HIV prevalence in Ukraine

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Purpose: Study of behavioral models of transgender people leading to high rates of HIV prevalence in Ukraine.
Methods: A quantitative study using the RDS method. This is the largest of its kind in the EECA countries: 438 transgender people were surveyed across Ukraine, including Crimea and the eastern regions of the country where military operations are taking place.
Results: 69% of transgender people in Ukraine did not use a condom during their most recent sexual intercourse. The main reasons for this were that sexual partners insisted on sex without condoms (28%) and the lack of condoms (23%). According to respondents' own reports, HIV prevalence among transgender people could be as high as 21%. At the same time, HIV infection specialists and other doctors in AIDS centers in Ukraine do not receive special training to work with transgender people, and transgender people with HIV are registered in health facilities according to their biological gender.
Conclusions: The data obtained suggest that, as in other countries, the risk of HIV transmission among transgender people in Ukraine is 50 times higher than among the general population.
The level of knowledge about HIV/AIDS and STI among transgender people needs to be raised, by means of targeted interventions, and access for transgender people to HIV services needs to improve, including through awareness training for doctors. There is also a need for advocacy work to improve the meaningful participation of trans people and their organizations in national anti-epidemic action.
The next steps should aim to ensure that the state recognizes the vulnerability of transgender people and explicitly includes transgender people in the list of groups with an increased risk of HIV infection. Transgender people should be included in national coordination mechanisms, in particular, the National Council for Countering Tuberculosis and HIV/AIDS.

PE11/5

Outreach services for HIV testing and prevention among female transgender commercial sex workers in Milan: different approaches for different populations?

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Purpose: Female-transgender commercial sex-workers (FTG-CSW) are disproportionally affected by HIV and have reduced access to HIV-testing and PREP. We describe two different testing strategies: an outreach program and an outpatient clinic dedicated to FTG-CSW.
Methods: In collaboration with a non-governative organization (NGO) providing counseling and help to TG persons, we organized (i)a mobile unit, one night a week, in TG prostitution sites in Milan, offering rapid oral tests and counseling about HIV prevention; (ii)a weekly evening outpatient clinic in the NGO headquarters, offering fingerstick tests and PREP care. The staff included a FTG peer-educator, a counselor, a psychologist and HIV-specialists. FTG-CSW were interviewed about sexual habits, history of STI, health needs and barriers.
Results: 57 FTG-CSW accessed our services between February and June 2019. First contact was the mobile unit in 39 and the outpatient clinic in 18 subjects. Table 1 shows their characteristics. Those reached on the street were younger than those self-presenting to the outpatient clinic. More than half of the subjects reported>6 months since thier last HIV-test. The most commonly

Subject characteristic	Mobile Unit (N=39)	Outpatient Clinic (N=18)
Age, years (Median, IQR)	33 (29-38)	41 (31-49)
Years lived in Milan (Median, IQR)	7 (1-15)	7 (1-18)
No of Sexual Intercourses per month (Median, IQR)	50 (30-90)	45 (10-60)
Gender reassigned by surgery	2 (5.3%)	2 (11.1%)
Country of origin		
Brazil	24 (63%)	7 (39%)
Peru	8 (21%)	8 (44%)
Other South American	4 (10%)	1 (6%)
Italy	1 (3%)	2 (11%)
Other	1 (3%)	0 (0%)
Undocumented	17 (47%)	7 (47%)
No access to the health system	20 (57%)	10 (62%)
Low education (≤9 years)	8 (22%)	1 (5%)
Self-reported condom use (any sex), less than 'Always'	13 (36%)	7 (41%)
Self-reported condom use (insertive sex), less than 'Always'	4 (12.5%)	5 (42%)
Self-reported condom use (receptive anal sex), less than 'Always'	4 (11%)	3 (17%)
Self-reported condom use (oral sex), less than 'Always'	18 (51%)	14 (82%)
Condomless sex in exchange for money	11 (31%)	4 (23%)
History of sexually-trasmitted infections	17 (44%)	8 (44%)
Time since last HIV testing		
>3 months	29 (76%)	14 (87%)
>6 months	20 (52%)	10 (62%)
Newly diagnosed HIV-infection	5 (13%)	0 (0%)

Table 1. Subject characteristics grouped by type of first contact (mobile unit or outpatient clinic)

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reported reason for delayed testing were difficult/uncomfortable access to testing-facilities (54%) and fear of stigma/discrimination (27%). Condomless sex was frequent and higher among self-presenting TG-CSW.
Street oral tests and fingerstick tests in the outpatient clinic were positive in 5/39 (12%) and 0/18 (0%), respectively. Among newly identified HIV-positive FTG-CSW, 4/5 were linked-to-care and 3 started treatment within 7 days from diagnosis. Monthly finger-stick testing and PREP in the outpatient clinic were offered to all subjects; 4 FTG-CSW initiated PREP.
Conclusions: Street-based rapid oral HIV testing in outreach settings among FTG-CSW is useful and brings to a significant number of new HIV-diagnoses. Creating a dedicated outpatient clinic was useful to implement PREP in this fragile population, but the benefit in terms of new diagnosis was null.

PE11/6

The impact of unstable housing on HIV treatment outcomes in people living with HIV/AIDS in an urban setting of Southern Europe

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Purpose: People living with HIV (PLHIV) with unstable housing (UH) face several barriers hindering access to care, adherence to antiretroviral therapy (ART), retention in care, and treatment success. Despite being on the rise, this phenomenon has been scarcely characterized in Southern Europe.
Method: A retrospective cohort study was conducted among all PLHIV>18-year-old who started or resumed ART between 2012 and 2018 in Hospital del Mar, Barcelona. Unstable housing was defined as living in the street or in temporary residences due to financially insecure situations. Multivariate Cox regression models were used to identify independent risk factors associated with a composite outcome of treatment failure, loss to follow-up and death (TF).
Results: We included 570 patients, contributing 1014 person-years of follow-up, with a median time of 21.35 months. Among them, 115 (20.17%) had UH. The baseline characteristics of people with UH included: mean age 41.81 years; male gender 77.4%; median HIV-RNA viral load 4.76 $\log_{10}$ copies/mL; median CD4 count 257 cells/mL; STR 47.8%; HIV acquisition through injection drug use 67%; alcoholism 29.6%; current drug use 64.3%; psychiatric disorder 36.5%; Idiomatic/cultural barrier 24.3%; and patient prejudgment 5.2%.
75.7% were non-adherent, 47% had inadequate immune recovery and 48.7% presented TF, compared to 20.7%, 21% and 18.2% in the non-UH group respectively (P<0.001). UH independently predicted TF (HR: 1.87; 1.22–2.85), after adjusting for HIV-RNA (HR: 1.27 per $\log_{10}$ increase; 95% CI 1.00–1.61); current recreational drug use (HR: 2.09; 95% CI 1.40–3.12) and patient prejudgment (HR: 2.16; 95% CI 1.23–3.80).
Conclusion: The proportion of UH was common in this Southern European urban cohort of PLHIV. PLHIV with UH had a high comorbidity burden and suboptimal ART outcomes, including poorer adherence, retention in care, adequate immune recovery and treatment success. Specific interventions are needed for this neglected population

PE11/7

Reflection of sex work criminalization in court judgements targeting to protect health, sanitary and epidemiological well-being

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Purpose: Sex workers remain a population severely affected by HIV epidemics, which is widely recognized. To expose the court practice in accordance with Article 6.11 of the Administrative Code of the Russian Federation, which provides for punishment of a fine for engaging in sex work, we looked into the contents of court decisions.
Method: We applied the content analysis to 250 magistrate's court judgements under the Article 6.11 made from June to December 2017 accessed online through an aggregator of court decisions 'Rospravosudiye'.
Results: The offender's request was stated only in 0.04% of the decisions; in 73% the accused women were physically absent in the court hearings. Witness testimonies were collected in 16.8% (42) judgements; in the court hearings there were no testimonies by a witness or police officer who drew up a report on detention. The presence of a lawyer was mentioned in two court judgements. In 92% (230) protocols, the offender did a guilty plea, that is, gave written confessions or pleaded guilty during a court hearing, and in 92.8% (232) judgements women received a fine of 21 - 28 Euros. The mass distribution of sexually transmitted diseases and HIV infection was referred as harm of prostitution in one of the 250 judgements. One case was initiated against a man, which indicates that under this article women are disproportionately prosecuted.
Conclusion: Although the public harm of sex work is interpreted as a cause a massive spread of sexually transmitted diseases and HIV infection, the court practice under Article 6.11 for engaging in prostitution has lost its original meaning to protect public health and focuses only on vague notion of morality. This legal uncertainty leads to deliberately unjust decisions by courts: the proof of guilt is practically absent, and the court practice focuses on guilty verdicts against women.

PE11/8

Caring for the Transgender HIV-positive patient

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Purpose: The stigma attached to gender nonconformity in many societies can result in the so called "minority stress", that may make transgenders more likely to avoid medical care and to escape the retention in care when suffering from chronic diseases. A health monitoring system targeting this population doesn't exist yet and data on demographics are lacking due to the fact that not every transgender person pursue an open medical path that leaves a record. The aim of this study is to describe the state of health of male-to-female HIVpositive transgender population attending the Infectious diseases Outpatient Service of our University Hospital in order to identify their needs and to improve their retention in care.
Methods: We collected data from all theHIVpositive transgender male-to-female patients attending the Infectious Diseases Outpatient Service of our Clinic from 1988 to 2018 with more than one access to the clinic, reviewing their outpatient clinical records and then performed a descriptive analysis.
Results: We collected data from 78 patients.48.7%(N=38) had<1 year of follow up. 51.3%had>1 year of follow-up with median follow-up of 11 years (IQR 7.1–16.4).Of total population, 53.8% ranged from 18 to 30 years old,43.6%(N=34) presented comorbidities(Table 1).MedianCD4 cell count at HIV diagnosis was212(IQR 72–350); 30.8%(N=24)of the population presented for the 1st time to our center with AIDS-defining events(mostly tuberculosis:

Demographic characteristics of the population

Total population N=78 (100%)

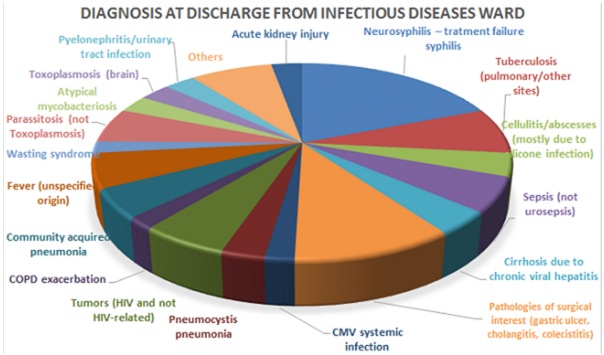
Age (categorical)	18–30	42 (53.8%)	HCV co-infected		4 (5.1%)
	31–40	26 (33.3%)	HBV co-infected		5 (6.4%)
	>40	10 (12.8%)	Comorbidities		34 (43.6%)
Nationality	Brazil	45 (57.7%)	Types of comorbidities	Cardiovascular/ Diabetes	16.6%
	Colombia	13 (16.7%)		Dyslipidemia/ Lipodystrophy	15%
	Argentina	7 (9.0%)		GERD	13.3%
	Peru	6 (7.7%)		Neurological	11.6%
	Ecuador	4 (5.1%)		Psychiatric (diagnosed)	8.3%
	Others	3 (3.9%)		Others	35.2%

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37.5%; Table 2). 42(53.8%)of the population was hospitalized at least once, with a median length of hospital stay of3 days(IQR 0–17.25);the most frequent diagnosis at discharge was neurosyphilis or treatment failed syphilis (19%;Image1)0.41%of the population had a history of benzodiazepine abuse. 39%used estrogens. Data about drugs and alcohol abuse were lacking.
Conclusions: Transgender patients are mostly young, are likely to have a sub-optimal adherence to outpatient follow-up, and tend to develop benzodiazepine abuse. An integrated and multidisciplinary medical, cultural and psychological approach is needed in order to maximize the overall health of this delicate category of patients and to permit a better retention in care.

HIV infection-related characteristics

CDC Group at HIV diagnosis	A	30 (38.5%)
	B	24 (30.8%)
	C	24 (30.8%)
AIDS-defining events at diagnosis (CDC C N=24)	Tuberculosis (pulmonary, other sites)	43.5%
	Cerebral Toxoplasmosis	10.2%
	Pneumocystis pneumonia	10.2%
	Cryptococcosis	7.6%
	CMV systemic disease	7.6%
	Others	20.5%



Diagnosis at discharge from Infectious Diseases ward

PE11/9

Association of current Estradiol use with carotid intimal media thickness among transgender women: a cross-sectional study

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Purpose: Epidemiologic studies suggest that transgender population has higher burden of cardiovascular (CV) risk factors and CV disease. We aimed to assess CV risk and investigate the relationship between current use of E2 or EE and carotid intima-media thickness (cIMT) in transgender women (transwomen).
Method: Cross-sectional evaluations of transwomen in the Transcendendo cohort in Rio de Janeiro, Brazil from August 2015 to February 2017. cIMT was measured by ultrasonography, following the Mannheim protocol. Increased cIMT was defined as a measurement above the 75th percentile. We tested the association of E2, EE or both with cIMT. Covariables included traditional cardiovascular risk factors, HIV status, drug use, and history of feminizing procedures. Framingham and ASCVD risk scores were calculated and compared with cIMT. Adjusted logistic regression models were fitted and odds ratios (OR) were used to assess the association of current use of the 3 hormone categories with cIMT.
Results: 308 transwomen were included; median age was 31 years (interquartile range - IQR=25–38), 53.8% had HIV infection. Among current hormone users (40.8%), the most frequent were estradiol (26.53%), ethinylestradiol (5.15) or a combination of both (9.18%). Median cIMT was 0.57 mm (IQR=0.52–0.64). In participants with increased cIMT, 11 (3.97%) and 24 (8.66%) were classified as high risk by the Framingham equation and ASCVD, respectively. In the final adjusted model, age (OR=1.14, 95% CI=1.08–1.20), systolic blood pressure (OR=1.05, 95% IC=1.01–1.09) and estradiol use (OR=0.34 95%IC=0.11–0.92) were associated with cIMT.
Conclusion: A negative association between cIMT and current estradiol use was found in transgender women. While conflicting results exist in the literature about estrogen replacement therapy in women, these data suggest cardioprotective effects of estradiol use without medical supervision in younger transwomen. Follow up studies are needed to confirm its safety and it might be considered as a choice of hormone for transwomen.

PE11/10

HIV and migrants: a demographic and clinical characterization of migrants under follow up at an Infectious Diseases Department in Lisbon, Portugal

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Purpose: Characterize the migrant population currently on follow-up at the Infectious Diseases Department of a Central Hospital (IDD) in Lisbon, Portugal, for Human Immunodeficiency Virus Infection (HIV).
Method: All patients currently attending follow-up appointments were identified, and cohort based on nationality was selected. Patient's charts were reviewed for confirmation of migrant status and characterization of HIV infection and clinical outcomes.
Results: Of the 348 patients identified, accounting for 11.5% of all patients under follow-up for HIV infection (n=3013), 230 were men with an average age of 49 years. Most of the patients are from Portuguese speaking countries, 49% from Brazil and 51% from African Portuguese Speaking Countries. Two-hundred and sixteen patients, 62%, were identified as economic migrants, and 6.9% (n=24) entered the country under health protocols between countries.The patients have been in Portugal for nine years on average, and 60.3% (n=210) were diagnosed in the year prior to entering the country or in the year of entrance. Regarding HIV infection, 94.25% (n=328) are HIV type 1 and three present HIV type 1 and 2 co-infection, mostly of probable sexual transmission, 79% (n=275), and 41% (n=143) of these of heterosexual risk. Sixty-two patients (17.8%) presented with opportunistic infections (OI) on diagnosis, in most cases active tuberculosis (6.3%, n=22), and more than one simultaneous OI in 4.6% (n=16). A hundred and thirty-two patients (37.9%) present co-infections of those 76 (57.6%) with Hepatitis B Virus. When first evaluated at IDD 67.8% of patients (n=236) were naive. All patients are currently under anti-retroviral therapy (ART), 87.4% (n=304) of whom have undetectable viral load.
Conclusion: Access to health care allows early diagnosis and adequate treatment. The migrant population's engagement in follow-up care leads to both good therapy adhesion and good immunovirological status contributing to control the HIV epidemic.

HIV cure

PE12/1

Comparison of three commercial kits for quantitative analysis of HIV-1 RNA produced in Russia

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Purpose: Viral load (VL) measuring is one of the main methods of HIV cure efficiency control. Unfortunately, the main viral variant used in design of quantitative PCR-kits is HIV-1 subtype B. However A6 subtype dominates in Russia and CRF03_AB, CRF02_AG and CRF63_02A1 are wide spreading as well.

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In this study we compared three Russian Real-Time-quantitative PCR-kits: AmpliSens HIV-Monitor-FRT (Monitor-FRT), RealBest RNA HIV quantitative (RealBest) and recently developed AmpliSens HIV-monitor-Duo-FL (Monitor-Duo).

Method: Plasma clinical samples with VL 590–2.05*10^6 copies/mL was analyzed. All samples (n=125) were tested using Monitor-FRT and Monitor-Duo. Using RealBest the part of collection (n=84) were tested as well. The simple linear regression and Bland-Altman analyses were carried out.Precision of kits was tested by analysis of NIBSC HIV-1 Standard 97/650, in three dilutions.

Effectiveness of different HIV-1 subtypes and CRFs quantification was tested using NIBSC References panels 12/224 and 13/214.

Results: In analysis of clinical samples a statistically significant correlation between all kits was found (with R^2>0.8) (Fig. 1). The highest convergence was found between Monitor-FRT and Monitor-Duo.

For 2nd WHO International Standard all assays demonstrated VL lower than real concentration (0.19, 0.34 and 0.53 log copies/mL for Monitor-Duo, Monitor-FRT and RealBest correspondingly). The best precision in HIV-1 subtypes' and CRFs testing was found for Monitor-Duo. The median VL-delta («real» minus «obtained») of log copies/mL for this kit was 0.19 (-0.13–0.91). For Monitor-FRT VL-delta was 0.49 (0.18–1.17) and for RealBest - 0.74 (0.32–1.75). The highest discordance was found for CRF13_cpx sample (1.17, 0.91 and 0.55 for Monitor-FRT, Monitor-Duo and RealBest correspondingly).

Conclusion: All three Russian HIV-1 VL-quantitative kits studied demonstrated high level of correlation and precision for HIV cure efficiency control. All kits revealed different HIV-1 group M subtypes and CRFs. Apparently high rate of VL delta for CRF13_cpx sample is result of mosaic structure of its genome.

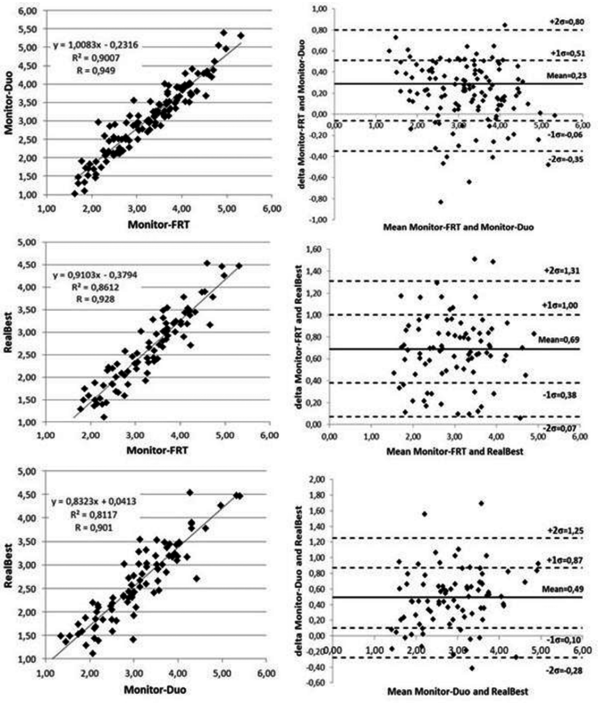


Figure 1. Comparison of kits by a simple linear regression (left) and Bland-Altman (right) analyses

PE12/2

Optimization of genotyping by phenotypic analysis of clinical HIV-1 subtype CRF01_AE isolates from South-East Asia

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Purpose: The latent HIV reservoir in lymphoid cells continues to be a major obstacle for curing HIV.

We reported (1) from the Swiss HIV cohort that, under ART, the viral tropism plays a role for decay and kinetics of the latent reservoir: Contrasting the untreated situation, the frequency of X4 tropic proviruses decreases in most patients on therapy, hinting a selective virus elimination and new perspectives for cure research. Hence the accurate determination of tropism appears crucial for strategies to eradicate HIV reservoir in patients.

Different phenotypic and genotypic tools are availiable for tropism-prediction, e.g. geno2pheno[coreceptor] (2), which has been validated on large HIV-1 subtype B cohorts. However, for other HIV subtypes tropism prediction proved to be difficult.

This study therefore aimed at improving the reliability of tropism prediction for subtype CRF01_AE.

Method: 45 HIV-1 clinical subtype CRF01_AE samples from Thailand were used for parallel phenotyping and genotyping. 15 of which were used to adapt the G2P algorithm, and 30 separate samples for functionally validating the new tool.

Results: Genotypic prediction was done by geno2pheno[coreceptor] and a new algorithm version. The results indicate an overcalling of X4 with a False-Positive-Rate cut-off (FPR) of 10%. In parallel, the tropism of most subtype CRF01_AE samples was phenotypically determined.

Conclusion: While the standard version of geno2pheno[coreceptor] overcalled X4-viruses for subtype AE, various adjustments for sequence, stringency and rules were tried. A significantly better prediction was obtained by lowering the FPR from 10% to 5%, indicating a more stringent ruling.

For phenotypic confirmation, several almost full-length clones of AE-isolates were generated, allowing to functionally determine the tropism of HIV-1 subtype AE variants by viral replication in the presence of selective inhibitors. The gained knowledge will help to improve prediction tools for other subtypes and be of utility for future strategies towards eradication of HIV.

HIV drug resistance

PE13/1

Darunavir resistance among patients exposed to protease inhibitors failing ARV therapy

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Purpose: Darunavir is the main protease inhibitor (PI) antiretroviral for salvage therapy, but previous PI use may limit treatment response to this drug.

Method: The HIV-1 RNA partial pol sequences (Sanger) from 1,696 patients failing antiretroviral regimen, genotyped from 2014 to 2017, were evaluated at Stanford db for drug resistance mutations (DRM) and genotypic susceptibility score (GSS) and at rega and NCBI for HIV subtype. Logistic regression analyses were performed to access clinical and laboratory variables associated to decrease of darunavir GSS.

Results: Mutations to NRTI (69.6%, 1181/1696) and to NNRTI (59.9%, 1016/1696) drug classes were common, and 27.5% (466/1696) had at least one major PI-DRM, most commonly M46 (14.7%, 250/1696), V82 (13.8%, 234/1696) and I54 (13.3%, 225/1696). Full activity to darunavir was predicted for 88% of the patients, but only 57% for those with at least one PI-DRM. Presence of a PI-DRM was strongly associated (p<0.001) to older age, use of more than two regimens, longer total time on treatment and presence of a NRTI mutation. A lower GSS to darunavir was independently associated to subtype F, NRTI mutations and exposure to darunavir and previous use of older PI (e.g. saquinavir, indinavir, nelfinavir).

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Conclusion: Among patients with PI-DRM, full activity to darunavir was compromised in many cases and efforts to detect failure at earlier time is warranted, particularly for cases treated in early HAART era or infected with HIV-1 subtype F, both associated to darunavir resistance. NRTI mutations may serve as a proxy for a minimal level of therapy adherence necessary for PI-DRM emergence.

Table 1. Logistic regression to evaluate the association of demographic and laboratory variables to DRV susceptibility

	Unadjusted Odds Ratio	P	95% CI	Adjusted Odds Ratio	P	95% CI
Age above 36 years	2.07	0.001	1.37–3.11	1.98	0.082	0.92–4.28
CD4+ T count >500 cells/mm^3	0.77	0.190	0.52–1.14	0.60	0.146	0.30–1.20
Time on treatment >7 years	2.70	0.000	1.70–4.30	1.11	0.769	0.60–2.24
Number of regimens >2	2.95	0.000	1.86–4.70	1.19	0.651	0.57–2.50
Exposure to IDV, SQV, NFV	3.75	0.000	2.54–5.53	3.11	0.000	1.65–5.85
LPV treatment	2.04	0.001	1.36–3.07	1.68	0.098	0.91–3.11
DRV treatment	8.17	0.000	4.96–13.47	3.95	0.000	1.83–8.54
HIV-1 polymerase subtype F	1.48	0.083	0.95–2.30	2.23	0.021	1.13–4.40

Association of darunavir genotypic susceptibility score (full activity, GSS=1 vs some degree of resistance, GSS 0–0.75) to variables at genotyping collection. Due to space constrain only variables with p<0.2 at unadjusted analyses are shown. Presence of NRTI resistance mutation is not included in the table as there was no case of darunavir resistance without a NRTI mutation (100% × 59%, p<0.0001).

PE13/2

Prevalence and factors associated to the detection (population and next generation sequencing) of archived 3TC resistance mutations in aviremic HIV-infected adults (GEN-PRO)

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Purpose: To evaluate in aviraemic participants the frequency of M184V/I and K65R/E/N in proviral DNA (pvDNA) by population sequencing (PS) and next generation sequencing (NGS), the concordance between techniques and predictive factors for persistence of mutations.
Methods: We analized pvDNA of HIV-infected participants on stable ART and virologically suppressed for ≧1 year by PS (whole blood) and NGS (PBMCs). Mutations were identified and quantified using the PASeq system (IrsiCaixa).
Results: 102 participants (Table 1): 50 without M184V/I and/or K65R/E/N in historical resistance genotype in plasma, and 52 with prior history. In the group with historical resistance, pvDNA analysis by PS showed M184V/I and/or K65R/E/N in 14/52 (26.9%). NGS detected mutations in >1%, >5% o >20% in 42/48 (87.5%), 36/48 (75%) and 22/48 (45.8%) respectively. (Figure 1)
Univariate analysis of factors associated to clearance/persistence of 3TC mutations in pvDNAby PS analysis showed that current ART including 3TC/FTC [OR 0.22 (CI95:0.05–0.92; p=0.038)] and triple therapy [OR 0.14 (CI95%:0.02–0.79; p=0.038)] were associated to clearance, while time on ART -per year- was associated with persistence [OR 1.14 (CI95%:0.99–1.33; p=0.77)]. Using NGS>20%, current treatment with triple therapy was associated with clearance [OR 0.13 (CI95%:0.03–0.60; p=0.009)], regimen including 3TC/FTC had a trend towards association with clearance (p=0.07) and time since HIV diagnosis with persistence (p=0.06). When analysed with NGS>5%, predictive factors for persistence were time since HIV diagnosis, [OR 1.16 (CI:95%1.02–1.32; p=0.023)] and IDU risk factor [OR 12.86 (CI:95%1.29–128.14; p=0.029)]. By NGS>1%, no predictive factors were found.
Conclusion: Historical 3TC mutations are not detected in pvDNA in the majority of patients using PS. NGS increases sensitivity, but with the 5% cutoff NGS still misses one quarter of historical mutations. A regimen including 3TC is associated with clearance of resistance mutations. The therapeutic relevance of detecting 3TC mutations in pvDNA by NGS requires further research (ART-PRO clinical trial, NCT03539224).

Table 1. Baseline characteristics

	Total population (n=102)	Historical mutations M184V/I and/or K65R/E/N (n=52)	No historical mutations M184V/I nor I65R/E/N (n=50)	p-value
Male sex, n (%)	77 (75.4)	36 (69.2)	41 (82.0)	0.132
Age (years), median (IQR)	51.2 (45.3–56.3)	52.3 (49.0–58.4)	47.6 (41.8–54.2)	0.017
Route of HIV transmission, n (%)				
- MSM	43 (42.1)	15 (28.8)	28 (56.0)	0.028
- Heterosexual	27 (26.4)	15 (28.8)	12 (24.0)	
- IDU	24 (23.5)	17 (32.7)	7 (14.0)	
- Other/Unknown	8 (7.8)	5 (9.6)	3 (6.0)	
Time since HIV-infection diagnosis (years), median (IQR)	18.4 (11.8–23.3)	21.9 (17.5–24.7)	12.7 (6.7–20.3)	<0.001
CD4 count (cells/mm^3) median (IQR)				
- Nadir	195 (91–320)	152 (84–262)	274 (96–383)	0.006
- Baseline	661 (506–866)	671 (507–882)	626 (500–853)	0.617
Time on ART (years), median (IQR)	17.0 (9.1–20.9)	19.3 (17.0–22.6)	9.7 (5.9–16.1)	<0.001
Current ART, n (%)				
- Including 3TC or FTC	71 (69.6)	24 (46.2)	47 (94.0)	<0.001
- 2NRTIs + NNRTI or bPI	56 (54.9)	21 (40.4)	35 (70.0)	
- 1NRTI + bPI	27 (26.4)	15 (28.8)	12 (24.0)	0.001
- bPI monotherapy	19 (18.6)	16 (30.8)	3 (6.0)	
Time on current ART (years), median (IQR)	4.1 (2.6–6.9)	4.5 (3.0–7.1)	3.5 (2.2–6.5)	0.428
Time of HIV viraemia suppression (years), median (IQR)	7.7 (5.1–12.1)	8.8 (5.7–12.3)	6.3 (4.2–10.9)	0.09

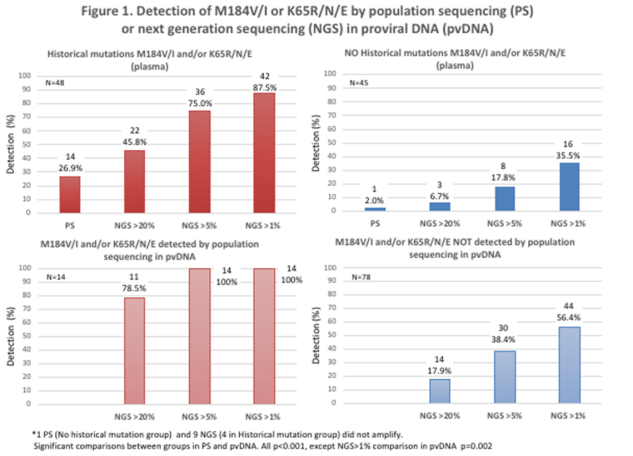


Figure 1. Detection of M184V/I or K65R/N/E by population sequencing or next generation sequencing in proviral DNA

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PE13/3

Accumulation of integrase strand-transfer inhibitor resistance mutations confers high level resistance to dolutegravir in HIV-1 non-B subtype viruses from patients failing raltegravir in Uganda

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[1]Western University, Microbiology and Immunology, London, Canada [2]Joint Clinical Research Centre, Center for AIDS Research Laboratories, Kampala, Uganda [3]Western University, Pathology and Laboratory Medicine, London, Canada [4]Joint Clinical Research Centre, Kampala, Uganda [5]University of Otago, Microbiology and Immunology, Dunedin, New Zealand

Purpose: There are limited data on susceptibility of HIV to integrase strand-transfer inhibitors (INSTIs) in low- and middle-income countries, mostly due to rare reports of failure on INSTI-based regimens and scarcity of patients with INSTI drug resistant mutations (DRMs).
Method: HIV non-B subtype infected patients (n=10) failing raltegravir (RAL)-based third-line treatment were selected for the study. Patient-derived HIV integrases with INSTI DRMs, and a control lacking DRMs were used to test for phenotypic susceptibility to INSTIs (DTG, RAL, and EVG). Cross resistance was assessed by Spearman's correlation coefficient test.
Results: Viruses with one primary mutation and accessory mutations (AMs) were susceptible to DTG but highly resistant to both EVG and RAL. For example, viruses with N155H had fold change (FC) increase in IC50 of 1.1 to 1.4, 21.4 to 77.6, and 10.1 to 18.7 to DTG, EVG, and RAL respectively. Viruses with N155H and AMs, (T97A, L74I, E157Q, G163R, M50L, and/or V151I) were susceptible to DTG but resistant to EVG (FC 56.7 to >100) and RAL (FC 29.1 to 44.7). Presence of Y143R/S with AMs (T97A, M50I, L74IM, G163R, D232N) had FC of 0.5 to 1.1 (DTG), 15.9 to >100 (EVG), and >100 (RAL). A virus with E138A, G140A, Q148R, and G163R showed resistance to all three INSTIs, FC of >111 for DTG and >1000 to either EVG or RAL. Among AMs, G163R conferred high level resistance to all INSTIs in presence of Y143R/S or N155H. The strong cross resistance was only observed between DTG and EVG (r=0.88, p=0.00075). Viral infectivity assay showed a 56% average loss in infectivity with mutant viruses.
Conclusion: Patients failing RAL are susceptible to DTG, but resistant to EVG and RAL. Multiple primary INSTI DRMs seem to confer high-level resistance to DTG. Thus, precaution is needed when switching RAL failures with multiple primary INSTIs DRMs.

PE13/4

Monitoring the prevalence of transmitted HIV drug resistance in Hungary

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Purpose: Transmitted HIV-1 drug resistance (TDR) may affect the success of first-line antiretroviral treatment. The aim of this study was to monitor the presence of HIV-1 strains carrying transmitted drug resistance-associated mutations (TDRMs) in newly diagnosed, treatment-naïve patients in Hungary. Extensive implementation of integrase inhibitors into the medical care initiated to investigate TDR of this drug class as well.
Method: 274 HIV-infected individuals diagnosed between 2013 and 2018 were included in the study; most of them belonged to the MSM (men who have sex with men) group. HIV-1 subtypes and TDRMs were determined by sequencing partial protease, reverse transcriptase and integrase coding regions of the *pol* gene. The sequences were analysed using the Stanford HIV Drug Resistance Database algorithm. Transmission clusters among patients were identified using phylogenetic analysis.
Results: Although subtype B HIV-1 strains were predominant (84.7%) in the study, non-B subtypes including A, F, CRF01_AE, CRF02_AG, C, D and G were also recorded. The overall prevalence of TDR was 9.1% (25/274; 95% CI: 6.3–13.1%). Most of TDRMs were detected in subtype B HIV-1 strains. Nucleoside reverse transcriptase inhibitor (NRTI)-associated mutations were the most frequent indicators of TDR (21/274; 7.7%; 95% CI: 5.1–11.4%), followed by mutations conferring resistance to protease inhibitors (PIs) (3/274, 1.1%; 95% CI: 0.4–3.2%) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) (2/274; 0.7%; 95% CI: 0.2–2.6%). Drug resistance of integrase inhibitors were tested in 136 newly diagnosed, untreated patients. Major integrase resistance mutation (T66A) was detected in 1 case (1/136; 0.7%; 95% CI: 0.1–4.1). Cluster analysis revealed potential transmission clusters with TDRM carrying samples.
Conclusion: Onward transmission of drug resistant subtype B HIV-1 strains accounted for the majority of TDR observed among treatment-naïve HIV-infected individuals in Hungary.

PE13/5

Predominant reverse transcriptase resistance mutations as barriers to achieving elimination of mother-to-child transmission of HIV in South Africa

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Purpose: The emergence of HIV drug resistance poses a significant threat to achieving the goal of elimination of mother-to-child transmission. In this study, we assessed the burden of HIV-1 drug resistance mutations (DRMs) within the context of the public sector prevention of mother-to-child transmission (PMTCT) programme in the Eastern Cape, South Africa.
Method: We conducted genetic analysis on viral isolates (n=80) from plasma samples of women with probable virological failure at delivery between January and May 2018 from two large maternity centres in the Eastern Cape using standard protocols. Partial pol gene covering 1030 bp were amplified and sequenced according to previously reported protocol. DRMs were determined by submitting the generated partial pol sequences to the Stanford drug resistance database for query on mutations associated with drug resistance in HIV viruses. We examined the correlates of DRMs using bivariate analysis.
Results: The age of parturient women ranged from 16–43 years. The majority of the parturient women were currently on Efavirenz-based regimen (first line ART) (82.5%) and had been on ART for more than 12 months (65.0%). The prevalence of DRMs was 72.5% (n=58). The CD4 count demonstrated a negative linear association with the DRMs (p=0.002). The predominant DRMs were K103N (n=43; 74.1%), M184V (n=28; 48.3%) and K65R (n=11; 19%). Among the parturient women on current treatment of EFV-based regimen; 79.1% already had K103N while nine patients on protease inhibitor-based regimen still harboured K103N. The majority of the M184V mutations were observed in parturient women on first line regimen (n=23; 82.1%).
Conclusion: We found a high prevalence of DRMs in women delivering their index babies at high viral loads in the study settings. Future studies should explore the point-of-care technology for reverse transcriptase-PCR for screening for common resistance mutations to guide appropriate neonatal prophylaxis and maternal therapy.

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PE13/6

Virologic failure and human immunodeficiency virus drug resistance in adolescents on antiretroviral therapy in Yaounde and Douala

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Purpose: HIV is a leading cause of death, among adolescents, likely due to poor monitoring and high risk of therapeutic failure in resource-limited settings. We sought to determine the rates of virologic failure (VF) and HIV-1 drug resistance (HIVDR) among adolescents receiving antiretroviral therapy (ART).
Method: A cross-sectional study was conducted among adolescents receiving ART in 10 Health Facilities of Douala and Yaounde in Cameroon from November 2018 to May 2019. Sociodemographic characteristics, ART regimens, adherence level and viral load (VL) were obtained from medical files. Genotypic HIVDR testing was performed for those experiencing VF (VL≥1000 copies/mL) with available sample and interpreted using the Stanford HIVdb algorithm. Bivariate analyses were performed, with $p<0.05$ considered statistically significant.
Results: Out of 1,316 adolescent files on ART, 233 (17.7%) had missing records of VL. Among those with VL results, adherence level ranged from 81.6% to 91.8% using different adherence assessment methods. Interestingly, 276/1083 (25.5%) were experiencing VF versus 807/1083 (74.5%) reported with viral suppression (VL <1000 copies/mL). HIVDR testing was successfully done for 45/57 (79%) available samples from those experiencing VF. Of relevance, VF was associated to suboptimal adherence (OR:0.039, p=0.000), distant residence (OR :1.5, p=0.01) and category one health facility (OR:2.8, p=0.02), age at ART initiation (OR:2.5, p=0.01) and baseline CD4 percentages (OR:2.1, p=0.001). Overall rate of acquired HIVDR was 93.3% (42/45), with a high rate of multiclass HIVDR-mutations (80%).
Conclusion: In Cameroon, VF is high among adolescents receiving ART, mainly attributed to poor adherence. Acquired HIVDR is frequent adolescents experiencing VF, with consistent rate of multi-drug resistance strains, which in turn limit future therapeutic options for transition to adult care. Thus, scale up of VL monitoring, timely detection of VF and prompt switching to PI-based second-line ART would limit the accumulation of HIVDR and ensure successful viral suppression.

PE13/7

Selection of integrase inhibitor (INI) resistance mutations in an INI experienced patient treated by Bictegravir

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Purpose: Very few data are available about the viral genetic resistance pathways in case of failure to Bictegravir (BIC).
Method: We described a case of an INI experienced patient with baseline N155H INI resistance mutation who had a virologic rebound while on Bictegravir containing regimen.
Results: A 30-year-old African American patient, diagnosed with HIV in 2008 and started HIV treatment in 2015 with TDF/FTC/EVG/c. This first ARV line was stopped due to poor adherence related to GI side effects. Genotypic testing performed after failure of TDF/FTC/EVG/c evidenced a M50I + N155H profile in HIV integrase gene and M184V in RT.
The patient reengaged in care in November 2018 and was treated with TAF/FTC/BIC and was followed at M1, M2 and M3 (Table 1). At M1 and M2, he harbored a good virologic plasma HIV RNA response, then failed at M3. At M3, Integrase gene sequencing showed selection of E138K, S147G, and R263K mutations in addition to the M50I and N155H resistance mutations already present at baseline. He received as subsequent regimen of TAF/FTC/DRV/c STR with a good virologic response.
Conclusion: This case report suggests that TAF/FTC/BIC should not be used in patient with previous selection of INI resistance mutation and this kind of patient should receive only Dolutegravir (DTG) 50 mg twice a day if an INI based regimen has to be used. Bictegravir is able to select various INI resistance mutations at least in viruses already harboring INI resistance.

Table 1.

Date	Plasma HIV RNA	CD4 cell count	Resistance testing	Treatment
Baseline	467,000	8	RT: M184V; Integrase: M50I+N155H	TAF/FTC/BIC
M1	32,000	30		TAF/FTC/BIC
M2	2,850	52		TAF/FTC/BIC
M3	88,400		RT: M184V; Integrase: M50I+R138K+S147G+ N155H+R263K	TAF/FTC/BIC
M4	1,650	86		TAF/FTC/DRV/c
M6	83	147		TAF/FTC/DRV/c

PE13/8

Impact of HIV-1 subtypes and integrase natural polymorphisms on virological response to first-line integrase inhibitors based regimens

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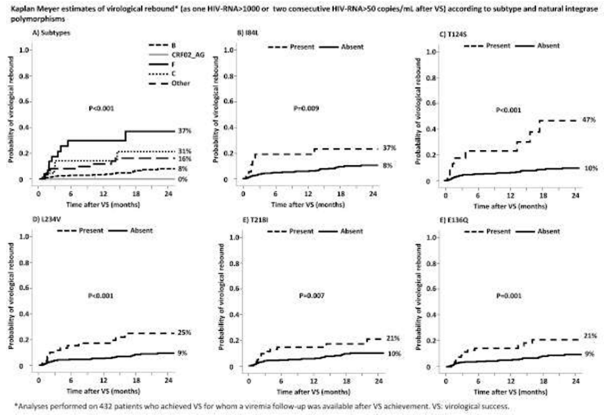
Purpose: We evaluated the virological response to first-line integrase-inhibitor (INI) based treatment in HIV-1 infected drug-naïve patients followed in Italy.
Methods: The impact of HIV-1 subtype and integrase polymorphisms on virological success (VS, HIV-RNA <50 copies/mL after ART-start) and virological rebound (VR, see Figure) was evaluated by survival analysis.
Results: 515 patients were analyzed: 336 infected with B subtype (65.2%), 36 F (7.0%), 28 C (5.4%), 24 CRF02_AG (4.7%) and 91 with other subtypes (17.7%). 222 (43.1%) patients were treated with dolutegravir, 166 (32.2%) with elvitegravir, 127 (24.7%) with raltegravir.
Two patients (0.4%) harbored one INI-major resistance mutation (MRM) at baseline (R263K and Y143YCHR, respectively), while 29 (5.6%) harbored ≥1 accessory INI RM (ARM).
Overall, by 12 months of treatment, the probability of VS was 94%. F-infected patients showed the lowest probability of VS (F: 85.1%; others: 91%, C: 96%; B: 96%; CRF02_AG: 100%; p=0.131). No associations with VS probability and the presence of ARMs or polymorphisms were found.
Overall, by 24 months after VS, the probability of VR was 12%. F-infected patients showed the highest probability of VR (37%, $p<0.001$) (Figure, Panel A). By evaluating the integrase polymorphisms, patients harboring I84L, T124S, K136Q, T218I or L234V (all associated with F-subtype) had a significantly higher probability of VR (Table; Figure, Panels B-F).

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By Cox multivariable analysis, adjusting for demographic, viro-immunological and treatment parameters, F-infected patients showed a higher relative hazard (95% C.I.) of VR (4.37 [1.77–10.79, p=0.001) compared to B-infected patients, regardless to the INI used.

Conclusion: Patients infected with CRF02_AG and B subtype showed the best virological control under first-line INI-based treatment, while F-infected patients showed a poorer virological control. The presence of F subtype-related polymorphisms may correlate with this phenomenon. Further investigations are needed to clarify these observations.

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Figure

Prevalence of integrase polymorphisms associated with virological rebound in drug-naïve patients treated with INIs

Integrase polymorphisms[a]	Overall Frequency n (%) (N=515)	Frequency among the most prevalent subtype in Italy, n (%)					P value (compared to B)[c]			
		B (N=336)	CRF02_AG (N=24)	F (N=36)	C (N=28)	Other (N=91)[b]	CRF02_AG	F	C	Other
I84L	41 (8.0)	4 (1.2)	0 (0)	**12 (33.3)**	0 (0)	**25 (27.5)**	0.590	**<0.001**	0.561	**<0.001**
T124S	30 (5.8)	8 (2.4)	0 (0)	**10 (27.8)**	2 (7.1)	**10 (11.0)**	0.444	**<0.001**	0.139	**<0.001**
K136Q	103 (20.0)	6 (1.8)	1 (4.2)	**31 (86.1)**	**22 (78.6)**	**43 (47.3)**	0.414	**<0.001**	**<0.001**	**<0.001**
T218I	83 (16.1)	16 (4.8)	4 (16.7)	**26 (72.2)**	**15 (53.6)**	**22 (24.2)**	0.013	**<0.001**	**<0.001**	**<0.001**
L234V	69 (13.4)	15 (4.5)	0 (0)	**23 (63.9)**	4 (14.3)	**27 (29.7)**	0.029	**<0.001**	0.025	**<0.001**

[a]Integrase polymorphisms have been defined as integrase amino acid substitutions with an overall prevalence ≥5%. By analyzing the integrase amino acid positions 1-263, 59 polymorphisms were found, 37 of them associated with HIV-1 subtypes. In the table, the prevalence of integrase polymorphisms that were associated with both subtype and virological rebound (VR) in drug-naïve patients receiving an INI-based first-line treatment is reported, overall and according with the most prevalent HIV-1 subtypes circulating in Italy.
[b]Other: 19 A; 16 CRF12_BF; 7 CRF01_AE; 5 CRF06_cpx; 5 CRF42_BF; 4 CRF47_BF; 3 CRF03_AB; 3 CRF17_BF; 3 CRF72_BF; 3 G; 2 CRF20_BG; 2 CRF28_BF; 2 CRF29_BF; 2 CRF51_01B; 2 CRF60_BC; 1 BC; 1 CRF_42BF; 1 CRF05_DF; 1 CRF07_BC; 1 CRF24_BG; 1 CRF34_01B; 1 CRF39_BF; 1 CRF43_02G; 1 CRF61_BC; 1 CRF71_BF; 1 D; 1 DF; 1 H.
[c]Chi-squared test corrected for multiple comparison (Benjamini-Hochberg correction, with a false discovery rate of 0.05 used to determine statistical significance) among 59 integrase polymorphisms tested.
In bold are indicated polymorphisms with P value <0.001 after Benjamini-Hochberg correction. INIs: integrase inhibitors.

Table

PE13/9

HIV-1 integrase inhibitor resistance associated mutations defined by majority and minority populations among individuals failing therapy

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Purpose: Integrase inhibitors (INIs) are recommended for ART-naïve individuals and are increasingly employed in switch and salvage regimens. This study examines the occurrence of INI major Resistance Associated Mutations (mRAMS) for both majority and minority populations and their impact on INI resistance (INI-R) in patients failing treatment.

Method: Genotypic antiretroviral resistance testing was performed using next generation sequencing for detection of mRAMS for majority and minority HIV populations and INI-R as defined in the Stanford University HIV drug resistance database. Assays were done on INI-experienced (INI-E) viremic persons (HIV RNA >200 copies/mL) failing therapy. Thresholds for mRAMs were defined as ≥10% for majority and 1–10% for minority populations.

Results: From 10/2015–12/2019, 293 individuals were prescribed INI regimens; 63 were considered treatment failures. Median age was 43 years (IQR: 30–51); 82.5% male; 88% African American; median HIV RNA: 41,426 (IQR: 10,749–97,942); median CD4: 281 (IQR: 110–385). Of those failing therapy, 86.0% had INI majority mRAMS. Minority INI mRAMS were found in 37.1%. INI-R defined by majority mRAMS was 7.9% for both first (G1) and second (G2) generation INIs and 33% for G1 INIs only. INI-R counting both majority and minority mRAMS was identified in 17.4% for both G1 and G2 INIs and 60% for G1 INIs only. Intermediate and high level INI-R defined by majority mRAMS was observed in 6.3% for G1 INIs and 0% of G2 INIs. With the inclusion of minority mRAMS, INI-R was 19% and 3.2% for G1 and G2 INIs.

Conclusion: Nearly all INI-E patients failing therapy had INI mRAMS; although INI-R remained low, particularly for G2 INIs. The clinical impact of minority INI mRAMS remains unclear. Long-term outcome studies are needed to resolve the clinical significance of minority mutations that impact susceptibility profiles of INIs.

PE13/10

HIV-1 diversity and antiretroviral resistance among bulgarian citizens infected abroad and foreigners registered with HIV/AIDS in bulgaria from 2012 to 2017 (preliminary analysis)

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Purpose: The aim of our study was to analyze HIV-1 diversity and the prevalence of antiretroviral resistance mutations among Bulgarian citizens who reported to be infected abroad and foreign individuals diagnosed and registered with HIV/AIDS in Bulgaria from 2012 to 2017.

Methods: In Bulgaria 274 individuals (190 Bulgarians and 84 foreigners) infected with HIV-1 abroad were diagnosed and registered from 2012 to 2017. 149 (54.4%) of them were heterosexuals (HET), 99 (36.1%) men who have sex with men (MSM), 20 (7.3%) people who inject drugs (PWIDs) and 6 (2.2%) MSM who inject drugs. Resistance mutations and HIV-1 diversity was analyzed in 108 (39.4%) randomly selected individuals. HIV-1 *pol* sequences were generated with TruGene and/or ViroSeq Genotyping Systems. Resistance mutations were determined using the Stanford HIVdb version 8.3. HIV-1 subtypes were defined using COMET v2.2. Phylogenetic relationships and possible clusters with resistance mutations were inferred by ML analysis with IQtree program and phylogenetic clusters were defined using ClusterPicker v1.2.3.

Results: The overall prevalence of the resistance mutations was 20.4% (22/108), comprising 6 (5.6%) to nucleoside reverse transcriptase inhibitors (NRTI) and 16 (14.8%) to non-nucleoside reverse transcriptase inhibitors (NNRTI). Dual resistance mutations were identified in 1 (0.9%) patient with both NRTI and NNRTI. The main HIV-1 clade was subtype B with 54 (50%) followed by subtype A1 15 (13.9%), unassigned 11 (10.2%), F1 8 (7.4), CRF01_AE 7 (6.5%) and 6 other subtypes and CRFs comprising 6% in total. Phylogenetic analysis identified phylogenetic clusters in different subtypes involving individuals infected abroad as well as patients infected in the country

Conclusions: High genetic diversity of HIV-1 subtypes have been introduced and disseminated in the country. Phylogenetic clusters demonstrate distribution of HIV-1 among different transmission groups of the populations. The prevalence of resistance mutations among analyzed individuals diagnosed with HIV/AIDS in Bulgaria is low.

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PE13/11

Analytical treatment interruption and its association with rearrangement of peripheral archived resistance mutations

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Purpose: Little is known about the impact of short-analytical antiretroviral-treatment interruption (ATI) and subsequent re-initiation of antiretroviral-therapy (ART) might have on archived major-resistance mutations (MRMs).
Methods: Seven chronically HIV-1 infected patients with HIV-RNA <50 copies/mL for ≥10 years, undergoing towards ATI (APACHE-study) were analysed for HIV-DNA (ddPCR) and pol-sequences (Illumina-MiSeq) before ATI, at viral-rebound (VR) during ATI and at achievement of undetectability after ART-resumption (post-ATI). These parameters were evaluated at three similar time-points in seven triple-ART-treated patients with HIV-RNA <50 copies/mL for ≥1 year (MODAT-study, control-group). Intra-patient prevalence of archived MRMs (Stanford-list), including Apobec3-related MRMs, was assessed at each time-point. Wilcoxon signed-rank and Mann-Whitney tests were used to test changes in MRM prevalence at different time-points, as appropriate.
Results: APACHE subjects experienced VR after ATI at a median (IQR) time of 4(3–7) weeks and, after ART resumption, achieved HIV-RNA <50 copies/mL in 24(4–29) weeks. Median (IQR) HIV-DNA was 982(692–1286) copies/10^6CD4$^+$T at T1, 1892(146–3798) at T2, and 992(553–2183) at T3, with no significant change in HIV-DNA overtime (p=0.37).
At baseline, 5/7 APACHE and 3/7 MODAT subjects carried HIV-DNA-MRMs with a median (IQR) intra-patient prevalence of 38.1(6.2–99.6) and 99.0(47.1–99.5) (p=0.46, Table). In APACHE, MRMs persisted during ATI in 2/7 (28.6%) and in 4/7 (57.1%) individuals at plasma level and in peripheral reservoir, respectively. Post-ATI, MRMs completely reverted in 2 individuals. Comparing pre- and post-ATI HIV-DNA sequences, MRMs with a baseline intra-patient prevalence <80% significantly decreased from pre- to post-ATI (intra-patient prevalence: 7.2 [1.8–29.8] vs. 0.0 [0.0–0.6], p=0.01). This decrease occurred mainly in APOBEC3-related MRMs (Table).
In MODAT-patients, no differences in MRM prevalence were found between baseline and follow-up (p=0.18).

Table. Major drug resistance mutations in protease and reverse transcriptase in patients enrolled in the APACHE and MODAT studies

Study	ID	Time 1[a]	Time 2[b]		Time 3[c]
	Sample	HIV-DNA	HIV-DNA	HIV-RNA	HIV-DNA
APACHE	A-001	PR: None RT: **D67N** (99.4%), K70R (99.6%), M184V (14.0%), T215I (85.6%), K219Q (99.8%)	PR: None RT: **D67N** (21.3%), K70R (99.7%), M184V (11.1%), K219Q (10.8%)	PR: None RT: K70R (99.6%)	PR: None RT: **D67N** (99.3%), K70R (99.7%), M184V (8.1%), T215I (89.9%), K219Q (99.8%)
	A-002	PR: None RT: **G190E** (5.1%)	PR: **D30N** (1.3%) RT: None	PR: None RT: None	PR: None RT: None
	A-009	PR: **M46I** (5.1%) RT: **D67N** (6.2%), **E138K** (7.3%)	PR: None RT: None	PR: None RT: None	PR: None RT: **M184I** (1.4%)
	A-011	PR: None RT: None	PR: None RT: None	PR: None RT: None	PR: None RT: None
	A-013	PR: None RT: None	PR: None RT: None	PR: None RT: None	PR: None RT: None
	A-014	PR: **M46I** (1.4%) RT: **D67N** (7.1%), **V106I** (99.3%)	PR: None RT: V106I (99.6%), Y188C (23.2%)	PR: None RT: **V106I** (99.7%), Y188C (97.0%)	PR: V82A (2.3%) RT: **V106I** (99.6%)
	A-015	PR: **V32I** (27.4%) RT: K65R (38.1%), K101E (38.0%), Y181C (42.5%), **M184I** (28.9%), **G190E** (1.9%)	PR: **M46I** (1.2%) RT: K65R (3.5%), Y181C (6.5%), **M184I** (3.6%), Y188H (1.3%)	PR: None RT: None	PR: None RT: None
MODAT	Sample	HIV-DNA	HIV-DNA		HIV-DNA
	T01-039	PR: None RT: M41L (94.2%), T215C (99.5%)	PR: None RT: M41L (51.3%), **M184I** (6.9%), T215C (99.4%)		PR: None RT: M41L (93.7%), T215C (98.6%)
	T01-040	PR: None RT: M41L (47.1%)	PR: None RT: M41L (73.9%)		PR: None RT: M41L (31.7%)
	T01-056	PR: None RT: None	PR: None RT: None		PR: None RT: None
	T01-058	PR: None RT: E138A (99.0%)	PR: None RT: E138A (98.8%)		PR: None RT: E138A (99.5%)
	T01-063	PR: None RT: None	PR: None RT: None		PR: None RT: None
	T01-066	PR: None RT: None	PR: None RT: None		PR: **M46I** (5.1%) RT: None
	T01-070	PR: None RT: None	PR: None RT: None		PR: None RT: None

[a] Time 1 corresponds to baseline for both the groups of patients; in particular, for APACHE patients Time 1 corresponds to the time before analytical treatment interruption (pre-ATI). [b] Time 2 corresponds to time of virological rebound during ATI for APACHE patients and to a similar time point for MODAT patients. [c] Time 3 corresponds to the time of undetectability achievement after ART resumption (post-ATI) in the APACHE patients and to a similar time point for MODAT patients. All the major drug resistance mutations (MRMs, Stanford list 2018) detected in HIV-1 protease and reverse transcriptase by Illumina MiSeq with a prevalence >1% have been considered at each time point. Apobec3-related MRMs are highlighted in bold. PR: protease; RT: reverse transcriptase.

Conclusion: This proof-of-concept study confirms that ATI does not affect the amount of post-ATI peripheral HIV-DNA but suggests that ATI may be associated with rearrangement of peripheral archived MRMs, and in some cases with their complete reversal.

PE13/12

A low level of darunavir resistance-associated mutation emergence in patients with virological failure during long term use of darunavir in people living with HIV, the French ANRS CO3 Aquitaine cohort

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Purpose: Ritonavir-boosted darunavir (DRV/r) is a protease inhibitor (PI) indicated for the treatment of naive and pretreated HIV infected patients since 2007. Our study aims to describe DRV/r treated-patients experiencing virological failure (VF) documented with HIV resistance testing.
Method: Data from patients belonging to the ANRS CO3 Aquitaine cohort treated with a regimen including DRV/r between February 2007 and December 2015 were analyzed. Baseline characteristics of patients with VF (defined by 2 consecutive plasma viral load (VL) >50 copies/mL) were compared to those without VF.We then described factors associated with VF as emergence of IAS DRV resistance-associated mutations (RAMs).
Results: 1458 patients treated with a DRV/r based regimen were included. Among them, 270 (18.5%) patients experienced VF with genotypic resistance tests performed during follow-up. DRV RAMs were detected in 29 patients (12%) at VF. These 29 patients had received a median of 10 lines of treatment before DRV/r initiation compared to 5 lines for patients without DRV RAMs (p<0.0001). Analysis of previous genotyping tests revealed that 25/29 patients had DRV RAMs before DRV initiation: 10, 9 and 6 patients had 2, 3 and 4 or more DRV RAMs respectively. VF had occurred under previous PI treatments. Dose of boosted DRV at VF was 1200 mg/day for 80 % of patients. For half of them, DRV was maintained after VF and controlled viremia was restored after modification of DRV-associated antiretroviral molecules or increased DRV dose. Finally, only 4/29 patients selected DRV RAMs after DRV/r initiation. All of them experienced previous VFs with other PIs without selecting DRV RAMs.
Conclusion: These results highlight the efficacy and the robustness of boosted darunavir since emergence of DRV RAMs appeared in less than 0.3% of patients receiving a DRV based regimen in our large cohort.

PE13/13

Patients infected with multi-class resistant HIV-1 and with viral suppression treated with no more than one active drug: comparison of historical resistance reports and drug resistance in proviral DNA

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Objective: Archived drug resistance-associated mutations (DRMs) may compromise virologic efficacy of antiretroviral therapy (ART). With deep sequencing (DS) assays, mutation patterns can be analyzed in proviral DNA at low frequencies. However, current data indicate that resistance testing

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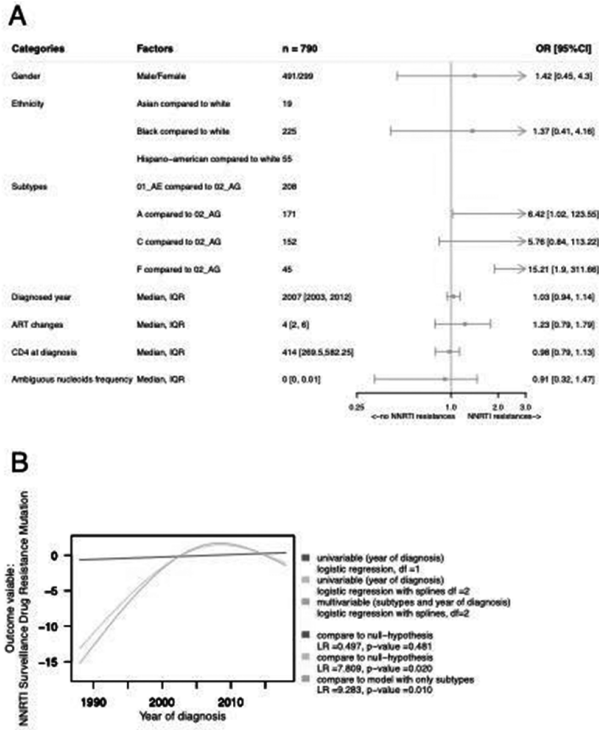
performed on HIV DNA lacks sensitivity compared with cumulative DRMs available from historical resistance testings (HRT) using plasma RNA.
Methods: LOWER is a multicenter study of patients with major DRMs (using Stanford-HIVdb v8.6.1) in ≥3 ART classes (of NRTIs, NNRTIs, PIs, INSTIs). This subanalysis describes mutational patterns in proviral DNA (after APOBEC filtering) in patients with viral suppression (<50 copies/mL) whose ART consisted of ≤1 active agent based on HRTs.
Results: In 16/195 patients with viral suppression, HRTs indicated that the genotypic susceptibility score (GSS) of current ART was ≤1. In 9 patients with a GSS of 1, fully active drugs were INSTIs (n=5), boosted PIs (n=2), and entry inhibitors (n=2). Among the 7 patients with a GSS <1, 3 cases were found to have a GSS=0. Median time of viral suppression in the 16 patients was 9.7 years. Even with a DS cut-off of <2%, many DRMs were not re-detected by DS and mean GSS increased from 0.69 (range 0–1) to 1.66 (0–3). In 11/16 patients, proviral drug resistance yielded a GSS increase of ≥0.5 for current ART, compared to HRTs. Only 1 patient had a GSS of <1 both in HRTs and in the proviral DNA.
Conclusion: Long-lasting viral suppression is possible in some patients with multi-class resistance, even when historical resistance reports suggest only one active agent (or even less) in the current ART regimen. GSS was higher using DS from proviral DNA, indicating that at least some DRMs could have been cleared from the latent reservoir over time.

PE13/14

Non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance in people living with HIV-1 (PLWH) subtype non-B from the Swiss HIV Cohort Study (SHCS)

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Purpose: The roll-out of antiretroviral therapy (ART) in resource limited settings (RLS), increases the spread of non-nucleoside reverse transcriptase inhibitors (NNRTI) drug resistance. With immigration of people living with HIV (PLWH) with subtype non-B, similar consequences could arise also in Western Europe.
Method: PLWH enrolled before March 2019 in the Swiss HIV Cohort Study (SHCS) and infected with HIV-1 non-B subtype (A, C, F, CRF01_AE, and CRF02_AG) were included. We analysed 790 PLWH that were treatment naïve at diagnosis and were diagnosed <1.5 years after estimated date of infection. The HIV-1 sequences from PLWH were analysed with HIVseq established by the HIV drug resistance database of Stanford University. Thereby, major NNRTI surveillance drug resistance mutations were analysed, according to Bennett et al., 2009. Logistic regression was used to identify the associations with NNRTI resistance.
Results: The prevalence of transmitted NNRTI resistance in the SHCS was 2.53% for non-B subtypes. We found that having an NNRTI resistance is associated with subtype A and F compared to CRF01_AE (odds ratio $(OR)_{univariable}$ [95% confidence interval (CI)] = 6.42 [1.02, 123.55], 15.21 [1.9, 311.66]) (see Figure A). Including the subtypes and the year of diagnosis with splines, the logistic regression model significantly improved the quality of the fit (p-value = 0.01), indicating a time dependence of NNRTI resistance in Switzerland for non-B subtypes (see Figure B).
Conclusion: This study shows that an increase of NNRTI resistance occurs not only in RLS but also in resource rich settings like Switzerland for non-B subtypes. Consequently, due to immigration from high HIV-1 prevalence countries, public health problems related to DR in RLS are also increasingly relevant in Western Europe. Close surveillance of transmitted drug resistance (TDR) remains important, given the ongoing widespread roll-out of integrase inhibitors in RLS, this may also apply to integrase inhibitors.



A: Identify associations with NNRTI resistance; B: Regression models with the year of HIV-1 diagnosis and HIV-1 subtypes

PE13/15

HIV-1 from antiretroviral-naïve and experienced patients lack capsid substitutions associated with GS-6207 in vitro resistance

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Purpose: HIV capsid (CA) plays an essential role in multiple stages of the viral replication cycle. In vitrocharacterization of the CA inhibitor GS-6207 revealed the high potency of the compound (0.1 nM EC50). Resistance selection experiments identified seven amino acid substitutions in CA protein associated within vitro resistance to GS-6207, all located near the GS-6207 binding site in CA. Genetic variations in gag can naturally occur depending on the HIV subtypes, immune pressure, and prior use of HIV protease (PR) inhibitors (PIs), as gag is the substrate for PR. Here we studied the prevalence of CA mutations associated with in vitroresistance to GS-6207 in antiretroviral therapy (ART)-naïve or -experienced people living with HIV (PLWH).
Method: Sanger sequencing was used to study the presence of GS-6207 *in vitro*-selected mutations (L56I, M66I, Q67H, K70N, N74D, N74S, and T107N in CA) in 3 large groups of PLWH: ART-naïve, ART-experienced without PI experience, and ART-experienced with PI failure with or without major PI resistance mutations (IAS-USA definition).
Results: Among the 1500 patients studied, the most prevalent HIV-1 subtypes were B and CRF 02 AG (Table 1). The majority of ARV-experienced patients with history of PI failure had at least 1 major PI resistance mutation (Table 2).

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None of the seven GS-6207 resistance mutations identified during *in vitro* selection experiments was detected among the 1500 patients studied.
Conclusion: In our large database (n=1500) of ART-naïve and experienced PLWH with various subtypes, no GS-6207 *in vitro*-associated mutations were observed. Therefore, previous PI failure and emergence of PI resistance mutations are not anticipated to impact potential resistance to GS-6207 in HIV-1 CA. This suggests a very low likelihood of pre-existence of resistance mutations to GS-6207 in the PLWH population and that GS-6207 has the potential to be effective regardless of treatment history or prior PI use.

Table 1.

HIV-1 Subtype distribution, % (n)	ARV-Naïve (n=500)	ARV-Experienced no PI use (n=500)	ARV-Experienced PI failure history (n=500)
B	37% (185)	42% (210)	56% (280)
CRF02_AG	46% (230)	48% (240)	37% (185)
F1	4.6% (23)	2.4% (12)	-
CRF06	4.4% (22)	3.8% (19)	3.4% (17)
A1	2.8% (14)	-	-
D	2.2% (11)	2.2% (11)	1.6% (8)
Other non-B	3.0% (15)	1.6% (8)	1.0% (5)

Table 2.

Number of Major PI Resistance Mutations, % (n)	ARV-Naïve (n=500)	ARV-Experienced no PI use (n=500)	ARV-Experienced PI failure history (n=500)
0	99.4% (497)	99.6% (498)	47.2% (236)
1	0.6% (3)	0.4% (2)	22.4% (112)
2	-	-	16.4% (82)
3	-	-	10.4% (52)
4	-	-	3.6% (18)

PE13/16

Long-term efficacy, safety and durability of ibalizumab in expanded access study

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Purpose: Ibalizumab (IBA) is a CD4-directed post-attachment HIV-1 inhibitor that blocks HIV-1 entry into CD4 cells while preserving normal immunological function. IBA, a long-acting humanized monoclonal antibody, is FDA-approved and under review by EMA.
We evaluated the long-term efficacy, safety and durability of IBA in study TMB-311.
Method: Patients in TMB-311 were enrolled in one of two cohorts:
Cohort 1: Patients rolled over from Phase 3 study TMB-301 or under an Investigator-sponsored Investigational New Drug (PI-IND) protocol upon completion of Phase 2 study TMB-202 continued on IBA at their current dosage in combination with an Optimized Background Regimen (OBR).
Cohort 2: Patients with no history of IBA treatment received a loading dose of 2000 mg of IBA followed by 800 mg IBA every 2 weeks in addition to an OBR. All patients continued receiving IBA until it became commercially available.
Results: *Cohort 1-TMB-301 (n=27):* At time of roll-over into TMB-311, 15 patients achieved viral load (VL) <50 copies/mL while 16 were virally suppressed by Year-2. Overall, patients averaged 2.1 years of IBA treatment, with 7 patients receiving IBA beyond Year-2.5, and some up to Year-2.8.
Cohort 1-TMB-202 (n=12): All 12 patients had an undetectable VL at time of last visit while on TMB-311. Patients were on IBA treatment for an average of 8.8 years (range of 7.8–9.5).
Cohort 2 (n=38): Twenty-four patients were treated with IBA for 24 weeks, with 11 (46%) achieving <50 copies/mL. Of 17 patients reaching Year-1 visit, 8 were undetectable. Overall, patients were on IBA treatment for an average of 0.9 years, with 17 for ≥1 year.
Overall, 39 of 77 patients (51%) in TMB-311 had undetectable VL.
IBA was well-tolerated and no unexpected IBA-related adverse events were reported.
Conclusion: Extended data from TMB-311 support the durable efficacy and long-term safety of IBA-based regimens.

PE13/17

Clinical impact of minority mutations in patients failing an integrase inhibitor-based regimen: what do clinicians do?

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Purpose: Next Generation Sequencing (NGS) is increasingly used to describe HIV antiretroviral drug resistance. However, the clinical consequences of minority mutations remains unclear. We examine how the addition of minority mutations affects the overall interpretation of genotype resistance reporting for Integrase Inhibitors (INIs) in INI-experienced (INI-E) patients failing INI-based ART.
Method: HIV genotypes for patients on ART therapy have been performed using NGS for detection of major HIV Resistance Associated Mutations (mRAMS) for majority and minority populations and INI-resistance (INI-R), defined by the Stanford University HIV drug resistance database. Assays were done on INI-E viremic persons (HIV RNA >200 copies/mL) failing therapy. Thresholds for mRAMS were defined as ≥10% for majority and 1-<10% for minority populations.
Results: Of 293 INI-E patients seen from 10/2015–12/2018, 63 were identified with presumed treatment failure. Median age: 43 years (IQR: 30–51); 82.5% male; 88% African American; median HIV RNA: 41,426 (IQR: 10,749–97,942); median CD4: 281 (IQR: 110–385). At failure, counting majority mRAMS only, 21 patients had INI-R (≥low level) with only 4 patients having intermediate or high level resistance. Of these four patients, two had changes to their regimen, one was lost to follow up and one patient had no changes to their regimen. At failure, including both majority and minority mRAMS, 39 patients had INI-R (≥low level) with 13 having intermediate or high level resistance. Within these 13 patients, 54% of them had changes to their regimen, 31% had no changes and 15% were lost to follow up.
Conclusion: Using NGS to identify minority mRAMS led to considerable changes in INI-R interpretation. The addition of minority genotypic susceptibility to the resistance report led clinicians to reject first or second generation INIs in 54% of patients. The clinical use of minority population mutations was inconsistent and further studies are needed for guidance.

PE13/18

Identification of HIV-1 transmission clusters in Croatia, 2014–2017: evidence for the forward spread of HIV-1 resistant variants

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Purpose: Phylogenetic analysis is a useful tool for identification of HIV-1 transmission clusters and analysis of biological characteristics of individual clusters. The aim of the study was to determine and characterize transmission networks that are responsible for the forward spread of HIV-1 infection and resistant variants in Croatia.
Method: We analyzed 403(95.9%) of 428 newly HIV-diagnosed persons who entered clinical care at the University Hospital for Infectious Diseases, Zagreb. The entire protease HIV-1 gene (PR, codons 1–99) and a part of the reverse transcriptase HIV-1 gene (RT, codons 1–240) were sequenced by using a validated in-house method. Mutations were determined by using Surveillance Drug Resistance Mutation list. HIV subtype was determined with Rega HIV-1 subtyping tool, version 3.0. Sequences subtyped as B were selected for phylogenetic inference. For each sequence in the dataset 10 closest sequences were determined with BLAST search. Phylogenetic trees were constructed with

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PhyML 3.0, while the Figtree version 1.4.3 was used for tree visualization. Transmission cluster were defined as sequences ≥3 patients from Croatian cohort with the approximate likelihood ratio test value >0.90.
Results: Subtype B was found in 368 (91%) of patients. The overall prevalence of transmitted drug resistance (TDR) was 16.4% (n=66/403). The most prevalent TDR patterns were T215S, 7.2% (n=29/403); K101E, 3.5% (n=14/403); T215S + L210W, 2.2% (n=9/403); V32I+I47V+T215E/D+L100I+K103N, 1.9% (n=8/403); M41L+T215L, 0.7% (n=3/403). Phylogenetic analysis identified 19 local transmission clusters, of which 5 (26%) clusters were responsible for the forward spread of resistant HIV-1 viral strains. Patients in clusters (n=347) were more frequently MSM (319/358 vs. heterosexuals 24/39, p<0.001), of younger age (median:35 vs 39 years, p=0.02) and had a recent infection (77/81 vs. chronic 270/322 p=0.009).
Conclusion: In this study we found a high prevalence of TDR and identified 5 local transmission clusters responsible for the spread of HIV-1 resistant strains.

PE13/19

High levels of resistance among HIV-1 treatment naive patients in Greece, a nationwide study: evidence for country and regional level transmission networks

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Purpose: The prevalence of HIV drug resistance among drug-naive HIV-infected individuals (baseline resistance) was previously estimated at 27.9% during 2006–2015, in Northern Greece.To investigatethe prevalence of resistance in the era of limited resistance testing in Greece
Method: We analyzed protease (PR) and partial reverse transcriptase (RT) sequences from 103treatment naïve patients obtained between 2016 and 2018 inNorthern Greece. The dispersal patterns of viruses with resistance were estimated by phylogenetic analysis using as references sequences sampled during 2006–2015, in Greece
Results: The overall prevalence of resistance was at 37.9% (39/103), with the highest prevalence to be for the NNRTIs (35.0%). For the N(t) RTIs and PIs low levels of resistance were detected at 2.9% and 1.0%, respectively. The dominant resistance mutations for NNRTIs were E138A (17.5%), and K103N (10.7%). Notably, the overall prevalence of resistance between 2016 and 2018 was higher than the previous ten years (37.9% versus 27.9%, p=0.04). Phylogenetic analyses showed that viruses with E138A and K103N resistant mutations originated from previous strains with the same resistance pattern found within phylogenetic clusters from Greece (local transmission networks, LTNs).
Conclusion: Our study showed that in the era of limited resistance testing, transmitted resistance (TDR) to NNRTIs continues to occur at increasing prevalence in Northern Greece. TDR originated from previously existing clusters of resistance. The existence of extensive local transmission networks in some areas, raise concern about the risk of TDR to other drug classes.

PE13/20

A phase 3b, open-label, pilot study to evaluate switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) in virologically-suppressed HIV-1 infected adult subjects harboring NRTI resistance mutations M184V/I +/- TAMs (GS-US-292-1824): week 24 results

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Purpose: Treatment with E/C/F/TAF in HIV-1-infected patients was shown to be effective and safe through 144 weeks though these 2 trials excluded participants with baseline nucleoside reverse transcriptase inhibitor (NRTI) resistance.
Method: This ongoing, prospective open-label, single arm, multicenter, 48-week trial is evaluating the efficacy and safety of switching suppressed participants to E/C/F/TAF from a stable regimen (≥6 months) of a third agent plus either F/tenofovir disoproxil fumarate (TDF) or abacavir/lamivudine. Enrollment required a historical genotype report showing M184V/I with up to 2 thymidine analog mutations (TAMs) and no evidence of previous virologic failure (VF) or resistance to boosted PIs or INSTIs. At screening, HIV-1 RNA <50 copies/mL was required with no evidence of additional NRTI or PI resistance mutations by proviral HIV DNA sequencing (GenoSure Archive, Monogram Biosciences). Primary objective was to evaluate the efficacy in maintaining HIV-1 RNA <50 copies/mL at Week 12 using pure virologic response (PVR). Participants who discontinued or had missing data were considered responders if they never had HIV-1 RNA ≥50 copies/mL at 2 consecutive visits and the last HIV-1 RNA was <50 copies/mL.
Results: Sixty-four participants were enrolled and switched to E/C/F/TAF (Table). Through Week 24, all participants (100%) had HIV-1 RNA <50 c/mL based on PVR; there were no virologic failures or emergent resistance. Six serious adverse events (AE) occurred in 5 participants (none study drug-related): squamous cell carcinoma, acute kidney injury and renal failure (with poorly controlled hypertension and diabetes), transient proteinuria (resolved on study drug), lung adenocarcinoma, and prostatic adenoma. Ten participants (16%) experienced a study drug-related AE (grade 1 or 2); one participant discontinued due to grade 2 muscle spasms.

Pooled Analysis of Pre-existing M184V/I among Virologically Suppressed Clinical Trial Participants who Switched Regimens to B/F/TAF

	Study 1844	Study 1878	Study 4030	Study 4449	Study 1474	Pooled B/F/TAF
Prior Regimen	DTG/ABC/3TC	Boosted PI + 2 NRTIs	DTG + F/TDF or DTG + F/TAF	EVG/COBI/F/TAF or any TDF-containing 3-drug regimen	Any 3rd agent + 2 NRTIs	-
Median B/F/TAF treatment duration (weeks)	117 (group 1); 50 (group 2)[a]	116 (group 1); 71 (group 2)[a]	48	54	48	63
Number switched to B/F/TAF	545	532	283	86	75	1521
HIV-1 RNA <50 c/mL at last visit	99% (537/545)	99% (525/532)	99% (282/283)	100% (86/86)	99% (74/75)	99% (1504/1521)
Baseline genotype available	96% (522/545)	93% (497/532)	84% (238/283)	98% (84/86)	15% (13/75)	89% (1354/1521)
Baseline M184V/I	3.3% (17/522)	12% (62/497)	20% (47/238)	3.6% (3/84)	23% (3/13)	9.7% (132/1354)
M184V/I HIV-1 RNA <50 c/mL at last visit	100% (17/17)	95% (59/62)	100% (47/47)	100% (3/3)	100% (3/3)	98% (129/132)
Treatment emergent resistance	0	0	0	0	0	0

a. Group 1: participants switched to B/F/TAF on Day 1 of study randomized phase; group 2: participants continued baseline regimen during randomized phase and switched to B/F/TAF in open-label extension phase

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Conclusion: E/C/F/TAF offers an effective, well tolerated switch option for patients with M184V/I. These data on continued virologic suppression despite pre-existing resistance are encouraging and warrant further follow-up.

Baseline Characteristics (n=64)

Median age, years (range)	52 (22–76)
Female, % (n)	27% (17)
Race,%, (n)	
White	69% (44)
Black	23% (15)
Median CD4 count, cells/mm^3, (range)	655 (107–1503)
Median weight, kg (range)	76 (44–164)

Resistance Mutations

Resistance mutations based on screening historic genotype		PVR at W24
M184V or M184I only	83% (53)	100%
M184V/I + 1 TAM [M41L (1), K70R (2), T215Y/F (4), K219E (1)]	12% (8)	100%
M184V/I + 2 TAMs [M41L+T215Y/F (3)]	5% (3)	100%
Regimen prior to switching: 2 NRTIs + PI + ritonavir or cobicistat	53% (34)	100%

PE13/21

Sustained viral suppression among participants with pre-existing M184V/I who switched to bictegravir/emtricitabine/tenofovir alafenamide

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Purpose: Pre-existing resistance can affect antiretroviral therapy efficacy in people living with HIV. One of the most common treatment-emergent resistance substitutions is M184V/I. This substitution can be transmitted, archived in the viral reservoir, and reactivated, even when genotyping shows wild-type virus. Studies 1844, 1878, 4030, 4449, and 1474 demonstrated the safety and efficacy of switching stably suppressed HIV-1-infected individuals to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF). In this pooled analysis, we investigated the prevalence of pre-existing M184V/I and impact on virologic outcomes.

Method: Participants enrolled were aged ≥18 years (studies 1844, 1878, and 4030), ≥65 years (study 4449), or 6 to <18 years (study 1474). Pre-existing drug resistance was assessed by historical genotypes and/or retrospective proviral DNA genotyping (GenoSure Archive® assay, Monogram Biosciences). Virologic outcomes were based on last available on-treatment HIV-1 RNA, where early discontinuation with HIV-1 RNA <50 copies/mL was considered suppressed.

Results: Altogether, 1521 participants switched to B/F/TAF and were treated for a median of 63 weeks (range 1–145 weeks; Table 1). Cumulative baseline genotypic data from historical and/or proviral genotypes were available for 89% (1354/1521). Pre-existing M184V/I was detected in 9.7% (132/1354) of participants: by proviral genotyping only (83%, 109/132), historical genotype only (9%, 12/132), or both (8%, 11/132). At baseline, participants with pre-existing M184V/I were 15–78 years old. At the time of analysis (≥48 weeks of B/F/TAF treatment), 98% (129/132) of participants with pre-existing M184V/I were suppressed compared to 99% (1504/1521) of the overall B/F/TAF study population. No B/F/TAF-treated participant developed new drug resistance.

Conclusion: Pre-existing M184V/I was detected in nearly 10% of suppressed participants' baseline genotypes, the majority of which was previously undocumented. High rates of virologic suppression in participants who switched to B/F/TAF, and the absence of treatment-emergent resistance, indicate B/F/TAF may be an effective and durable treatment for suppressed patients with archived M184V/I.

PE13/22

Absence of naturally existing resistance against the HIV-1 capsid inhibitor GS-6207 in HIV-1 primary isolates

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Purpose: GS-6207 is a first-in-class HIV capsid (CA) inhibitor in clinical development as a long-acting agent. Processing of the gag polyprotein is linked to multiple stages of the viral cycle, and natural gag polymorphisms found in viral isolates could be linked to loss of potency, as seen for maturation inhibitors (MI), also targeting gag. Here we studied the potency of GS-6207 in HIV-1 primary isolates from people living with HIV (PLWH) in the context of gag polymorphisms.

Method: The HIV-1 gag-protease fragment from 55 HIV-1 primary isolates from treatment-naïve (TN; n=18) and treatment-experienced (TE; n=37) PLWH were cloned into the pXXLAI proviral DNA. HIV-1 constructs were transfected into 293T cells and viral isolates were harvested after 48 hours. Susceptibility (EC_{50}) of the HIV-1 isolates to GS-6207 and controls was measured in a 5-day multi-cycle assay in MT-2 cells and compared to wild-type.

Results: GS-6207 displayed potency with an EC_{50} of 95 pM, with minimal variability across all 55 isolates tested (Table). In contrast, resistance to the protease inhibitors (PI) darunavir and atazanavir was high in TE isolates with PI resistance mutations. Antivirals from the MI class (bevirimat [BVM] and GSK-3532795) displayed reduced potency in isolates with naturally occurring gag polymorphisms known to affect MI activity. NRTI control displayed limited variation from wild-type, reflecting the wild-type sequence in reverse transcriptase in these HIV isolates.

Conclusion: GS-6207 exhibited high potency that was not affected by the presence of gag polymorphisms and/or protease mutations present in primary isolates, underscoring the absence of naturally occurring resistance against GS-6207, in contrast to maturation inhibitors. This confirms that the mode of action of GS-6207 is distinct from that of maturation inhibitors. Additionally, viral isolates from TN and TE PLWH were equally susceptible to GS-6207, underlining its potential for treatment in PLWH regardless of their treatment history.

Mean Drug Susceptibilities

	Mean Drug Susceptibilities (EC50 Fold-Change from Wild-Type Control, [range])				
Patient Isolates	GS-6207	BVM	GSK-3532795	ATV	DRV
Treatment-Naïve (n=18)	0.8 [0.6–1.2]	>46 [2.3–>67]	>393 [1.1–>1761]	0.8 [0.5–1.8]	0.8 [0.4–1.3]
Treatment-Experienced (n=37)	0.8 [0.5–1.2]	>36 [0.5–>67]	>353 [0.5–>1761]	148 [0.5–791]	99 [0.5–555]

PE13/23

Impacts assessment of home based care program over adherence to ART among adolescence living with HIV and AIDS in Blantyre Malawi

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Purpose: To assess the impacts of home based care program over promoting adherence among adolescence on ART and viral load suppression.

To identify factors that influence adherence among adolescence on ART.

Adherence to HIV antiretroviral therapy (ART) is a critical determinant of HIV-1 RNA viral suppression and health outcomes. However, HIV infected adolescents and youth tend to be less adherent to antiretroviral therapy (ART) and have significantly lower rates of virological suppression which results in re-infecting others.

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Method: A sample of 2157 adolescence on ART in different health centres in Blantyre rural was selected assessed from 2016 and 2018. These were in 30 support groups under Senior Chief Kapeni, Blantyre. Weekly home visits were done to provide counselling and sanitation trainings where we targeted parents and guardians, at least 45 focus group discussions were done, 25 key informants interviews with parents, guardians, adolescence on ART, health service providers. Data were collected three times, during baseline, mid and end line. Data was analysed by using excel.
Results: 56% of adolescence who were provided care and support by their parents or guardians reported in improved health than before starting ART, 14% of adolescence living without parental care or guardians, reported little change, the fact be, they have little time to concentrates on medication, rather they use time for searching everyday basic need. 653 adolescence defaulters were identified and retained on care. At least 1981 adolescence were vitally suppressed. Health service providers reported that, at adolescence that has no close relative likely miss the dates for collecting medication. Misbehaviour of health services providers hinders adolescence access the medication.
Conclusion: Adherence to ART can be achieved if the whole family where one is on ART treatment take part in treatment and linked with health service providers. Families has to be supported.

PE13/24

Correlation of results analysis drug resistance of HIV-1 among patients with virological failure by next-generation sequencing and traditional population sequencing

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Purpose: Achieving the goal "90-90-90" requires a significant increase the number of HIV-1 infected patients on ART. It entails an increase of viral drug resistance (DR) testing application. For this aim traditional "Sanger"-sequencing is used in Russia.However, the implementation of next-generation sequencing (NGS) approach may be used for DR-testing as well. Nonetheless,NGS must be validated before.The purpose of this study was to compare the results of DR-analysis HIV-1 pol-gene (protease and reverse transcriptase, 2083–3344) obtained by NGS and "Sanger"-sequencing for viruses derived from patients with virological failure.
Method: Plasma samples from 45 HIV-infected patients who experienced virological failure were analyzed by "Sanger"-sequencing and NGS with 1%/5%/10%/20% sensitivity thresholds to minor viral populations. Analysis of pol-sequences obtained and DR-analysis were carried out using BioEdit,MEGA and HIVdb program of Stanford database.
Results: DR to at least one antiretroviral drug was detected in 45 patients by NGS with 1% threshold and in 43 patients by NGS5%/10%/20% and "Sanger"-sequencing.DR to PI was found in 15 patients by NGS1%,in 10 patients by NGS5%/10%/20% and in 9 patients by "Sanger"-sequencing.DR to NRTI was detected in 42 patients using NGS1% and in 40 patients using all the other sequencing methods.Finally,DR to NNRTI was detected in 35 patients using NGS1%, in 31 using NGS5%/10%, in 30 using NGS20% and in 29 patients using "Sanger" sequencing.All mutations detected by "Sanger"-sequencing were found using NGS1%.Altogether 377,288,268 and 241 DR mutations were detected by NGS 1%/5%/10%/20% respectively and 229 DR mutations were detected by traditional sequencing (Fig. 1).Some of mutations detected by NGS changed the patients DR-profile. However,the best conjunction of sensitivity and specificity was found for NGS5%.
Conclusion: NGS with a threshold of 5% can be used for routine DR-testing and epidemiological surveillance.This will provide additional clinically relevant information about the resistance profile of patients and help reduce the risk of treatment failure.

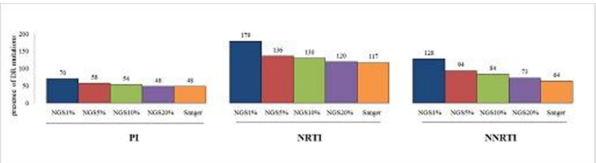


Figure 1. DR mutations identified by "Sanger" and NGS

PE13/25

Analysis of the latent reservoir of a patient infected with HIV under PrEP by single full-length HIV-1 amplification

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Purpose: Antiretroviral therapy fails to cure HIV-1 leading to a life-long disease. The reason for the failure is the latent reservoir which is established shortly after initial infection. The latent reservoir is characterised by replication-competent proviruses inside CD4+ cells which do not display active viral gene expression during ART. It demonstrates a remarkably strong long-term stability for which the reasons are not entirely clear. A better understanding of the latent reservoir could lead to a functional cure for the disease.
Method: In this work two single genome amplification approaches (published by Lee et al. 2017 and Brunner et al. 2016) were compared concerning to efficiency and success rate. The assay published by Lee was less complex and faster to implement than the assay proposed by Brunner, so it was validated and extensively performed for one patient who experienced an HIV-1 infection during pre-exposure prophylaxis by SGA and next-generation sequencing of full-length HIV-1 DNA.
Results: We demonstrated that the assay by Lee was highly sensitive for single genome amplification (SGA) by using a specialised cell-line containing integrated provirus. Overall, 22 proviruses generated by the assay were extensive analysed with respect to clonality, deletion/insertion, hypermutations and stop mutations, intact open reading frames, and resistance mutations. The proviral landscape involved resistance associated mutations M184I and M184V inside the reverse transcriptase, which indicates a new developing resistance against 3TC/FTC and not a transmitted 3TC/FTC resistance. In summary, 14% of the analysed population were genome intact, 9% had extensive hypermutations, and 50% contained large internal deletions.
Conclusion: This proviral full-length HIV-1 SGA implements a promising new rapid method which circumvents the limitation of the viral outgrowth assay. By intensive sequence analysis this assay allows a precise characterization of the latent reservoir to advance and improve cure strategies.

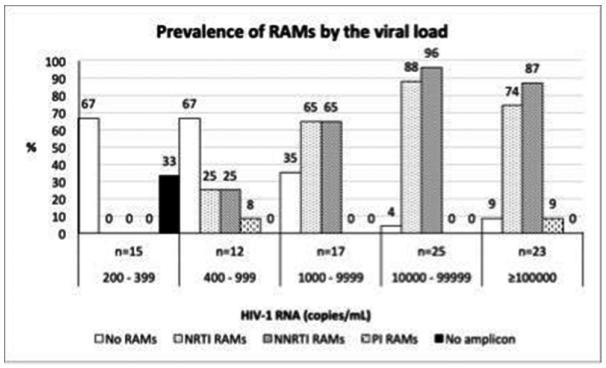
PE13/26

Drug resistance profile according to HIV-1 viral load after long-term exposure to antiretroviral treatment in the absence of routine virological monitoring: results from a programmatic cohort in sub-Saharan Africa

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Purpose: To assess the extent of HIV-1 drug-resistance according to the viral load in a programmatic cohort in Ghana.
Method: The study recruited consecutive patients from 4 out-patient clinics in 2018. HIV-1 RNA was quantified with Xpert HIV-1 Viral Load (Cepheid, Sunnyvale, US). Plasma samples underwent population sequencing if the viral load was >200 copies/mL. Major resistance-associated mutations (RAMs) and genotypic susceptibility scores (GSS) were determined using the Stanford HIV Drug Resistance database (v8.8).
Results: The study included 333 subjects on ART. Median ART exposure was 8.9 years (IQR 5.7–11.3) and most (297/333, 89·2%) were on a NNRTI-based regimen. HIV-1 RNA was quantifiable (≥40 copies/mL) in 164/333 (49.2%)

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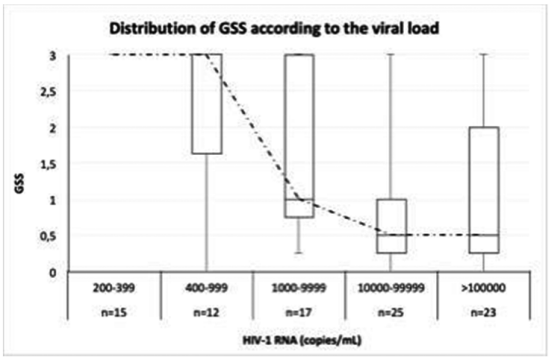


Figure 1a, 1b

(median 2.6 log copies/mL; IQR 2·0-4·4) and 71/333 (21.3%) had a viral load >1000 copies/mL. A total of 87 patients with sufficient sample underwent resistance testing, 65/71 (91.5%) with viral load ≥1000 copies/mL and 22/30 (73.3%) with viral load 200–999 copies/mL (Table 1). Prevalence of ≥1 NRTI, NNRTI or PI RAM was 53/87 (60.9%), 59/87 (67.8%) and 3/87 (3.4%), respectively. Prevalence of ≥1 RAM increased by viral load stratum (Figure 1A) and the GSS decreased in parallel (Figure 1B). No RAMs were detected in 15 patients with viral load 200–400 copies/mL. Among 12 patients with viral load 400–999 copies/mL, 4 (33·3%) had ≥1 RAM, most commonly M184V/I and K103N/S. Patients with viral load ≥1000 copies/mL had more extensive resistance (median 2 RAMs; IQR 1–3], and more complex resistance patterns: 35/65 (53·8% had M184V/I and K103N/S, 20/65 (30·8%) had ≥1 discriminatory RAM (other than M184V/I), and 24/65 (36·9%) had ≥1 TAM. CRF02_AG was the most prevalent subtype (66/87, 75·9%).

Conclusion: Co-existence of high viral loads and complex drug resistance patterns was common especially in patients with viral load ≥1000 copies/mL, whose ART should be promptly managed.

PE13/27

In vitro analysis of replicative capacity and phenotypic susceptibility of integrase mutant HIV-2 viruses

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Purpose: We aimed to assess replicative capacity and phenotypic susceptibility to INSTI of various resistance profiles observed in INSTI-experienced HIV-2-infected patients.

Method: Site-directed mutants (SDM) harboring T97A, E92Q+T97A, T97A+N155H, N155H, E92Q+T97A+N155H INSTI resistance-associated mutations, as well as insertions after codon 231 (231ins): GK, GYKGK, SREGK, YREGR and GIRGK, were constructed. SDM viral stocks were obtained by transfecting HEK293T cells with plasmid DNA. *In vitro* SDM phenotypic susceptibility to INSTI was measured, using the ANRS peripheral blood mononuclear cells (PBMC) assay. Viruses were co-cultured with fresh uninfected phytohemagglutinin-stimulated PBMC, with 10-fold dilutions of the antiretroviral drug, ranging from 1000 to 0.1 nM. Supernatant HIV-2 viral load was quantified at 3 and 4 days post-infection. Replicative capacity of SDMs with 231ins was assessed by measuring HIV-2 viral load at day 3, 7 and 14.

Results: Mutant viruses harboring 231ins did not present impaired replicative capacity, except 231insGIRGK mutant which exhibited a 43-fold lower viral replication than the wild-type virus at day 14 (Figure 1). SDM with 231insGK was resistant to raltegravir and cabotegravir, but remained susceptible to dolutegravir and bictegravir (Table 1). SDMs harboring a 5-amino-acids insertion were resistant to all integrase inhibitors. Phenotypic susceptibility to cabotegravir and raltegravir was impaired in presence of E92Q and/or N155H (6-to-75 fold-change), while bictegravir remained active on the 5 mutants.

Conclusion: Viruses with N155H mutation pathway, which is the most commonly observed mutation in INSTI-experienced HIV-2-infected patients, remained susceptible to bictegravir, offering a therapeutic option for patients infected by such viruses. Through this work, we also obtained new data on the recently described 231ins resistance pathway, using site-directed mutagenesis, showing no impact on viral fitness, and confirming the decreased susceptibility to first-generation INSTI and cabotegravir. Resistance to second-generation INSTI occurred only for mutants with 5-amino-acids insertion, limiting their use in clinical practice.

Table 1. Phenotypic susceptibility to INSTI of HIV-2 site-directed mutants

Mutant	Bictegravir, IC50, nM (Fold-change)	Cabotegravir, IC50, nM (Fold-change)	Dolutegravir, IC50, nM (Fold-change)	Raltegravir, IC50, nM (Fold-change)
ROD (wild-type)	3.0	3.3	2.9	2.4
231insGK	3.5 (1.2)	**68 (21)**	4.5 (1.6)	**172 (72)**
231insGYKGK	**118 (39)**	**139 (42)**	**78 (27)**	**182 (76)**
231insSREGK	**25 (8.3)**	**70 (21)**	**14 (4.8)**	**39 (16)**
T97A	4.2 (1.4)	6.6 (2.0)	3.3 (1.1)	2 (0.8)
E92Q+T97A	2.0 (0.7)	**248 (75)**	Not done	Not done
T97A+N155H	0.9 (0.3)	**51 (15)**	**64 (22)**	**48 (20)**
E92Q+T97A+N155H	0.8 (0.3)	**29 (8.8)**	**33 (11)**	**15 (6.3)**
N155H	1.7 (0.6)	**42 (13)**	1.1 (0.4)	**24 (10)**

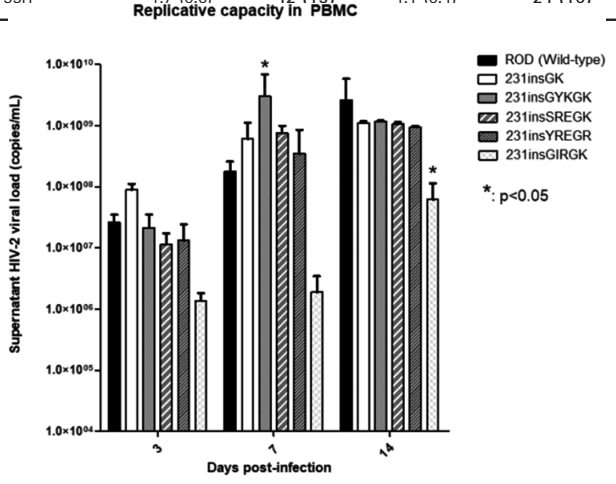


Figure 1. Replicative capacity of HIV-2 site-directed mutants harboring an insertion after codon 231

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PE13/28

Treatment simplification with two-drug regimens: impact of transmitted drug resistance mutations in residents of South-East Austria

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Purpose: Two-drug regimens may be preferable to induce and/or maintain viral suppression, while decreasing lifetime cumulative drug exposure and potential long-term toxicities. In this study, the prevalence of transmitted drug resistance mutations (DRMs) to dolutegravir (DTG), lamivudine (3TC), and rilpivirine (RPV) currently used for two-drug regimens was investigated in residents of South-East Austria representing an area with a population of more than 1 million. The local HIV-1 transmission network was reconstructed to gain deeper insight into transmitted HIV-1 DRMs in this population.
Method: The study population included 192 ART-naïve residents of South-East Austria with newly diagnosed HIV-1 infection between 2013 and 2018. Before initiation of ART, resistance testing based on Sanger sequencing data of the reverse transcriptase (RT) and integrase (IN) genes was performed using the Stanford University Genotypic Resistance Interpretation tool. The genetic transmission network was reconstructed; shared DRMs were defined as any DRM present in genetically linked individuals.
Results: The frequency of any clinically relevant DRM against DTG, 3TC, and/or RPV at time of diagnosis was 15.6% (30/192 patients). Of 192 patients, one (0.5%) showed resistance against DTG, 8 (4.2%) patients against 3TC, and 25 (13.0%) patients against RPV. Transmission network analysis found 42.7% (82/192) genetically linked patients forming 26 clusters, ranging in size from 2 to 10. Of the 30 patients harboring any DRM, 18 (60%) were members of 6 different clusters. Of those, 15/18 (83.3%) were shared DRMs.
Conclusion: In residents of South-East Austria, two-drug regimens may be used in the majority of patients. More than half of patients harboring any clinically relevant DRM were found to be part of clusters.

PE13/29

Baseline resistance to Doravirine depends on the algorithm used for interpretation

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Purpose: In this work, we report the results on the prevalence of Doravirine (DOR) associated mutations and clinical relevant resistance by using Stanford, RIS and ANRS algorithms.
Method: The prevalence of DOR associated mutations, as described by Soulie *et al.* 2018 (https://doi.org/10.1093/jac/dky464) was evaluated. Clinically relevant TDR were investigated using the latest versions of Stanford, RIS and ANRS Algorithms.
Results: Our cohort included 617 patients. The prevalence of DOR associated mutations was: V106M (n=1, 0.2%), V108I (n=3, 0.5%), Y188L (n=1, 0.2%), F227L (n=1, 0.2%) and Y318F (n=1, 0.2%). Those mutations were detected in 5 patients, making an overall prevalence of 0.8%. Interpretation of clinically relevant resistance by RIS and ANRS algorithms came up with 0.3% of resistance; when using Stanford algorithm, we obtained a prevalence of 4.9%, driven by the presence of V106I mutation (n=27, 3.9%), which Stanford scores as low-level resistance.
Conclusion: Transmitted Drug Resistance to Doravirine is very low in Spain in 2018 by using RIS/ANRS algorithms. The exact role of V106I mutation on DOR resistance should be further investigated.

PE13/30

Baseline resistance to EACS first line recommended antiretroviral regimens in newly diagnosed patients in Spain

C Guerrero Beltrán[1], MJ Pérez-Elias[2], J Pérez Stachowsky[3], M García-Álvarez[4], JA Iribarren[5], C Robledano[6], M Montero[7], S García-Bujalance[8], JR Blanco[9], M Rivero[10], LJ García-Fraile[11], N Espinosa[12], C Rodríguez[13], A Aguilera[14], A Vanrrell[15], D Dalmau[16], A Iborra[17], A Imaz[18], JL Gómez-Sirvent[19], J Peraire[20], J Portilla[21], E Caballero[22], F García[23] and CoRIS

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Purpose: We report the prevalence of clinically relevant resistance to first-line regimens recommended by EACS in the newly diagnosed patients in Spain in 2018
Method: The latest version (8.8) of Stanford HIV Drug Resistance Algorithm was used to investigate clinically relevant resistance, defined as any level of resistance different from susceptible or potential low-level resistance, to the latest update of EACS first-line regimens. Depending on the availability of fasta sequences in RT, Pro and Integrase, we studied resistance to ABC/3TC/DTG, TDF/FTC/DTG, TDF/FTC/BIC and TDF/FTC/RAL in 320 patients, TDF/FTC/RPV in 694 patients and TDF/FTC/DRV in 457 patients.
Results: Clinically relevant resistance to ABC and TAF/TDF was 0.7% (5/694), to 3TC/FTC was 0.3% (2/694), to RPV was 5.8% (40/694), and to RAL was 1.3% (5/394). No clinically relevant resistance to DRV, DTG or BIC was found. Clinically relevant resistance to first-line regimens recommended by EACS 2018 was as follows:

a) ABC/3TC/DTG, TDF/FTC/DTG and TDF/FTC/BIC: two patients (0.6%) showed resistance to at least 1 drug in the regimen, and 1 patient (0.3%) resistance to 2 drugs;
b) TDF/FTC/RAL, 6 patients (1.8%) showed resistance to at least 1 drug, and 1 patient (0.3%) to 2 drugs;
c) TDF/FTC/RPV: 45 patients (6.5%) were resistant to 1 drug in the regimen, and 2 (0.3%) to 2 drugs;
d) TDF/FTC/DRV: four patients (0.9%) showed resistance to 1 drug in the regimen, and 1 (0.2%) to 2 drugs.

No patient shared resistance to all 3 drugs in the regimen.
Conclusion: Clinically relevant baseline resistance to EACS protease- and integrase inhibitors-based regimens in HIV newly diagnosed patients in Spain remains very low. On spite of NNRTI resistance levels, caution on baseline resistance must be taken when starting a Rilpivirine based regimen.

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PE13/31

A retrospective evaluation of a national home infusion provider's approach to medication adherence of parenteral ibalizumab-uiyk in the alternate-site and homecare setting

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Purpose: Ibalizumab-uiyk (ibalizumab), is a parenteral CD4-directed post-attachment HIV-1 inhibitor, approved in the United States 2018, for treatment of HIV-1 infection heavily treatment-experienced adults with multidrug resistant HIV-1 in combination with oral anti-retroviral therapy (ART), who are failing their current ART regimen. (Package Insert).
The objective of this study was to demonstrate that medication adherence strategies would impact both the oral ART regimen compliance and ibalizumab infusions. The clinical infusion pharmacists' expertise would synergistically focus on medication adherence for the total regimen.
Methods: A retrospective analysis evaluated medication compliance using this care management model. Data collected began in May 2018. Dosing was given per manufacturer guidelines: a loading dose followed by a maintenance dose every 2 weeks. If a maintenance dose is missed 3 plus days beyond 2-weeks, an additional loading dose is required. Scheduling, clinical management, and adherence to both oral ART and ibalizumab regimen was imperative. Adherence to oral ART was based on documented patient assessments and confirmation of refill history. Coordination of care and communication data was collected.
Results: Data from 73 patients representing a total of 1005 intravenous infusions of ibalizumab was studied. Seventeen patients missed 19 doses for reasons listed in Table 1. 62 of 73 patients (85%) continued to receive ibalizumab infusions as scheduled. Eleven patients discontinued treatments listed in Table 1. Only two patient discontinued the regimen due to non-compliance. Three patients discontinued due to side effects. Oral ART compliance achieved was 89% listed in Table 2.
Conclusions: Patients receiving Ibalizumab can be successfully treated at home or in an alternate-site setting. Eight-five percent (85%) of studied patients continued to receive treatments every 2 weeks as planned. Medication adherence strategies were inclusive of oral ART. Ibalizumab provides a new treatment for oral ART resistant patients.

PE13/32

Prevalence of HIV-1 drug resistance among patients with antiretroviral therapy failure in Moscow region, Russia

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Purpose: In the Moscow region HIV-infected people accessible to public health reached 33,340 by the beginning of 2019, and ART coverage was 69%. The increase in number of people receiving antiretroviral therapy requires monitoring of acquired HIV drug resistance (DR) and enhancing surveillance of transmissible resistance
Method: We analyzed demographic and virological data from 896 ART patients attended the Moscow Regional AIDS Center in 2012–2019. Plasma samples were genotyped using ViroSeq ™ HIV-1 test-system and interpreted using the Stanford HIV DR database
Results: The average age of patients was 35 years (range 1–67). The proportion of men and women was 58.5% and 41.5%, respectively. The duration of treatment in all patients was at least 6 months, and all had a virological failure in the historyFor all the years studied, the virological failure was not associated with resistance-associated mutations (RAMs) in 143 (16%) patients. Among these cases, no dependence on gender or transmission route has been identified.
753 (84%) patients had single or multiple RAMs, resulting in HIV DR to one or more classes of ART.
Among those with HIV DR mutations identified, 54 % had NRTIs + NNRTIs mutations, 32% — NRTIs only, 8% — NNRTIs only, 3 % — NRTIs + PI, 2% — NRTIs + NNRTIs + PI and 1% — PI only. The most common RAMs were M184V/I (74.5%), L74V/I (11.5%), K65R (7.6%) to NRTIs, G190A/S/E (39.3%), K103N/S 28.0% to NNRTIs and M46I/MI/LV/ML (32.8%) to PI
Conclusion: High prevalence of circulating NRTIs + NNRTIs, NRTI- and NNRTI-resistant HIV-1 variants was observed in experienced HIV-1-infected patients in Moscow Region. HIV DR surveillance in the Moscow region should be strengthened to prevent the spread of multi-drug resistance and cross drug resistance and to strengthen the long-term success of ART

PE13/33

HIV-1 drug resistance surveillance among parturient women on anti-retroviral therapy in the Eastern Cape, South Africa: implications for elimination of mother-to-child transmission

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Background: The emergence of HIV drug resistance poses a significant threat to achieving the goal of elimination of mother-to-child transmission. In this study, we assessed the burden of HIV-1 drug resistance mutations (DRMs) within the context of the public sector prevention of mother-to-child transmission (PMTCT) programme in the Eastern Cape, South Africa.
Methods: We conducted genetic analysis on viral isolates (n=80) from plasma samples of women with probable virological failure at delivery between January and May 2018 from two large maternity centres in the Eastern Cape using standard protocols. Partial pol gene covering 1030 bp were amplified and sequenced according to previously reported protocol. DRMs were determined by submitting the generated partial pol sequences to the Stanford drug resistance database for query on mutations associated with drug resistance in HIV viruses. We examined the correlates of DRMs using bivariate analysis.
Results: The age of parturient women ranged from 16–43 years. The majority of the parturient women were currently on Efavirenz-based regimen (first line ART) (82.5%) and had been on ART for more than 12 months (65.0%). The prevalence of DRMs was 72.5% (n=58). The CD4 count demonstrated a negative linear association with the DRMs (p=0.002). The predominant DRMs were K103N (n=43; 74.1%), M184V (n=28; 48.3%) and K65R (n=11; 19%). Among the parturient women on current treatment of EFV-based regimen; 79.1% already had K103N while nine patients on protease inhibitor-based regimen still harboured K103N. The majority of the M184V mutations were observed in parturient women on first line regimen (n=23; 82.1%).
Conclusion: We found a high prevalence of DRMs in women delivering their index babies at high viral loads in the study settings. A point-of-care PCR for screening for common reverse transcriptase resistance mutations to guide appropriate neonatal prophylaxis and maternal therapy should be implemented in the country

PE13/34

Antiretroviral Resistance patterns in HIV-1 infected patients failing to second-line in Bamako, Mali

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Introduction: More than 20 years, patients remained on first-line ARV treatment coupled with a lack of virological follow-up, a late switch in second line which increase the virological failures for second line ART in Africa. All of these factors could have a negative impact to archive the goal of the last 90% of the UNAIDS in sub-Saharan Africa. We aimed to evaluate the prevalence of ART resistance patterns in HIV-1 infected patients in second-line virological failure in Mali.
Method: We recruited HIV-1 infected patients who failed to their second-line ART. The patients have been recruited from Bamako clinical care centers from March 2013 to December 2016. Protease and reverse transcriptase genes were sequenced by a commercial (Viroseq) and in house (ANRS) methods. The results were interpreted using the latest versions of Stanford algorithm.
Results: We included 309 patients who failed to their second line treatment (VL≥1000 copies/mL). Female sex was predominant with (%) 227/309, the median age was 35 years [18 and 70 years], the median of viral load was 57,086 copies/mL [1040 and 2,000,000 copies/mL], the median of CD4 count was 194 cells/mm^3 [2 and 1660 cells/mm^3]. The CRF02_AG was the most

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predominant HIV-1 subtype with 71% of cases and 62.46% of our patients were exposed to last six ARV molecules. The prevalence of resistance to different classes of ARV was as follows: 65.37% to NRTI, with M184V (61.81%), 61.49 to NNRTI with Y181C/I/V (22.98%), and V82F/T (2.3%) and L76V (0.05%).
Conclusion: These data show a high prevalence of NRTIs and NNRTI but less than 10% of PI resistance. The LPV remain sensitive in many patients this suggere the use better virological monitoring and good tools for poor adherence detection.

HIV-associated and non HIV-associated tumours

PE14/1

Prevalence of anal dysplasia among persons living with human immunodeficiency virus (HIV)

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Purpose: The study aimed to investigate the prevalence of anal dysplasia and describe the clinical characteristics of HIV-infected patients with anal dysplasia enrolled in services at a primary HIV/STI treatment hospital in the Philippines, a country experiencing one of the fastest growing HIV epidemics.
Method: This cross-sectional study was conducted from November 2017 to April 2018. Data were obtained through patient interview and chart review after informed consent. Anal pap smear using the conventional technique was performed and interpreted by a single pathologist.
Results: 371 patients were included in the analysis. The mean age was 32 years and more than 90% were male. The overall prevalence of abnormal anal cytology was 25.1% (n=93), of which 51.6% were classified as atypical squamous cells of undetermined significance (ASCUS), 37.6% low-grade squamous intraepithelial lesion (LSIL), 8.6% atypical squamous cells cannot rule out HSIL (ASC-H), and 2.2% high-grade squamous intraepithelial lesion (HSIL). There was a higher prevalence of anal dysplasia among HIV patients who identified themselves as homosexual ($p = 0.002$) or bisexual ($p = 0.003$), practiced receptive anal intercourse ($p = 0.015$), had ≥ 5 lifetime sexual partners ($p = 0.052$), had a CD4 T cell count ≤ 200 cells/mm^3 ($p = 0.388$), and with WHO HIV clinical stages 3 and 4 ($p = 0.014$).
Conclusion: Results of this study were comparable and consistent with previous studies. Findings underscore the need for further investigation on routine screening of anal dysplasia among HIV-patients in the Philippines, especially male having sex with male (MSM).

PE14/2

HIV infection is associated with reduced survival among hepatocellular carcinoma cases from an urban referral hospital: Kampala, Uganda

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Purpose: Hepatocellular carcinoma (HCC) rates appear to be increasing with prolonged survival among HIV infected patients. This study described the impact of HIV-infection on HCC prognosis.
Methods: Eligible HCC patients attending the Mulago National Referral Hospital in Kampala, Uganda, were enrolled into a case-control study between March 2015 and February 2018. Standardized methods were used to collect clinical, ultrasound and laboratory data at enrolment and a follow-up telephone call was made at one, three, six and twelve months post-enrolment to determine vital status of HCC cases. Kaplan Meier curves and Cox regression analyses were used to assess determinants of HCC survival.
Results: Of 372 HCC cases,18% were HIV-infected. HCC cases generally presented with multifocal disease (72%) with a median duration of symptoms of 4 months (IQR 1–84). None of the cases had received any curative treatment for HCC. Overall, 310 (83.3%) HCC case deaths were reported within one year following diagnosis. Median survival was 5 months from symptom onset and 1.5 months from diagnosis. HIV infected HCC cases had a median survival of 4 months. In multivariable analysis after adjusting for age, sex and ALT levels, HIV infection was independently associated with a 47% increased mortality risk (HR 1.47, 95% CI:1.08–1.99, p 0.012).
Conclusion: Despite overall rapid mortality, HIV-infected HCC cases had a poorer prognosis compared to HIV negative HCC patients. Clinical and ultrasound-based screening algorithms which are relatively affordable should be explored for early HCC diagnosis and linkage to care, in these resource-limited settings where HIV is prevalent.

PE14/3

High prevalence of anal and cervical dysplasia in a cohort of HIV-infected women, but low prevalence of concomitant lesions

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Purpose: Incidence of Anal Intraepithelial Neoplasia is higher in HIV-1-women compared with HIV-uninfected women. HIV-1-infected women have an increased risk of an invasive anal squamous cell carcinoma (IASCC) compared to HIV-uninfected women. Published data on prevalence of anal intraepithelial lesions are scarce in these women. The aim of this study was: estimate prevalence of anal-cervical lesions, prevalence of concomitant lesions and the associated predictive factors in a cohort of HIV-1women.
Methods: Cross sectional study performed between 2008–2018. HIV-1-infected women from single tertiary care center in Catalonia-Spain were included. Anal/cervical cytology was performed, High-resolution anoscopy/colposcopic biopsy was performed in women with ASCUS, LSIL, HSIL anal/cervical cytology.
Results: 514 HIV-1-infected women were included: mean (SD) age, 42 (10) years; median (SD) of HIV diagnosis time, 14.1 (6.9) years; 261 (53%) women has a CD4 T-cells <200 cel/μL. Anal cytology [n (%)] was: normal [280 (54%)], ASCUS [61(12%)], LSIL [81(16%)], HSIL [37(7%)] and unsatisfactory [55 (11%)]. 107 anal biopsies [n (%)] were performed: normal [20 (19%)], AIN1 [51(48%)], AIN2 [21(19%)], AIN3 [12(11%)], non-evaluable [3 (3%)]. Cervical cytology was not available in 20 women: normal [313(63%)], ASCUS [60 (12%)], LSIL [99(20%)] and HSIL [20 (4%)] and unsatisfactory [2(0.4%)]. 67 cervical biopsies were performed: normal [16(24%)], CIN1 [28(42%)], CIN2 [15 (22%)], CIN3 [6(9%)], other diagnosis [2 (3%)]. The prevalence of concomitant SIL in anal and cervix was 5%, correlation coefficient: 0.377. No predictive factor was associated with concomitant lesions. Conclusions
Prevalence of anal canal intraepithelial lesions was similar to the prevalence of cervical intraepithelial lesions in HIV-1women. The prevalence of concomitant lesions in anal and cervix was low. In front of the lack of results on effectiveness of the screening programs for cancer prevention in anal canal, our results suggest that this preventive strategy in anal canal (and cervix) is advisable for HIV-1-infected women.

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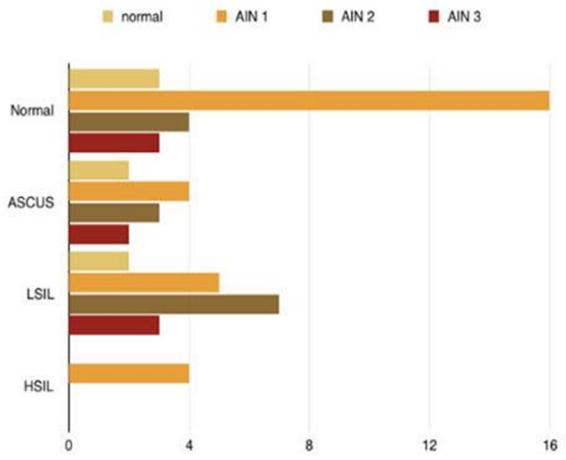


Figure 3. Correlation between anal cervical and histological anal lesions at baseline. Bivariate analysis Comparison of frequencies between groups by Fisher's exact test. Correlation coefficient: 0.377

Basal characteristics of the population		Cohort of patients included in the study n = 494
Age (years)	Media (DE)	42,2 (10,1)
Time since the diagnosis of HIV (years)	Media (DE)	14,1 (6,9)
Antiretroviral treatment time (years)	Media (DE)	9,7 (6,5)
Basal CD4 cel/uL	Media (DE)	589 (343)
Nadir CD4 cel/uL	Media (DE)	225 (125)
Nadir CD4 <200 cel/uL	%	52,6%
Viral Load <50 copies/mL	%	76%

Table 1. Basal characteristics of the sample.

PE14/4

Malignant and benign skin lesions in HIV-1 infected people

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Purpose: In cART era, the incidence of AIDS-defining cancers decreased while there is a persistence of non-AIDS defining cancers. Whether HIV patients are at increased risk of melanoma and non-melanoma skin cancer (NMSC) is not well documented. Compared with HIV-uninfected persons, the HIV-infected counterparts have a higher risk for subsequent squamous cell carcinoma (SCC) but not basal cell carcinoma (BCC), with a dose-response relationship with lower CD4 count and higher viral load. Aim of this study was to assess the presence of cutaneous malignancies in HIV-1 patients.
Methods: A monocentric cross-sectional study was conducted on HIV-infected patients consecutively visited (February-May 2019). A single expert dermatologist assessed the presence of skin lesions. All suspicious lesions were biopsied and evaluated by a dermatopathologist. Clinical history of HIV infection and laboratory data were recorded. The characteristics of the patients with or without NMSC were compared by chi-square test for categorical variables and T-test for independent samples for continuous variables.
Results: NMSC was diagnosed in 17/96 patients (17.7%,15 SCC and 2 BCC), melanoma in 2 patients (2.1%). Other lesions were: 6 actinic keratoses (6.2%), 7 seborrheic keratoses (7.3%), 5 atypical nevi (5.2%). Patients with NMSC were older (mean difference 7.8 years, SD 2.6, p=0.003) than non-NMSC patients, while no differences were found regarding photodamage, family history for NMSC/melanoma, CDC class, time from HIV diagnosis, nadir CD4 cell count, log10 zenith viral load, current CD4 cell count, time on antiretroviral therapy, exposure to different antiretroviral drug classes.
Conclusions: Our study showed that SCC was more common than BCC regardless of the state of immunological reconstitution, time of HIV diagnosis, nadir or current CD4 cell count. Two patients were diagnosed with melanoma (a Superficial Spreading Melanoma and a nodular melanoma), suggesting that dermatological evaluation can be very important for early diagnosis of non-AIDS related skin cancers.

PE14/5

Results of HPV-testing for anal screening in HIV-infected women

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Introduction: Occurrence rate of anal cancer is comparatively rare and accounts for approximately 1–2% of all tumors of the gastrointestinal tract in the general population. The cancer of the anal canal is usually associated with the human papillomavirus (HPV). The risk group for this disease is women with HPV-infected in cervix. HIV-infected women have a higher risk of papillomavirus infection, malignancy and persistence than HIV-negative women.
Purpose: to study the prevalence of HPV high carcinogenic risk (HCR) in anus among HIV-infected women.
Method: We examined 99 HIV-infected women from Moscow region during 2018–2019. There was performed HPV-test from anus and cervix (with the determination of 14 types of HPV HCR - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) for all women.
Results: Young women up to 40 years predominated in the study group. There were diagnosed with HPV of HCR in anus in 47 (47.5%) of them: 62% (29/47) HPV detection was in cervix (maximum 7 genotypes in one sample) and 38% (18/47) without HPV in cervix (maximum 3 genotypes in one sample). Frequency of determination types of HPV HCR in anus is: 16–32%,51–25.5%, 68–23.4%, 56–17%, 45- 14.9%, 52–12.8%, 31–10.6%,39–10.6%, 58 - 10.6%,18- 8.5%, 33- 8.5%, 59–8.5%,66–6.4%, 35–4.2%.
Conclusion: HIV-infected women have a high incidence of HPV infection and a wide range of detectable genotypes of HCR HPV with the highest incidence of HPV infection. The results should be used to develop anal screening using HPV testing for at least 13 HCR HPV genotypes.

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PE14/6

COHORT SDT (Granada): decrease of the incidence of HSIL+ in the anal mucosa of HIV+ patients MSM after the performance of a screening, diagnostic and therapeutic program (2010–2018)

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Purpose: Our main objective was to analyze the incidence of HSILs and ASCC (HSIL+) in anal mucosa of HIV+ MSM, and the risk factors related.
Method: The study included consecutive HIV-infected MSM between May 2010 and December 2018. Data were gathered at baseline and annually on their sexual behavior, CD4 and CD8 levels, HIV viral load of HIV, and anal cytology, HPV PCR, and high-resolution anoscopy. Patients with normal anoscopy and LSIL were evaluated annually.There were two options for patients with HSIL: mucosectomy with electric scalpel by the coloproctology (from May 2010 onwards); or self-administration of 5 % imiquimod 3/times weekly/16 weeks (from November 2013 onwards). When ASCC was detected, patients were referred to the oncology department. Between May 2012 and May 2014, the quadrivalent HPV vaccine was administered to 66 patients.
Results: Among the 405 patients, 87.2 % had at least two control anoscopies with a median follow-up of 36 months (IQR: 12–69). 88 HSIL cases and 3 ASCC cases were diagnosed. The incidence of HSIL was 30.86/1,000 patient-years, and ASCC 81.22/100,000 patient-years. 49 HSILs were treated by mucosectomy and 34 with imiquimod. None of the treated patients of HSIL progressed to ASCC. We found significant reductions in HSIL+ between 2010 and 2018 (42.9% *vs.* 4.1%, p=0.034). Risk factor related to HSIL+ were HPV 11 (OR 4.153; CI95% 1.85–9.3), HPV 16 (OR 2.74, CI 95% 1.189–6.34), HPV 53 (OR 3.67, CI95% 1.141–11.79); HPV 61 (OR 13.98, CI 95% 3.74–52.2); HPV 68 (OR 2.773 CI 95% 1.121–6.86); presence of Low and High-Risk HPV (OR 1.058; CI95% 1.003–1.116), and low CD4 nadir (OR1.002; CI95% 1–1.004).
Conclusion: The reduction in HSIL+ rate observed in our patients may be attributable to the bundle of measures adopted at our center. The chronic mixture infection by HPV and low level of CD4 nadir were related to HSIL.

PE14/7

Prospective longitudinal study on immunogenicity and safety of vaccination against human papillomavirus (HPV) with the 9valent vaccine in HIV-positive women, the Papillon study: preliminary results on tolerance and safety

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Purpose: Guidelines on HPV vaccination in HIV-positive women recommend preferentially 9valent vaccine in 3 doses but there are currently no data on this strategy. We present preliminary results on tolerance/safety of this vaccine in women with well-controlled HIV infection.
Method: The Papillon study (EUDRACT 2018-000228-33/NCT NCT03391921) is an ongoing prospective trial in HIV-positive women, aged 15–40 years, on cART with HIV RNA <400 cp/mL, randomized to receive either 2 (0.6 months) or 3 doses (0, 2, 6 months) of 9 valent vaccine (Gardasil9®MSD). Antibodies against HPV vaccine genotypes and HIV parameters are measured at baseline and month 7 (one month after last vaccine dose). Vaccine tolerance/safety is evaluated by a specific questionnaire performed once between day 2 and 7 after each dose.
Results: Between June 2018 and June 2019, 90 women were vaccinated with 188 doses (3 doses n=41, 2 doses n=57, 1 dose n=90 women). At baseline, median age was 35 years, CD4 656/μL, 93% had HIV RNA <50 cp/mL. After a median follow-up of 165 days, there was no serious adverse event; 62% (56/90) of women had mild to moderate transient local reaction, mostly local discomfort during 2 days. Headaches were reported in 9.6% (18/188) of vaccine episodes with one patient having severe headaches within 24 hours of the first dose and during 3 days; this adverse event was possibly related to vaccination and further vaccination was discontinued because it had affected the patient's daily activities. In all other cases, headaches were of minor severity (requiring paracetamol intake in 10/17 episodes) and vaccination was pursued. At month 7, median CD4 was 699/μL and 95% had HIV RNA <50 cp/mL.
Conclusion: Vaccination against HPV with the 9 valent vaccine is safe and well tolerated in HIV-positive women with the same tolerance profile as in HIV-negative women. HPV vaccination does not impact the control of HIV infection.

PE14/8

Cancer trends and outcomes in a cohort of people living with HIV

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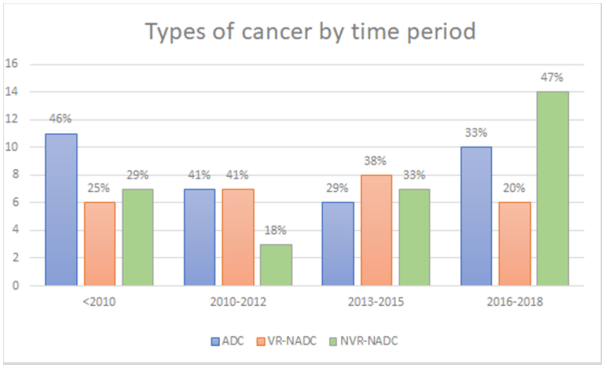
Purpose: the aim of our study was to evaluate cancer cases in terms of diagnoses, management and outcomes in our cohort of people living with HIV (PLWHIV) in the HAART era.
Method: we performed a retrospective study including PLWHIV with a diagnosis of cancer in the last 15 years. We collected data about diagnosis, type of cancer, staging, treatment and cause of death. We considered four groups depending on the year of diagnosis (<2010, 2010–2012, 2013–2015, 2016–2018). Furthermore, we divided cancers in AIDS-defining cancer (ADC), virus-related non-AIDS-defining cancer [(HCV, HBV, EBV and HPV), VR-NADC] and not-virus-related and non-AIDS-defining cancer (NVR-NADC).
Results: we enrolled 83 patients for a total of 92 cases of cancer. Seven patients had two different cancer, and one patient had three. Demographic, clinical and virologic data have been summarized in Table 1. Although the number of cases was similar in each group, the temporal distribution was different (Figure 1). ADC diagnoses were more frequent before 2010. On the contrary, NVR-NADC showed an increasing trend in the last 3 years-period. VR-NADC were, instead, stable during the years. Sixteen (17.4%) subject were naïve at the diagnosis of cancer and 14 of them had an ADC (11 Kaposi's Sarcoma, 3 Non-Hodgkin Lymphoma) and 2 a testicular cancer.
We observed 38 (45.78%) deaths with a median survival of 6.2 (IQR 1.4–14.4) months. Thirtytwo (84.21%) patients died in the first 2 years after the diagnosis. NVR-NADC showed the highest mortality rate (51.6%), especially when diagnosed late (81.2%). An advanced cancer at the diagnosis was the strongest predictor of mortality (aHR 23.59, CI 3.08–180.67).
Conclusion: NVR-NADC showed a progressive increase in the last years and where associated with an advance stage and high mortality rates in PLWHIV. Specific preventive and screening campaignes are needed in this population.

Demographic, clinical and virologic data

Male	66 (79.5%)
Caucasian	81 (97.5%)
Risk Factor: Heterosexual; MSM; IDU; Unknown	17 (20.5%); 22 (26.5%); 41 (49.4%); 3 (3.6%)
Smoking: Yes; Previous smoker	53 (63.8%); 6 (7.2%)
Coinfection: HCV; HBV; HCV+HBV	37 (44.6%); 5 (6%); 7 (8.4%)
CDC staging: A; B; C; Unknown	3 (3.6%); 23 (27.7%); 54 (65.1%); 3 (3.6%);
Patients on treatment; Viral load <50 copies/mL; Naïve	63 (68.5%); 53 (57.6%); 16 (17.4%)
CD4 nadir (median), cells/mm^3	126 (IQR55–254)
Deaths	38 (45.8%)

MSM: Men who have Sex with Men; IDU: Injection Drug User; IQR: Interquartile Range

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Types of cancer by time period

PE14/9

Rate of HCC occurrence and associated risk factors in a multicentric cohort of HIV/HCV co-infected patients treated with DAAs

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Purpose: After the introduction of direct-acting antivirals (DAAs), the natural history of HCV infection has changed, with effects on HCV-related events after the Sustained Virologic Response (SVR) in cirrhotic individuals. Our study aimed to determine the rate and the predictors of HCC in a HIV/HCV co-infected population of cirrhotic individuals treated with DAAs-regimens.
Method: We retrospectively studied all cirrhotic HIV/HCV individuals treated with DAAs, from October 2014 to January 2017 at the Departments of Infectious Diseases in five Italian hospitals, observing our patients from the day they started DAAs therapy, and analyzed their characteristics with multivariate COX regression to find independent prognostic factors for HCC occurrence.
Results: We included 178 HIV/HCV co-infected patients: 76.4% were male and the median age was 52 (IQR 49–55) years. After a median of 13 months, HCC occurred in 15 patients (8.4%), 3 of them being recurrences, with a rate of HCC recurrence of 50% and median disease-free survival of 14 months. At the univariate analysis we found that HCV genotype, Child Pugh Turcot (CPT) score, CD4-linfocytes-nadir and cART administration at baseline were significantly different between patients who developed HCC and patients who did not. Furthermore, patients with a previous history of HCC showed a higher risk of developing a second event (*Table 1*). After adjusting for confounders, HCV genotype 1b, higher CPT score and history of HCC remained independently associated with HCC occurrence (*p-value 0.005*, *0.01* and *<0.001* respectively), otherwise cART administration at baseline was a protective factor (*p-value 0.03*; *Table2*).
Conclusions: As we expected, in our cohort, HCC occurrence was associated to the severity of liver disease, HCV genotype 1b, and previous history of liver cancer. What moreover came out is the need of a deeper investigation of the role of immunovirological control of HIV as a protective factor for HCC.

Table 1. Baseline characteristics of overall population, with comparison of patients with and without HCC through COX univariate regression

Variable (expressed as median and interquartile range or absolute value and percentage)	Overall N=178	No HCC N=163 (91.6%)	HCC N=15 (8.4%)	p-value
Age	52 (49–55)	52 (49–55)	52 (50.2–55)	0.472
Male	136 (76.4%)	123 (75.5%)	13 (86.7%)	0.334
HCV genotypes				
1a	72 (40.4%)	69 (42.3%)	3 (20%)	
1b	14 (7.9%)	11 (6.7%)	3 (20%)	**0.033 (HR 5.71)**
2	4 (2.2%)	4 (2.4%)	0 (0%)	0.998
3	59 (33.1%)	52 (31.9%)	7 (46.7%)	0.111
4	28 (15.7%)	26 (16%)	2 (13.3%)	0.539
Other	1 (0.6%)	1 (0.6%)	0 (0%)	0.999
Naive to HCV therapies	100 (56.2%)	94 (57.7%)	6 (40%)	0.171
CPT score (23 missing)	5 (5–6)	5 (5–6)	6 (5–7.5)	**0.019 (HR 1.43)**
CP-A	125 (80.6%)	116 (82.9%)	9 (60%)	
CP-B	28 (18.1%)	23 (16.4%)	5 (33.3%)	
CP-C	2 (1.3%)	1 (0.7%)	1 (6.6%)	
HCC history	6 (3.4%)	3 (1.8%)	3 (20%)	**<0.001 (HR 8.58)**
Nadir CD4 (55 missing)	151 (68–289)	148 (68–266)	328 (126.5–469.5)	**0.009 (HR 1.01)**
ART administration	173 (97.2%)	160 (98.2%)	13 (86.7%)	**0.009 (HR 0.13)**

Table 2. Factors independently associated with HCC occurrence at COX multivariate regression

Variable	HR (CI 95%)	p-value
Age	1.09 (0.96–1.24)	0.178
Male	1.76 (0.22–14.09)	0.592
CPT score	1.55 (1.1–2.18)	**0.012**
HCV genotype 1b	12.82 (2.18–75.19)	**0.005**
HCV genotype 3	3.72 (0.87–16)	0.077
Naive to HCV therapies	0.47 (0.14–1.64)	0.238
HCC history	16.47 (3.52–76.98)	**<0.001**
cART administration	0.12 (0.02–0.85)	**0.034**

Human genomics

PE15/1

Genetic characterization of the near full-length genome of an HIV-1 A1/C/D/K/B unique recombinant form from the Eastern Cape, South Africa: a case report

OV Adeniyi

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Purpose: HIV-1 sub-type C is the predominant circulating virus in South Africa, a country with the world's largest HIV epidemic. There have been anecdotal reports of non-C subtypes of HIV-1 in different parts of the country in the past two decades. Though, Eastern Cape has the third largest HIV epidemic by province in South Africa, very little information exists on the genetic diversity of HIV in this understudied region of the country.
Method: This paper presents the genetic analysis of a mosaic recombinant variant of HIV-1 from a pregnant woman from Mdantsane, Eastern Cape, South Africa. Preliminary analysis of the partial *Pol* gene of the RNA sequence showed inter-subtypes recombination of C and D, thus, prompting a detailed analysis of the full-length genomic sequence. The REGA HIV sub-typing tool version 3.0 was used to analyse the full sequence for recombination pattern. Sequences were multiply aligned with Clustal X and phylogenetic trees generated by the neighbour-joining method.
Results: The full sequence analysis revealed a mosaic pattern comprising recombinant C/D (in the *pol* gene), recombinant A1/C/D (in the *gag* gene) and predominant B subtype in the *env-nef* gene. The accessory genes consist of: recombinant B/K in the Vpu gene and other subtypes: C (Vpr and Vif genes) and B (Nef gene).
Conclusion: This is the first report of this mosaic pattern of HIV-1 in South Africa. However, the clinical and epidemiological implications of this variant remains unclear. More studies are needed to fully understand the genetic diversities of HIV in the country.

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PE15/2

Impact of KIR and their ligands (HLA allele) on susceptibility to selected viral opportunistic conditions and HIV plasma viral load in HIV+ patients

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Purpose: To assess the influence of KIR/HLA allele on occurrence of Herpesviridae AIDS-defining conditions, HPV infection, pretreatment TCD4+ cell count and HIV-RNA, baseline TCD4+/TCD8 ratio as well as nadir TCD4+ count.
Method: Study included 310 HIV-positive patients. Among them 70 (22.6%) had the history of shingles, 36 (11.6%) - HPV clinical manifestation, 38 (12.3%) - CMV, EBV, HHV-8 and HSV diseases defining AIDS. Genotyping of 16 variants of KIR, HLA-A Bw4+, HLA-B Bw4+Ile80, HLA-B Bw4+Thr80, HLA-B Bw4+Asp77,Thr80, HLA-C1 Asn80 and HLA-C2 Lys80 was performed with PCR-SSP, statistical analysis with chi-square test and U Mann-Whitney test.
Results: Patients with a history of HPV infection were found significantly more likely to carry KIR2DS3 (p=0.002), KIR2DL5all (p=0.004) or KIR2DL5gr2 (p=0.0003) alleles. Among these patients HLA-C1Asn80, KIR2DL3 and compound KIR2DL3/HLA-C2 were less frequent compared to those without HPV manifestation (p=0.03, p=0.02 and p=0.003, respectively). Expression of compound KIR3DS1/HLA-B Bw4+I80 and genotype HLA-C1/HLA-C2 tended to link with lower frequency of shingles (p=0.05 and p=0.06, respectively). No significant differences in frequency of the analysed KIR and HLA genotypes between patients with and without AIDS-defining illnesses with CMV, HSV, EBV and KS-HV were found. Higher pretreatment HIV-RNA was found in patients expressing KIR2DS1 (p=0.038), KIR2DS2 (p=0.041), KIR3DS1 (p=0.023), KIR2DL2 (p=0.018), KIR2DL5exp (p=0.019), KIR3DS1/3DL1 (p=0.008) and following compounds - KIR2DL2/HLA-C1 (p=0.0006), KIR2DL2/HLA-C2 (p=0.023), KIR2DS1/HLA-C1 (p=0.015), KIR2DS1/HLA-C2 (p=0.004), KIR2DL2/2DL3/HLA- C1 (p=0.01). The only genetic variant connected with lower baseline viral load was haplotype A of KIR (p=0.0003). KIR2DL5gr2 was related to lower nadir TCD4+cell count (p=0.038).
Conclusion: 1. Six variants of KIR and HLA allele both alone and in pairs were found to influence/modify the occurrence of HPV-related diseases among HIV-infected patients.
2. Expression of selected KIR variants, compounds and KIR haplotype A is affecting HIV replication.

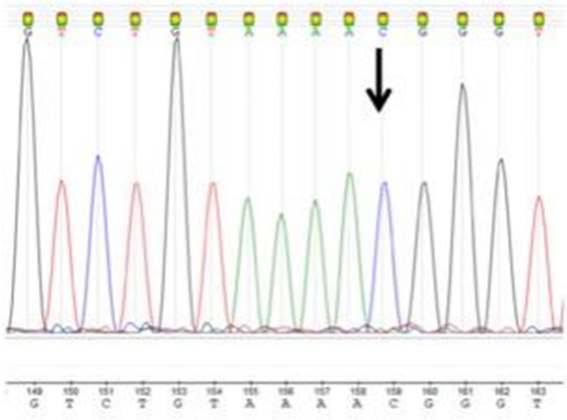
PE15/3

The identification and causal analysis of aberrant CD4 counts in an HIV cohort in Southern Alberta, Canada

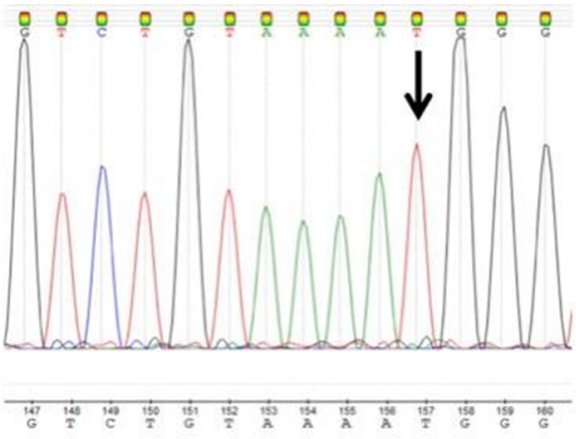
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Background: The CD4 count is used as the most robust surrogate marker for HIV disease immunosuppression. A potential confounder (genetic diversity of the OKT4 receptor) in the correct enumeration of CD4 cells was described in 1981 but has subsequently received little attention. We report on a series of cases where this mutation compromised the results of a new commercially available monoclonal antibody leading to highly aberrant results.
Methods: After a routine satisfactory comparative analysis (200 samples) a new commercial monoclonal antibody (BioLegend: T4-FITC anti-human CD4 antibody) was introduced in flow cytometry CD4 testing. In 5/1980 patients receiving care at the Southern Alberta HIV Clinic who had, despite clinical and virologic stability, experienced an apparent sudden >99% decline in CD4 cells we undertook Sanger sequencing.
Results: All cases had central to east African ethnic background. Their CD4 measurement was aberrant with only one commercial monoclonal product. A homozygous mutation of the OKT4 epitope in the V3 domain of the CD4 explained the complete absence of CD4 cell recognition in these five patients. We also identified heterozygosity leading to correct count but a 50% reduction in immunofluorescence.
Conclusions: HIV care programs need to be aware that reagents and assays reflect a changing profile of the HIV epidemic, noting host genetics. Despite significant developments in laboratory methods, allowing for more accurate and efficient CD4 reporting, ongoing vigilance is required of both lab professionals and clinicians to identify false test results and pursue programmatic improvements.



DNA chromatogram of homozygous wild type CD4



DNA chromatogram homozygous OKT4 deficient. The arrow denotes position 868 in the CD4 gene

PE15/4

Placental gene expression profiles and pathways in HIV-1 positive Cameroonian women under ART

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Purpose: A major consequence of in-utero exposure to HIV/ART is increased morbidity and mortality in infants during postnatal life. The causes and mechanism(s) underlying these conditions are not well understood. The placenta plays a key role in the development of a healthy fetus, and normally functioning placentas increases the chances of improved health later on in their childhood. We hypothesized that HIV-1 infection causes alterations in the functioning of the placenta, which impedes the holistic development of the fetus. The aim of this study is was to conducted a genome-wide study investigating changes in the gene expression and pathways in women infected by HIV-1 under ART.
Method: In a cross-sectional survey, 102 women (31 HIV-1 positive under ART, and 71 uninfected woman) were enrolled. Median viral load was 682 copies/ul and women were on variable lengths of treatment. Placenta biopsies

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excised from 9 HIV-1-positive women and 8 HIV-uninfected women were carefully selected and gene expression was measured using Illumina Human HT-12 v 4.0 BeadChip microarray. Next, genes presenting a 2-fold ratio as compared to the control group were entered into Ingenuity Pathway Analysis (IPA) in order to determine genes specifically regulated in the placenta of HIV-1-infected women.
Results: Overall, 61/47323 genes were significantly dysregulated in placenta from HIV-1+ women compared to the HIV- controls. These genes encoded components of canonical signaling pathways: "Epithelial Adherens Junction", "Phagosome Maturation", "Gμ12/13", "14-3-3-mediated", "HIF1a", "CDK5", and the "Remodeling Epithelial Adherens". Predictor networks indicated that the placenta of HIV-1-infected had upregulations in genes that confer organismal injury and abnormalities.
Conclusion: The gene expression in the placenta is different between HIV-1/ART and uninfected counterparts, and highlights specific genes such as those related to injury. This might underwhelm the sound development of the fetus and consequently the well-being of the off-spring in later life

PE15/5

Functional clustering and association of HLA class I alleles to viral load in HIV-positive and ART-naïve participants from the INSIGHT START study

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Background: Previous studies on host-viral genomics in HIV+ patients found associations between HIV-1 viral load (VL) and HLA class-I alleles. Statistical analyses of HLA alleles have been challenging due to high polymorphism and variable allele frequencies among populations. To overcome this, we explored functional clusters of HLA class-I alleles based on predicted epitopes to increase statistical power.
Methods: Viral sequencing data from 3785 HIV+ participants enrolled in the START study was used to assemble HIV consensus sequences from 35 countries. We translated these sequences into 1.03 million putative HIV-1 peptides (9-mers) and predicted their binding affinities to 259 HLA class-I alleles using netMHCpan 4.0. This predicted cohort-specific immunopeptidome was used to group alleles by hierarchical consensus clustering into a single high-confidence tree of functional relationships (Fig. 1). Associations of $\log_{10}$(VL) to each functional cluster were tested by linear regression using imputed HLA alleles from 2546 ART-naive participants and adjusted by sex, self-reported race and country. Multiple testing was controlled by a false discovery rate (FDR)-based procedure using a q-value <0.05 to identify associations.
Results: Two functional groups were associated with a lower VL, one composed of HLA-B*57:01, B*57:02, and B*57:03 (β -0.32, q-value 1.77E-07; Fig. 2) and a pair of HLA-C*08 alleles (β -0.29, q-value 0.043; Fig. 2). In contrast, an HLA-B*44 cluster showed an association with higher VL (β 0.15, q-value 0.005; Fig. 2). Among the 13 alleles implicated by these 3 functional clusters, only two (HLA-B*57:01 and B*57:03 Fig. 2) were detected at individual allele level.
Conclusions: Consensus clustering of HLA alleles based on predicted epitopes provides functional groups to efficiently explore associations with VL. Three significant functional clusters were found containing both previously reported HLA alleles (HLA-B*57) and novel candidates whose predicted epitope profiles closely resemble those of other alleles affecting HIV-1 VL that were not detected at individual allele level.

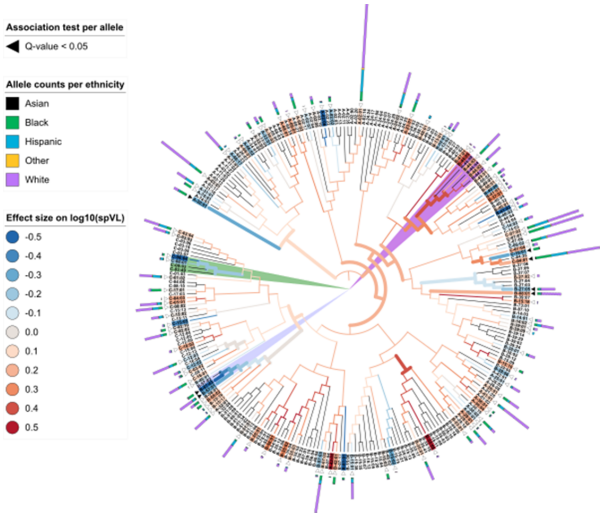


Figure 1. Dendrogram of 259 HLA class I alleles based on predicted binding affities to HIV

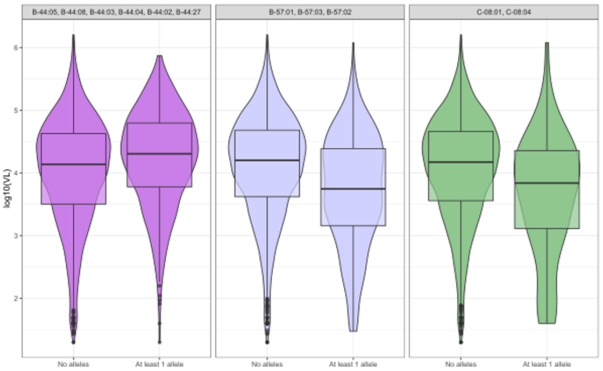


Figure 2. Boxplots and violin plots of HIV-1 VL in carriers and non-carriers of reported HLA nodes

PE15/6

miRNA expression profiling in subcutaneous adipose tissue of monozygotic twins discordant for HIV infection: validation of differentially expressed miRNA and bioinformatic analysis

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Purpose: Variability in metabolic complications of combination Antiretroviral Treatment (cART) has been linked not only to theraphy, but also to host genetic factors. MicroRNAs (miRNAs) are small noncoding RNAs regulating gene expression. The model of two monozygotic twins differing only for HIV-infection could allow to better comprehend cART miRNAs regulation, independently of genetic background.
Methods: A profiling of 2577 mature miRNA in subcutaneous adipose tissue (SAT) of twins was investigated by GeneChip® miRNA 4.1 array. Real-time PCR was performed to validate differentially expressed miRNAs. Target genes of deregulated miRNA were predicted by miRDB database (prediction score >70) and enrichment analysis was carried out with Panther, a platform using Gene Ontology and Panther pathways as annotation data set.

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Results: Twin A, HIV$^+$ on therapy with tenofovir, emtricitabine and efavirenz, was affected by peripheral and face lipoatrophy; no comorbidity was reported for Twin B, HIV$^-$. They differed significantly for BMI (21.8 vs 27.3, twin A vs twin B) but not for glucose, lipid profile, liver enzymes and blood pressure. 95 mature miRNAs differentially expressed (FC $\geq$ 2 or $\leq$2) in the twin A respect to the B were identified: 30 were up-regulated, whereas 65 were down-regulated. mir-15b-5p, mir-127-3p (upregulated), mir-122-5p and mir-3620-5p (downregulated) were validated by Real-Time PCR. Prediction target analysis identified 914 genes. Pathway enrichment analysis of genes targeted by miRNAs showed their involvement in Cadherin signalling (a key protein in the adherens junction), Fibroblast Growth Factor, Notch signalling (a critical pathway for kidney development), T cell activation and Wnt signaling (involved in pathogenesis of neuroinflammation in the Central Nervous System).
Conclusions: This analysis could provide some preliminary information on genes targeted by mir-15b-5p, mir-127-3p, mir-122-5p and mir-3620-5p in SAT. Further researches could deepen the link between deregulated miRNAs and comorbidities reported in people HIV-affected.

PE15/7

Factors influencing late presentation into care of HIV disease

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Purpose: Late presentation and care entry with advanced HIV infection remains an obstacle in achieving UNAIDS90-90-90 goals. The aim was to analyze association between selected genetic chemokines CCR5Δ32(rs333), CCR2(rs1799864), CCR5promoter (rs1799988) and CX3CR1(rs3732378) as well as HLA-B5701, HLAC-35 SNP, and late presentation.
Method: Cross-sectional clinical immunologic and viral data of 25.9% (n=224) female and 74.1% (n=639) male patients were linked with above genetic markers. Late care entry was defined as baseline CD4 count <350 cells/μL, advanced HIV disease was defined as baseline CD4 count <200 cells/μL or AIDS at diagnosis. For statistics Chi2 or U-Mann Whitney tests were used, as appropriate.
Results: Overall frequency of late presenters in the analyzed group was 50.9% (n=443), with 35.8% (n=311) with advanced HIV disease. In the late presenter group HLA-B5701 allele was less common 5% (n=21) compared to patients with baseline CD4 count >350 cells/μL or without AIDS 8.9% (n=24) p=0.02; association with HLA-B5701 allele was also noted when CD4 count and clinical stage at baseline were analyzed separately 5.2% (n=21) for CD4 count <350 cells/μL vs 8.9% (n=24) for >350 cells/μL, p=0.02 and 4.7% (n=16) for symptomatic infection and AIDS at care entry vs 8.6% (n=17) for asymptomatic cases, p=0.02. Presence of CCR5Δ32 allele was more common among asymptomatic patients 18.9% (n=40) compared to symptomatic infection or AIDS at baseline 12% (n=42), p=0.03. In advanced HIV disease HLA-B5701 was less common 4.1% (n=12) compared to patients entering care early 8.4% (n=33),p=0.04. Protective effect was observed for the CCR2 A allele with the frequencies of 0.7% (n=2), 16.3% (n=49) and 83% (n=249) for AA, AG and GG genotypes on AIDS or CD4 count <200 cells/μL patients, and 1.2% (n=5), 24.3% (n=99), 74.5% (n=245) among patients without AIDS or with CD4 count >200 cells/μL.
Conclusion: Protective clinical effects of HLA-B5701,CCR5Δ32 and CCR2 were confirmed. Genetic variants may positively affect patients survival in populations with high frequencies of advanced HIV disease and late care entry.

Immunology

PE16/1

Immunological and metabolic effects of dasatinib treatment in IL7-stimulated CD4+ T-cells subpopulations

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Introduction: IL7 plays an important role in long-term maintenance of immunological memory through the homeostatic proliferation of T-lymphocytes. HIV-1 infects preferentially memory CD4+ subsets and their IL7-mediated expansion can be a mechanism to perpetuate and expand the viral reservoir. Dasatinib, a tyrosine kinase inhibitor currently used in treatment of chronic myeloid leukemia, can counteract IL7 effects, restoring HIV-1 restriction and blocking the expansion of the reservoir. However, immunological and metabolic changes induced by IL7 and/or dasatinib stimulation in CD4+ T-cells subsets, have not been explored in depth.
Methods: Purified CD4+ T-cells were treated with IL7 and/or dasatinib. CD4+ T-cell subpopulations, T-cell activation markers and T-cell receptors expression, infectivity levels, were estimated by flow cytometry immunophenotyping. Metabolic rates were assessed with a Seahorse XF96 analyzer. Statistical analysis was performed by Wilcoxon test.
Results: IL7 stimulation induced significant changes in frequency and distribution of CD4+ subsets and the expression of T-cell activation markers. IL7-treated cells were more susceptible to HIV-1 infection that was increased in different CD4+ subpopulations. IL7 induced metabolic changes in CD4+ T-cells, increasing both glycolytic and mitochondrial respiration rates. Dasatinib was able to induce the following effects in IL7-treated cells: (a) restored the frequency of CD4+ T-cell subsets, mainly of naïve and central memory cells; (b) reduced the expression of HLA-DR and CD69 in CD4+ T-cells; (c) induced changes in the expression of CD25 and CD127 in CD4+ T-cells and some CD4+ subpopulations; (d) reduced the infectivity levels, similarly among CD4+ T-cells subpopulations; and, (e) decreased glycolytic metabolism rates in CD4+ T-cells.
Conclusion: IL7 induced immunologic and metabolic changes in CD4+ T-cells leading to increased HIV-1 infection, and dasatinib counteracted some of these effects. These results provide new insights on the role of interleukins in HIV-1 reservoirs maintenance and the potential role of tyrosine kinase inhibitors in cure strategies.

PE16/2

New T- and B-lymphocytes production and T-cell receptor diversity in young adults perinatally infected by HIV

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Objectives: To evaluate immunosenescence (defined as reduced production of new lymphocytes, restriction of T-cell receptor repertoire and telomeres shortening) in perinatally-infected children with very long-lasting HIV infection.
Methods: We compared thymic and bone marrow output (quantifying the number of T-cell receptor excision circles (TRECs) and K-deleting recombination excision circles (KRECs)), telomere length (TL) and T-cell repertoire (analyzed by means of CDR3 spectratyping analysis) of 21 perinatally HIV-infected subjects (pHIVy), with a mean of 27 years of infection, with those of 19 age-matched non-perinatally HIV-infected patients (np-HIVy), with a mean duration of HIV infection of 4.5 years, and of 40 age-matched healthy controls (HC).
Results: TRECs and KRECs levels were similar among pHIVy, npHIVy and HC (Fig. 1), while median TL in peripheral blood cells was significantly lower in both pHIVy and npHIVy than in HC (Fig. 2). The mean proportion of human T cell receptor beta variable (TRBV) subgroups with normal profiles was significantly lower in samples obtained from HIV-infected patients compared to HC (16.8% and 18.8% vs 27.5%).The proportion of TRBV chains with shifted profiles was not different, while that with restricted TRBV profiles was significantly higher in pHIVy than in HC (49.5% vs 35.5%) and mono/oligoclonal TRBV cells were higher in npHIVy than in HC (11.4% vs 2.9%). A negative correlation was found between the percentage of TRBV perturbations and CD4/CD8 ratio ($r = -0.81$; $P < 0.0001$) and CD4$^+$cell count ($r = -0.63$; $P < 0.05$).
Conclusions: A normal thymic output together with an increased telomere length and a reduced T-cell diversity in perinatally HIV-infected subjects could be explained by the shift of newly produced cells into memory subsets. This phenomenon may allow to control viral infection and maintain peripheral homeostasis.

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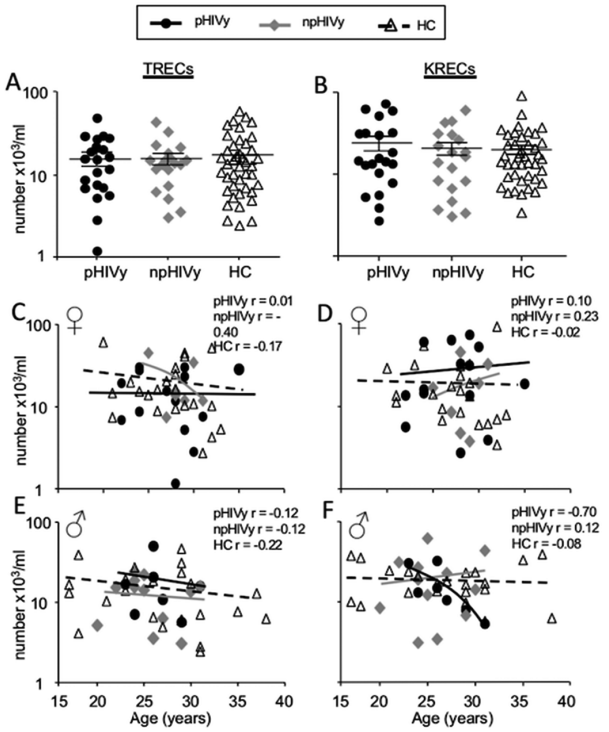


Figure 1. TRECs (A) and KRECs (B) in pHIVy, npHIVy and HC.TRECs (C, E), KRECs (D, F) according to gender

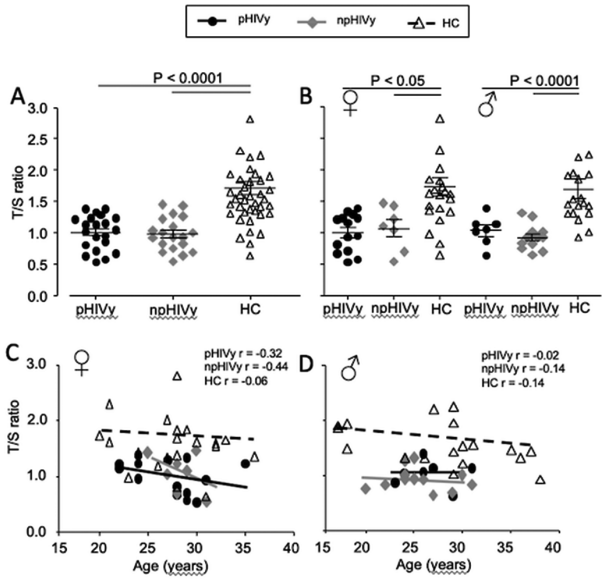


Figure 2. Telomere length in pHIVy, npHIVy, HC (A) and age according to gender (C, D)

PE16/3

In Vivo modelling of mechanisms of HIV-1-related monocyte dysfunction

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Purpose: Monocyte/macrophage (M/M)-related (rather than T-cell) inflammation and immune activation may contribute to morbidity and mortality in chronic treated HIV-1 infection. However, the mechanisms of HIV-1 related M/M dysfunction remain poorly defined *in vivo*.

Method: Using the Bone Marrow/Liver/Thymus humanized mouse (BLT), we assessed the direct early effect of the HIV-1 clone 89.6 on expression of (co) receptors important for HIV-1 pathogenesis and/or M/M function. Protein expression and function (endocytosis) in human monocyte subsets (CD14+, CD14+CD16+, CD14+CD16-) was assessed at baseline and after 4 weeks of HIV-1 infection using flow cytometry. Pairwise group comparisons used Wilcoxon rank-sum tests.

Results: Over 4 weeks of HIV-1 infection, expression [% of parent (not shown) and/or Median Fluorescence Intensity (MFI) of CD4 and CXCR2 declined in all monocyte subsets in the HIV1+ group (n=10). CXCR4 MFI increased only in hCD14+hCD16+ monocytes in the HIV1+ group (not shown). % CCR5 expression increased only in hCD14+hCD16- monocytes in the HIV1+ group. % CD16 expression increased similarly in monocytes of both the HIV1+ and HIV-1- group (n=10) (not shown). CCR2 expression did not change in any monocyte subset in both groups. % CX3CR1 increased only in hCD14+hCD16+ monocytes in the HIV1+ group. % PhRhodo positivity and MFI declined (suggesting impaired endocytosis) only in hCD14+hCD16+, monocytes in the HIV1+ group. The most notable effects in the HIV1+ group were increase in CCR5 expression in hCD14+hCD16- monocytes, decrease in CD4 and CXCR2, increase in CX3CR1 and reduction in % PhRhodo+ in hCD14+hCD16+ monocytes (Table).

Conclusion: HIV-1 directly downregulates CD4 and CXCR2 in monocytes, impairs monocyte function and upregulates CX3CR1 in proinflammatory CD14+CD16+ monocytes. Our data complement prior *in vitro* data that CD16+ monocytes are preferentially susceptible to HIV-1 entry and demonstrate the direct impact of HIV on human M/M function and chemokine expression *in vivo*.

Table

Table Parameter (selected)	Wk 0 HIV- (n=8)	Mean Fold Change relative to wk 0	p value	Wk 0 HIV+ (n=10)	Mean Fold Change relative to wk 0	p value
MFI CX3CR (CD14+CD16+)	395 (339, 531)	1.17	0.69	346 (259, 448)	2.30	0.02
MFI CXCR2 (CD14+CD16+)	260 (181, 339)	1.12	1.00	352 (326, 441)	0.81	0.23
MFI CD4 (CD14+CD16+)	196 (191,228)	0.98	0.99	261 (247, 299)	0.70	0.002
% PhRhodo Red (CD14+CD16+)	78.4 (69.6, 86.5)	1.76	0.25	83.4 (79.18, 87.63)	0.66	0.02
% CCR5 (CD14+CD16-)	10.04 (9.09, 12.40)	3.49	0.03	15.60 (12.35, 19.33)	2.50	0.002
% CX3CR (CD14+CD16-)	9.58 (6.99, 12.00)	1.58	1.00	6.43 (5.40, 7.85)	2.02	0.03
MFI CXCR2 (CD14+CD16-)	210 (162, 226)	1.09	0.44	236 (224, 282)	0.73	0.002
% PhRhodo Red (CD14+CD16-)	7.61 (6.72, 14.0)	1.20	0.44	11.75 (10.78, 13.25)	0.85	0.04

PE16/4

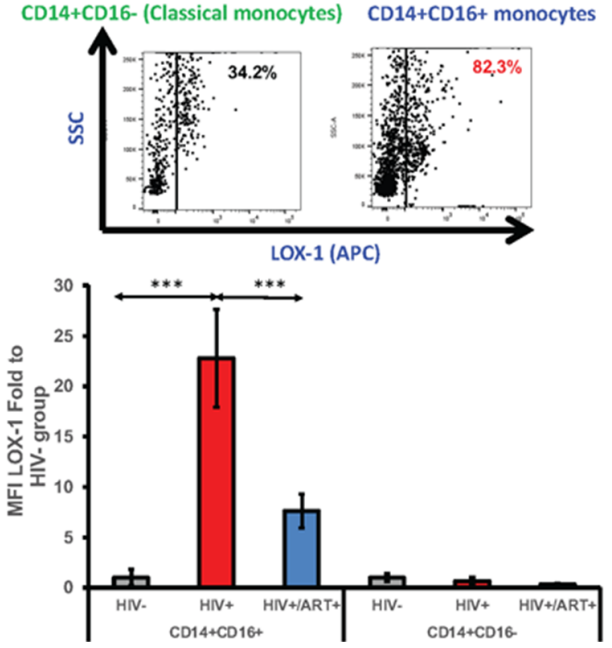
Lectin-like oxidized low-density lipoprotein (LOX-1) is elevated in proinflammatory monocytes in chronic treated HIV

W Mu, P Hamid, A Kossyvakis, H Nguyen, S Sen Roy and T Kelesidis
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Purpose: The mechanisms of HIV-1 related Monocyte/macrophage (M/M) dysfunction remain poorly defined *in vivo*. Both oxidized lipids and HIV-1 are known to impact M/M and lipid rafts, specialized membrane domains enriched in signalling machinery important for atherogenesis. Proinflammatory CD14+CD16+ monocytes have higher content of lipid rafts compared to classic CD14+CD16- monocytes. We hypothesized that scavenger receptors that bind oxidized lipids such as the Lectin-like oxidized low-density

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lipoprotein (LOX-1) are upregulated in lipid raft enriched CD14+CD16+ proinflammatory monocytes in chronic treated HIV and this receptor may drive proinflammatory properties of CD14+CD16+ monocytes.
Method: Using the Bone Marrow/Liver/Thymus humanized mouse (BLT), we assessed the direct effect of the HIV-1 clone 89.6 on expression of LOX-1. BLT mice (n=32) were split in 3 groups: A) HIV uninfected (n=8), B) HIV infected viremic, no antiviral therapy (ART)(n=12), C) HIV infected aviremic, on potent ART (n=12). Protein expression in monocyte subsets was assessed after 12 weeks of HIV-1 infection and potent antiviral therapy using flow cytometry and whole blood staining with anti-human antibodies. Group comparisons used Wilcoxon rank-sum tests.
Results: Over 12 weeks of HIV-1 infection, expression [% of parent (not shown) and/or Median Fluorescence Intensity (MFI) of LOX-1 in CD14+CD16+ monocytes increased in the HIV-1+/ART group compared to the HIV- group by a mean of 22-fold (Figure). Protein membrane levels of LOX-1 in CD14+CD16- monocytes decreased in the HIV1+ group compared to the HIV- group. LOX-1 in CD14+CD16+ monocytes remained elevated in the HIV/ART group by a mean of 8-fold compared to the HIV- group.
Conclusion: HIV-1 directly upregulates LOX-1 in CD14+CD16+ monocytes. Despite potent ART, elevated levels of LOX-1 in these monocytes persist and may drive their proatherogenic properties by binding oxidized lipids.



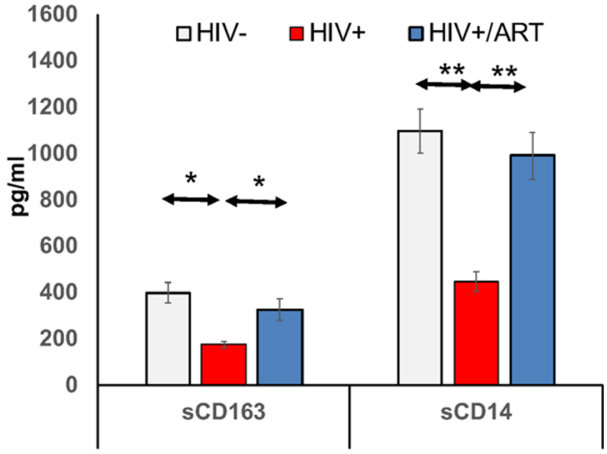
Figure

PE16/5

In vivo dissection of the impact of HIV-1 versus antivirals on immune activation in chronic treated HIV

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Purpose: Monocyte/macrophage (M/M)-related (rather than T-cell) inflammation and immune activation may contribute to morbidity and mortality in chronic treated HIV-1 infection. Observational human studies cannot dissect the differential effects of HIV versus antivirals (ART) on M/M activation. We used a physiologically relevant humanized mouse model of chronic treated HIV to dissect *in vivo* HIV- and/or ART-driven impact on biomarkers of human M/M activation.
Method: The C57BL/6 *Rag2−/−γc−/−CD47−/−* Bone Marrow/Liver/Thymus mice do not develop early graft versus host disease and thus HIV- and/or ART-driven changes on immune activation can be dissected in vivo. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. The groups were: A (n=5): uninfected (HIV-); B (n=10): HIV+; C (n=15): HIV+. Biomarkers of human M/M activation sCD163 and sCD14 were determined by Luminex Assays. Results are described as mean and SEM and t-test was used for statistical analysis.
Results: HIV-1 induced a mean 59% and 56% reduction in plasma h-sCD14 and h-sCD163, respectively, in infected compared to uninfected mice ($p< 0.05$). Potent ART for 12 weeks suppressed viremia within 4 weeks and induced a mean 49% and 38% increase in h-sCD14 and h-sCD163 ($p< 0.05$) in HIV+/ART+ compared to HIV+ mice ($p< 0.05$).
Conclusion: Our in vivo model provided unique mechanistic insight about differential effects of HIV-1 versus potent ART on M/M activation. HIV-1 reduced biomarkers of M/M activation (possibly due to cytotoxic effects of HIV-1), whereas ART increased h-sCD163 and h-sCD14. These mechanistic data complement prior data from observational human studies that biomarkers of M/M activation remain elevated in chronic treated HIV despite potent ART and suggest that ART rather than HIV-1 per se drives the increase in plasma levels of sCD163 and sCD14.



Figure

PE16/6

Differential impact of HIV-1 versus antivirals on systemic inflammation in chronic treated HIV

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Purpose: Despite potent antiviral therapy (ART), increased inflammation persists in chronic treated HIV-1 infection and may contribute to morbidity. Observational human studies cannot dissect the differential effects of HIV versus ART on inflammation. We used a physiologically relevant humanized mouse model of chronic treated HIV to dissect *in vivo* HIV- and/or ART-driven impact on human cytokines and chemokines.
Method: The C57BL/6 *Rag2−/−γc−/−CD47−/−* Bone Marrow/Liver/Thymus mice do not develop early graft versus host disease. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. The groups were: A (n=5): uninfected (HIV-); B (n=10): HIV+; C (n=15): HIV+/ART. Human and murine cytokines and chemokines were determined by Luminex Assays. Results are described as mean and SEM and t-test was used for statistical analysis.
Results: HIV-1 induced a mean >45% reduction in plasma h-IL-1b, h-IL-6, h-IL-8, h-IL-10, h-IL-18 and h-TNF-a and a mean >20% increase in plasma h-CCL3, h-CCL5, h-CX3CL1 and h-CXCL10 in infected compared to uninfected mice ($p< 0.05$, Table). Potent ART for 12 weeks suppressed viremia within 4 weeks and induced a mean >20% increase in human cytokines. ART induced a mean >20% increase in h-CCL2 and hCXCL1 and a mean 55% increase in murine TNF-a in HIV+/ART+ compared to HIV+ mice ($p< 0.05$).
Conclusion: Our in vivo model provided unique mechanistic insight about differential effects of HIV-1 versus potent ART on human cytokines and chemokines. HIV-1 reduced human cytokines (possibly due to cytotoxic effects of HIV-1 on human immune cells), whereas potent ART did not affect or even increased human chemokines and m-TNF-a. These mechanistic data complement prior data from observational human studies and suggest that ART contributes to systemic inflammation in chronic treated HIV.

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Table

	Uninfected (pg/mL; mean±SEM)	HIV (fold to HIV-; mean±SEM)	HIV/ART (fold to HIV-; mean±SEM)	P values (#: HIV+ vs HIV-, ^: HIV+/ART+ vs HIV+)
h-IL-1b	3.4±1.2	0.513±0.047	1.176±0.161	0.020#, 0.001^
h-IL-6	94.8±37.9	0.035±0.008	0.972±0.220	0.008#, 0.001^
h-IL-10	23.2±8.1	0.151±0.017	1.050±0.164	0.002#, <0.001^
h-TNF-a	92.2±33.1	0.156±0.017	0.844±0.084	0.003#, <0.001^
h-CCL2	40.7±15.1	1.571±0.297	3.342±0.485	0.143 #, 0.006^
h-CCL3	14.6±4.8	1.282±0.040	1.309±0.059	0.057 #, 0.710 ^
h-CCL5	9.0±2.9	1.966±0.094	2.126±0.129	<0.001 #, 0.329^
h-CX3CL1	14.4±4.8	2.446±0.242	2.536±0.305	<0.001 #, <0.820^
h-CXCL10	4.5±1.6	2.086±0.249	1.461±0.164	0.004#, 0.056^

PE16/7

Correlation between blood telomere length and CD4$^+$ CD8$^+$ T-cell subsets in HIV-1-positive individuals with long-term virological suppression on antiretroviral therapy

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Purpose: People living with HIV have shorter blood telomere length (TL) than the general population possibly due to an accelerated aging of the immune system. To further investigate the relationship between blood TL and HIV immune dysregulation we have assessed correlations between blood TL and T cell subsets in long-term treated HIV-positive persons who have been virologically suppressed more than 10 years.

Method: TL was measured in whole blood samples by qPCR (T/S ratio). Fresh PBMCs were analyzed using flow cytometry. The following CD4$^+$ and CD8$^+$ T cell subsets were included in the analysis: Recent Thymic Emigrants (RTE) (CD31$^+$ CD45RA$^+$), Naïve (CD45RA$^+$ CD27$^+$), Central Memory (CD45RA$^-$ CD27$^+$), Effector Memory (CD45RA$^-$ CD27$^-$), TEMRA (CD45RA$^+$ CD27$^-$), Senescent (CD28$^-$ CD57$^+$), Exhausted (PD1$^+$) and Activated (CD38$^+$ HLA-DR$^+$). Associations were calculated using the Spearman correlation.

Results: Characteristics of the 152 participants appear in Table 1. Mean blood TL: 0.960 (standard deviation=0 .165) was significantly correlated with age (rho=-0.321, P< 0.0001) and total CD4$^+$ (rho=0.182, P= 0.025), but not with total CD8$^+$ nor with CD4$^+$/CD8$^+$ ratio. In the CD4$^+$ population (Figure 1A), TL was positively correlated with RTE (rho=0.225, P=0.005). By contrast, a negative correlation was found with TEMRA (rho=-0.221, P=0.006), activated (rho=-0.219, P=0.007), senescent (rho=-0.196, P= 0.016) and effector memory cells (rho=-0.187, P= 0.021). In the CD8$^+$ compartment (Figure 1B), TL was positively correlated with naïve cells (rho=0.289, P< 0.001) and negatively associated with TEMRA (rho=-0.292, P< 0.001) and senescent cells (rho=-0.171, P=0.035). After adjusting correspondingly by total CD4$^+$ and CD8$^+$ counts in a linear regression model, TL remained significantly associated with CD4$^+$ TEMRA (P=0.011), senescent (P=0.025) and RTE cells (P=0.048), and CD8$^+$ TEMRA (P=0.001), naïve (P=0.017) and senescent cells (P=0.025).

Conclusion: In our cohort of HIV-positive participants with long-term treated infection, blood TL correlated with the differentiation state of the T-cell compartment.

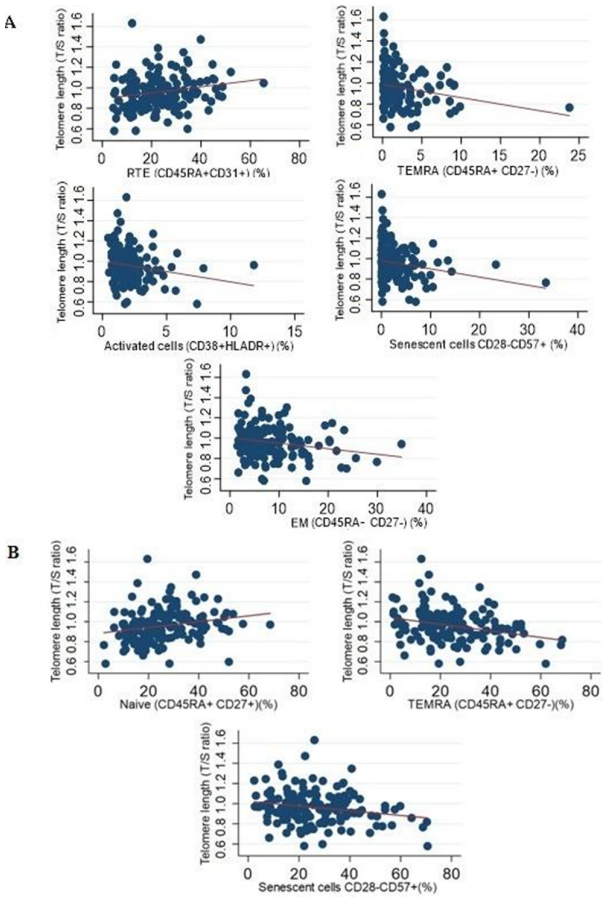


Figure 1. Correlation between TL CD4+ (A) and CD8+ (B) T-cell subsets

Table 1. Participant characteristics

Characteristic	
Age, y	53.5
Sex, %	
-Female	25.66
Ethnicity, %	
-White	92.76
-Other	7.24
Route of HIV transmission, %	
-Parenteral	30.92
-Sexual	66.45
-Unknown	2.66
Current tobacco use, %	
-No	50.66
-Yes	49.34
Current alcohol use, %	
-No	38.82
-Yes	61.18
HCV coinfection, %	
-No	66.45
-Yes	32.89
-Unknown	0.66
Time with HIV load <50 copies/mL, y	11
T- cell count, cell/mL	
-CD4+	759.57
-CD8+	684.41

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PE16/9

Phenotypical recovery of the T-cell pool following switch to dual and triple INSTI-based cART

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Purpose: Integrase strand transfer inhibitors (INSTIs) are used in first-line and switch strategies as dual combination therapy, yet their impact on the persistent immunological changes of treated HIV infection is unknown. We evaluated T-cell homeostasis in subjects switching to dual and triple INSTI-based therapy during viral undetectability.

Method: Retrospective study on HIV-infected subjects on suppressive NNRTI- or PI-based triple cART regimens switched to dual or triple INSTI-containing therapies.

T-cell immunephenotype was studied pre-switch and at 6 (T6) and 12 months (T12) after switch during stable viral suppression. Peripheral blood was stained with the fluorochrome-based antibodies to study T-cell naïve (CD45RA), memory (CD45R0), activated (CD38), and CD127-expressing subpopulations. Mann-Whitney and Wilcoxon tests were used for statistics.

Results: 45 dual-INSTI and 164 triple-INSTI individuals were identified (Table 1). Despite CD4+ count increases in triple-INSTI (Fig. 1A), stable CD4/CD8 ratio was registered in both groups (Fig. 1B).

Analysis of T-cell homeostasis revealed the selective expansion of naïve CD4+ T-cells in dual-INSTI (Fig. 1C) and stable kinetics of naïve CD8+ T-cells in both groups (Fig 1D). Sustained increases of CD127-expressing CD4+ cells were detected in dual- and triple-INSTI subjects (Fig. 1E), yet growth of the CD8+CD127+ subset was observed only in the former (Fig. 1F). In contrast, a contraction of memory CD8+ T-cells was noted in triple-INSTI (Fig. 1G), coupled with the increase of the activated CD8+ pool which translated into significantly higher CD8+CD38+ cells compared to dual-INSTI at T12 (Fig. 1H).

Conclusion: Switching to a dual INSTI-based regimen in the course of viral suppression may aid immunological recovery of the T-cell pool, featuring the expansion of the CD127-expressing and naïve CD4+ T-cell subsets. Future studies need to confirm these preliminary findings which appear to support the immunologic efficacy of dual INSTI-based regimens in sustaining a more favourable T-cell immunephenotype in peripheral blood.

	Dual INSTI N=45	Triple INSTI N=164	p value (Dual vs Triple)
Sex (M) n, (%)	35 (77)	127 (77)	1
Age in years (median, IQR)	54, 45-65	47, 41-53	**0.0005**
HIV epidemiology			
MSM, n (%)	11 (24)	61 (37)	0.1
Heterosexual, n (%)	12 (27)	59 (36)	0.4
IVU n (%)	12 (27)	30 (18)	0.2
AIDS n (%)	12 (27)	45 (27)	1
HCV RNA positivity, n (%)	3 (7)	3 (2)	0.11
HBsAg positivity, n (%)	3 (7)	9 (5)	0.7
TPPA positivity, n (%)	15 (33)	44 (27)	0.45
Smokers, yes, n (%)	15 (33)	59 (36)	0.86
Nadir CD4/uL (median, IQR)	234, 148-412	235, 103-370	0.29
CD4/CD8 ratio when cART naïve (median, IQR)	0.31, 0.24-0.45	0.34, 0.18-0.49	0.75
Zenith HIV RNA load, log10 cp/mL (median, IQR)	5.09, 4.06-5.55	4.76, 4.12-5.40	0.6
Time of HIV RNA undetactability at switch, months (median, IQR)	59, 25-85	61, 31-85	0.85
cART pre-switch (n, %)			
NNRTI	13 (29)	54 (33)	0.7
PI	14 (31)	97 (59)	**0.00012**
other	18 (40)	13 (8)	**<0.0001**
CD4/uL at switch (median, IQR)	624, 420-920	581, 414-756	0.23
CD4/CD8 at switch (median, IQR)	0.68, 0.46-0.94	0.73, 0.49-0.97	0.39

Table 1. Demographic Characteristics of Study Subjects

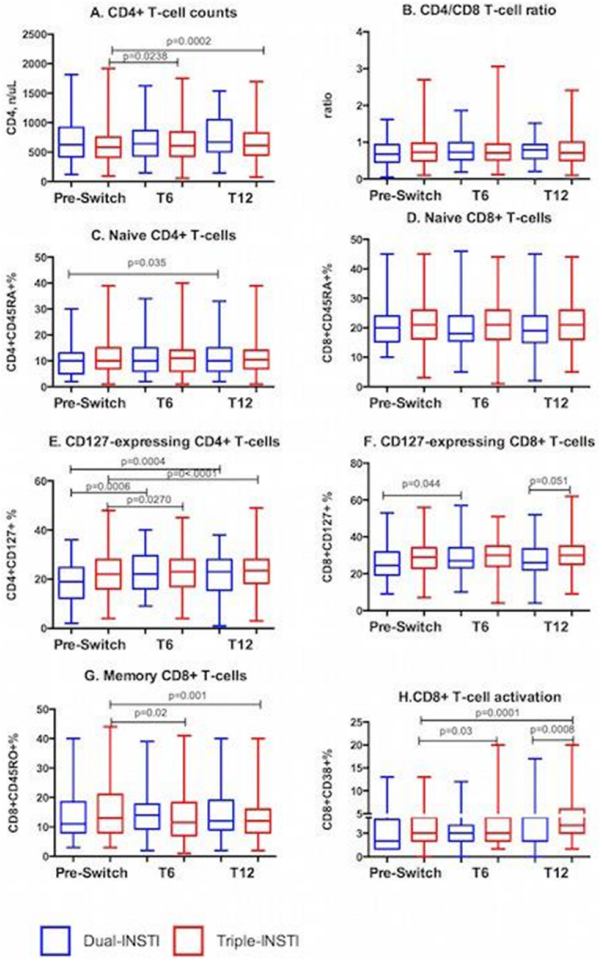


Figure 1. T-Cell Homeostasis in dual- and triple-INSTI treated subjects

PE16/11

Expression of PD-1 in a population of double-negative T cells ($CD3^+CD4^-CD8^-$) in HIV-infected patients – the preliminary study results

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Purpose: Double-negative T cells ($CD3^+CD4^-CD8^-$; DNT) are heterogeneous populations; in healthy people they account for approximately 1–3% of all $CD3^+$ cells in peripheral blood. Their function has not yet been fully understood, but it is believed that they play a role in regulatory processes, and the PD-1^+ subsets generate the majority of proinflammatory cytokines.

The aim of the study was to evaluate PD-1^+ DNT cells, depending on the type of TCR receptor in HIV-infected patients receiving antiretroviral therapy.

Method: Fifteen HIV infected individuals on antiretroviral treatment, with undetectable HIV-RNA, were included to the study (12 men [80.00%], 3 women [20.00%]; mean age 41 years [SD: 7], mean $CD4^+$ cells 441/μL [SD: 213]). DNT were selected from PBMC with flow cytometry: CD3-V450, CD4-PerCP-5.5, CD8-APC-H7, TCRαβ-FITC, TCRγδ-PE-CY7, PD1-V500. Amount of study cells in blood volume were calculated from complete blood count test. U Mann-Whitney test were used for statistical analysis. Applying the Bonferroni correction the significant p-value was established as $p < 0.016$.

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Results: Table 1 presents the results.
Conclusions: The TCD$\gamma\delta^+$ subpopulation predominates among DNT cells in HIV infected patients treated with antiretroviral therapy. The PD-1 is the surface protein of most DNT cells, but is more common in TCR$\alpha\beta^+$ subpopulations than TCR$\gamma\delta^+$.

Table 1. DNT cells subpopulations and frequency of PD-1+ cells

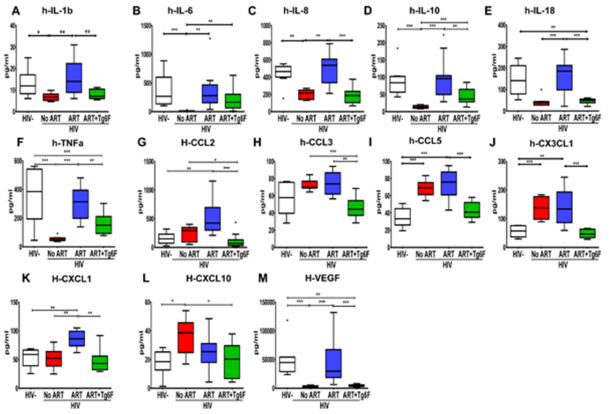
	All DNT cells	DNT TCR αβ+ cells	DNT TCRγδ+ cells	P (DNT TCR αβ+ vs DNT TCRγδ+)
cells/μL	mean 54.5 (SD: 36.7)	median 9.2 (IQR: 5.4–15.9)	median 37.4 (IQR: 7.0–69.2)	0.0235
%	mean 5.3 % of CD3+ (SD: 2.2)	median 24.0 % of DNT (IQR: 9.9–45.8)	median 75.9 % of DNT (IQR: 54.4–90.1)	0.0014
PD1+ (%)	mean 60.1 (SD:16.0)	median 70.9 (IQR: 68.0–80.2)	median 51.6 (IQR: 41.6–67.2)	0.0023

PE16/12

Targeting inflammation in chronic treated HIV with oral ApoA-I mimetics

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Purpose: Novel therapies are needed to attenuate inflammation in chronic treated HIV infection. ApoA-I peptides (such as 6F) mimic HDL, bind oxidized lipids and endotoxin and attenuate proinflammatory mechanisms. The 6F was expressed as a transgene in tomatoes (Tg6F) and reduced cardiovascular disease in mice. Tg6F can be translated to human diet. We used a physiologically relevant humanized mouse model of chronic treated HIV to study whether Tg6F attenuates *in vivo* HIV- and/or ART-driven impact on biomarkers of M/M activation.
Method: The C57BL/6 *Rag2−/−γc−/−CD47−/−* Bone Marrow/Liver/Thymus mice do not develop early graft versus host disease. After 4 weeks of infection with the 89.6 HIV-1 virus, mice (n=40) were treated with daily emtricitabine, tenofovir, raltegravir for up to 12 weeks. Oral ApoA-I mimetics were given as Tg6F (at 0.06% by weight of diet) to HIV+/ART-treated mice (n=20) after suppression of viremia with ART. The groups were: A (n=10): uninfected (HIV-); B (n=10): HIV+; C (n=20): HIV+, ART; D (n=20): HIV+/ART/Tg6F. Human cytokines and chemokines were determined by Luminex Assays. Results are described as median and interquartile range and Wilcoxon signed-rank test was used for statistical analysis.
Results: Potent ART induced a mean >15% increase in human cytokines (Figure) compared to HIV viremic mice. ART induced a mean >30% increase in h-CCL2, hCXCL1, murine IL-1b and TNF-a in HIV+/ART+ compared to HIV+ and uninfected mice ($p < 0.05$). Tg6F attenuated all ART-induced increases in m-TNF-a, m-IL-1b and human cytokines and chemokines except for h-IL-6 and h-CXCL10.



Figure

Conclusion: Tg6F attenuated ART-induced increase in inflammation. Given that Tg6F is not absorbed systemically, our model confirms that gut dysfunction is a major instigator of inflammation in chronic treated HIV. Further studies are needed to determine whether oral ApoA-I mimetics can be a novel strategy to attenuate inflammation in chronic treated HIV.

PE16/13

Poor recovery of T-cell receptor repertoire despite long-term antiretroviral therapy

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Purpose: Despite antiretroviral therapy (ART), people living with HIV (PLWH) remain at greater risk of several infectious and non-communicable comorbidities. Persisting immunological deficits might contribute to this excess burden of non-AIDS disease. Previous work has suggested that the T cell receptor (TCR) repertoire is highly disordered in untreated HIV infection and does not recover after three months of ART. We sought to establish whether these T-Cell receptor repertoires normalise with long-term antiretroviral therapy.
Methods: Peripheral blood samples from HIV positive participants using ART and HIV negative individuals participating in a prospective cohort study were analysed. TCR receptor sequences were amplified and sequenced and bioinfomatic pathways were followed using previously established TCR assignation software.
Results: Samples were analysed from 27 HIV positive and 22 HIV negative individuals and compared to data from 16 PLWH before and after initiation of antiretroviral therapy analysed in previous work. The HIV positive group on ART had evidence of good immune reconstitution, with median (IQR) CD4 counts of 685 (457–848) cells/μL and undetectable HIV viral loads.
TCR repertoires remained abnormal when compared to HIV negative individuals, with a lower diversity and greater inequality of receptor repertoires. This had not normalised after more than 10 years of ART. In a specific evaluation of the population of Mucosal-Associated Invariant T (MAIT) cells, these were found to be severely depleted in HIV infection prior to ART and had not recovered with ART.
Conclusions: These results suggest that the disrupted TCR repertoire associated with HIV infection does not normalise with long-term ART. Possible explanations could be permanent changes in T cell populations that do not recover with antiretroviral therapy, or on-going chronic inflammation causing bias in the TCR repertoire. If confirmed in larger studies, these findings help explain the greater incidence of infectious and non-communicable comorbidities among PLWH.

Moderated ePosters I: basic science

PE17/1

Abdominal adipose tissue is associated with alterations in tryptophan–kynurenine metabolism and markers of systemic inflammation in people living with HIV

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Purpose: While both adipose tissue accumulation and tryptophan (Trp) metabolism alterations are features of HIV infection, their interplay is unclear. The primary aim was to evaluate associations between abdominal adipose

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tissue, alterations in the kynurenine (Kyn) pathway of Trp metabolism, and systemic inflammation in people living with HIV (PLWH). Exploratively, we investigated possible associations between Kynurenines and lipids.

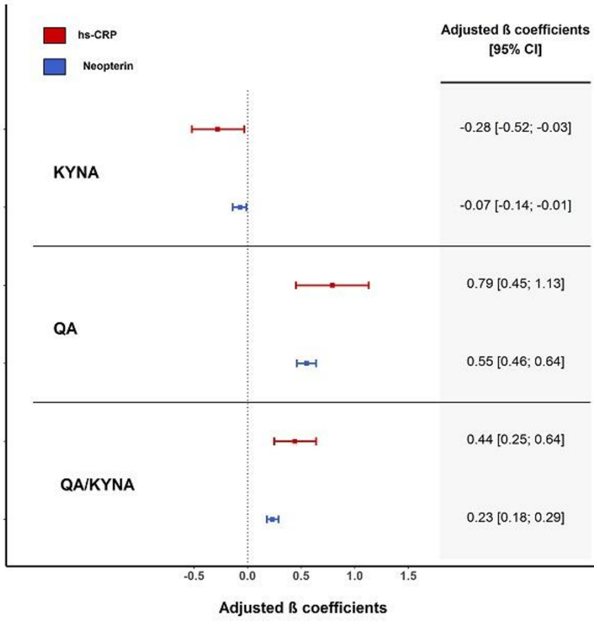
Method: 864 PLWH and 75 uninfected controls were included from the COCOMO study. Abdominal adipose tissue was measured using waist-to-hip ratio. Venous blood was collected and analyzed for Kyn and Kyn catabolites, neopterin, high-sensitivity CRP (hs-CRP), and lipids. Linear regression models were used to test associations in PLWH. The ratio between quinolinic and kynurenic acids (QA/KYNA) was used as measure of the flux through the branch of the kynurenine pro-inflammatory pathway catalyzed by kynurenine 3-monooxygenase.

Results: PLWH had higher KTR than uninfected individuals (p-value < 0.001). In PLWH, increase in waist-to-hip ratio was associated with higher KTR (p-value 0.009), QA/KYNA ratio (p-value 0.006), markers of systemic inflammation (p-value < 0.001) and with lower KYNA concentration (p-value 0.019) (Table 1). Increase in QA/KYNA ratio was associated with higher hs-CRP (p-value < 0.001) and neopterin concentrations (p-value < 0.001) (Figure 1). In contrast, KYNA concentration was associated with lower hs-CRP (p-value 0.025) and neopterin concentrations (p-value 0.034) (Figure 1). Kyn metabolites were associated with lower concentrations of LDL and total cholesterol after controlling for confounders (Figure 2).

Change in % of outcome per 0.5 unit increase in waist-to-hip ratio

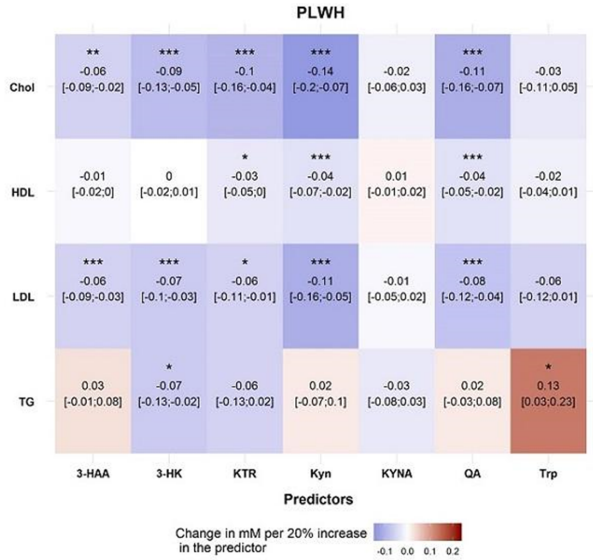
Outcome	Crude β-coefficient [95% CI]	p-value	Adjusted β-coefficient [95% CI]	p-value
KTR	31 [17; 46]	<0.001	19 [5; 37]	0.009
QA/KYNA	44 [22; 69]	<0.001	33 [8;66]	0.006
KYNA	11 [-21;42]	0.505	-18 [-31; -3]	0.019
QA	52 [30; 76]	<0.001	9 [-3; 34]	0.151
hs-CRP	431 [232; 749]	<0.001	232 [80; 504]	<0.001
Neopterin	19 [1; 37]	0.033	15 [-6; 40]	0.160

Abbreviations: PLWH, people living with HIV; KTR, kynurenine-to-tryptophan ratio; QA/KYNA, quinolinic acid-to-kynurenic acid ratio; QA, quinolinic acid; KYNA, kynurenic acid; hs-CRP, high sensitivity CRP. Confounders included in multivariable models were age, sex, smoking, origin, BMI, and Kyn (only when QA/KYNA, KYNA, and QA as dependent variables)



Association of KYNA, QA, and QA/KYNA ratio with markers of systemic inflammation in PLWH adjusting for age, sex, smoking, origin, BMI, WHR, Kyn

Conclusions: In PLWH, abdominal adipose tissue was associated with increased QA/KYNA ratio, suggesting activation of pro-inflammatory pathway of Kyn metabolism, with reduction of anti-inflammatory molecules, and increase of markers of systemic inflammation. Interestingly, Kyn metabolites concentrations were negatively associated with lipid levels. Taken together, our results suggest dysregulation of Kyn metabolism associated with abdominal adipose tissue accumulation to be a potential source of inflammation in HIV infection.



Change in lipids levels per 20% increase in KTR and kynurenine catabolites after adjusting for age, sex, smoking, BMI, and anti-dyslipidemia treatment

PE17/2

Integrase inhibitor negatively affects CD8 T-cell function

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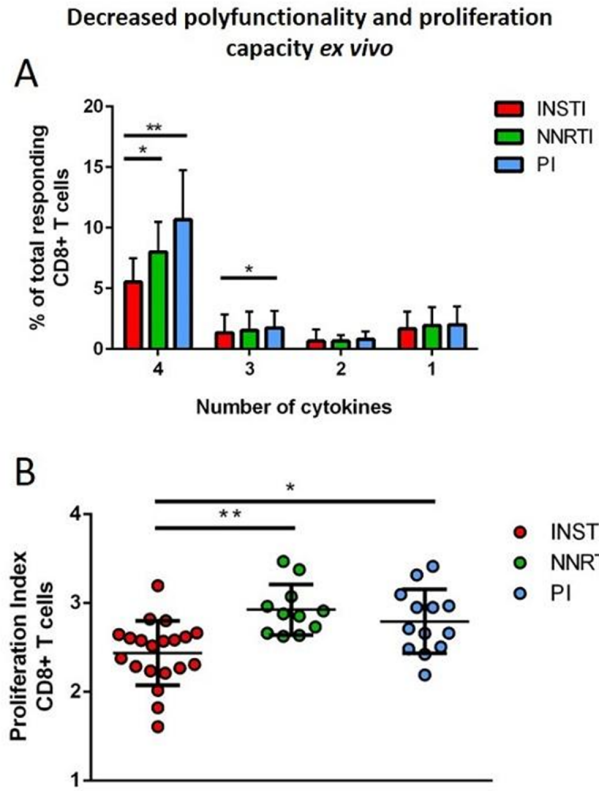
Purpose: Although HIV-specific CD8 T-cells are effective in controlling HIV-infection, they fail to clear infection even in the presence of antiretroviral therapy. Here, we describe a negative impact of ART on CD8 T-cell activity and function.

Method: We performed ex vivo proliferation assays and determined cytokine polyfunctionality of PBMCs from treated HIV+ individuals. We analyzed PBMCs from HIV+ and healthy individuals via FACS to determine functional properties of CD8 T-cells in the presence of ART drugs.

Results: We first assessed the cytokine polyfunctionality of CD8 T-cells from treated HIV+ individuals directly ex vivo and observed a decline in the multifunctional response of these cells in individuals treated with INSTI-based ART regimen compared to both PI- and NNRTI- ($p< 0.05$) based regimens. Given the reduced function, we next performed ex vivo proliferation studies and observed a significantly lower proliferation index of CD8 T-cells in individuals treated with INSTI (2.43 ± 0.36) compared to both PI ($p< 0.05$) and NNRTI ($p< 0.01$). We then co-cultured CD8 T-cells with different drugs individually and could observe reduced functional properties with significantly lower expression of IFNγ ($p< 0.01$), IL-2 ($p< 0.01$) and TNFα ($p< 0.01$) only after treatment with INSTI-based regimens. Furthermore, we determined whether this decreased cytokine expression also affects the new-synthesis and secretion of cytolytic molecules in presence of different ART regimens. Indeed, previously activated and INSTI-treated CD8 T-cells demonstrated reduced expression of perforin and granzyme B compared to PI and NNRTI ($p< 0.001$) treated cells. We next used a live cell imaging assay to determine the migratory capacity of CD8 T-cells. Only dolutegravir-treated cells showed less migration activity after SDF1α stimulation compared to NRTI regimens ($p< 0.05$).

Conclusion: Our data show that the choice of ART can have a significant impact on CD8 T-cell effector function and may have important implications for eradication strategies.

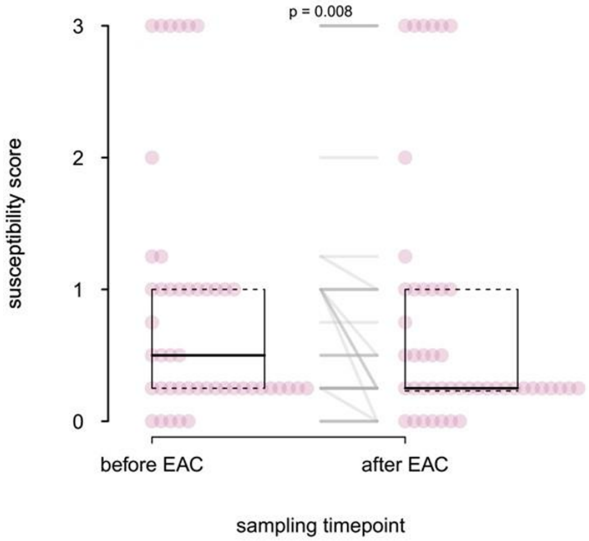
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Decreased polyfunctionality and proliferation capacity ex vivo

had a decreased score after the EAC period (*Figure*). Susceptibility was low already before EAC, with 59.6% of participants harbouring HIV-1 that was not fully susceptible to any of the drugs in their regimen.

Conclusion: Levels of HIVDR were high before starting EAC, indicating extensive time already spent on a failing regimen. A minority of participants acquired further HIVDR during the EAC period. The benefit of EAC in avoiding unnecessary regimen switches should be critically assessed against the risk of developing (additional) HIVDR.



Susceptibility scores (pink dots) before and after EAC in the study population (N = 47). Grey lines connect samples of the same individual. Box plots indicate the median (bold horizontal line) and the interquartile range (IQR; dashed horizontal line). P-value derived using sign test.

Figure

PE17/3

The evolution of HIV-1 drug resistance during the 3-month WHO-recommended enhanced adherence counselling period

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Purpose: Since HIV-1 drug resistance (HIVDR) testing is rarely available in resource-limited settings, the World Health Organization recommends that patients taking antiretroviral therapy (ART) with a viral load (VL) ≥1000c/mL undergo enhanced adherence counselling (EAC) and repeat VL testing three to six months thereafter. A second VL≥1000c/mL triggers switching to second-line ART. We aimed to assess the risk of further HIVDR acquisition during the EAC period.

Method: In the CART-1 study (NCT02126696) in Lesotho, 93 participants on ART with a VL ≥1000c/mL repeated VL testing after EAC. Seventeen (18.3%), 12 (12.9%) and 64 (68.8%) had a second VL of < 80, 80–999, and ≥1000c/mL. Paired plasma samples (before/after EAC) were available from 47 participants with sustained VL ≥1000c/mL, and were analysed for HIVDR in the consensus sequence using Illumina MiSeq next-generation sequencing and Minvar-v2.2. To calculate drug susceptibility scores, HIVDR according to Stanford HIVdb-v8.8, namely high-level, intermediate, low-level, potential low-level, and susceptible, were assigned values of 0.00, 0.25, 0.50, 0.75, and 1.00. The scores of each drug in a participant's three-drug regimen were added to an overall susceptibility score (range:0.00–3.00), with lower scores indicating lower susceptibility (higher resistance).

Results: Median susceptibility scores dropped significantly from 0.5 (IQR=[0.25,1]) before EAC to 0.25 (IQR=[0.25,1],p=0.008) after EAC. Forty individuals (85.1%) experienced no change in susceptibility, while 7 (14.9%)

PE17/4

Replication-competent HIV-1 reservoirs form in mucosal tissue macrophages of patients under antiretroviral therapy

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Purpose: HIV-1 eradication requires the elimination/reduction of the HIV-1-reservoir pool mainly characterized within T-cells. However, residual viremia in HIV-1-infected cART-suppressedindividuals originates from T-cells but also from macrophages that posses all required characteristics to form an additional long-lived HIV-1 reservoir. Hence, macrophages, initially targeted by HIV-1 upon genital mucosa infection, are tissues-resident cells that resist the cytopathic effects of HIV-1 infection, are long-lived, can self-renew, accumulate infectious virus in intracellular virus-containing compartments (VCC), and produce infectious virus upon stimulation *in-vitro*.

Methods: We used whole penile tissues from HIV-1-infected cART-suppressedindividuals with undetectable plasma viral load obtained upon transgender-surgery and searched by PCR, FISH and microscopy for HIV-1 DNA, RNA, p24 and intact virions. Tissue viral outgrowth was used to detect infectious reactivation-competent viruses.

Results: We show that urethral macrophages contain integrated HIV-1 DNA, RNA, proteins and intact virions in VCCs, whereas viral components remain undetectable in urethral T-cells. Moreover, urethral cells release replication-competent infectious HIV-1 following specific re-activation with the macrophage activator lipopolysaccharide (LPS), while the T-cell activator phytohaemagglutinin (PHA) is ineffective. HIV-1 urethral reservoirs localize preferentially in a newly identified subset of intermediate M1/M2 macrophages, highly expressing CD206, IL-1 and IL-4-receptors, but not CD163. Finally, macrophage reservoirs form longlasting conjugates with CD8+T-cells resisting killing suggestive of a mechanism of enhanced inflammation that participates in reservoir persistence.

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Conclusions: Altogether, we demonstrate that tissue-macropahges establish replication-competent reservoir in cART-supressed patients, thereby challenging the dogma that HIV-1-reservoirs principally reside in T-cells. As the molecular and cellular characteristics of HIV-1-reservoir in tissue-macrophages differ from that in T-cell, we anticipated that reservoir dynamic and eradication strategies in this two cell types will diverge.Systematic investigation of the presence of HIV1–reservoirs in other human tissues is now clearly necessary, especially for shock and kill strategies aimed at reservoir elimination.

PE17/5

Skin tissue resident memory T cells (T_{RMs}) are depleted in HIV infection and reconstituted by an early begin of ART

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Purpose: PLWHIV have increased risk of skin and mucosal cancer, like HPV-related neoplasia, despite of ART. T_{RMs} are abundant in the skin and widely recognized for their anticancer role in peripheral tissues. Our project aims at investigating the effect of HIV infection on the skin T_{RMs}.
Method: We collected skin biopsies from individuals of two cohorts: (1) patients with a long history of HIV and a late begin of cART, currently under therapy; (2) recently diagnosed patients who received ART and were re-biopsied one year after infection. We quantified T_{RMs} via immunofluorescent staining and automated *in situ* analysis (Tissue-FAXS). We performed DNA And RNA-Scope on the skin of HIV+ patients and SIV chronically infected untreated macaques.
Results: Skin T_{RMs} were strongly depleted in both human cohorts, indicating that the depletion happens early in the course of HIV infection. The number of T_{RMs} correlated with the *nadir*, suggesting that skin T_{RMs} are lost in advanced HIV disease and never reconstituted. Surprisingly, our most recent results show that if ART is started early, the skin TRMs population is reconstituted one year after ART begin. Moreover, we could recently detect HIV-DNA by DNA-Scope in the cells of the papillary dermis of patients with a long history of HIV. Finally, skin of SIV chronically infected macaques showed the presence of SIV RNA and DNA in the cells of the papillary dermis.
Conclusion: Skin T_{RMs} are severely depleted upon HIV infection but can be properly reconstituted if ART is started early. Our DNA and RNA-Scope staining in untreated macaques suggest a direct depletion of skin T cells by SIV. The fact that we could detect a few HIV+ cells via DNA-Scope in the skin of PLWHIV under ART, suggests that the cells of the papillary dermis might represent an underestimated reservoir for HIV.

PE17/6

Baseline and emergent genotypic and phenotypic results in HIV-1-infected, heavily treatment-experienced (HTE) participants meeting protocol-defined virologic failure (PDVF) criteria through week 96 in the fostemsavir (FTR) phase 3 BRIGHTE study

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Purpose: FTR is a prodrug of temsavir (TMR), a first-in-class, investigational attachment inhibitor that binds to HIV-1 gp120, preventing viral attachment and entry into host CD4+ T-cells. Here, we present Baseline and emergent virologic results among participants experiencing PDVF through 96-weeks of FTR-based therapy.
Method: BRIGHTE is a Phase 3 trial evaluating FTR in HTE patients with multidrug resistant HIV-1. Participants were assigned to the Randomized (RC; 1–2 ARV classes remaining) or Non-randomized Cohort (Non-RC; zero classes remaining). Glycoprotein (gp)-120 substitutions that potentially influence susceptibility to TMR include: S375H/I/M/N/T, M426L/P, M434I/K, M475I.
Results: Overall, 45% (162/358) of participants had relevant gp120 substitution(s) at Baseline, and median TMR IC50FC was 0.99-fold from reference. Through WK96, 23% (63/272) of RC and 49% (49/99) Non-RC participants met PDVF criteria. Rates of PDVF among RC participants were

	Randomized Cohort FTR 600mg BID		Non-Randomized Cohort FTR 600mg BID	
Baseline Disease Characteristics	Total (N=272)	PDVF[a] (N=63)	Total (N=99)	PDVF[a] (N=49)
Median Baseline HIV-1 RNA (log10 c/mL) Median Baseline CD4+ (cells/mm^3)	4.66 99.5	4.86 60	4.31 41	4.53 19
Baseline Genotypic Substitutions of Interest[b], n (%)	Total (N=263)[c]	PDVF n/n (%)	Total (N=95)[c]	PDVF n/n (%)
Participants WITHOUT gp120 Substitutions of Interest Present at Baseline	141 (54)	31/141 (22)	55 (58)	26/55 (47)
Participants WITH gp120 Substitutions of Interest Present at Baseline	122 (46)	31/122 (25)	40 (42)	21/40 (53)
S375H/I/M/N/T M426L/P M434I/K M475I	86 (33) 32 (12) 17 (6) 3 (1)	21/86 (24) 11/32 (34) 4/17 (24) 0	25 (26) 14 (15) 2 (2) 1 (1)	12/25 (48) 8/14 (57) 0 1/1 (100)
Baseline Temsavir IC50 Fold Change[d] Summary Statistics	Total (N=263)[c]	PDVF (N=62)[c]	Total (N=96)[c]	PDVF (N=48)[c]
Geom. Mean Median Min. Max.	2.70 0.99 0.05 6651.28	4.12 1.38 0.11 6651.29	2.37 0.94 0.04 9398.14	4.36 1.49 0.14 9398.15
Baseline Temsavir IC50 Fold Change[d] Category, n (%)	Total (N=263)[c]	PDVF n/n (%)	Total (N=96)[c]	PDVF n/n (%)
≤1-fold >1-10-fold >10-100-fold >100-1000-fold >1000-fold	132 (50) 63 (24) 34 (13) 16 (6) 18 (7)	29/132 (22) 14/63 (22) 9/34 (26) 4/16 (25) 6/18 (33)	49 (51) 26 (27) 9 (9) 7 (7) 5 (5)	22/49 (45) 12/26 (46) 4/9 (44) 6/7 (86) 4/5 (80)

a. PDVF was defined as: Before Week 24: confirmed or last available prior to discontinuation HIV-1 RNA ≥400 c/mL following confirmed suppression to <400 c/mL, or >1 log10 increase in HIV-1 RNA above nadir where nadir is ≥40 c/mL; On or after Week 24: confirmed or last available prior to discontinuation HIV-1 RNA of ≥400 c/mL.
b. Includes only gp120 substitutions of interest: S375H/I/M/N/T, M426L/P, M434I/K, and M475I. M426P and M434K were not present in this study population at Baseline.
c. Number of evaluable participants.
d. IC50FC is FC compared to a reference virus that has an IC50 of approximately 1 nM in the Monogram PhenoSense Entry assay.

Table 1. Key Baseline Characteristics

n (%)	Randomized Cohort FTR 600mg BID plus OBT[a] (N=272)	Non-Randomized Cohort FTR 600mg BID plus OBT[a] (N=99)
Participants meeting PDVF	63 (23)	49 (49)
Participants with HIV-1 RNA <40 c/mL after meeting PDVF	17/63 (27)	5/49 (10)
Emergent Genotypic Substitutions of Interest[b] at Failure[c]	Randomized Cohort (n=50)[d]	Non-Randomized Cohort (n=44)[d]
Participants WITHOUT Emergent gp120 Substitutions of Interest	26 (52)	11 (25)
Participants WITH Emergent gp120 Substitutions of Interest[e]	24 (48)	33 (75)
S375H/I/M/N/T M426L/P M434I/K M475I	15 (30) 16 (32) 5 (10) 6 (12)	22 (50) 21 (48) 4 (9) 5 (11)
TMR IC50 FC at Failure[c]		
Median Change in Baseline TMR IC50 FC	1.7-fold (n=53)[d]	470-fold (n=45)[d]
Participants WITHOUT Emergent gp120 Substitutions of Interest	0.9-fold (n=26)	0.7-fold (n=11)
Participants WITH Emergent gp120 Substitutions of Interest[e]	511-fold (n=24)	2260-fold (n=32)
TMR IC50 FC Categories at Failure[c]	(n=51)[d]	(n=44)[d]
≤1-fold >1-10-fold >10-100-fold >100-1000-fold >1000-fold	15 (29) 4 (8) 6 (12) 9 (18) 17 (33)	2 (5) 4 (9) 3 (7) 8 (18) 27 (61)

a. OBT, optimized background therapy
b. Includes only gp120 substitutions of interest: S375H/I/M/N/T, M426L/P, M434I/K, and M475I. M426P and M434K were not present in this study population at Baseline.
c. On-treatment resistance testing data is shown at the time of confirmed VF where available, or the time of suspect VF or a time point nearest, but subsequent, to the VF time point.
d. Number of evaluable participants.
e. Most frequent emergent substitutions were M426L (RC 16/50,32%; Non-RC 21/44, 48%) and S375N (RC 13/50, 26%; Non-RC 17/44, 39%), including mixtures.

Table 2. Treatment-Emergent Genotypic and Phenotypic Changes to TMR Among Participants Meeting PDVF

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comparable regardless of Baseline virologic factors: 22% (31/141) without vs. 25% (31/122) with relevant gp120 substitutions, and 22% (29/132) with IC50FC ≤1-fold vs. 29% (10/34) with TMR IC50FC >100-fold (Table 1). 52% (26/50) of RC and 25% (11/44) Non-RC participants with PDVF had no treatment-emergent gp120 substitutions of interest, among whom median change in Baseline TMR IC50FC was < 1-fold. Median increase in IC50FC in participants with emergent gp120 substitutions at failure was 511-fold for RC and 2,260-fold for Non-RC (Table 2).
Conclusion: Through WK96, PDVF in RC participants was comparable to previous ARV trials conducted in similar populations. Pre-treatment gp120 substitutions of interest and TMR IC50FC were not reliably predictive of PDVF among RC participants. Non-RC participants, with zero fully active ARVs, experienced higher rates of PDVF, emergent gp120 substitutions of interest, and greater median increase in Baseline TMR IC50FC. Overall, emergent gp120 substitutions of interest correlated with higher median increase in TMR IC50FC. A clinical cut-off for FTR has not yet been determined.

Moderated ePosters II: clinical science

PE18/1

Are women living with HIV in increased risk of complications to birth when planning elective caesarean section? A Danish nation wide population based study

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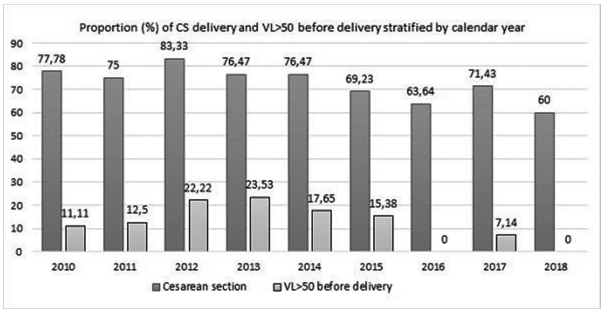
Objectives: Regardless of viral suppression two-thirds of women living with HIV (WLWH) in Denmark deliver by caesarean section (CS) and half of the elective CS (ECS) are performed due to mothers request. The aim of the study was to investigate if planning ECS increases risk of obstetric complications compared to planning vaginal delivery in WLWH.
Method: Retrospectively, all WLWH in Denmark giving birth to live born singletons from 2002–2014 were included. Data was retrieved from medical records and national registries. The risk of obstetric complications comparing planning ECS to vaginal birth was estimated through multivariate logistic regression adjusted for mode of delivery, viral load, year of birth and maternal age.
Results: 389 WLWH were included. All were in antiretroviral treatment at delivery, 86% had HIV-RNA < 40copies/mL and 21% had previously had a CS. No MTCT was seen. During pregnancy and in collaboration with a gynaecologist 50.4% planned ECS, 44% without medical indication.
Children born by WLWH planning vaginal delivery did not have increased risk of low APGAR-scores (<7)(3% vs. 2%, aOR 1.7, 95% CI 0.1–22.7, p=0.68) or prolonged hospitalization (>3 days)(31% vs. 52%, aOR 1.9 95% CI 0.8–4.3, p=0.12) compared to children born by WLWH planning ECS. No differences between groups were observed regarding postpartum bleeding (38% vs. 20%, aOR 0.6, 95% CI 0.2–1.6, p=0.29), infections (2% vs. 3%, aOR 1.5, 95% CI 0.2–14.6, p=0.72) or prolonged maternal hospitalization (>3 days) (37% vs. 69%, aOR 1.6, 95% CI 0.7–3.4, p=0.26). WLWH planning ECS had lower risk of emergency CS (32% vs. 20%, aOR 0.5, 95% CI 0.29–0.85, p=0.01) compared to WLWH planning vaginal delivery.
Conclusion: To a high extent WLWH still plan to give birth by ECS without medical indication. No increased risk of most obstetric complications was however seen when comparing WLWH planning vaginal delivery to planning ECS. Overall WLWH can safely plan a vaginal delivery.

PE18/2

Cesarean section is still the most common mode of delivery among HIV-positive women in Central Poland

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Background: In the context of effective ART and viral suppression (VS) it is expected that cesarean section (CS) would be less common mode of delivery for HIV-positive pregnant women. At the same time the proportion of CS deliveries in general Polish population increased from 19.6% in 2000 to 42.2 % in 2014 (Euro-Persista). Here we investigate the trends over time in CS among HIV-positive women under integrated gynecological care in Warsaw.
Methods: We reviewed medical records of all pregnancies in 2006–2017. We compared indications for mode of delivery as identified by HIV clinic's gynecologist (HCG) and the final delivery mode (FDM). In statistical analyses we used kappa agreements and non-parametric tests as appropriate.
Results: Of 112 births with known mode of delivery (70.9% of all pregnancies) 103 were with known indication for mode of delivery. 70 (62.5%) mothers were on cART before pregnancy, 6 (5.3%) started after 28th week of pregnancy, 96 (85.7%) had VS before delivery. In total 83 (74.1%) of deliveries were by CS, but HCG indicated the need for CS in 58 (51.8%). The proportion of CS deliveries did not vary over the calendar years (p=0.969). The proportion of women with HIV RNA>50 copies/mL varied from maximum of 23.5% in 2013 to zero in 2016 and 2018 (0.689), figure. In 77 (68.7%) cases of CS indication by HCG and FDM agreed (kappa agreement of 0.49 [CI 0.32–0.66]). Of 20 cases of CS performed contrary to HCG recommendation 18 were explained by gynecological/obstetrical indication.
Conclusions: Despite most women being on ARV before pregnancy and predominant VS before delivery CS remains the most common mode of delivery among HIV-positive pregnant women. This was could be explained by obstetrical indications and reflects the trends in overusing and liberalization of indications for CS in general Polish population.



Figure

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PE18/3

The Swiss Mother and Child HIV Cohort Study (MoCHiV), a unique opportunity to monitor and adapt measures to prevent HIV mother to child transmission

A Brunner[1], A Scherrer[2,3], A Traytel[2,3], C Kahlert[4,5], K Aebi-Popp[6], E Bernasconi[7], P-A Crisinel[8], A Duppenthaler[9], H Guenthard[2,3], B Martinez de Tejada[10], P Paioni[11], M Stoeckle[12], N Wagner[13], I Hoesli[1], C Rudin[14] and and the Swiss HIV Cohort Study (SHCS) and the Swiss Mother and Child HIV Cohort Study (MoCHiV)

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Background: The Swiss Mother and Child HIV Cohort Study (MoCHiV) is an on-going multicenter, interdisciplinary and prospective observational cohort study, providing longitudinal data on HIV-infected mothers and children in Switzerland. Here we describe the study's coverage of changes in recommendations for the prevention of HIV mother-to-child transmission (MTCT) and assess these changes on patients data.

Methods: We evaluated data from MoCHiV and the linked Swiss HIV Cohort Study (SHCS) database and describe changes at different time points when recommendations were changed.

Results: The study includes a total of 1248 mother-and-child pairs, 281 HIV-infected children and 1571 HIV-exposed uninfected (HEU) children. The most common mode of acquisition of maternal HIV-infection was heterosexual (77%). In 2016, 42 deliveries were registered and all of them received combined antiretroviral therapy (cART) during pregnancy and 40 (95%) had a non-detectable HIV plasma viral-load (pVL) at time of delivery. 36% of children were born by vaginal delivery, 45% by elective cesarean-section and 19% by secondary cesarean section. Since 2009 when vaginal delivery in women with undetectable pVL was recommended, the rate in elective cesarean section has steadily decreased *(Figure 1)*. MTCT also has decreased continuously to less than 1% due to the increasing suppression of HIV pVL (*Figure 2+3)*. Recently, neonatal post-exposure-prophylaxis has been discontinued in children born to HIV-infected mothers with fully suppressed HIV pVL in the last trimester. In 2018 new recommendations on breastfeeding were published in Switzerland.

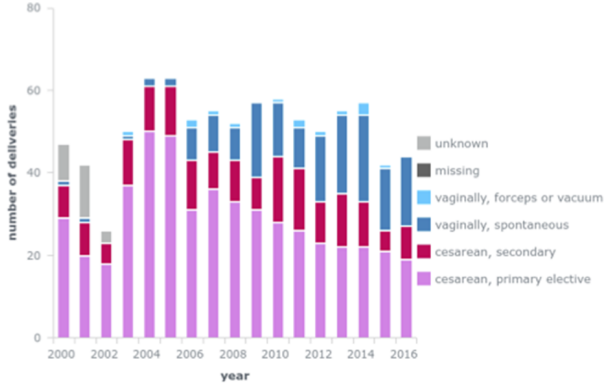


Figure 1. Mode of delivery in HIV-infected women 2000–2016

Conclusion: The MoCHiV study offers a unique longitudinal data-collection and contributes to national and international HIV research and to changing recommendations. Thanks to the very high effectiveness of maternal treatment, any other preventive measure, including treatment of the newborn, could be abandoned, when mother HIV pVL is undetectable at birth.

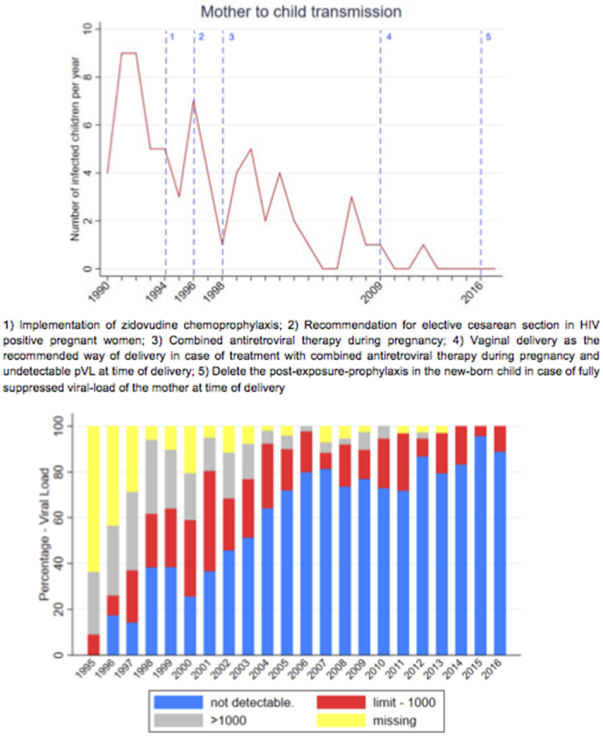


Figure 2/3. MTCT and changes of Swiss guidelines/Changes of pVL over time

PE18/4

Influence of HCV co-infection and hepatitis C treatment on risk of chronic kidney disease in HIV positive persons

L Peters[1], L Ryom[1], C Oprea[2], Q Li[3], A Rauch[4], C Boesecke[5], V Uzdaviniene[6], D Sedlacek[7], J Llibre[8], K Lacombe[9], L Nielsen[10], E Florence[11], I Aho[12], N Chkhartishvili[13], J Szlavik[14], G Dragovic[15], C Leen[16], H Sambatakou[17], T Staub[18], M Laguno[19], H Elinav[20], J Tomažič[21] and A Mocroft[3]

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Purpose: HCV infection has been associated with increased risk of chronic kidney disease (CKD). We investigated the impact of HCV cure

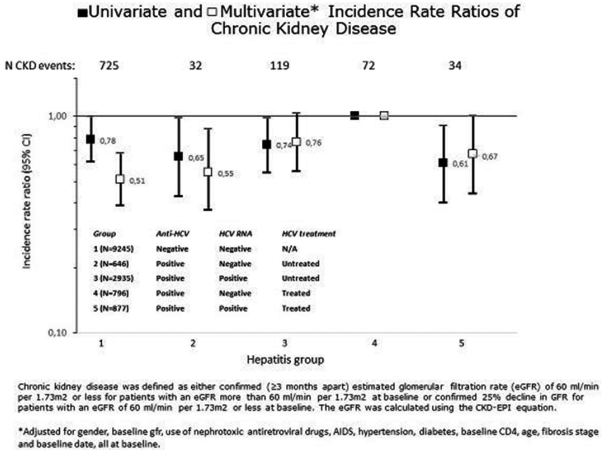
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on the risk of CKD in HIV/HCV co-infected individuals in the EuroSIDA study.

Method: HIV-positive persons with known HCV status and ≥3 serum creatinine measurements after 1/1/2004 were included in five groups based on time-updated HCV-RNA and use of HCV treatment: 1) HCV-uninfected 2) spontaneously resolved HCV, 3) Chronic untreated HCV, 4) Successfully treated HCV, 5) HCV-RNA positive after starting HCV treatment. Poisson regression was used to compare incidence rates of CKD between HCV groups.

Results: We included a total of 14,499 HIV-positive persons; 5254 (36.2%) were anti-HCV positive at baseline. The majority were male (74%), White (85%), and on cART (88%) with a median age of 43 years and CD4 cell count of 467 cells/μL. During 104816 person-years of follow-up (PYFU); median 6.6 (IQR 3.0–11.6) per person, 982 (6.8%) developed CKD; crude incidence rate/ 1000 PYFU (95% CI) was 9.4 (8.8–10.0). After adjustment, all groups had lower rates of CKD compared to group 4, although this was marginally significant for groups 3 and 5 (Figure). Analysis in those without F3/F4 fibrosis showed similar results. Excluding persons treated with DAA-only therapy in groups 4 and 5 attenuated the differences in CKD incidence between group 3–5. After adjustment, compared to group 4, group 3 had a 5% decreased incidence of CKD (aIRR 0.95; 95% CI 0.65–1.38) and a 16% reduced incidence in group 5 (aIRR 0.84; 95% CI 0.52–1.36).

Conclusion: This large study of >5000 HIV/HCV co-infected persons found no evidence that successful HCV treatment reduced the incidence of CKD. Confounding by indication, where those with highest risk of CKD were prioritized for HCV treatment, especially in the DAA era, may contribute to these findings.



Univariate and Multivariate Incidence Rate Ratios of Chronic Kidney Disease

PE18/5

The hepatitis C continuum of care among HIV-infected individuals in Austria

M Rappold[1], M Gisinger[2], D Chromy[3], B Schmied[4], A Öllinger[5], E Wallner[6], A Zoufaly[7], A Egle[8], M Kanatschnig[9], R Zangerle[2] and for the AHIVCOS Group

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Purpose: The use of DAAs in the Austrian HIV Cohort Study was strongly associated with clinics providing DAAs directly compared to clinics who have to refer patients to hepatologists (Fig. 1). Here, we evaluated whether this difference diminished 18 months later.

Method: Patients seen after 2013 were studied up to March 2019. Stages of the continuum included patients HCV-antibody tested, anti-HCV positive, HCV-RNA tested, ever HCV-RNA positive, remaining HCV-RNA positive without therapy, treatment, the composite of ongoing therapy and sustained virologic response (SVR), and SVR alone. Reinfections were thus captured and taken as failing SVR. Multivariable logistic regression models were performed to identify factors associated with DAA use.

Results: Among 6152 HIV positive patients, HCV antibody test was not performed in 360(5.9%) and 1223(19.9%) had a positive antibody test, of whom 1208(98.8%) were HCV-RNA tested and 975(79.7%) were ever HCV-RNA positive (55.6% with genotype 1 and 23.9% with GT3). Among the 821 individuals that remained HCV-RNA positive, 606(73.8%) individuals initiated HCV treatment, 403(66.5%) received DAAs without interferon and 203(33.5%) interferon based regimens. The composite endpoint of ongoing therapy and SVR occurred in 579(70.5%) patients and 547(66.6%) achieved SVR (Fig. 2). Significant differences between HIV clinics, according to providing DAAs directly or not were found for all treatment related stages. DAA use was strongly associated with clinics providing DAAs (OR 3.89; 2.55–5.93) and with older age (<30 OR 0.18; 0.08–0.39; 30–50 OR 0.35; 0.24–0.51) compared to being 50 years of age or older, but was not associated with transmission category, sex, origin and HCV genotype.

Conclusion: Despite being "en route" to eliminate HCV from HIV/HCV co-infected individuals, there is still a difference in access to DAA use. To improve and hasten this process a "no matter who provides HCV therapy" strategy is warranted.

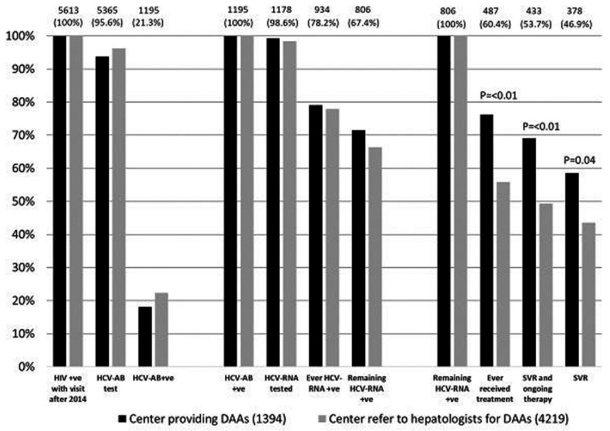


Figure 1. HCV Continuum of Care September 1st 2017

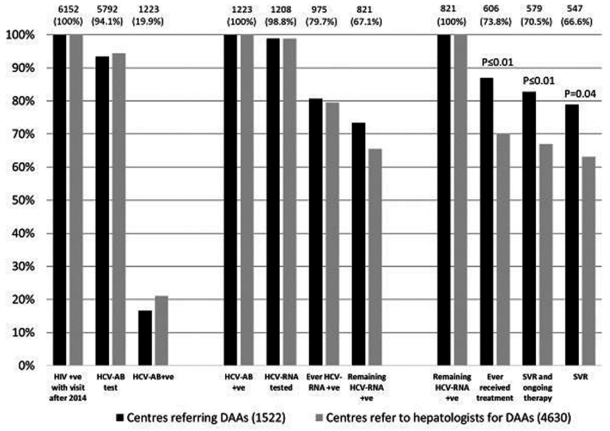


Figure 2. HCV Continuum of Care March 1st 2019

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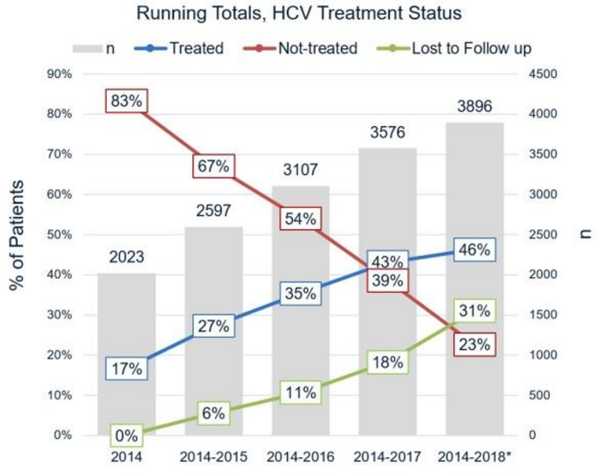
PE19/1

Untreated HCV in HIV/HCV-coinfected US population remains common despite the availability of curative therapies

R Elion[1], K Althoff[2], J Eron[3], J Gillman[4], R Haubrich[5], G Huhn[6], S Milligan[7], A Mills[8], K Mounzer[9,10], G Moyle[11], J Radtchenko[7], S Santiago[12], P Sax[13,14] and D Jayaweera[15]

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Purpose: To determine the HIV/HCV population never treated for HCV since the availability of direct-acting antivirals (DAAs) in a US network of HIV treatment centers.
Method: We collected EMR data specific to coinfected patients in care between 1 Jan 2014 to 31 Oct 2018 from 10 HIV treating clinics in the US. Index date was set as the latter of confirmed coinfection or 1 Jan 2014. Patients were classified as "treated", "lost to follow up (LTFU)" (no evidence of treatment or cure and no longer in care at practice), or "untreated" (no evidence of treatment or cure, in care with detectable HCV).
Results: Of 3,896 patients, 1,479 were diagnosed as HIV/HCV-coinfected prior to 2014 and the remaining 2,417 were new cases. Median (IQR) follow was 32.2 (10.1–52.2) months. At the end of the observation period, 882 (23%) patients remained untreated, 1,210 (31%) LTFU, and 1,804 (46%) treated. [FIGURE] Median (IQR) follow for untreated patients was 40.9 (11.3–54.1) months. For patients classified as LTFU, median (IQR) time from index to date of last care was 10.2 (1.8–27.9) months with observation of 39.0 (23.5–54.2) months. For treated patients, median (IQR) time from index to treatment was 14.2 (3.9–28.5) months.
Conclusion: Despite the availability of highly effective HCV therapies, in this cohort of HIV/HCV-coinfected patients, less than half had evidence of receiving treatment. Given the more rapid progression of liver disease among people with coinfection, better strategies are needed to optimize patient engagement and provide timely HCV treatment to this population.



HIV/HCV patients by HCV Treatment Status, 2014 to 2018

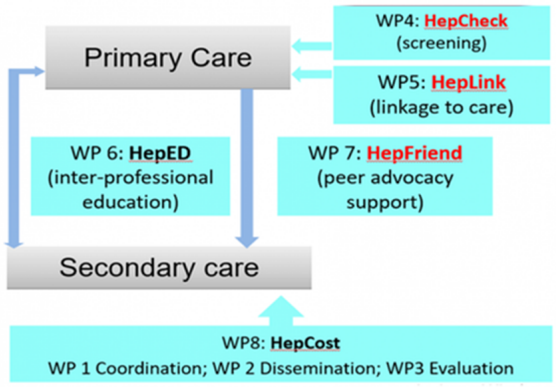
PE19/2

HepCare Europe – a model of integrated care in Romanian HCV/HIV co-infected patients from key populations

C Oprea[1,2], I Ianache[1], S Lazar[1,2], I Popa[1], A Kosa[1], A Luca[1], I Petre[3], S Florescu[1,2] and E Ceausu[1,2]

[1]Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Bucharest, Romania [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania [3]Carusel, Bucharest, Romania

Purpose: HepCare Europe, a project co-funded by the European Commission, aims to improve access to HCV screening, diagnosis and treatment in patients from key populations, through outreach to the community and integration of primary and secondary care services.(Figure) The objective of our study was to evaluate the implementation of HepCare model at Victor Babes Clinical site, Bucharest (SVB)
Method: Prospective study on HIV/HCV co-infected and HCV mono-infected patients from key populations enrolled in Hepcare at SVB between April 2016 and April 2019. Statistical analysis was performed using SPSS vs. 20.0.
Results: Out of 525 persons screened with rapid oral tests for HCV (HepCheck), 230 (43.8%) had positive HCV antibodies and 73.0% (168/230) were linked-to-care (HepLink). The majority were males (85.7%), injecting drug users (IDUs) (92.2%), with a median age of 35 years (IQR 30, 39). Advanced fibrosis (METAVIR >9 kPa) was diagnosed by Fibroscan in 27.5% of those evaluated (82.1%) and HCV-RNA was detectable in 81.1%. There were significant differences in risk factors between HCV/HIV co-infected and HCV mono-infected patients (Table). Median CD4 cell count/μL and HIV-RNA (log10copies/mL) were 483 (IQR 290, 646) and 2.74 (IQR 1.27, 4.67), respectively, only 35.7% having undetectable HIV viral load. DAA was initiated in 24 IDUs, 22 achieving SVR and 2 were non-responders (genotype 3). Within



HepCare Europe Project - Work Packages

Characteristics in patients from key populations linked to care– comparison between HIV/HCV and HCV mono-infected patients

		Total n=168	HIV-positive n=70	HIV-negative n=98	p value
Homeless	n (%)	61 (36.3)	37 (52.8)	24 (24.4)	<0.0001
Imprisonment	n (%)	89 (52.9)	42 (60.0)	47 (47.9)	0.83
Opioid substitution treatment	n (%)	85 (50.5)	32 (45.7)	53 (54.0)	1.81
Injecting drug use	n (%)	155 (92.2)	70 (100)	85 (86.7)	0.001
Sharing needles	n (%)	82 (48.8)	51 (72.8)	31 (31.6)	<0.0001
Type of drug Heroin New psychoactive stimulants Mixed abuse	n (%)	30 (17.8) 57 (33.9) 73 (43.3)	7 (10.0) 16 (22.8) 51 (72.8)	24 (24.4) 42 (42.8) 24 (24.4)	<0.0001
Alcohol abuse	n (%)	67 (39.8)	41 (58.5)	26 (26.5)	<0.0001
Fibrosis stage (METAVIR score)	Median (IQR)	7.0 (5.4, 9.3)	7.0 (6.0, 9.5)	7.0 (5.3, 9.3)	0.372
HCV-RNA (log10UI/L)	Median (IQR)	6.11 (5.48, 6.52)	6.30 (5.77, 6.66)	5.50 (5.16, 5.88)	0.047

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HepEd, 241 HCPs were trained on HCV management during 3 educational HCV Masterclasses. HCV informative flyers and booklets were created and disseminated to patients and peers. Peer support sessions (HepFriend) were successfully attended by 64 (38%) patients.
Conclusion: HIV/HCV co-infection was high among IDUs and associated with multiple risk factors and increased HCV-RNA levels. Socio-economic barriers and the lack of pangenotypic DAAs limited the treatment and outcomes in this group. This is the first pilot study on managing patients with HIV/HCV from key population in Romania.

PE19/3

Prélib: evaluating a newly launched Canadian provider of innovative internet-based services for self-directed HIV and STI screening

M Regimbal-Ethier[1,2], K Benomar[1,2], V To[2] and M Quesnel[2]
[1]Prelib, Montreal, Canada [2]Clinique Medicale Quorum, Montreal, Canada

Purpose: Technology-enabled STI screening paradigms are promising for addressing barriers to testing uptake, yet few such services exist. Prélib, a new clinic in downtown Montréal, aims to provide accessible, convenient, and judgement-free screening by innovatively combining internet-based risk assessment with on-site self-sampling. Being one of the first of its kind, Prélib offers a unique opportunity to evaluate the uptake, feasibility, and acceptability of this model.
Method: Prélib offers Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), syphilis, hepatitis B (HBV), hepatitis C (HCV), and HIV screening to people age >15 years according to local guidelines. Uptake, feasibility and acceptability were assessed based on rates of completing online profile, questionnaire, payment and appointment scheduling, and on-site self-sampling steps and HIV/STI prevalence. Sign-in and sampling are self-directed with video instruction, except blood draws performed by a nurse. Results and follow-up instructions (except positive syphilis, HBV, HCV, and HIV results) are communicated securely online. Observational data span from December 1, 2018 (launch) to May 8, 2019. Outcomes and client characteristics were summarized using descriptive statistics.
Results: Prélib registered 708 profiles within 5 months post-launch, 66.5% of whom attended appointment (Table 1). Completion rates for each step were >75% (lowest was observed for payment/scheduling).

Table 1. Summary of screening completion rates

Step of screening process	N	% of previous	% overall
Created profile	708	100%	100%
Completed questionnaire	664	93.8%	93.8%
Scheduled appointment (all)	502	75.6%	70.9%
Scheduled appointment within study period	492	n/a	69.5%
Attended an appointment	471	95.7%	66.5%

Table 2. HIV and STI prevalence among those tested with results available during the study period

	N/N tested	Prevalence (%)		N/N tested	Prevalence (%)
Any HIV/STI	29/443	6.5%	NG (any extragenital)	11/113	9.7%
CT (any)	16/443	3.6%	NG (anal swab)	1/106	0.9%
CT (urogenital)	11/442	2.5%	NG (oral swab)	10/112	8.9%
CT (anal swab)	7/106	6.6%	Syphilis	4/430	0.9%
NG (any)	12/442	2.7%	HBV	1/213	0.5%
NG (urogenital)	3/441	0.7%	HCV (anti-HCV)	0/121	0%
			HIV	0/425	0%

Among 471 appointment attendees, mean number of partners in the past 2 months was 2.6[median=2], 25.5% were men who have sex with men, 74.1% reported condomless anal or vaginal sex, and 23.6% reported first-time screening. STI prevalence was 6.5%, driven by NG and CT (Table 2). Extragenital NG and CT were most prevalent. No HIV or HCV infections were identified.
Conclusion: Prélib demonstrated feasibility and acceptability following launch, based on high screening completion rates and STI prevalence comparable to local clinical practice, and reached many high-risk and first-time testers.

PE19/4

Employment of people living with HIV approaching that of the HIV-negative population irrespective of migrant status and sexual orientation

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[1]Karolinska Institutet, Department of Medicine Huddinge, Stockholm, Sweden [2]Uppsala University, Centre for Clinical Research Västmanland, Västerås, Sweden [3]Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden

Purpose: To assess employment in the Swedish HIV cohort over twenty years compared to the HIV-negative population (HNP).
Method: From the Swedish Total Population Registry we identified all people born between 1940 and 2000 (n=8 587 629) in Sweden and linked them with the Swedish National HIV Registry (n=9 492) and the Longitudinal Integration Database for Health Insurance and Labor Market Studies. Prevalence ratios (PR) of employment were calculated using Poisson regression. Predictors of employment (age, sex, education, origin and civil status) were adjusted for (adjPR). For people living with HIV (PLWH) we adjusted for CD4 count, suppressive antiretroviral therapy (ART) (HIV-RNA <50 [<500 before 2004] copies/mL) and mode of HIV-transmission. Trends in employment were illustrated in scatterplots with overlaid prediction plots.
Results: PLWH were less likely to be employed than HNP but with decreasing difference over time (adjPR 0.6, 95% CI 0.6–0.6 in 1996, adjPR 0.7, 95% CI 0.7–0.7 in 2006 and adjPR 0.9, 95% CI 0.9–0.9 in 2016) (Fig. 1). Migrant women with HIV had the largest increase of employment (Fig. 2) and the negative association between migrant status and employment decreased between 1996 (adjPR 0.7, 95% CI: 0.6–0.9) and 2016 (adjPR 0.9, 95% CI 0.9–1.0). Suppressive ART associated with employment 2006 (adjPR 1.2, 95% CI 1.1–1.3) and 2016 (adjPR 1.3, 95% CI 1.2–1.4)) but not in 1996 (adjPR 1.1, 95% CI 0.9–1.2). Low CD4 count (<200) associated with reduced employment (adjPR 0.7, 95% CI 0.6–0.8). Employment of PLWH with present/former intravenous drug use (IVDU) was persistently low (Fig 2).

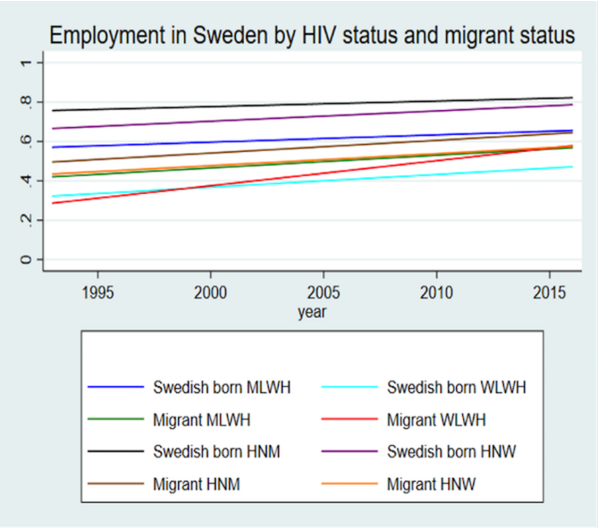


Figure 1. MLWH: men living with HIV, WLWH: women living with HIV, HNM: HIV-neg men, HNW: HIV-neg women

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Conclusion: To our knowledge, this is the first study of employment in PLWH including a whole nation. Employment of PLWH increased over time, particularly in migrants, and was associated with suppressive ART and high CD4 count.People with former IVDU are an important target group for policies promoting employment.

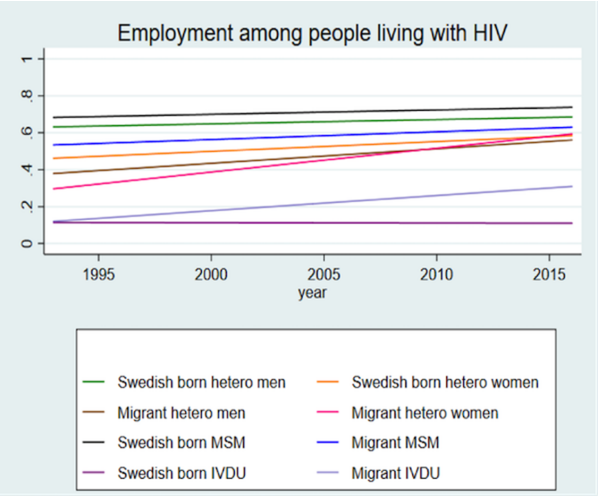


Figure 2. Employment in PLWH. MSM: men who have sex with men, IVDU: former/present intravenous drug use

PE19/5

Retention in care and virological suppression in naïve HIV-infected transgender women initiating treatment in Argentina: 48-week results (TRANSViiV study)

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Purpose: Prevalence of HIV infection in transgender women (TGW) in Argentina is 34%. Stigma and discrimination in the health sector hinder access and retention. We aimed to evaluate retention in care and antiviral efficacy among naïve TGW initiating first-line therapy in a trans-sensitive HIV service. ClinicalTrials.gov Identifier NCT03033836.
Method: Naïve TGW without NRTI resistance (IAS-USA) with any value of plasma viral load HIV-1 (pVL) initiated dolutegravir 50 mg plus tenofovir/emtricitabine QD, and were followed at weeks 4, 8, 12, 24, 36 and 48. Psychosocial questionnaires and adherence were administered at admission, weeks 24 and 48. The trans-sensitive HIV service included a multidisciplinary team. Retention (primary outcome) was defined as the proportion of individuals retained along the 48 weeks of the study. Viral suppression at <50 copies/mL was evaluated using snapshot algorithm and as per protocol analysis.
Results: 61 out of 75 TGWs screened were enrolled. Characteristics at baseline (median): age 28 years, HIV-1 RNA 46,908 copies/mL (40% >100,000 copies/mL,). CD4+ T-cell count 383 cells/mm^3 (19% <200).
At week 48, 77% were retained, and 72% had pVL HIV <50 copies/mL (97% per-protocol). 48-weeks median adherence was 86.3%. Fourteen patients (22%) were discontinued or lost to follow-up, however 79% of them had undetectable pVL at the last visit. Median CD4 cell count was 665 cells/mm^3. Incidental syphilis was diagnosed in 29.5% of the participants. One patient died due to meningeal TB. No major tolerability/toxicity issues were observed. Preliminary analysis at week 24 of the factors associated with failure of retention were: police harassment and drug/alcohol-related problems.
Conclusion: Retention is the major issue among TGW initiating treatment. Most defaults were due to external factors, without association of HIV treatment. Strategies to increase retention in care are urgently needed to achieve 90/90/90 among this specific population.
Supported by a ViiV-IIR-grant

PE19/6

Addressing the needs of female sex workers in Switzerland: model of care beyond STI testing

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Purpose: In Switzerland, sexwork is legal and regulated with an estimated 20 000 female sexworkers (FSW) in the country. FSW are at high risk of sexually transmitted infections (STI), but have reduced access to prevention and treatment because of stigmatization, language barriers, and financial concerns. We aimed to identify a suitable model to engage FSW in health care.
Method: The Basel Aids center (www.ahbb.ch) opened an anonymous "walk in clinic" called "lady-check" for one afternoon per week. This clinic includes translators, a gynecologist, a specialist nurse and a collaborating pharmacy. Clients pay only 20 Euro at registration for counselling, screening for STIs, contraception advice, a full gynaecological examination including cervical cancer smear and vaccination against hepatitis B. The service is anonymous.
Results: From March 2016 to July 2019, 350 women attended comprising 872 clinical visits during 328 office hours. 125 (36 %) women were from Eastern Europe and 118 (34%) from South America and the Caribbean. 23 (8.4%) of cervical cytologies were abnormal necessitating referral for colposcopy. There were 11 unplanned pregnancies requesting referral for medical abortion. STIs were identified and treated in 43/350 (15%) of women: Chlamydia 30/382 (7.8%), Gonorrhoea 15/382 (3.9%) and Syphilis 8 (2.4%). No FSW (504 tests) tested HIV positive. All women were counselled on HIV/STI prevention and condom use. In addition, oral hormonal contraception, implants or IUDs were prescribed as indicated. Overall, we administered 187 Heptitis B vaccine doses.
Conclusion: FSW are willing to engage in health care services including gynaecological care, if these are easily accessible, affordable and anonymous. FSW had high rates of asymptomatic bacterial STIs, requiring antibiotic treatment and many FSW were not previously vaccinated against Hepatitis B.

Morbidity/mortality in the era of cART

PE20/1

The association of rare HLA alleles with clinical disease progression in HIV-positive cohorts with varied treatment strategies

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Purpose: The Strategic Timing of AntiRetroviral Treatment (START) and The Strategies for Management of Antiretroviral Therapy (SMART) trials demonstrated that ART can partly reverse clinically defined immune dysfunction induced by HIV replication. Control of HIV replication is influenced by human leukocyte antigen (HLA) alleles. Whether HLA alleles also independently influence risk of clinical events reflecting immune dysfunction is unknown and is explored here.
Method: In HIV+ individuals from the START and SMART trials, we assessed associations between imputed HLA alleles (102 class I and 83 class II alleles), and the following endpoints: AIDS, infection-related cancer, herpes virus-related AIDS events, chronic inflammation-related conditions and bacterial pneumonia. We used Cox regression to estimate the hazard ratios (HRs) for the

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risk of clinical events for HLA allele carriers versus non-carriers. Models were adjusted for sex, age at trial entry, geographical region, race, time-updated CD4+ count and HIV viral load and stratified by trial treatment groups. HLA class I and II alleles were analysed separately, and the Benjamini-Hochberg procedure was used to limit the false discovery rate (FDR) to <5% (*q*-value <0.05).

Results: Among 4,829 participants, there were 132 AIDS events, 136 chronic inflammation-related conditions, 167 bacterial pneumonias, 45 infection-related cancers and 44 herpes virus-related AIDS events. After FDR correction, we found several associations with a q-value <0.05 (Table 1): HLA-DQB1*06:04 and HLA-DRB1*13:02 for AIDS (HR [95% CI] 2.63 [1.5–4.6] and 2.25 [1.4–3.7], respectively), HLA-B*15:17 and HLA-DPB1*15:01 for bacterial pneumonia (4.93 [2.3–10.7] and 4.33 [2.0–9.3], respectively), and HLA-A*69:01 for infection-related cancer (15.26 [3.5–66.7]). The carriage frequencies of all alleles with a q-value <0.05 were ≤10% (Table 1).

Conclusion: This hypothesis-generating study suggests that certain rare HLA alleles may influence risk of specific, clinical immune dysfunctional phenotypes irrespective of the effect of ART. Validation of these observations in other larger cohorts is required.

Table 1. Adjusted hazard ratios for HLA class I and II alleles associated with clinical events in HIV-positive individuals (n=4,829) from the START and SMART pooled cohorts who provided consent for the genomics substudy. All associations with a *q*-value <0.05 in the multivariable model are shown.

Clinical event (no. of events[a])	Allele	Participants with predicted HLA, n(% of cohort)	HLA allele carriers and non-carriers, n(% with predicted HLA)		Events among allele carriers and non-carriers[b], n(%)	Multivariable[c]	
						HR (95% CI)	q-value
AIDS (n=132)	HLA-DQB1*06:04	4,671 (96.7)	Non-carriers	4,452 (95.3)	108 (2.4)	1	
			Carriers	219 (4.7)	15 (6.8)	2.63 (1.5-4.6)	0.041
	HLA-DRB1*13:02	3,800 (78.7)	Non-carriers	3,410 (89.7)	79 (2.3)	1	
			Carriers	390 (10.3)	22 (5.6)	2.25 (1.4-3.7)	0.041
Bacterial pneumonia (n=167)	HLA-B*15:17	3,963 (82.1)	Non-carriers	3,921 (98.9)	127 (3.2)	1	
			Carriers	42 (1.1)	7 (16.7)	4.93 (2.3-10.7)	0.005
	HLA-DPB1*15:01	4,479 (92.8)	Non-carriers	4,423 (98.7)	142 (3.2)	1	
			Carriers	56 (1.3)	7 (12.5)	4.33 (2.0-9.3)	0.015
Infection-related cancer (n=45)	HLA-A*69:01	4,598 (95.2)	Non-carriers	4,585 (99.7)	42 (0.9)	1	
			Carriers	13 (0.3)	2 (15.4)	15.26 (3.5-66.7)	0.027

[a]Total number of events in the pooled cohort.

[b]The total number of events among allele carriers and non-carriers will vary depending on the number of HLA-predicted participants at each HLA locus.

[c]Multivariable analysis: Time to first event adjusted for time-updated $\log_2$CD4+ count, time-updated $\log_{10}$viral load, race, geographical region, sex and age at baseline and stratified by trial treatment groups.

Table 1.

PE20/2

Neutrophil-to-lymphocyte ratio compared to CD4+:CD8+ T-cell ratio as a predictor of non-AIDS events in treated people living with HIV

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Purpose: In the ART era non-AIDS events have emerged as the leading cause of morbidity and mortality for people living with HIV (PLWH). CD4+/CD8+ T-cell ratio has been shown to be incrementally associated with non-AIDS defining events (NADEs), while neutrophil-to-lymphocyte ratio (NLR) predicts cardiovascular mortality in the general population, and has previously been linked to excess cardiovascular mortality in PLWH. We evaluated the role of NRL in predicting NADEs compared to CD4+/CD8+ T-cell ratio in PLWH.

Method: A retrospective analysis was performed on adult PLWH enrolled in the UCD-ID Cohort who commenced antiretroviral therapy (ART) after 2001. Clinical events, demographics and laboratory data were collected. Association of NLR and CD4+/CD8+ T-cell ratio (measured prior to event) with progression to first NADE was assessed using Cox regression models. Predictive performance of models was assessed using the C-statistic.

Results: Of 550 PLWH, 317 (58%) were male, 220 (40%) African and 131 (24%) injecting drug-users. At ART initiation median (IQR) age was 34 (29–40) years, and nadir CD4+ count 187 (80–284) cells/mm^3. 135 NADEs occurred in 2557 person-years of follow-up (crude incidence 5.3/100 PYFU (95% CI 4.50–6.30)), commonest being pneumonia (n=39), liver disease (n=17), cardiovascular disease (n=14) and non-AIDS malignancies (n=12). NADEs incidence rate across all quintiles of NLR were similar, and did not scale as the NLR increased. In unadjusted models, both lower pre-event CD4+/CD8+ T-cell ratio and higher NRL were associated with increased NADEs (p<0.001, p=0.05 respectively, Figure1). After adjustment for confounders, only CD4+/CD8+ T-cell ratio remained independently associated with the incidence of NADEs (Table1). Models containing pre-event CD4+/CD8+ T-cell ratio predicted NADEs better than pre-event NLR (C-statistic; 0.73 vs 0.68 respectively, Table2).

Conclusion: This study suggests NLR does not have predictive value for NADEs in PLWH. Further studies are needed to assess its clinical utility for specific NADEs in this population.

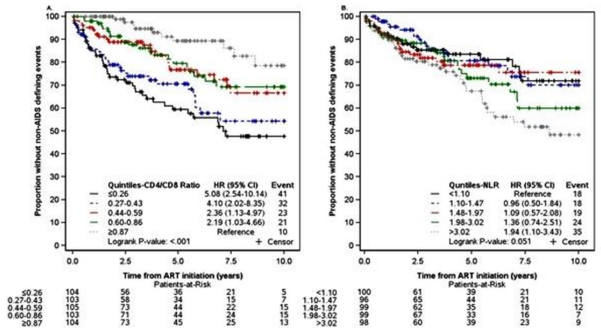


Figure 1. KM curves for time to first non-AIDS event

Table 1. Adjusted Cox regression model for time to first non-AIDS event

	HR (95% CI)	P-value	HR (95% CI)	P-value
Age at ART initiation (per 10 years)	1.27 (1.03-1.58)	0.0283	1.44 (1.16-1.80)	0.0012
Gender		<.0001		<.0001
Female	Reference		Reference	
Male	0.39 (0.26-0.58)		0.43 (0.29-0.66)	
Ethnicity		0.0136		0.0884
Caucasian	Reference		Reference	
Non-Caucasian	0.55 (0.34-0.88)		0.62 (0.36-1.07)	
Mode of HIV transmission		0.1318		0.0114
Non-injecting drug use	Reference		Reference	
Injecting drug use	1.40 (0.90-2.18)		1.80 (1.14-2.84)	
Pre-event CD4+/CD8+ ratio		<.0001		
≤0.26	4.85 (2.42-9.70)			
0.27-0.43	3.62 (1.77-7.41)			
0.44-0.59	2.10 (1.00-4.42)			
0.60-0.86	1.99 (0.94-4.24)			
≥0.87	Reference			
Pre-event NLR				0.5144
<1.10			Reference	
1.10-1.47			0.81 (0.41-1.58)	
1.48-1.97			0.83 (0.42-1.62)	
1.98-3.02			0.81 (0.41-1.60)	
>3.02			1.20 (0.63-2.26)	

Table 2. Harrell C statistics for Cox regression models predicting events during follow-up

	Unadjusted Cox Model	§Adjusted Cox Model
	C Statistic (95% CI %)	C Statistic* (95% CI %)
Model with quintiles of CD4+/CD8+ T-cell ratio	0.67 (0.62–0.71)	0.73 (0.69–0.76)
Model with quintiles of neutrophil/lymphocytes ratio	0.57 (0.52–0.62)	0.68 (0.63–0.73)

§Adjusted for age, gender, ethnicity and HIV transmission risk group

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PE20/3

Factors associated with virologic failure in women with HIV: Condesa specialized clinics, Mexico City

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Purpose: To identify factors associated with virologic failure (VF) in women with HIV, patients of two clinics in Mexico City.
Method: An observational cross-sectional study. Carried out among women patients at the Condesa Clinics between January 2014 and December 2018. All patients were pregnant (Cohort pregnant women) and had been undergoing HAART (highly active antiretroviral treatment) for at least six months and possessed complete medical records. Convenience sampling, prevalence, odds ratio, chi^2 and attributable risk were analyzed using SPSS24.
Results: 169 women with HIV from the Condesa Specialized Clinic (CSC) and CSC-Iztapalapa.143 in statistical analysis, 15% (n=16) failed to follow up. Median age, 28 years (SD 6.1). Education: 47% completed middle school. Unpaid employment: 78%. 74% have a stable partner. 85% with virologic suppression and 15% with virologic failure (VF). Women with chronic HIV (n=67), 41% with VF at the time of first medical consultation in pregnancy: VL 16,355 copies/mL (SD 261891 c/mL), at the third quarter before birth 97% with VL <200 c/mL, at present 85% VL <200 c/mL. CD4 (cells/mm^3): 381 c/mm^3 (SD 224), 432 c/mm^3 (SD 185) and 427 c/mm^3 SD 241) respectively. 61% serodiscordant couples. Women with recent diagnosis of HIV (pregnancy scrutiny, n=76) first viral load 22,106 c/mL (SD 41285 c/mL), before birth 95% with VL<1000 c/mL, at present 95% VL<200 c/mL, 5% in VF. CD4 (cells/mm^3): 302 c/mm^3 (SD 214), 375 c/mm^3 (SD 257) and 581 c/mm^3 (SD 332) respectively; 47% concordant couples. In both, the probability of VF in women who experienced domestic violence was 3.1 OR (SD 1.3–9.9, p 0.01) and in those receiving antiretroviral treatment with protease inhibitor (PI) the probability of VF was 2.9 OR (SD 1.1–7.5, p 0.03).
Conclusion: In this study we observed two factors associated with VF; identifying the associated factors is useful in developing intervention strategies. If we eliminated domestic violence, the VF decreases 73% and if we change HAART without PI, VF decreases 66%.

PE20/4

Causes of death among a cohort of HIV-infected adults in rural Tanzania

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Purpose: Nearly half of AIDS-related deaths occur in East and Southern Africa, yet data on causes of death (COD) are scarce. We determined COD and factors associated with cause-specific mortality among HIV-infected persons in rural Tanzania.
Method: We included adults (≥15 years) enrolled in the Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) in 2005–2016, with follow-up through 2016. We classified COD as HIV-related or non-HIV-related with sub-classification into comprehensive classes. Among adults enrolled from 2013 onwards (when COD were systematically recorded), we assessed cause-specific mortality using cumulative incidences, and associated factors using Cox proportional hazard models.
Results: Among 8409 adults, 816 (10%) had died by the end of 2016, among whom COD were available for 358 (44%), with missing COD mainly before 2013 (Figure 1). The leading identified COD were tuberculosis (107 (30%)), non-AIDS-related infections (58 (16%)), and AIDS-related infections (52 (15%)). Among 2574 adults enrolled from 2013 onwards, 74 (3%), 24 (1%) and 22 (1%) died from HIV-related, non-HIV-related and unknown causes, respectively. One-year cumulative incidences of HIV-related and non-HIV-related mortality were 0.03 (95% confidence interval 0.02–0.04) and 0.009 (0.006–0.01), respectively (Figure 2). Factors associated with HIV-related mortality were hospitalisation, not having an HIV-positive partner, advanced WHO stage, lower CD4 count, and not initiating ART at enrolment. Factors associated with non-HIV-related mortality were older age, living closer to the clinic, and hospitalisation.
Conclusion: Despite access to ART, HIV-related mortality rates were higher than non-HIV-related mortality rates. Tuberculosis was the leading identified COD, emphasising the need for continued improvements in screening and management. Documentation of COD improved over time; methods to uniformly capture deaths and causes are recommended. The lower non-HIV-mortality rates among those living further from the clinic may be due to undocumented deaths; further efforts to track and retain participants in care are needed.

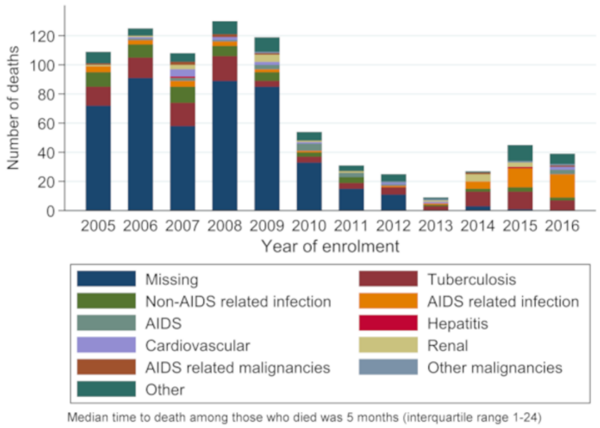


Figure 1. Causes of death among adults.

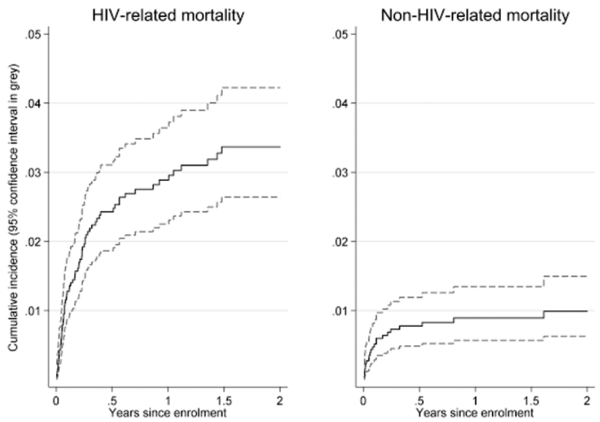


Figure 2. Cause-specific cumulative incidences of HIV-related and non-HIV-related mortality.

PE20/5

Predictors of early mortality among adult HIV-infected patients on antiretroviral therapy in a Kenyan pastoralist community: a retrospective cohort study

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Purpose: Policy changes have enabled scale up of antiretroviral therapy to patients with HIV infection irrespective of their CD4 count in low and middle-income settings. However, high rates of early mortality continue to be

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documented. In addition, predictors of this phenomenon among adult HIV-infected patients in pastoralist communities in Kenya are largely unknown.
Method: This was a retrospective cohort study carried out between January 2014 and December 2017 among HIV-infected patients being followed up at the Baringo County Referral Hospital, Kabarnet, Kenya. Patient files were used to extract the required patient information. Kaplan-Meier, as well as Cox proportional hazards regression models, were used to assess for independent predictors that contributed to mortality of these patients over time.
Results: 332 patients were studied over a median follow-up period of 27.6 months (IQR: 18.5–36.2 months), with a female to male predominance of 1.4:1, a median age of 41 years (IQR: 35–48 years), and a median pre-treatment CD4 count of 207 cells/mm^3 (IQR: 81–316 cells/mm^3). Overall, 6.6% (n=22) of the patients were documented to have died during the study period, with estimated mortality at 3.1% (n=11; 95% CI: 1.9–5.9%) in month 3, 5.1% (n=2; 95% CI: 3.2–8.1%) in month 12, 7.1% (n=5; 95% CI: 4.7–10.6%) in month 24, and 7.1% (n=0; 95% CI: 4.7–10.6%). Independent predictors of mortality were male sex (aHR: 4.90; 95% CI: 1.81–13.27), immunosuppression (CD4 $\leq$ 50 cells/mm^3 [aHR: 3.09; 95% CI: 1.32–7.24], CD4 $\leq$100 cells/mm^3 [aHR: 2.93; 95% CI: 1.24–6.91], and WHO stage III & IV [aHR: 2.80; 95% CI: 1.20–6.55]), and TB/HIV co-infection (aHR: 18.39; 95% CI: 4.71–71.81).
Conclusion: Mortality was noted to be high, especially among the first three months of follow-up, mostly due to immunosuppression and TB/HIV co-infection. Hence, early diagnosis, with expeditious commencement of therapy and frequent follow-up is vital to minimize these numbers.

PE20/6

Trends in underlying causes of death in HIV – infected patients from 2016 to 2018 in Ukraine: a cohort study

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Purpose: Death level in PLHIV in Ukraine remains high. We aimed to examine changes in causes of death in PLHIV over the period 2016–2018.
Method: A retrospective cohort study was conducted at Poltava Regional HIV Center in which routinely collected data for PLHIV enrolled and followed up between January 2016 and December 2018 were abstracted from the clinic's database. Patient follow up was initiated from the day of the first visit in clinic until exit by death, transfer out or loss to follow up. Percentage of deaths for each cause across calendar years was analyzed using Chi-square test.
Results: 268 of the 3559 study participants died during 9706 person-years of follow- up (crude incidence mortality rate, 2.7 per 100 person-years [95% CI 2.2–3.3]). 147 people were transferred out and 85 lost-to-follow-up. Compared with those that survived (n=3059), we recorded a higher proportion of deaths in men - 176 (65%) vs 1553 (50.7%), intravenous drug use risk for HIV acquisition - 94 (35.1%) vs 885 (28.9%), presented for care late in course of their HIV infection 126 (47.1%) vs 793 (25.9%), hepatitis C virus-positive - 185 (69%) vs 1850 (60.5%), previous AIDS diagnosis -173 (64.5%) vs 1070 (34.9%) (p<0.001), never exposed to ART 92 (34.3%) vs 176 (5.8%)(p<0.001). The most common causes of death were AIDS-related causes, followed by liver disease, and cardiovascular disease.

Table 1. Specific causes of death, 2016–2018

	Number of deaths (%)
Total death	268 (100%)
AIDS-related, including:	164 (61.2%)
- tuberculosis	80 (29.8%)
- toxoplasmosis of brain	33 (12.3%)
- pneumocystis pneumonia	12 (4.5%)
Liver-related (chronic viral hepatitis)	59 (22.0%)
Cardiovascular disease (CVD)-related	16 (5.9%)
Other or unknown, including:	29 (10.9%)
- drug overdose	17 (6.4%)

While AIDS remained the most common cause of death throughout the period 2016–2018 (62.6%–63.5%), the percentage of liver-related deaths increased (12% to 25.3%) and CVD- related deaths increased (2.6% to 10.6%), p<0.05, χ^2 test.
Conclusions: AIDS remained the most common cause of death over the period 2016–2018 in Ukraine. The percentage of liver-related and CVD-deaths increased, making it the joint leading non-AIDS cause of death with AIDS-related deaths.

PE20/7

Dynamic of CD4+/CD8+ ratio in late presenters: impact on clinical outcomes

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Purpose: To evaluate whether CD4+/CD8+ cell ratio (CD4/CD8) measured over time is associated with the development of AIDS-defining events (AE), non-AIDS defining events (NAE) and mortality in HIV+ late presenter (LP) individuals from the cohort of the Spanish HIV/AIDS Research Network (CoRIS).
Method: Late presentation was defined as HIV diagnosis with CD4+cell count $\leq$350 cells/μL or an AIDS defining event within 6 months of enrolment. Cox proportional hazard models allowing time-varying covariates were used to estimate hazard ratios (HR) for the association between time-varying CD4/CD8 and the first AE, the first NAE (cardiovascular, kidney, liver, neoplasms, bone, neuropsychiatric, metabolic or other event) and death. Models were adjusted for CD4+cell count and age, as time-varying covariates, transmission category, country of origin, educational level, presence of HCV antibodies, presence of HBV surface antigen and HIV-RNA at enrolment.
Results: Of the 10,486 out of 15,509 CoRIS participants by November 2018 included in the study, 4,643 were LP [prevalence: 44.3% (95% CI: 43.3; 45.2)]. Among LP, 159 patients had at least one AE [incidence: 0.61 (95% CI: 0.52; 072)×100 person-years], 593 experienced at least one NAE [incidence: 2.53 (95% CI: 2.33; 2.74)×100 person-years] and 213 died [mortality rate: 0.79 (95% CI: 0.68; 0.90)×100 person-years]. CD4/CD8<0.4 over time was associated with an increased risk of AE [HR: 1.79 (95% CI: 1.09; 2.96)] and NAE [HR: 1.25 (1.01; 1.55)], mainly cardiovascular events, as detailed in table 1 and with all-causes mortality [HR: 1.37 (0.96, 1.95)].

Association between CD4+/CD8+ ratio and the first non-AIDS event in late presenters (N=4,643)

	N of HIV+ late presenter individuals with at least one NAE and CD4/CD8 <0.4/CD4/CD8 ≥0.4	Incidence rate x 100 person-years (95% CI)	Adjusted HR for CD4+/CD8+ <0.4 vs ≥0.4
Cardiovascular events	38/45	0.35 (0.28; 0.44)	1.97 (1.18, 3.29)
Kidney events	18/38	0.24 (0.18, 0.31)	0.87 (0.41, 1.84)
Liver events	15/18	0.14 (0.10, 0.20)	0.60 (0.27, 1.37)
Neoplasms	58/83	0.60 (0.51; 0.71)	1.06 (0.68, 1.64)
Bone Events	32/62	0.40 (0.32, 0.49)	1.31 (0.78, 2.18)
Neuropsychiatric events	47/62	0.46 (0.38; 0.56)	1.45 (0.87, 2.40)
Metabolic events	38/61	0.42 (0.34, 0.51)	1.57 (0.93, 2.65)
Other events	6/3	0.04 (0.02, 0.07)	0.78 (0.20, 2.98)

Conclusion: Low CD4/CD8 measured over time was associated with increased risk of AE, NAE and mortality regardless of CD4+cell count. These preliminary findings supports the predictive role of variation of CD4/CD8 over time and the need for further research on therapeutic tools, whether antiretroviral therapy or not, to improve the recovery of the CD4/CD8.

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PE20/8

Retrospective investigation into the causes of death in HIV-infected patients from Bonn in the era of combined Anti-Retroviral Therapy

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Purpose: Countless investigations have attested to the decline of deaths attributed to AIDS in HIV positive patients since the introduction of combined Anti-Retroviral Therapy (cART). The goal of this investigation was to examine this transition and systematically determine the causes of death in the previous decade in the Bonn cohort of HIV infected people.
Method: For the purposes of this investigation 81 patients from Bonn who died between 2010 and 2018 were recorded. Along with the underlying causes of death, patient data such as pre-mortem laboratory parameters, comorbidities und comedications were collected and descriptively analyzed.
Result: The median age at death was 51 years (IQR 45.8–60.0), 81% were men. The median lifespan with HIV infection was 15.66 years. 88.9% of the patients received antiretroviral therapy until the time of their death. 70% of the patients had an undetectable HIV viral load at last check .The median of the last CD4 Helper Cell count before death (<12 Months) was 260.5 Cells/μL. In 17.2% of the cases the cause of death was an AIDS defining illness: 6.1% Pneumocystis jirovecii Pneumonia, 4.9% other AIDS defining illness, 3.7% Non-Hodgkin-Lymphoma and 1.2% Wasting Syndrome. Non-AIDS associated malignancies (19.8%) were the most common cause of death. Cardiovascular disease represented 13.6% of the deaths respectively before Non-HIV associated infections (12.3%). 7.4% of the patients, all of whom were coinfected with chronic hepatitis, suffered from diseases of the liver. 6.2% of the patients committed suicide, 8.6% died of other causes, and in 14.8% of the cases the cause of death remained unknown.
Conclusion: Non-AIDS associated malignancies and cardiovascular disease are increasingly leading to the death of HIV infected people in the area of Bonn. The trend of decreasing mortalities attributed to AIDS was confirmed. These results are due to consistently implemented antiretroviral therapy and highlights their importance.

PE20/9

Reduced utility of early procalcitonin in HIV febrile patients admitted to the emergency department

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Purpose: To investigate the role of procalcitonin (PCT) in the Emergency Department (ED) as early assessment of febrile patients and to investigate its prognostic role on in-hospital mortality.
Method: We retrospectively evaluated data of all HIV-infected patients who were admitted to ED and then hospitalized with fever as the main symptom from 2008 to 2017. QSOFA score was used to assess the severity of clinical presentation. Chi-square test and logistic regression were used to assess the factors independently associated to the use of PCT and to assess the prognostic prediction value of PCT assessment in terms of in-hospital mortality rate.
Results: Study population consisted in 579 patients: 65.3% males; median age 47 years (IQR 40-53). Median length of hospital stay after ED admission was 11 days (IQR 6-20). At ED admission, medianCD4 cell count was 222 cell/mm^3 (IQR 64-445) and median plasma HIV-RNA was 1612 cp/mL (IQR 19-139431). In 52% of the cases, HIV serostatus was already known at ED admission (60% of them were on cART from at least 6 months) and in13% of cases the patients presented with AIDS defining events. QSOFA score was>0 in 8%of the population (N=47).PCT was performed in14%of patients (N=82). At multivariate analysis, factors associated with the use of PCT were: to be female (p=0.029), of older age (p=0.012), already diagnosed with HIV infection (p=0.04) and to have presented positive blood cultures at admission (p=0.025). Having performed PCT didn't affect mortality neither in patients with QSOFA score>0 (p=0.939) nor in those with QSOFA=0 (p=0.183).
Conclusion: The decision to perform early PCT test in HIV febrile patients is guided by the clinical presentation and by some demographic characteristics such as female gender, older age, known HIV infection. The prognostic relevance of early determination of PCT is poor. An integrated approach including biomarkers dosage, validated sepsis scores, and involvement of antibiotic stewardship team, is desirable to improve outcome in this kind of patients.

In-hospital deaths according to QSOFA in HIV positive patients admitted to Emergency Department (ED) with fever tested or not with Procalcitonin (PCT)

			PCT in ED		
QSOFA			NO PCT in ED N (%)	PCT in ED N (%)	Total N (%)
QSOFA=0	In-hospital death	No N (%)	434 (94.3)	65 (90.3)	499 (93.8)
		Yes N (%)	26 (5.7)	7 (9.7)	33 (6.2)
		Total N (%)	460 (100)	72 (100)	532 (100)
QSOFA>0	In-hospital death	No N (%)	30 (81.1)	8 (80)	38 (80.9)
		Yes N (%)	7 (18.9)	2 (20)	9 (19.1)
		Total N (%)	37 (100)	10 (100)	47 (100)

PE20/10

Patients with HIV and HCV in intensive care treatment: admission criteria and trends in the intensive care unit (ICU) at the University Hospital of Bonn 2014–2019

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Purpose: Patients with chronic HIV- and HCV-infection require specialized, multidisciplinary intensive care in case of uncontrolled HIV infection/opportunistic infections and/or decompensated liver disease. Here we analyze admission characteristics and trends over time in HIV, HCV and HIV/HCV co-infected patients admitted to the intensive care unit (ICU) at University Hospital of Bonn during January 2014 to June 2019.
Method: We performed a retrospective survey of all patients admitted to the ICU with HIV infection and chronic/recent history of HCV infection.
Available clinical data of all patients with regard to sex, age, medical history, admission criteria, duration of stay and outcome were analyzed.
Results: Overall, 210 patients were included (median age 51.3 years, female/male 60/150) with a total of 288 ICU admissions. Median duration on ICU was 3 days. 46 patients died on ICU.
Admission criteria differed in HIV, HCV and HIV/HCV co-infected patients. HIV patients (42 patients, 58 admissions) were predominantly admitted due to opportunistic infections (37.9%), sepsis (24.1%) and cardiopulmonary disease (18.97%). HCV patients (148 patients, 205 admissions) were mostly admitted due to liver disease (22.9%), sepsis (21.95%) and intoxication/drug abuse (20.0%).
20 HIV/HCV co-infected patients were were admitted because of sepsis (32.0%), opportunistic infections (20.0%) and intoxication/drug abuse (20.0%).
During the observation period we saw a constant trend of admissions of HIV patients due to infectious diseases. Admissions of HCV patients due to complications of liver disease was considerably decreasing.
Conclusions: The high number of HIV patients admitted to ICU due to acute infections reflects the ongoing high proportion of HIV late presenters. The decreasing trend of HCV patients admitted due to sequelae of liver disease probably shows the impact of DAA therapy on clinical course of HCV infection reducing morbidity and mortality.

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PE20/11

Burden of disease in PLWH harboring a 4-class drug resistant virus: data from PRESTIGIO Registry

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Purpose: To date, there are no data on survival and burden of disease in people living with HIV-1 (PLWH) harboring a 4-class drug resistant (4DR) virus (NRTI, NNRTI, PI, INSTI).
The aim of the study was to evaluate the survival and the incidence of AIDS and non-AIDS-related events in this fragile population.
Method: Cohort study on PLWH, recorded in the PRESTIGIO Registry, with a documented 4DR virus.
We estimated the incidence of death, AIDS and non-AIDS-related clinical events recorded after 4DR occurrence (baseline, BL).
Non-AIDS related events included: non-AIDS related malignancies, major adverse cardiovascular events (MACE), cirrhosis, chronic kidney disease (CKD), diabetes.
Incidence rates (IR) were expressed per number of person-years of follow-up (PYFU) since BL and estimated by univariate Poisson regression.

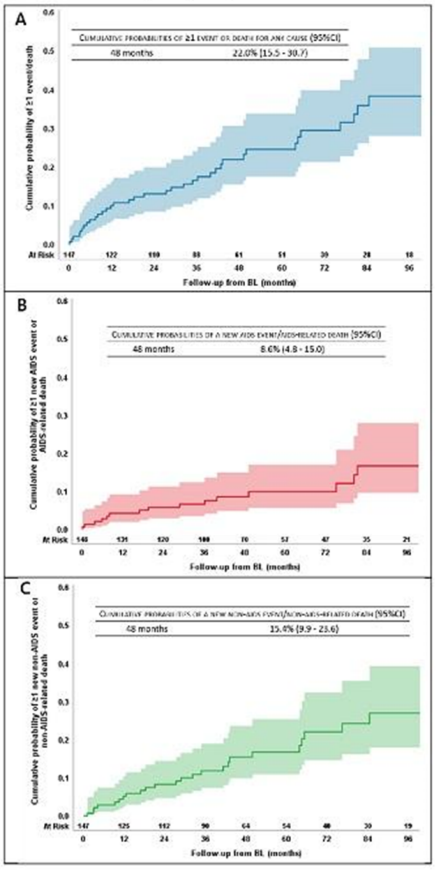
Table 1: Baseline characteristics of the 148 PLWH and 4-class drug resistant virus.

Characteristics	OVERALL (n=148)
Age (years)	49 (44-53)
Male Gender	115 (78%)
HCVAb Positive	31(30%)
HBsAg Positive	2 (2%)
Years since HIV diagnosis	20.4 (16.2-24.5)
Years of ART	16.8 (14.0-19.7)
Pre-ART HIV-RNA (log_{10} copies/mL)	5.18 (4.95-5.67)
Nadir CD4+ (cells/µL)	92 (18-203)
Previous AIDS events	58 (39%)
Previous non-AIDS event	32 (22%)
Diabetes	9 (6%)
Cirrhosis	1 (0.7%)
Malignancies	25 (17%)
MACE	4 (3%)
CKD (eGFR <60 mL/min/1.73m^2)	3 (2%)
HIV-RNA (log_{10}copies/mL)	3.49 (2.37-4.48)
CD4+ (cells/µL)	346 (169-600)
CD8+ (cells/µL)	946 (629-1284)
CD4+/CD8+ ratio	0.35 (0.20-0.61)

Baseline characteristics of the 148 PLWH and 4-class drug resistant virus.

Time to any clinical event/death for any cause or AIDS event/AIDS-related death or non-AIDS event/non-AIDS-related death were estimated by Kaplan-Meier curves.
Results: Overall, 148 PLWH were evaluated: median age was 49 years (IQR=44–53), 78% males. Patients' characteristics are reported in Table 1.
During a median follow-up of 47 months (IQR=32–84), 38 PLWH had 62 events/death for any cause (12 died, 17 non-AIDS-defining malignancies, 3 AIDS-defining malignancies, 15 AIDS events, 6 MACE, 6 CKD and 3 cirrhosis): IR=9.12/100-PYFU (95% CI=6.85–11.39).
Fifteen PLWH developed 24 new AIDS events or had AIDS-related death: IR=3.52/100-PYFU (95% CI=2.12–4.94).
Twenty-six PLWH developed 38 non-AIDS events or non-AIDS-related deaths: IR=5.59/100-PYFU (95% CI=3.81–7.37).
Time to any clinical event/death for any reason, AIDS event/AIDS-related death or non-AIDS event/non-AIDS-related death are shown in Figure 1.
Conclusion: Among PLWH with 4DR, the burden of disease due to both AIDS and non-AIDS related events is still an issue, even in recent years.
Interestingly, 32% of the recorded clinical events were malignancies, 27% non-AIDS-defining malignancies.

Figure 1 - Time to occurrence of ≥1 event/death (panel A), AIDS event/AIDS-related death (panel B) and non-AIDS event/non-AIDS-related death (panel C) among 148 PLWH and 4-class drug resistant virus.



Time to ≥1 event/death (panelA), AIDS event/death (panelB) and non-AIDS event/death (panelC).

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PE20/12

Changing pattern of hospital admissions due to medical conditions in HIV-infected subjects in a European public health care system with free access to antiretroviral treatment

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Purpose: Reasons for hospitalizations in HIV-infected subjects might vary along recent years due to universal ART and achievement of high rates of HIV suppression, particularly in developed countries with universal free ART and access to health-care.
Method: We analyzed admissions of HIV-infected subjects to internal medicine/infectious diseases Dept. from October 2016-September 2018 in a University tertiary hospital in Barcelona.
Results: We identified 243 admissions (1.5 admissions/subject) with a mean stay of 11.2 days. Of them, 73.2% were male, median age 49.8 years, median 361 CD4+ cells. Alcohol or drug (including IV) abuse was present in 24.7% and 23.5%, respectively, and 56.4% had prior HCV coinfection. Most (93%) subjects were previously diagnosed of HIV, only 5.4% were newly diagnosed during the admission. Mortality was 4.9%, and was associated with neoplasia (p=0.020). Plasma HIV-1 RNA was <50 copies/mL in 53.1% (129/243), and 40.0% had >200 copies/mL. Having an AIDS-defining illness (p=0.007) or lower CD4 count (p=0.026) were associated with longer hospital stays. Being female (p=0.069) or having an undetectable HIV-1 plasma RNA (p=0.14) were associated with trends towards shorter hospitalizations. Last ART retrieval from the pharmacy was significantly shorter in those with undetectable plasma HIV-RNA (37.9 vs 162.0 days, p<0.001). The main diagnostics were infections not related to HIV (n=133, 53.9%), of which 69.2% were respiratory infections. Only 14.6% had AIDS-defining illnesses.
Conclusion: The main diagnostics were respiratory infections not related to HIV . Mortality was 5% and was only associated with neoplasia. AIDS-defining illnesses and lower CD4 counts had longer hospital stays. Most subjects were already diagnosed of HIV and had lost their link to health care and withdrawn their ART. These subjects not only fuel hospital admissions but also HIV transmission to the general population. Active public health strategies should be designed to relink them to viral suppression.

PE20/13

Association of non-adherence to antiretroviral therapy with cardiovascular outcomes in virologically suppressed persons living with HIV: the Swiss HIV Cohort Study

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Purpose: Suboptimal adherence to antiretroviral therapy (ART), even if enough to achieve and sustain viral suppression, has been associated with enhanced residual inflammation. We aim to investigate whether incomplete ART adherence in the persons living with HIV (PLWH) with virologic suppression is associated with increased cardiovascular disease (CVD) outcomes.
Method: PLWH prospectively enrolled in the SHCS were included in this analysis if they started ART between 2003 and 2017, had at least 6 months of viral suppression (RNA<50 copies/mL) and no history of CVD. The association between incomplete adherence to ART, defined as any missed doses by self-report, and a composite outcome for a CVD event (myocardial infarction [MI], revascularization, cerebral hemorrhage, stroke, and/or death due to cardiovascular event), was evaluated using Cox proportional hazard ratio (HR) models. Models were adjusted for the Framingham 10-year risk score (FRS), family history of CVD, ethnicity, HIV transmission group, and $CD4^+$ T-cell count, and HIV-1 RNA upon ART initiation.
Results: A total of 6,188 PLWH were included in the analysis (74% male) with a median age of 39 (range: 17–80). FRS was 10–20% and >20% in 18% and 9% of participants, respectively. Median participant follow-up was 8 years (IQR: 5–11), with a median of 13 adherence questionnaires (IQR: 7–21). In total, 181 (3%) participants experienced a CVD event: revascularization (43%), stroke (22%), MI (20%), death (12%), and hemorrhage (3%). After adjusting for confounders, suboptimal adherence was associated with an increase in CVD events (HR: 1.35, 95% CI: 0.85–2.17).
Conclusion: Among PLWH with virologic suppression, there was a trend towards incomplete ART adherence being associated with an increased risk of a CVD event, emphasizing the possible role of non-adherence to ART as a driver of clinical non-AIDS outcomes. Future studies in other cohorts should further confirm this association to understand its clinical implications.

PE20/14

Differences in social and mental well-being of long-term survivors among people who inject drugs and other participants in the Swiss HIV Cohort Study: 1980–201

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Purpose: People living with HIV who were diagnosed before highly active antiretroviral therapy (HAART) was available and who survived at least 15 years after HIV diagnosis, termed pre-HAART long-term survivors (LTS), form a particularly vulnerable population. We study social, clinical and mental factors of LTS in the Swiss HIV Cohort Study, with a particular focus on people who inject drugs (PWID).
Method: We compared PWID LTS with those LTS, who were most likely infected through sexual contact, i.e., men who have sex with men (MSM) and heterosexuals (HET). By using phylogenetic methods, we selected an additional group of heterosexual LTS who most likely shared a social network with PWID (presumed because of phylogenetic HIV clustering) at the time of HIV infection, termed clusteredHET. Social and clinical factors at the time when the HIV diagnosis was at least 15 years ago were compared among these three study groups using logistic regression.
Results: Overall, 1,663 of 5,686 (29.2%) PWID were LTS. We found significant differences between PWID LTS and MSM/HET LTS regarding self-reported depression (59.4% vs 43.9%, OR=1.8, p<0.001), being in prison (30.6% vs 7.3%, OR=5.1, p<0.001), and work ability of less than 50% (59.6% vs 28.9%, OR=5.1, p<0.001). ClusteredHET were less vulnerable with respect to these variables than PWID LTS but more at risk compared to MSM/HET LTS, indicating that clusteredHET are closer to PWID with regard to social and mental aspects compared to all MSM/HET.
Conclusion: Despite the overwhelming success of harm reduction programs for PWID in Switzerland, special care for HIV-infected PWID is still needed today, with emphasis on mental health and social integration of PWID LTS.

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PE20/15

Low pre-ART CD4 count is associated with increased risk of clinical progression or death even after reaching 500 CD4 cells/μL on ART

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Purpose: Although the clinical disadvantages of initiating ART at low CD4 counts have been clearly demonstrated, it is unclear whether any excess risk remains after reaching relatively safe CD4 levels. We explore whether persons who started ART with <500 CD4 cells/μL but increased their CD4 count above this level, have from this point onwards, similar risk of clinical progression/death with persons starting ART with ≥500 CD4 cells/μL.

Method: Data were derived from a multicenter Greek cohort study (AMACS). Adults, starting boosted PI, NNRTI or INSTI based ART, ≥2000 were eligible, provided they either started ART with ≥500 CD4 cells/μL ("High CD4") or started with <500 CD4 cells/μL but surpassed this threshold while on ART ("Low CD4"). Baseline was ART initiation ("High CD4" group) or the date of first exceeding 500 CD4 cells/μL ("Low CD4" group). Survival analysis, allowing for competing risks, was used to explore the risk of clinical progression/death (AIDS/AIDS-death or serious non-AIDS events-SNAEs i.e. Myocardial Infarction, Stroke, End-Stage Renal Disease, non-Decompensated Liver Disease, non-AIDS Malignancies, non-AIDS deaths).

Results: The study included 3,819 persons: 645 in the "High CD4" and 3,174 in the "Low CD4" group. Median (IQR) follow-up time was 43 (25, 83) and 61 (32, 98) months, respectively. In total, 223 events (93 fatal, 130 non fatal; 39 AIDS related and 184 SNAEs) were observed. Overall, there was no significant difference in disease progression between the two groups but further stratification of the "Low CD4" group revealed that those initiating ART with <200 CD4 cells/μL were at higher risk for clinical progression or death after baseline, compared to those in the "High CD4" group (**Table**).

Conclusion: Individuals starting ART with <200 cells/μL remain on increased risk of clinical progression/death even after reaching or surpassing 500 CD4 cells/μL. These patients should be closely followed.

Results from Cox proportional hazards or Fine & Gray models for competing risks. All estimates are adjusted for potential confounders.

CD4 at cART initiation (cells/μL)	aHR	95% CI	p	aHR	95% CI	p
	AIDS/AIDS-death or SNAE			SNAE (AIDS/AIDS-death as compet. risk)		
350–499/500+	1.268	(0.786, 2.046)	0.331	1.194	(0.709, 2.011)	0.504
200–349/500+	1.336	(0.865, 2.063)	0.192	1.082	(0.677, 1.728)	0.742
<200/500+	2.225	(1.422, 3.481)	<0.001	1.826	(1.133, 2.942)	0.013
	AIDS/AIDS-death (SNAE as compet. risk)			Total mortality		
350–499/500+	1.184	(0.377, 3.718)	0.772	0.996	(0.489, 2.027)	0.991
200–349/500+	2.015	(0.786, 5.168)	0.145	1.209	(0.651, 2.245)	0.549
<200/500+	3.161	(1.159, 8.619)	0.025	2.032	(1.049, 3.933)	0.035

PE20/16

A comparative analysis on blood pressure in HIV-infected individuals versus uninfected controls residing in Sub-Saharan Africa: a narrative review

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Purpose: Elevated blood pressure is a well-documented risk factor for cardiovascular disease and mortality in Sub-Saharan Africa (SSA). With SSA also affected by high Human Immunodeficiency Virus (HIV) infection rates, it remains controversial whether the HIV-infected population has a higher cardiovascular risk than the general population. We, therefore reviewed the literature comparing blood pressure estimates in treated HIV-infected populations against untreated and/or uninfected controls from SSA.

Methods: We conducted a narrative review through PubMed and EBSCO Discovery Service (EDS) to determine the estimates of raised blood pressure and hypertension in the HIV-infected individuals versus uninfected controls (01 January 2005 to 11 November 2018).

Results: After review, we included 14 eligible studies from six countries including 26,302 participants that compared treated HIV-infected, versus untreated and uninfected controls. Studies involving 24,696 participants reported lower blood pressure and/or prevalence of hypertension in treated HIV-infected patients compared to uninfected controls. Studies comprising of 3,536 participants reported higher blood pressure and hypertension prevalence in the treated HIV-infected group than uninfected counterparts, whereas studies with 6,379 participants showed no difference in blood pressure and/or prevalence of hypertension. When comparing HIV patients with and without antiretroviral treatment, studies with 10,304 patients showed treated patients to have lower blood pressure and/or prevalence of hypertension, one study indicated higher blood pressure and/or prevalence of hypertension and studies with 5,806 patients showed no difference in blood pressure and/or prevalence of hypertension than untreated infected patients.

Conclusion: The majority of the findings in this review indicate lower or similar blood pressure and/or prevalence of hypertension in treated HIV-infected individuals compared to untreated and uninfected controls from SSA. It is imperative to further clarify these findings to provide reliable tools for screening and monitoring raised blood pressure in HIV-infected patients.

PE20/17

Causes of death in AIDS/HIV-infected patients at the hospital of infectious diseases in St. Petersburg, Russia

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Purpose: St. Petersburg, Russia and its surrounding Leningradskaya oblast (LO) have the high incidence of HIV-infection, involving the epidemic 1.2% of

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the population of LO. The cause-of-death data on HIV-infected were analyzed for better understanding the urgent clinical and public health interventions.
Method: Causes of mortality in HIV type 1 infected patients in the largest infectious diseases hospital in St. Petersburg in the year 2015 and associations of prognostic factors with cause-specific mortality were analyzed.
Results: Among 2,516 patients died 383 (15.2%, 257 males, 126 females; mean age 36 years; SD:7.5).
Among the dead, the advanced HIV/AIDS stage (CDC category C3) was diagnosed in 319 out of 355 (92.7%). CD4-positive count varied 0-665 (median 33 cell/mcl [10;97]). In 116 (30.3%) patients HIV-infection were diagnosed for the first time. In 256 (66.8%) it lasted more than one year, but only 6 (2.3%) of them received effective antiretroviral therapy (ART). In total, 96 (25.1%) patients had started but 54/96 (56.3%) interrupted ART.
The most frequent opportunistic infection was tuberculosis (n=176, 45.9%), with the generalization in 149 (38.9%) patients, caused by mono/polyresistant Mycobacteria in 40 from 47 (85.0%) analyzed cases. Tuberculosis became the main reason of death (135, 35%), following with pneumonia (n=80, 20.9%), encephalitis (n=65, 17%) and cancer (n=24, 6.7%).
In total, cancers were detected in 31 (8.1%) patients. Patients with CD4≥65/μL had higher risk for development of cancer (adjusted (by age and sex) OR=2.2, 95% CI: 1.00–4.78) and dying from it (adjusted OR=3.2, 95%:CI). No association between cancers and gender, HIV-infection stage and duration and ART was observed.
Conclusion: An active program for early detection of HIV, initiation of ART, detection of associated diseases and precancers will help prevent the development of diseases and deaths related to HIV/AIDS, which will lead to an increase in the life expectancy of HIV-infected in Russia.

PE20/18

Dynamics and structure of mortality of HIV-positive people in Ukraine

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Purpose: Analysis of dynamics, structure of HIV-positive people mortality, effectiveness of antiretroviral therapy in Ukraine during the period of 2014–2018.
Method: A retrospective descriptive epidemiological analysis based on the national report forms.
Results: During 2014–2018, the mortality rate of HIV-positive people in Ukraine increased (from 5.9 to 6.8 thousand), with 28449 people deseased. In the age-gender structure, 65% of deaths occurred among men, 35% – among women, 80% of all deaths were reported in the 25 to 49 age group. 56% people that died were infected with the HIV virus due to unprotected sexual contacts, and 41% – as a result of injecting drug use.Of all deaths, 60% were HIV - associated, 37% were diseases not related to HIV-infection and other causes - 3%. Among HIV-associated deaths 58% occurred due to AIDS. On average, 3.3 thousand AIDS-deaths are recorded annually. The mortality rate increased from 8.0 per 100,000 population in 2014 to 8.9 in 2018. HIV/TB was the leading cause AIDS-related deaths: 64% in 2014 and 51% in 2018. The mortality rates not related to HIV-infection diseases increased from 36% to 38%. The number of deaths from tuberculosis decreased by 1.7 times.
43% of people who died were receiving antiretroviral therapy. Treatment coverage raised from 39% in 2014 to 46% in 2018. The proportion of patients who died of HIV/TB while receiving therapy was 51.0%.
The highest levels mortality being registered in Dnipropetrovska, Odeska, Mykolaivska oblasts.
Conclusion: It is necessary to optimize preventive measures aimed at early detection of HIV-positive people, their linkage to medical care, improvement of epidemiological surveillance system, completeness and quality of collected data regarding the causes of death, taking into account the existing tendency of increasing AIDS mortality rate against the background of significant spread of tuberculosis among deceased, their insufficient coverage by antiretroviral treatment.

Mother-to-child transmission

PE21/1

HIV infection in pregnant women and children in Switzerland: how effective are measures for preventing mother-to-child transmission?

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Purpose: In 2004, recommendations were published in Switzerland in order to prevent mother-to-child transmission (MTCT) of HIV (Bulletin FOPH 53/2004:1008-1011). The recommendations were approved by the Swiss Federal Commission for Sexual Health and included combination antiretroviral therapy, caesarian section and avoidance of breastfeeding. The objective was to evaluate the effectiveness of MTCT-prevention in women with Swiss versus non-Swiss nationality (distribution of nationalities see Table 1).
Method: Analysis of Swiss HIV notification data on (a) children infected by MTCT in 1990–2018 and (b) women diagnosed during pregnancy in 2004–2018.
Results: Rates of HIV infections in children were substantially lower after 2004, particularly in children with Swiss nationality (Table 2). The overall rate was higher for non-Swiss than for Swiss children (Odds Ratio non-Swiss vs. Swiss: 2.46 [1.87–3.21], p<0.0001). During 2004–2018, HIV diagnoses declined in both Swiss and non-Swiss women (Figures 1 and 2). 5.0 % of HIV-diagnosed Swiss women (N=716) were pregnant at diagnosis, compared to 18.8 % of non-Swiss women (N=1778, z=8.4, p<0.0001). The rate of HIV diagnoses in women who were pregnant at diagnosis was 2.11 per million Swiss women, versus 46.4 per million non-Swiss women (Odds ratio Swiss versus non-Swiss 0.044 CI [0.031–0.061], p<0.0001; reference population are the 15–44 year-old women in Switzerland).
Conclusion: MTCT of HIV in Switzerland declined following the recommendations published in 2004. However, rates of HIV infections were twelve times higher in non-Swiss children than in Swiss children. This is partly explained by non-Swiss women being three times more likely to be diagnosed with HIV than Swiss women when tested during pregnancy. The results indicate that prevention of MTCT is less effective in non-Swiss than in Swiss women.
Prevention measures need to be improved for foreign women in order to further reduce MTCT of HIV in Switzerland.

Table 1. Nationality of women diagnosed with HIV during 2004–2018

Nationality	Number of HIV diagnoses	Percentage of Total
Swiss	717	28.7%
European (non-Swiss	209	8.4%
African	1073	43.0%
American (North, Middle, South)	119	4.8%
Asian	158	6.3%
Oceanian	34	1.4%
Unknown	186	7.4%

Table 2. Rate of HIV infected children per 100,000 live births in Switzerland by nationality of the children and birth period

Nationality	Birth period	Mean rate	Odds ratio [CI]*	p-value
Swiss	1990–2003	13.6	1	
Swiss	2004–2018	0.54	0.042 [0.017–0.103]	<0.0001
non-Swiss	1990–2003	28.0	1	
non-Swiss	2004–2018	6.3	0.225 [0.139–0.364]	<0.0001

*2004–2018 versus 1990–2003; CI: 5% Confidence interval

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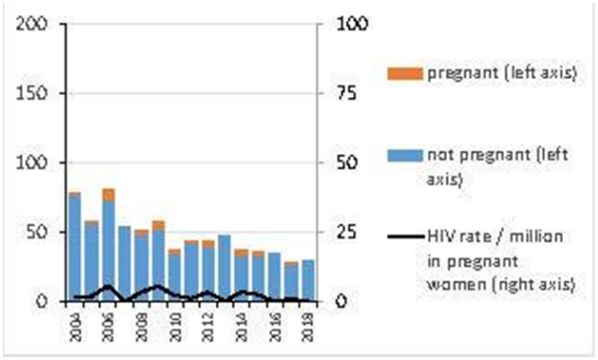


Figure 1. Yearly HIV cases in Swiss women by pregnancy status and rate per million Swiss women

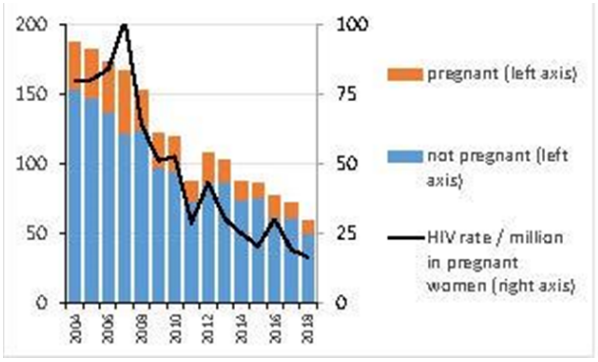


Figure 2. Yearly HIV cases in non-Swiss women by pregnancy status and rate per million non-Swiss women

PE21/2

No evidence for induced glucuronidation of dolutegravir in HIV-infected pregnant women

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Purpose: Dolutegravir (DTG) exposure is moderately decreased (by approximately 30 %) during pregnancy. One possible explanation for this decrease could be increased glucuronidation through induction of UGT1A1, which has been described in pregnancy. Therefore, we examined the metabolic ratio of DTG-glucuronide (DTG-gluc)/DTG in plasma during pregnancy and postpartum.

Methods: An open-label, multi-centre, observational, phase IV study was conducted in HIV-infected pregnant women recruited in HIV treatment centers in Europe (PANNA Network). We collected intensive steady-state 24-h pharmacokinetic (PK) curves during the third trimester of pregnancy and 3–7 weeks postpartum for women treated with once daily 50 mg DTG as part of antiretroviral treatment. The geometric mean (GM) DTG-gluc $AUC_{0-24\ h}$ and DTG $AUC_{0-24\ h}$ were determined with non-compartmental analysis. Next, the molar metabolic ratio of DTG-gluc $AUC_{0-24\ h}$/DTG $AUC_{0-24\ h}$ was calculated. We compared the molar metabolic ratio in third trimester vs. postpartum with the Wilcoxon signed-rank test.

Results: 14 third trimester and 9 postpartum PK curves were available to determine the $AUC_{0-24\ h}$ of both DTG-gluc and DTG. GM (%CV) $AUC_{0-24\ h}$ of DTG-gluc was 4.60 (65) h·mg/L in the third trimester and 3.94 (44) h·mg/L postpartum. Geometric mean ratio (90% CI) $AUC_{0-24\ h}$ for DTG-gluc in third trimester vs. post-partum was 1.04 (0.83-1.31). The median (IQR) molar metabolic ratio was 0.11 (0.07-0.12) in the third trimester and 0.08 (0.05-0.09) postpartum (third trimester vs. postpartum; p=0.164).

Conclusion: No significant difference in the molar metabolic ratio DTG-gluc $AUC_{0-24\ h}$/DTG $AUC_{0-24\ h}$ in pregnancy was observed. It is unlikely that induction of UGT1A1 is the major driver of decreased DTG exposure in pregnant women.

PE21/3

Comparative analysis of clinic and laboratory parameters and frequency of mother-to-child transmission of HIV among HIV-positive pregnant women with marked immunodeficiency and normal immunological status

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Purpose: Comparative analysis of clinic and laboratory parameters and frequency of mother-to-child transmission among HIV-positive pregnant women with marked immunodeficiency or without it.

Methods: Comparative retrospective and prospective evaluation of clinic and laboratory test values for 1333 women with HIV that gave birth in the time period between 2014 and 2017 in Saint-Petersburg. All pregnant women were divided into two groups: 1st group - 139 womenwith marked immunodeficiency (CD4 <200 cells/μL), 2nd group - 1194 patients without immunodeficiency
(CD4- 201 cells/μL and more). Statistical analysis was done with the analytics software Statistica 10.

Results: One pregnant woman in ten (10.4%, n=139) had the marked immunodeficiency. The number of pregnant women with immunodeficiency has declined between 2014 and 2017
(p<0.001). The groups are similar in age (1st group - age 28±3.7, 2nd group - age 31±4.7), way of transmission (sexual transmission - 61.2 % of pregnant women in the 1st group, 70 % in the 2nd group). Certain differences were identified for some parameters (see the table).

Conclusions: For the HIV-positive pregnant women the marked immunodeficiency is a risk factor for development of anemia, preterm delivery and mother-to-child transmission. Timely diagnosis of HIV and immunodeficiency for women of reproductive age together with early administration of HAART before pregnancy allow to lower significantly the frequency of preterm delivery and mother-to-child transmission.

Clinical and laboratory parameters in groups of pregnant women

Parameter	Group I	Group II	p
Drug injecting during pregnancy, %	9	3.5	<0.01
Pregnant women with HCV coinfection, %	53	42	<0.05
Anemia in Pregnancy, %	77	62	<0.001
Beginning of HAART before pregnancy, %	19	34	<0.001
CD-4 lymphocyte count on the date of pregnancy registration at healthcare institution, cells/μL (%)	126.6 (12)	517 (27.7)	<0.001
CD-4 lymphocyte count before delivery, cells/μL (%)	242.4 (18.4)	615.8 (36.6)	<0.001
Percentage of preterm delivery, %	26	17	<0.05
Frequency of HIV mother-to-child transmission, %	2.2	0.6	<0.001

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PE21/4

Analysis of perinatal HIV transmission cases in St. Petersburg

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Purpose: To analyze the causes of perinatal HIV transmission in St. Petersburg for the period from 2014 to 2018, to determine the risk factors for mother-to-child transmission of HIV infection and ways to reduce this indicator.
Method: A retrospective analysis of 86 medical records of HIV-infected children with perinatal transmission, born 2014–2018 in St. Petersburg and other regions of the Russian Federation, as well as medical records of their mothers, was carried out.
Results: Of the 86 cases of perinatal HIV transmission, 49 children were born to HIV-infected mothers in St. Petersburg, 23 children infected through breastfeeding, and 14 children are from other regions of Russia. The majority of mothers who gave birth to children in St. Petersburg and infected them in utero or during childbirth, HIV infection was diagnosed before pregnancy (58%), 22% during pregnancy, 12% during childbirth and 6% - time of infection detection is unknown. The sexual way of infection was the main one in the mothers of the group under discussion - 63% (n=31), half of the mothers sought medical help (49%), the average duration of treatment was 21 weeks of gestation. 13 women (27%) actively consumed drugs. ARVD during pregnancy received 37% of mothers, starting at an average of 24.5 weeks of pregnancy, 72% of them had impaired treatment adherence. The average time of receiving HAART was 5 weeks. The average level of HIV RNA in the blood of mothers before delivery was 86,397 copies/mL. Abandoned antiretroviral medicine - 49% (n=24). 29 mothers (59%) received prophylaxis at birth. 23 out of 86 children were infected during breastfeeding, 74% of women were seronegative during pregnancy.
Conclusions: The main reasons for the implementation of perinatal HIV transmission is the refusal to prevent socially prosperous women or the violation of adherence to ARV

PE21/5

Geopolitical assessment and relevance for acceptance of vaginal delivery in good controlled HIV-infected pregnant women in Japan

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Purpose: The aim of this study was to examine and identify relevance of acceptance of vaginal delivery, as the delivery mode in good controlled HIV-infected pregnant women in Japan, in comparison with conventional elective caesarean section delivery from some geopolitical points (number of patients, medical assurance system
et al.) of view.
Method: This study was researched by the Group of Epidemiological Study on P-MTCT in Japan. This group is a multicenter prospective observational study group in which 983 HIV-infected pregnant women are enrolled and their infants prospectively followed between1984 and 2016. Data on 564 obstetrics facilities enrolled were analyzed between 2015 and 2017.
Results: Only 76 of 564 obstetrics facilities (13.4%) agreed with vaginal delivery as the delivery mode in good controlled HIV-infected pregnant women. And 64 of 76 obstetrics facilities (84.2%) could be analyzed in detail. But only 6 of 64 obstetrics facilities (9.4%) could accept vaginal delivery as the delivery mode in good controlled HIV-infected pregnant women unconditionally. Finally, vaginal delivery in good controlled HIV-infected pregnant women could be accepted in only 6 of 564 obstetrics facilities (1.1%)
Conclusion: New guideline in which vaginal delivery is admitted as the option of the delivery mode of HIV-infected pregnant women were published in March,2018 in Japan. But our findings suggested that only 6 of 564 obstetrics facilities (1.1%) can accept vaginal delivery for good controlled HIV-infected pregnant women. Considering recent Japanese obstetrics circumstance (very few number of HIV-infected pregnant women:30~40 a year and medical understaff power, good enough medical assurance system et al.), it seems to be that it will take a lot of time to accept vaginal delivery in general as the delivery mode in good controlled HIV-infected pregnant women in Japan

PE21/6

Pregnancy outcomes in HIV-positive women: a retrospective national cohort study from the "Grigorios AIDS Clinic" in Cyprus

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Purpose: provide national data on pregnancy outcomes among HIV-positive women in Cyprus.
Method: retrospective cohort study, including HIV-positive pregnant women followed at Cyprus' HIV referral clinic. Demographic, clinical and laboratory data were collected from medical records and analyzed using JMP®, Version 14. SAS Institute, NC.
Results: Between 1986 and 2019, 29 HIV-positive women with 34 pregnancies were followed at "Grigorios AIDS Clinic"in Cyprus. The majority were of European origin (17/29), followed by those of African origin (11/29) and one patient from Asia. Patients' age at pregnancy diagnosis was 28.73 (±4.06) years (mean±95% CI), whereas mean gestational age at time of pregnancy confirmation was 14.65 (±2.97, 95% CI) weeks. Mean $CD4^+$ T-cell count at time of pregnancy diagnosis was 454.64 (±92.59, 95% CI). Viral load (VL) was undetectable in only 3/34 pregnancies; the remaining 31/34 had a mean VL of 1.017×10^5 ($\pm0.67\times10^5$, 95% CI) copies/mL. All patients were initiated on antiretroviral therapy (ART). At time of delivery, 27/34 pregnancies had undetectable VL whereas the remaining 7 had a mean VL of 8.172×10^3 copies/mL. Mean $CD4^+$ T-cell count was 749.76(±145.48, 95% CI). Mode of delivery was scheduled cesarean section regardless of VL. Both mother and newborn received AZT during and following delivery respectively. Out of 35 newborns (one twin pregnancy), 33 were HIV-negative at 24 months of age whereas one was found HIV-positive. Positivity was attributed to mother's poor compliance to ART. One newborn is currently at 6 months of age and is HIV negative.
Conclusion: This is the first report of Cyprus' national data on pregnancy outcomes of HIV-positive women. Between 1986 and 2019, one case of perinatal HIV transmission has been recorded and attributed to mother's poor compliance to ART.

PE21/7

New-born infants from HIV positive women: five years experience of Infectious Diseases Hospital Iasi

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Purpose: In the North-Eastern region of Romania most of the female HIV-positive population is sexually active at a child-bearing age. In Romania, there is a strict protocol regarding HIV vertical transmission. We aim to evaluate the efficiency of this protocol and the degree of appliance, reflected in the HIV status of new-born infants from HIV-positive mothers for a period of 5 years.
Method: Of the 1442 patients actively monitored in the HIV/AIDS Regional Center in Iasi, Romania, 46.5% are female. We evaluated retrospectively the files of all new-born infants from HIV-positive mothers for a period of 5 years.(January2012-December 2016)

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Results: In the period mentioned above, 163 children were born (36 in 2012, 38 in 2013, 26 in 2014, 27 in 2015, 36 in 2016); one death occurred 10 days after birth, due to multiple organ malformations; the lowest weight at birth was 750 g; three of the children (1.8%) had a detectable viral load at birth; in two cases we could not evaluate the viral load; 161 children were born through caesarean section; two were born through natural labour (1.2%), one of which at home. Mothers received treatment with lopinavir/ritonavir +zidovudine/lamivudine through the whole pregnancy in 111 cases, other antiretroviral regimens in 43 cases, and in 9 cases the mothers did not receive any treatment, being tested for HIV at birth. For all new-borns prohylaxis was made with zidovudine+lamivudine for 6 weeks. Three children remained positive at 18 months, and therapy for them consisted of zidovudine+lamivudine+nevirapine.
Conclusion: Evaluation of pregnant HIV-positive women and prophylaxis for new-born infants in the evaluated period was conducted according to protocols, which resulted in a small percentage of HIV-positive children (1.8%).

PE21/8

Risk factors for peripartum virological failure in South African pregnant women on anti-retroviral therapy: East London Prospective Cohort Study

OV Adeniyi and East London Prospective Cohort Study Group
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Background: South Africa government implemented the World Health Organization Option B+ (life-long highly active anti-retroviral therapy - HAART) in 2015 as a strategy towards achieving the goal of elimination of mother-to-child transmission of HIV. This study investigated the HIV-1 RNA plasma viral load suppression at delivery in a cohort of pregnant women on HAART, and risk factors for peri-partum virological failure in Eastern Cape Province, South Africa.
Methods: This is a sub-analysis of the East London Prospective Cohort Study database designed to monitor the treatment outcomes of mother-infant pairs across three large maternity services in Eastern Cape, South Africa. Quantitative PCR assays (viral load) were conducted within 24 hours of delivery and categorised as; full suppression (lower than limit of detection), low level viraemia (VL=20-999 RNA copies/mL) and virological failure (VL≥1000RNA copies/mL). Logistic regression model analysis was performed to determine the risk factors for peripartum virological failure.
Results: Among all the participants (N=1709), 57.2% achieved full viral suppression at delivery, 25.3% had low level viraemia and 17.5% had virological failure. Younger age ≤ 25 years, unemployment, pre-conception awareness of HIV status, poor adherence, partner non-disclosure and lifestyle behaviours (alcohol consumption and cigarette smoking during pregnancy) were significantly associated with peri-partum virological failure. In multivariate (LR) analysis, after adjusting for confounding factors, poor adherence, pre-conception awareness of serostatus and unemployment were the independent significant determinants of peri-partum virological failure with consequent 20 cases of in-utero MTCT of HIV (1.2%).
Conclusion: Significant progress towards elimination of MTCT has been achieved in the study settings. However, health system strengthening and social support will be crucial towards addressing the identified risk factors of virological failure in South Africa.

NASH

PE22/1

Assessment of non alcoholic fatty liver disease in a cohort of HIV mono-infected patients

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Introduction: NAFLD is a substantial social problem in Western countries due to metabolic syndrome increasing and lack of effective treatment. Early recognition and risk stratification of asymptomatic patients could lead to a significant challenge. Considering HIV population NAFLD is commoner, progress faster and cause non-AIDS related disease. Despite the availability of the new noninvasive techniques and serologic markers of fibrosis there is a lack of systematic study for their validation among those patients.
Purpose: Aim of this study is to assess the performance of non-invasive tools for screening and diagnosis of NAFLD among HIV patients, identify the associated risk factor and identify a diagnostic algorithm.
Methods: This is a retrospective observational study involving HIV clinics of Pavia's Policlinico San Matteo. We collected data of 128 HIV patients without viral coinfection, history of alcoholic abuse or other liver abnormalities between 2014 and 2016. Steatosis and fibrosis evaluation has been performed by the biochemical scores Fatty Liver Index (FLI), NAFLD fibrosis score and by controlled attenuation parameter (CAP) evaluated with FibroScan.
Results: 42% of patients resulted positive for NAFLD presence at Fibroscan with CAP evaluation and 22% at FLI. 41% of patients in positive CAP group had a positive FLI score. Contrary, only 8% in CAP negative group presented a positive FLI.
We found a significant statistical correlation between FLI and CAP: FLI score was positive and higher in CAP positive patients, with an AUROC of 0.758. Multivariate model showed that higher BMI and triglycerides levels were significantly associated with NAFLD.
Conclusion: Latest scores and non-invasive diagnostic techniques, CAP particularly, are promising tools requiring further study to obtain a validation also among HIV patients. Between the score Fatty Liver Index is the most useful to identify people at risk of NAFLD which deserve to be investigated and successively examine with CAP.

PE22/2

Non-alcoholic fatty liver disease (NAFLD) and related metabolic disorders among HIV-infected patients in the country of Georgia

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Background and Purpose: The burden of liver-related morbidity and mortality remains high among HIV-infected patients. Whilst prevalence and mortality rates associated with viral hepatitis in HIV-infected individuals have been declining, rates associated with NAFLD are increasing. NAFLD is emerging concern for individuals with HIV. Pathogenesis of NAFLD and reasons for progression to NASH and ESLD are not fully elucidated, but metabolic disorders seem to be main drivers. Importantly, HIV and NAFLD are both associated with increased risk of cardiovascular disease (CVD).
Methods: Total of 187 HIV mono-infected patients with NAFLD were studied. NAFLD was diagnosed based on ultrasound and Controlled Attenuation Parameter (CAP) by transient elastography (TE-FibroScan). Among patients with moderate (S2) (CAP>268 and ≤280 dB/m) and severe steatosis (S3) (CAP >280 dB/m) following metabolic parameters were studied: Central obesity (waist circumference ≥94 cm (males), ≥80 cm (females) or BMI>30 kg/m^2), Triglycerides ≥150 mg/dL, Total Cholesterol-TC ≥200 mg/dL, LDL-cholesterol≥130 mg/dL, HDL-cholesterol <40 mg/dL in males, <50 mg/dL in females, blood pleasure (BP≥130/85 mmHg), fasting plasma glucose (FPG)≥100 mg/dL, or previously diagnosed T2DM/prediabetes.
Results: Among 187 HIV mono-infected NAFLD patients 151 (80.7%) had moderate (S2) or severe steatosis (S3). Mean age -46 years, 81% - males, mean CD4+ cell count - 590 cells/μL, 98.5% on ART. Among 151 NAFLD patients dyslipidemia was revealed in 121 subjects (80%), 67% (n=81) had atherogenic dyslipidemia defined as elevated triglycerides and decreased HDL-c, mixed dyslipidemia in 21 subjects (17.5%), IFG/T2DM in 19 subjects (13%), hypertension in 52 (35%) patients and overweight/obesity in 37 subjects (25%). No significant metabolic changes were associated with mild steatosis (S0–S1).
Conclusion: TE can be considered as useful tool for early detection of NAFLD in HIV-infected patients and timely intervention might reduce liver-related morbidity and even CVD risk. Further studies emphasizing ART's association with metabolic disorders are needed.

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PE22/3

Non-alcoholic fatty liver disease is a significant predictor of cardiovascular risk in HIV-infected patients

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Purpose: The association between non-alcoholic fatty liver disease (NAFLD) and cardiovascular disease in the general population has been largely confirmed while in people living with HIV (PLWH) has not been assessed yet. We aimed to evaluate the impact of NAFLD and liver fibrosis on cardiovascular risk in PLWH.
Method: 982 HIV-monoinfected patients from three retrospective cohorts (LHivPA in Palermo; LIVEHIV in Montreal; MHMC in Modena) were included. All patients underwent FibroScan. NAFLD was defined as controlled attenuation parameter (CAP) ≥288 db/m in the absence of significant alcohol intake (<20 g/die), which was excluded for all the included patients. Significant fibrosis was defined as liver stiffness measurement (LSM) >7 kPa. Cardiovascular risk was evaluated with Atherosclerotic Cardiovascular Disease (ASCVD) Risk Estimator, according to American College of Cardiology and categorized as: low if <5%, borderline if 5%-7.4%, intermediate if 7.5%-19.9% and high if ≥20%. Patients with previous cardiovascular events were considered as high risk.
Results: The mean age of the population was 53 years, 74% were males, 450 (46%), 130(13%), 264(27%) and 138(14%) were in low, borderline, intermediate and high ASCVD risk classes, respectively. The prevalence of previous cardiovascular events was 8.4%. NAFLD and liver fibrosis were found in 20% and 17% of the population, respectively. The distribution of ASCVD risk classes by NAFLD and fibrosis category is depicted in the Table.

Distribution of Atherosclerotic Cardiovascular Disease Risk Classes by NAFLD and significant liver fibrosis categories.

		ASCVD Risk Classes			
	n=982	Low	Borderline	Intermediate	High
NAFLD (CAP≥288 db/m)	n=196	76 (39%)	14 (7%)	70 (36%)	36 (19%)
Without NAFLD (CAP<288 db/m)	n=786	37 (48%)	115 (15%)	195 (25%)	102 (13%)
Significant liver fibrosis (LSM>7 kPa)	n=168	57 (34%)	23 (13%)	59 (35%)	29 (17%)
Without liver fibrosis (LSM≤7 kPa)	n=814	393 (48%)	107 (13%)	205 (25%)	109 (14%)

Overall, intermediate and high risk classes were more frequent in patients with steatosis (p<0.001). Notably, by multivariate ordinal regression analysis, NAFLD (OR 1.50, 95% CI 1.05–2.14, p=0.03), BMI≥30 (OR 1.85, 95% C.I. 1.38–2.49, p<0.001) and time since HIV diagnosis (OR 1.03, 95% CI 1.03–1.06, p<0.001) were independent factors associated with a higher ASCVD risk. No association was found between fibrosis and ASCVD risk classes.
Conclusion: NAFLD is a strong predictor of cardiovascular disease in PLWH. Early recognition of NAFLD may allow to implement life-style modification and treatment to prevent cardiovascular disease.

PE22/4

Non alcoholic fatty liver disease diagnosed by non-invasive markers in HIV-infected patients

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Purpose: After curing chronic hepatitis C, non-alcoholic fatty liver disease (NAFLD) is the main cause of liver damage in HIV-infected subjects. The identification of subjects with NAFLD with simple tools is an important challenge for HIV-infected subjects nowadays. Our objective was to screen a large cohort of stable HIV-infected subjects for liver steatosis with available non-invasive markers.
Method: Cross-sectional study in a 4009 HIV-infected subjects from a single Clinical Unit. We analysed the demographic, clinical and last analytical records of all patients with HIV infection followed regularly in our cohort. We calculated steatosis markers (HSI, TyG), fibrosis markers (APRI, FIB4) and analysed CAP (controlled attenuated parameter) whose value >238 dB/m diagnoses liver steatosis >5%, and transient elastography (TE) by Fibroscan®. Non-invasive markers were calculated with the last available laboratory test records done no earlier than 6 months before the cross-sectional study date, in February 2109.
Results: The main clinical and demographic characteristics: females 20%, transmission route MSM 47%, hetero 22%, IDU 23%, ethnicity 85% Caucasian, CDC stage C 23%, median nadir CD4+ cell count 220 (103–336), actual CD4+ cell count 697 (505–914), 93% with undetectable HIV viral load, median BMI 25 kg/m^2 (23–28). Less than 1% of subjects have a non-treated chronic hepatitis B or C. Non-invasive markers and metabolic parameters are shown in table 1.
Conclusion: Currently at least one out of every 3 patients infected with HIV has hepatic steatosis. Insulin resistance and hypertriglyceridemia, key components of metabolic syndrome, have a very high prevalence in this population. Although advanced fibrosis is not very prevalent at present, the

Table 1: Non-invasive markers and metabolic parameters

Metabolic parameters N (%)	Diabetes Mellitus	335/4009	8%
	Diabetes Mellitus or abnormal fasting glucose	509/4009	13%
	Dyslipemia	1937/4009	48%
	Hypertriglyceridemia	1313/4009	33%
	HTA	1136/4009	28%
	Metabolic syndrome	637/4009	16%
NAFLD N (%)	Clinical records	736/3261	24%
	HIS	1033/3493	30%
	TyG >8.38	2461/3913	63%
Insulin resistance N (%)	TyG >4.68	1645/3913	42%
Advanced liver fibrosis N (%)	FIB-4 >2.67	199/3914	5%
	APRI >0.5	49/3574	1%
Transient elastography N (%)	CAP >238 db/m	1031	53%
	Liver stiffness >9.6 Kpa	272/2153	13%

Table 1. Non-invasive markers and metabolic parameters

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high prevalence of insulin resistance and NAFLD would cause it to increase significantly in the coming years. Non-invasive markers of hepatic steatosis and fibrosis are an easy-to-use tool what should be routinely implemented in the care of patients infected with HIV.

PE22/5

Global prevalence of liver impairment in HIV population in direct antiviral agents (DAA) era: the role of fatty liver disease

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Purpose: Our objectives are to analyze the global prevalence and causes of hepatic impairment in the HIV-infected population and to know the role of NAFLD in this population
Methods: Cross-sectional study was conducted in our HIV outpatient clinic between March and May 2017. Sociodemographic, clinical, analytical, and abdominal ultrasound (US) performed in the 24 previous months were collected.
Results: 373 consecutive HIV-infected patients were included. Median age 50 (IQR 42–55); 75.1% men, median CD4 691 cells/mm^3 (IQR 468–891). Undetectable HIV viral load in 89.8%.
Hepatic impairment triggers were: HCV (+) 146 (39%) 82 of them already cured with DAAs, AgVHBs(+) 3.7%. We found persistently abnormal high transaminase levels in 108 patients (28.9%), which was significantly associated with male gender [OR (IC95%), 2.1(1.1–3.9)] and having fatty liver in US [OR (IC95%), 2.1(1.2–3.2)].
In 79 (21%) some grade of NAFLD was described in abdominal US. We managed to identify the underlying cause of liver impairment in 59/108 patients, albeit it remains unclear in 49/108 (13.1 % of the whole population). We found significant association with abdominal ultrasound fatty liver and the duration of antiretroviral treatment exposure (p=0.005) and age (p<0.001)
Conclusion: Even though 1/3 of the HIV-infected population has persistently elevated transaminases, in 13% of them, the cause remains unclear. Taking into account that fatty liver is described in 21% of this population, we must consider NAFLD of paramount importance in this population. NAFLD is associated with duration of antiretroviral exposure and age. We need further research that will allow us to understand this emerging problem in the HIV-infected subjects.

Novel consultations, remote care – telemedicine, mobile applications

PE23/1

Harnessing mobile technology for health worker capacity building to improve quality of care in resource-constrained settings

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Purpose: With the high health worker: patient ratio, there has been increased task-shifting of physician responsibilities to mid-level practitioners but the corresponding capacity building for these health workers to provide quality HIV care is limited and costly. The Infectious Diseases Institute (IDI), a private non-profit organisation affiliated to Makerere University, is bridging this capacity development gap through its flagship innovation - the Advanced Treatment Information Centre (ATIC). ATIC provides a toll-free line through which health workers are linked to in-house medical officers, physicians, pharmacists, and laboratory experts for interactive telephonic consultation on HIV and infectious diseases patient management.
Method: In December 2016, ATIC extended working hours through a mobile app, to include after-office hours, weekends and public holidays in a bid to increase health worker access to this resource.
Results: Since 2004, ATIC has handled over 20,000 information requests - the majority (70.1%) are on clinical management of patients with specific interest in ART initiation (8.5%); ARV administration and dosing (39.4%); drug interactions (2.4%); adverse drug reaction management (13.1%); management of treatment failure (6.7%); ARV logistics 2.6 %; while 3.7% inquire about laboratory investigations for HIV and other infectious diseases. In December 2018 ATIC received 1,456 information request compared to 907 in December 2016 - a 60.5% rise.
Conclusion: Mobile technologies can facilitate effective linkage between experts and health workers to enhance their capacity in clinical patient management, accurate diagnosis and health supplies management. The ATIC toll-free call centre provides an effective model for capacity-building in resource-limited settings. However, the efficacy and cost-effectiveness of call centres for health worker capacity-building hasn't been determined and data from similar resource-constrained settings is limited. We aim to evaluate impact and cost effectiveness of this service in the future.

PE23/2

Feasibility, uptake and acceptability of the EmERGE mHealth app in individuals living with stable HIV in five European countries

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Purpose: To assess the feasibility, usability & acceptability of a co-designed mHealth supported pathway of care for individuals living with stable HIV.
Methods: Following a detailed background assessment, a co-design process was facilitated with community and clinicians at five diverse clinical sites across Europe, informing the development of the platform (Figure 1) within a reduced visit pathway of care.



Figure 1. EmERGE platform

Individuals living with stable HIV (based on WHO criteria) are seen annually by their clinician with interim bloods drawn (6 & 18 months); results checked, encrypted and pushed securely to their mobile device alongside medication, appointment and other information.
Data are reported on uptake, usability (System Usability Scale (SUS)) and experience over the first year.
Results: The platform was successfully co-designed, developed and integrated into hospital ICT systems at the five sites; GDPR compliance was ensured.
2251 participants enrolled in the study: uptake varied by site (10%-37% of respective cohorts). Reasons for non-participation included: clinician engagement (change to practice; lack of virtual tariff; perceptions of digitalising clinical work); patient choice (change to current pathway; no smart phone; confidentiality); technical aspects & research questionnaires also contributed.
Of the 1439 individuals with 12 month data available to May 2019: 1222/1316(92.7%) were male; median age 44 (range 20–75); 1077/1288(83.6%) MSM; and 271/1318(20.6%) non-national at site. Viral load was undetectable at 12 months in 1229/1241(99%); no SAEs related to the pathway were reported.
Usability rating was excellent: median SUS score 85/100 (IQR 70–95) & patient reported experience positive: 82.9% rated their experience as good/excellent; 94.2% would recommend to a friend.
Conclusions: The EmERGE pathway is a feasible and acceptable option in the menu of care for individuals living with stable HIV. Uptake has varied by site and learning gives insights into factors affecting roll out of such options. To date usability and reported experience is very good.

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PE23/3

Attracting people who use drugs to HIV prevention and care programs via darknet and messengers: evidence from St. Petersburg, Russia

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Purpose: Darknet online-platform for selling illegal psychoactive substances (IPS) Hydra, as well as Telegram and KakaoTalk messengers, have become the main sources of IPS for people who use drugs in St. Petersburg. Also, the drug scene has been rapidly changing since 2015. The most popular IPS, apart from cannabioids, are new psychoactive substances (mephedrone, α-PVP, etc.), as well as amphetamine, methampetamine, MDMA. The use of heroin and methadone has been decreasing steadily. It means that HIV prevention and care programs aimed at intravenous drug users who had been using opioids mainly should be updated.
Method: Charitable fund "Humanitarian Action" has been working in the field of HIV prevention among PWIDs and sex workers since 2001. Each year more than 5,000 people receive services of the fund, including syringes exchange, HIV, HCV and HBV testing, linkage to HIV care, etc. The fund sought to update its methods of attracting PUDs to HIV prevention and care. The deputy director of the fund contacted Hydra to provide this platform with the information on the fund's activities. Also, he gave 2 interviews to the Telegram channel of Hydra. An active drug user - one of the clients of the fund - created and developed chats and public channels of the fund in Telegram and KakoTalk messengers.
Results: 2 interviews for Hydra generated more than 100,000 views. Telegram chat has more than 820 members, public channel - more than 960 subscribers. Case managers and peer counselors of the fund connect with clients via these messengers directly to remind them of ARV intake, of a visit to the doctor, etc.
Conclusion: Darknet, as well as Telegram and KakaoTalk messengers, should be actively used by harm reduction and HIV prevention and care programs to attract PUDs to testing and linkage to care.

PE23/4

People living with HIV (PLHIV) and their doctors: adopters and sceptics, and those opened to e-health

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Purpose: To identify profiles of PLHIV and doctors regarding e-health.
Methods: Multicenter online survey conducted in October 2018 in France including 279 PLHIV and 229 physicians. A multiple correspondence analysis followed by a mixed unsupervised classification was implemented.
Results: Three groups of PLHIV were identified: group 1 "adherent to e-health" N=121 (43%) more often over 60 (G1 8% G2 29%, G3 40%), more likely to receive other treatments than antiretrovirals (G1 25% G2 47% G3 54%); group 2 "technology sceptics" N=86 (31%) more often women and having at least one child (G1 29%, G2 56%, G3 41%); group 3 "Internet adopters" N=72 (26%) more often under 49 (G1 65% G2 30% G3 27%) and MSM (G1 64%, G2 24% G3 44%), more likely to use mobile applications for wellness/health (G1 64%, G2 19%, G3 10%) and connected objects (G1 47% G2 13% G3 13 %).
Among doctors, three groups emerged: group 1 "strongly confident in e-health" N=95 (41%) more often using mobile applications for wellness/health (G1 23%, G2 38%; G3 43%), more likely to accept the prescription assistance software (G1 50% G2 61% G3 72%); group 2 "strongly opposed to e-health" N=80 (35%), more numerous to agree that e-health challenges confidentiality (G1 64% G2 39% G3 27%); group 3 "open to e-health" N=44 (19%) more often infectiologists (G1 63% G2 86% G3 73%), more likely to believe that medical applications are useful for patient information/education (G1 58% G2 91% G3 87%).
No link was found between the groups of PLHIV and doctors.
Conclusion: While world literature about e-health describes adopters and sceptics, a third profile appears in both PLHIV and doctors, but without a direct link: those who pay attention to e-health to improve their health condition and doctors who find a benefit to patients and/or for their exercise.

PE23/5

Fitness tracking wearable devices and a dedicated smart phone app (MySAwH App) to predict quality of life in PLWH: a multi-centre prospective study

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Objective: My Smart Age with HIV (MySAwH) is a multi-centre prospective ongoing study based on collection of physical function data and patient-related outcomes through a dedicated smart-phone app (MySAwH App). Our objective was to describe health changes assessed with frailty index (FI), collected by health professionals, and a health measure called intrinsic capacity (IC) index which explores 5 different health domains: locomotion, vitality, sensory, cognition, psychosocial. FI and IC were used to predict quality of life (QOL) and health score (HS) at follow-up.
Methods: We included 261 PLWH >50 years from Italy (128), Australia (100) and Hong Kong (33). Baseline and follow-up (9 months) were performed. Frailty was measured with a 36-item FI, while 27-item IC index was self-assessed with fitness tracking wearable devices and a MySAwH app. QoL and HS were evaluated with EQ5D5L questionnaire.
Results: Mean age was 56.94 years; 88.12% men. Median CD4 was 657 c/μL (480–817 IQR) and 252 (98.05%) patients had undetectable HIV viral load. Mean FI at baseline and follow-up were 0.22 (±0.1) and 0.2 (±0.09) respectively, p<0.001. Mean IC at baseline and follow-up were 0.69 (±0.12) and 0.71 (±0.12), p=0.27. Median QoL at baseline and follow-up were 0.88 (0.8–1 IQR) and 0.9 (0.83–1 IQR), p<0.03. Mean HS at baseline and follow-up were 7.6 (±1.68) and 7.63 (±1.56), p<0.001. In a multivariate logistic model, predictors for a good HS at follow-up were baseline IC (OR=6.74, 3.86–11.77) and recruitment site (Hong Kong (OR=1.25, 1.01–1.54)). Predictors for QoL were baseline IC (OR=7.62, 4–14.51) and recruitment site (Hong Kong (OR=1.33, 1.05–1.69)).
Conclusion: FI and IC are performative tools that can be used in research and clinical setting to describe respectively disease and health status in PLWH. IC score in comparison to FI displayed higher sensitivity to predict both QoL and self-perceived health in PLWH.

PE23/6

The efficiency of introducing the EmERGE Pathway of care for stable Croatian PLHIV

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Purpose: Estimate the cost-effectiveness of introducing a mHealth supported Pathway of Care for clinically stable people living with HIV in Zagreb. The EmERGE Pathway enables individuals to receive HIV treatment information on their smart-phone via the mHealth App.
Method: 293 study participants predominantly used HIV outpatient services, the focus of the costing study. Unit costs were linked to mean per patient year (MPY) use of HIV services. Data on use of services were collected retrospectively one-year before and prospectively one-year after the introduction of the mHealth Pathway, enabling annual cost of HIV service provision to be estimated. Annual costs were combined with outcome data, changes in CD4 count and Viral Load one-year before and after the introduction of the mHealth Pathway. Costing were calculated in Croatian Kuna and converted to Euros.
Results: Mean outpatient visits decreased from 5.2 (95% CI: 4.9 to 5.5) to 4.75 (95% CI: 4.5 to 5.0) MPY. The annual costs of service provision were €8,885.30 (95% CI €8,833.90 to €8,938.60) pre-mHealth and €8,716.20 (95% CI €8,673.40 to €8,761.40) post-mHealth; clinic visits and tests comprised

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10% of total costs, ARVs 55% and other pharmacy costs 35% of annual costs. No significant differences in CD4 counts were observed between periods and Viral Load remained undetectable during each period with no significant difference between pre-mHealth and post-mHealth values.
Conclusion: Annual cost pre- and post- mHealth Pathway decreased by 2%. Cost for ARVs and Pharmacy services were the greatest cost drivers. Participants remained clinically stable after the introduction of mHealth Pathway of Care, which has been an efficient intervention. Future efficiencies can be anticipated with introduction of the Pathway across the clinical site. Additional analyses will include other outcomes such as quality of life (PROQOL-HIV), self-management (PAM13) and patient out-of-pocket expenditures.

PE23/7

'The 4th 90': a preliminary assessment of change in quality of life over 1 year of the EmERGE study: PROQOL-HIV and EQ-5D-5L, a descriptive analysis

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Purpose: To assess the potential effect on Quality of Life (QoL) of a co-designed reduced visit pathway of care for individuals living with stable HIV.
Methods: People living with stable HIV across five diverse clinical sites in Europe were invited to take part in the EmERGE study - whereby individuals are seen once instead of twice a year by their clinician - with interim visits supported via an mHealth platform.
We report descriptively on QoL outcomes at baseline (M0) and month12 (M12) available to May 2019. For PROQOL-HIV, the mean change in score is reported by domain. For EQ-5D-5L, some vs. no problems (as proportions) are reported by dimension.
Results: PROQOL-HIV was completed by N=1868/2230 (83.8%) at M0 and 966/1439 (69.2%) at M12. At M0, domain scores were generally high across sites (median score for each≥75/100), except for stigma (median=50,IQR 25.0–87.5) with some variation by site. Mean differences (M12-M0) for all domains were small relative to their SDs, indicating little change (Table 1). Participants' general health was good at M0, (2.4% rated their health as <fair) and at M12 had improved for N=151/912(16.6%), worsened for 261(28.6%), unchanged for 500(54.8%).
EQ-5D-5L was available on N=2115/2230 (95.5%) at M0, and N=1018/1439(70.1%) at M12. Mean health today was 84.3(SD=13.1), M0, and 83.4(SD=13.7), M12. At both M0&M12, >75% of respondents reported no problems with mobility, self-care or usual activities; a smaller majority reported no pain/discomfort or anxiety/depression: proportions for these domains were lower (8.8%&6.6%, respectively) at M12 (Table 2).
Conclusions: Preliminary results show QoL was high across PROQOL-HIV domains, except stigma, which scored lowest. Changes over time were small; stigma improved at four out of five sites. QoL was similarly high on EQ-5D-5L dimensions. Observed reductions in general health and/or QoL may be explained by a ceiling effect in this healthy population with high QoL.

Table 1. Mean (SD) of changes between M0 & M12 for domains fo PROQOL-HIV by site

Change in PROQOL-HIV	Antwerp			Barcelona			Brighton			Lisbon			Zagreb		
between m0 & m12	n	mean	sd	n	mean	sd	n	mean	sd	n	mean	sd	n	mean	sd
Physical Health and Symptoms	165	-2.1	14.1	208	-5.0	13.1	245	-1.8	13.7	123	-1.0	13.6	227	-1.4	12.8
Body Change	163	-0.4	16.3	208	-6.8	20.3	250	-2.1	16.9	126	-2.1	14.9	229	-0.4	16.2
Social relationships	169	0.4	16.6	210	-2.3	15.9	255	-0.6	14	127	-0.4	15.8	233	0.6	13.9
Intimate relationships	168	2.0	22.3	208	-6.4	25.5	250	-2.2	22.5	127	-1.6	20.3	230	1.7	21.4
Stigma	167	6.4	29.4	211	-1.1	30.3	253	1.9	26.2	128	4.1	27.4	230	3.8	33.8
Emotional distress	165	0.0	17.3	209	-4.3	20.6	251	-3.2	19.4	126	-2.8	18.2	232	1.0	18.3
Health concerns	166	-0.4	20.2	207	-5.1	19.9	252	-1.2	17.4	126	-0.8	21.9	231	0.9	16.8
Treatment impact	159	-0.8	9.5	204	-2.6	11.3	243	-1.0	10	124	-0.2	9.7	230	0.3	11.2

Table 2. Number (%) of respondents (n) reporting no problems per domain of EQ-5D at M0 & M12

Reporting no problems with	Baseline			Month 12		
	n	N	%	n	N	%
Mobility	1933	2151	89.9	918	1047	87.7
Self-care	2099	2154	97.5	1014	1046	96.4
Usual activities	1938	2154	90.0	927	1047	88.5
Pain or discomfort	1621	2159	75.1	693	1046	66.3
Anxiety of depression	1347	2159	62.4	584	1046	55.8

PE23/8

Measuring empowerment in EmERGE mHealth platform users: a descriptive analysis of interim data

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Purpose: To assess the potential effectiveness of a co-designed reduced visit pathway of care for individuals living with stable HIV in terms of empowerment (which encapsulates patient confidence, skills and knowledge to self-manage health and care).
Methods: People living with stable HIV across five diverse clinical sites in Europe were invited to take part in the EmERGE study - whereby individuals are seen once, instead of twice, a year by their clinician - with their interim visit supported via an mHealth platform.
We report here on preliminary data on the primary outcome, empowerment, measured by PAM-13 (Patient Activation Measure-13) at baseline (M0) and 12 months (M12).
Results: PAM-13 was available on 2112/2251 (93.8%) of participants at M0 and 1026/1439 (72.3%) at M12. The overall proportion of participants at low activation Levels (L) 1&2 was 12.4% (261/2112) at baseline, ranging from 10.5% in Antwerp to 13.5% in Zagreb. At M12, the overall proportion was 14.1% (145/1026), ranging from 9.0% in Zagreb to 17.1% in Barcelona.
Change in activation from L1&2 at baseline to L3&4 at M12 was achieved by 63/101 (62.4%) L1&2 baseline participants whilst 93/891 (10.4%) of baseline participants at L3&4 had dropped to L1&2 by M12; 836/992 (84.3%) did not switch between L1&2 and L3&4.
The distribution of participants across each of the four levels of PAM-13 was similar across sites at baseline with≥86% of participants with the highest levels of activation. At four out of five sites, the proportion at L3&4 is currently lower at M12 than at M0.
Conclusions: The majority of participants had a high level of empowerment at baseline. Over 60% of respondents in the lowest categories of PAM-13 (L1&2) at baseline shifted to L3&4 in M12. The proportion of participants at low activation levels was similar between sites. Follow-up continues until October 2019.

Other coinfections/sexually transmitted infections

PE24/2

High rates of ocular and neurosyphilis in a large German, city-based university hospital: lessons learned on ocular syphilis

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Purpose: Incidence of syphilis is rising, mainly among the high-risk group of men having sex with men (MSM). Syphilis can range from uncomplicated to more complicated clinical infections, including ocular syphilis (OS). A stage-adopted treatment is standard of care and recommendations advise to treat OS according to neuro-syphilis-treatment. However, data on detailed understanding of OS remain sparse.
Method: Retrospective cohort study of sero-active syphilis cases at University Hospital Klinikum rechts der Isar, Munich from 08/2008 to 06/2018 with focus on ocular involvement. Cases were defined according to definition of Centers for Disease Control (CDC).
Results: In total, data sets of 90 patients (93% male), average age 47 years (IQR 38–54 years) were analyzed. Patients positive for HIV (PLWH) accounted for 48% and 51% were MSM. 24 (27%) were diagnosed with OS, resulting in 36 affected single eyes. Visual acuity reduction was the most frequent symptom (96%). Papillitis (61% of affected eyes), vasculitis (44%) and posterior uveitis (42%) were the most frequent diagnostic findings (*Table 1*). In total (in cases with OS), 11% (0%) were in primary, 13% (13%) in early secondary, 53% (83%) in late secondary, 17% (0%) in latent and 6% (4%) in tertiary stage of infection. 48% of the patients underwent lumbar puncture, of which 54% were defined as neurosyphilis cases (57% of OS). Overall treatment regimens (treatment in OS) consisted of 20% (33%) intravenous ceftriaxone, 42% (13%) intramuscular benzathine penicillin, 20% (33%) intravenous penicillin G, 7% (13%) combination of penicillin G, intramuscular benzathine penicillin and ceftriaxone and 3% (0%) doxycycline. In 8% (8%) the patients were lost for treatment.
Conclusion: The majority of syphilis patients was male and PLWH. Around one quarter presented with OS, almost all cases had visual acuity reduction. This finding highlights OS as a relevant and probably often underdiagnosed complication of secondary syphilis.

Table 1. Detailed description of ocular syphilis and eye involvement

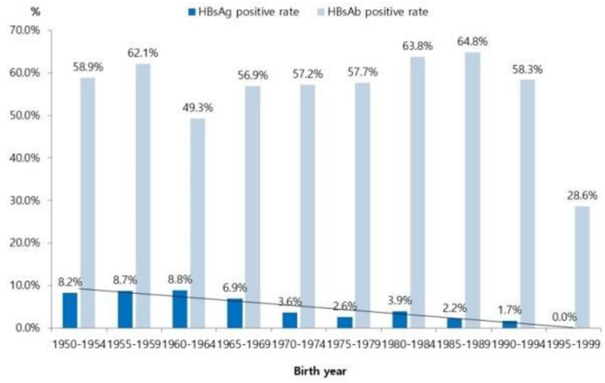
Classification of uveitis/eye involvement	n (%)
Anterior uveitis	5 (14)
Intermediate uveitis	5 (14)
Posterior uveitis	15 (42)
Panuveitis	4 (11)
Papillitis	22 (61)
Vasculitis	16 (44)
Chorioretinitis/Retinitis	12 (33)
Vitritis	7 (19)
Iridocyclitis	5 (14)

PE24/3

Decreasing rate of HIV and HBV co-infection in nationwide Korean HIV/AIDS cohort and its meaning

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Purpose: Hepatitis B vaccination is important in people living with HIV (PLHIV) since both viruses have the same transmission routes and co-infection has greater morbidity. In South Korea, hepatitis B virus (HBV) vaccination was introduced in 1983, and become a national immunization program (NIP) vaccination in 1995. We aimed to evaluate the effect of HBV vaccination program and current hepatitis B virus surface antibody (HBsAb) positive rate in HIV patients in South Korea.
Methods: The Korea HIV/AIDS cohort is a multi-center, prospective study consisting of 15 university hospitals nationwide with ongoing enrollment of HIV-infected adult patients older than 18 years. We analyzed 1,093 HIV individuals enrolled in Korea HIV/AIDS cohort age under 70 between December 2006 and December 2016. We investigated the prevalence of HIV/HBV co-infection (HBsAg positive) rate and HBsAb positive rate based on yearly changes of 5 year intervals.
Results: Mean age of enrolled patients was 47 years old. In total 1,093, HIV/HBV co-infection rate was 5.2% (57/1093). HBV co-infection prevalence rate was the highest (8.8%, 12/174) in 1960–1964 birth year patients and the lowest (0%, 0/7) in the 1995–1999 birth year patients. Decreasing linear trend of HBV co-infection rate was observed according to 5 year interval changes. No hepatitis B co-infection has been identified since 1995 birth year (24-year-old at present) in our national HIV cohort study. HBsAb positive rate was 58.1% (635/1093) in total HIV population. After introduction of hepatitis B vaccination, HBsAb positive rate was the highest 64.8% (59/91) in 1985–1989 birth year patients.
Conclusion: The national HBV vaccination programs seem to be effective in decreasing the HBV co-infection rate in Korean HIV population. However, HIV population still have low HBsAb positive rate. Therefore, we should give an effort to increasing HBV vaccination rate in the HBV susceptible host, especially HIV patients.



Decreasing HIV/HBV co-infection incidence rate according to the birth year of 5 year intervals

PE24/5

Prevalence of syphilitic hepatitis among HIV-infected patients in Istanbul, Turkey, a region with increasing incidence of syphilis and HIV infection

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Purpose: The aim of this study is to determine the prevalence of syphilitic hepatitis among HIV-infected individuals diagnosed with acute syphilis.
Method: Between January 2016 and June 2019, a retrospective analysis of HIV-infected individuals who regularly attended a tertiary clinic in Istanbul, was performed. -Cases of syphilitic hepatitis were identified according to the following criteria: (I) VDRL/RPR-confirmed *T. pallidum* infection occurring after or simultaneously diagnosed with HIV infection (II) elevated liver enzyme laboratory tests, including alkaline phosphatase (ALP), that resolved after penicillin treatment, and (III) exclusion of other causes of hepatitis
Results: Among 933 HIV-infected patients, 74 (7.9%) were diagnosed with any stage of syphilis based on RPR and TPHA results, 72 of them were male, and all patients were Caucasian. Concurrent syphilis and HIV infections were diagnosed in 7 of 74 patients.
Out of 74 patients 6 (8.1%) had syphilitic hepatitis. Moreover, 2 of these 6 patients were simultaneously diagnosed with syphilis and HIV infection. Within the cohort demonstrating syphilitic hepatitis, all of them selfidentified as men who have sex with men (MSM). All of the 6 patients were diagnosed in the early stage of syphilis and they were treated with a single dose of benzathine penicilin. The following symptoms were recorded: mucocutaneus lesions (n=5), chancre (n=4), pharyngitis (n=2) and jaundice (n=1). Rapid remission of clinical and biochemical abnormalities following treatment were seen in all hepatic involved patients.
Conclusion: The rates of hepatic involvement in HIV-syphilis coinfection were higher in predominantly MSM populations. Immune dysregulation and entry of spirochetes via rectum are possible mechanisms to explain an increased risk of hepatic involvement in HIV-syphilis co-infected population. Therefore, all syphilitic hepatitis patients were MSM in our cohort. Lower rates of MSM

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individuals may contribute to the lower prevalence observed in our patients as compared to previous reports in the literature.

PE24/6

Seroconversion rate after yellow fever vaccine in HIV-positive patients

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Background: Yellow fever (YF) vaccine is a live attenuated vaccine inducing protecting Neutralizing Titers of antibodies (NT Ab) in 99% of immunocompetent vaccines at one month. Data on seroconversion rate in HIV-positive patients (p) are scarce.
Objectives: To assess seroconversion rate by measuring NTAb in HIV (p) in the year before and after YF vaccine and to identify risk factors for lack of seroconversion.
Methods: A retrospective study in two Belgian AIDS Reference Center. Demographics, HIV history and YF immunization data were extracted from HIV databases. Plasma samples from the year before and after YF vaccination (≥ 30 days after immunization) were analyzed for YF NTAb by plaque reduction neutralization test (PRNT90). Primary endpoint was seroconversion rate (YF NTAb increasing from undetectable to ≥1/10).
Results: Hundred HIV p., negative for YF at baseline and immunized with one YF vaccine, were included: 51% female, 68% African, median age at vaccination 38 years; 79% on antiretroviral therapy (ARV), 65% with undetectable viral load before immunization, median CD4 509/μL, median nadir CD4 211/μL.
After YF vaccine 84/100 p. developed protective NTAb. Age, ethnicity, nadir CD4 count, duration of HIV infection, CD4 in the year before immunization had no influence on seroconversion rate, while not being on ARV or having a detectable HIV viral load before or during immunization was a risk factor for lack of seroconversion (p=0.0005).
Conclusions: Not being on ARV or with undetectable HIV viral load was the only identified risk factor for lack of seroconversion after YF vaccine. A second dose of vaccine, should be considered in such circumstances. A multicentric study to assess seroconversion rate and duration of protection after YF immunization in HIV patients on a larger scale is currently underway.

PE24/7

Low seroprevalence of syphilis infection among key populations in Togo in 2017: a national cross-sectional survey

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Purpose: To estimate the seroprevalence of syphilis among males who have sex with males (MSM), female sex workers (FSW) and drug users (DU) in Togo.
Methods: A cross-sectional bio-behavioral study was conducted in August and September 2017 using a respondent-driven sampling (RDS) method in eight major cities in Togo.A standardized questionnaire was used to record socio-demographic data and sexual behavior patterns. A blood sample was taken and SD Biolane Duo VIH/Syphilis rapid test was used to test for HIV and syphilis.
Results: A total of 2,158 key populations (678 MSM, 1,003 FSW and 477 DU), with an average age of 27.6 years (standard deviation 8.8 years) participated in the study. Prevalence of syphilis was 0.6% (95% CI= [0.3–1.0]) with no statistical significance between the three groups: null among MSM, 0.8% among FSW (95% CI= [0.37–1.63]) and 1.1 % among DU (95% CI= [0.39–2.57]). There was no relation between HIV status and syphilis (p=0.236). Among the 298 HIV-positive people, none was diagnosed with syphilis.
Conclusion: Findings from this study reveal a low prevalence rate of syphilis among key populations in Togo. Specific interventions into HIV prevention programs should be reinforced to eliminate syphilis in Togo.
Key words: Syphilis, HIV, seroprevalence, key populations, Sub-Saharan Africa.

PE24/8

Socio demographics, sexual behavior and clinical manifestations of HIV+ and HIV- patients diagnosed with syphilis, Brussels 2017–2019

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Purpose: To compare patient characteristics, sexual behavior and clinical manifestations of HIV positive (HIV+) and HIV negative (HIV-) patients with syphilis.
Method: Prospective observational study performed in the largest HIV reference center and STI clinic of Brussels. Inclusion criteria were adult patient with a new episode of syphilis. Both patient and physician filled a survey. Data on demographics, socioeconomic, sexual behavior, chemsex, stage of syphilis, clinical manifestation, concomitant STI, PrEP use, CD4 and viral load in HIV+ patients were analysed. Descriptive statistics were used with Wilcoxon or Fisher's exact tests.
Results: Between October 2017 and May 2019, 136 patients were included: 62 HIV+ and 74 HIV-. Most were men (97%), 90% MSM. There was no difference in gender, sexual orientation, origin and socioeconomic status between the 2 groups. HIV- were slightly older than HIV+ (40 vs 36 years, p=0.02). High risk sexual behaviors including chemsex were frequent in both groups (see Table 1). Among HIV+, 97% (60/62) were treated with a VL <200 cp/ml. Among HIV-, 30% were on PrEP and 19% started PrEP after syphilis diagnosis. Two-thirds of patients had symptoms of primary or secondary syphilis. Proportion of neurosyphilis was similar in both groups. Among asymptomatic patients, HIV+ had more frequently early latent syphilis while HIV- had more late latent syphilis or of unknown duration (p<0.01). Previous syphilis infection was more frequent in HIV+ (74% vs 37% in HIV-, p<0.01). Median RPR was similar in both groups.
Conclusion: HIV+ and HIV- patients with syphilis have a similar profile with high risk sexual behavior including infrequent condom use, sex under influence and multiple partners. Among asymptomatic patients, HIV+ were diagnosed at earlier stage probably due to regular blood test. Strategies to detect syphilis earlier should be developed, such as more frequent testing, particularly in HIV-MSM not on PrEP.

		All patients n=136	HIV positive n=62	HIV negative n=74	p	Missing data
Occasional partners		97 (76%)	38(70%)	59(80%)	0,29	8
Number of partners in the last 12 months (median, Q1-Q3)		6 (3-20)	5(3-17)	8(3-20)	0,5	
Use of condom for penetration in the last 12 months					0,35	13
	Always	15(12%)	7	8		
	Always except with stable partner	14(11%)	3	7		
	Sometimes	68 (55%)	28	40		
	Never, even with multiple partner	14(11%)	9	5		
	Never because only one stable partner	10(8%)	3	7		
Unprotected sex under influence		47 (40%)	23	24	0,18	18
	Alcohol	32(68%)	12	20	0,03	
	Cannabis	12(25%)	6	6	1	
	Ecstasy	16(34%)	6	10	0,36	
	Cocaine	22(47%)	9	13	0,39	
	Crystal methamphetamine	13(27%)	6	7	1	
	GHB	22(47%)	11	11	1	
	Mephedrone	6(13%)	3	3	1	
	Ketamine	10(21%)	4	6	0,72	
	Slam (injecting drug)	19(14%)	7	12	0,46	

Table 1. Sexual behaviors in patients with syphilis

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PE24/9

Risk factors and prevalence of syphilis, gonorrhea and chlamydia infections in the Swiss HIV cohort study

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Purpose: To assess risk factors and prevalence of sexually transmitted infections (STIs) in the Swiss HIV Cohort Study (SHCS).
Methods: STIs reported by patients or treating physicians within the last 6 months of study visit are recorded in the SHCS since October 2017. Demographic, clinical and behavioral characteristics were prospectively collected at the 6-monthly follow-up visits. We calculated prevalence and used logistic regression to assess risk factors for episodes of STIs.

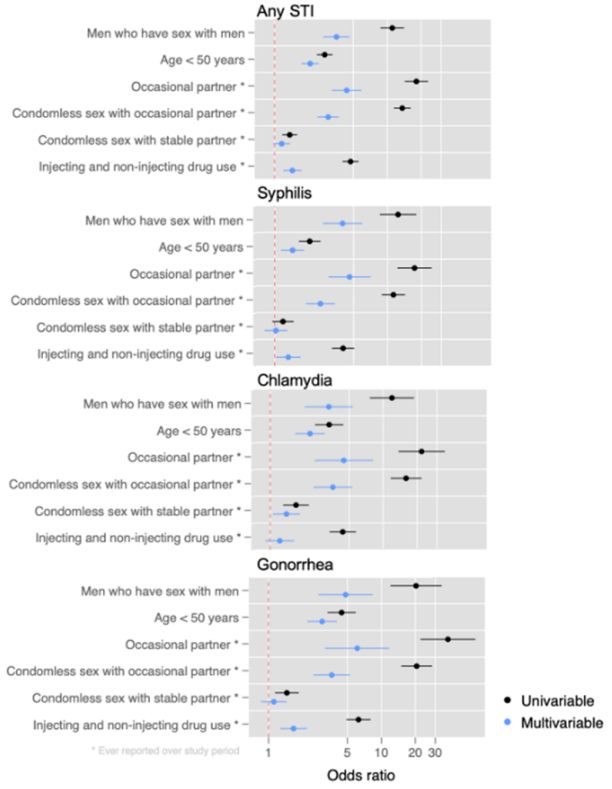


Figure. **Risk factors for reported sexually transmitted infections (STIs) among participants in the Swiss HIV Cohort Study. Univariable odds ratio (OR, black) and multivariable adjusted odds ratio (aOR, blue) and 95% confidence interval. (Note: logarithmic scale)**

Results: Between October 2017 and March 2019, 728 SHCS participants reported 1,001 episodes of STIs among 9,824 patients under follow-up. The most frequent STI was syphilis, with 368 reported episodes, followed by gonorrhea (309), chlamydia (255) and others (not specified, 69). Half of STI episodes were symptomatic (501, 50%). Patients reporting an episode of STI were predominantly male (96%), men who have sex with men (MSM) (89%) and younger (median age 44 vs 52) than those without STI. Prevalence of ever having an STI among MSM was 14% and ranged between 1.0% and 4.4% among other transmission groups.
In univariable analysis, the strongest risk factors for STIs were having had occasional partners (odds ratio (OR) 18.1, 95% confidence interval [11.5–16.1]) and condomless sex with an occasional partner (OR 13.6 [14.0–23.0]) (Figure). In multivariable analysis, risk factors included MSM (adjusted odds ration (aOR) 3.6[2.8 -4.7]), having occasional partners (aOR 4.5[3.3–6.0]), condomless sex with an occasional (aOR 3.3[2.7–4.1]) or steady partner (aOR 1.2[1.0–1.4]), as well as being younger than 50 years (aOR 2.2[1.9–2.6]) and injecting and non-injecting drug use (aOR 1.4[1.2–1.7]), and were similar across different STIs (Figure).
Conclusion: Prevalence of STIs in the SHCS was 14% among MSM and less than 5% among other transmission groups. Risk for STIs exceeded 3-fold among MSM compared to any other transmission group, and 4-fold among participants having occasional partners.

PE24/10

Predictors of serofast state after treatment for syphilis in HIV-infected patients

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Objectives: Nontreponemal serologic tests such as rapid plasma reagin (RPR) tests are used to monitor treatment response, because they usually correlate with disease activity. Syphilis and human immunodeficiency virus (HIV) coinfected patients may experience slower decline in RPR titers which is referred to as serofast status. Risk factors for serofast status in which nontreponemal antibodies persist after treatment are not completely understood. Goal of this study was to evaluate risk factors for serofast state after treatment in HIV-infected patients.
Methods: From April 2016 to June 2018 671 HIV+ patients were tested for syphilis using Treponema pallidum particle agglutination assay (TPPA). Among the TPPA positive patients, medical records were screened for documented syphilis infections with evaluable data. Serofast state was defined as lack of 4-fold decrease in RPR titers during a 6 months follow-up period in the absence of symptoms of syphilis. Baseline characteristics were tested as predictive factors of serological failure using univariable analysis.
Results: 224 patients (33.4%) were tested positive in TPPA assay and in 135 patients at least one previous syphilis infection was documented in case records. 53 out of 135 patients (39.3%) experienced serological failure. Serofast state was associated with higher number of previous infections (p=0.01) and fewer usage of adjunctive therapy with corticosteroids (p=0.001). Adjunctive corticosteroids, used for the prevention of the Jarisch-Herxheimer reaction and not for treatment of syphilis, led more often to serological cure in late syphilis (p=0.002), while it had no influence in early syphilis (p=0.15). Type of syphilis treatment (one versus three doses of benzathine penicillin-G) did not affect serological cure rates.
Conclusion: Corticosteroid usage for prevention of the Jarisch-Herxheimer reaction was associated with serological cure. Although serological response is the most commonly used surrogate method to assess the efficacy of syphilis treatment, the biological significance of the serofast state remains unclear.

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PE24/11

A proactive approach to assess rising STIs among different at-risk groups of MSM in the early era of PrEP: a real-world clinical care setting

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Purpose: MSM are at particular risk of STIs due to sexual behavior and substance use. HIV PrEP may increase this risk, mainly by means of risk compensation. In our center, a proactive approach combining education about STIs has been proposed to all patients PrEP users. Our aim was to comparatively assess incident STIs among different at-risk groups—PLWHIV, HIV-negative (HIV-neg) PrEP and no-PrEP users—seen at our center early after PrEP implementation, as well as to evaluate different types and sites of STI in these groups.
Method: Clinical data were retrospectively collected on all consecutive MSM seen at the Infectious Diseases Department (European Hospital Marseille, France), between September 2016 and October 2018. STI screening is performed systematically among all at-risk patients followed in our center. STI incidence rate (IR) was assessed among groups of patients for the whole period (P), as well as separately for the first (P1) and second year (P2) of the study period.
Results: Medical records of 636 MSM participants were reviewed, of whom 447 were PLWHIV, and 189 were HIV-neg, including 105 PrEP-users. Overall STI incidence rate ratio (IRR) was higher in HIV-neg (irrespective of use of PrEP) when compared to that of PLWHIV. In multivariate analysis, STI risk was significantly higher among HIV-neg no-PrEP users compared to PLWHIV, while not different between PLWHIV and PrEP users.
STI incidence globally increased during the first 2 years after PrEP approval among PLWHIV and no-PrEP users while it remained rather stable for HIV-neg PrEP users. The HIV-neg no-PrEP group remained at higher risk of STI than PLWHIV and PrEP users during the two periods.
Conclusion: These results underline that a proactive approach of an efficient follow-up of and information on MSM participants since PrEP approval may have prevented an increase of the incidence of STIs among HIV-neg individuals.

PE24/12

Profiles of multidrug resistant gonorrhea in HIV-infected patients attending an urban hospital in Uganda

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Purpose: There's increasing anti-microbial resistance of Neisseria gonorrhea to conventional anti-microbial therapy. There's limited data on *N. gonorrhea* resistance among HIV-infected patients in developing countries. The objective of this operational research was to estimate the prevalence of culture positive *N. gonorrhea* resistance among HIV-infected patients diagnosed with culture positive N. gonorrhea.
Method: Prospective operational study carried out from June 2018 to July 2019, in HIV-infected persons who presented with either an abnormal vaginal discharge or penile discharge and tested culture positive for *N. gonorrhea*.
Results: A total of 511 HIV-infected patients accessed services from the STI program. Of 511 patients, 279 (54%) presented with either an abnormal vaginal discharge or penile discharge. Among the 279 samples that were cultured, *N. gonorrhea* was isolated in 23 (8.2%) cultures. Although *N. gonorrhea* was more amongst the male participants compared to their female counterparts: 65.2% vs. 34.8%, this was not statistically significant (p=0.84). Median age of the participants diagnosed with *N. gonorrhea* was 33 years (IQR: 29.5–39.0) and 12 (52.2%) with WHO clinical stage III/IV. Six (26.1%) sensitivity profiles were unavailable due to inability of the *N. gonorrhea* isolate to grow on subculture. In 15/17 (88.2%) *N. gonorrhea* cultures, there was sensitivity to either Cefoxitine, Augmentin, Ceftriaxone, Cefuroxime, Penicillin, Chloramphenicol or Streptomycin. Ceftriaxone resistance, the current recommended first-line therapy was present among 3/17 (17.6%) of the patients. Interestingly, 2/17 (11.8%) cultures showed total antimicrobial resistance.
Conclusion: Development of MDR *N. gonorrhoea* is especially concerning as it is difficult to treat, provides long term risks of gonorrhoea and increases HIV drug resistance to partners. There's need for continued *N. gonorrhea* sensitivity surveillance in HIV patients, as well as the general public to inform management choices, especially in resource-limited settings where syndromic management of STIs is performed.

PE24/13

Sexually transmitted diseases clinic in a Portuguese Infectious Diseases unit

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Introduction: Sexually transmitted diseases (STDs) represent a major risk factor for HIV infection. Their prevention and treatment have a significant impact in individual and public health.
Objectives: To characterise the patients attending our consultation and their STDs.
Methods: Review of clinical records of patients attending the STD consultation between June 2017 and June 2019. Statistical analysis was performed using *IBM SPSS25®*.
Results: A total of 425 patients attended the STD consultation. Their mean age was 30.5 yo (min 18, max 68), mostly male (n=376; 88.5%) from which 78.8% were men who have sex with men (MSM). Five (1.2%) were transgender females. Two thirds (n=284, 66.8%) were Portuguese. Most of the patients (n=297; 69.8%) had a high education level. Six patients were sex workers. The main reasons for consultation were: symptoms compatible with STDs (35.6%), evaluation for PrEP (31.3%), high risk sexual exposure (24.9%), positive screening for a STD (6.7%).
We diagnosed a total of 188 infections in 148 patients: Syphilis, 55 cases (incidence of 12.9%); Gonorrhoea, 53 cases (12.5%); Chlamydia 48 cases (11.3%); Condyloma acuminatum 11 cases (2.6%); *Mycoplasma genitalium* 10 cases (2.4%); Candidiasis 5 cases (1.9%); Genital herpes 2 cases (0.5%) and Molluscum contagiosum 1 case (0.23%). HIV infection was diagnosed in three patients. At the first visit, 31 patients had two STDs diagnosed and 10 had three STDs diagnosed. Sixty-one patients met criteria and started PrEP during follow-up; nine patients met criteria and were informed but did not want to start PrEP.
Conclusion: Approximately one third (34.8%) of the patients that attended our consultation were diagnosed with at least one STD. We proposed PrEP in 47% of them. The incidence of HIV was 0.7%. Target-based campaigns can be an important measure to alert people in other risk groups beside MSM.

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PE24/14

Quantification of DNA human papillomavirus 16 and 18 in anal cells improves the prediction of high grade anal intraepithelial neoplasia in HIV patients

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Objective: To analyze the value of quantitative HPV-DNA16 and 18 in anal cells for screening of high grade anal intraepithelial neoplasia (HGAIN) in HIV-patients.
Methods: Cross sectional study between 2017–2019. Inclusion criteria: HIV infection, >18 years-old and risk factors for anal cancer. Exclusion criteria: previous HPV-vaccine. HGAIN was diagnosed by biopsy (AIN II-III) and guided by a high resolution anuscopy (HRA). We determined anal cytology, qualitative DNA-HPV 16,18 and other high risk (HR) subtypes (Cobas®6800-4800); quantitative DNA-HPV16,18 (qDNA-HPV) (Taqman-primers) in all patients. To calculate DNA-HPV cop./human-cells, we quantified 18S rRNA in anal cells (ThermoFisher-Scientific). ROC areas were calculated for best cut-off of qDNA-HPV16 and qDNA-HPV18. Sensitivity (S), specificity (Sp), positive predictive values (PPV), negative predictive value (NPV) were calculated to the different screening tests with their Kappa coefficients and p-value.
Results: 56 patients were included. Age 43.2±8.5 years; 48.2% smokers; 19.6% previous AIDS; CD4+:852±379 cel/uL; HIV-VL <50 cop/mL 96.5%; previous STI 71.4%. HR-HPV, HPV-16 and HPV-18 was detected in 85.7%, 42.9% and 17.9% respectively; Cytology was abnormal (ASCUS, LSIL or HSIL) in 19.6% (n=11). HGAIN-biopsy: 19.6% (n=11); low grade anal intraepithelial neoplasia (LGAIN): 25% (n=14). Abnormal cytology and DNA-HPV-16 were significantly more frequent in HGAIN-biopsies (p<0.05). qDNA-HPV16 was higher in HGAIN-biopsies: 864 cop./human-cells (IQR:80–3941) vs non-HSIL: 40 cop./human-cells (2–693), p=0.09 (Table 1). In Table 2, we show the S, Sp. PPV, NPV of cytology and virological variables for the prediction of HGAIN.
Conclusions: A qualitative DNA-HPV detection in anal cells is high sensitive for HGAIN diagnosis, but shows a low specificity and low PPV. Quantification of viral load of qDNA-HPV16 or qDNA-HPV18 in anal cells increases the specificity and PPV for HGAIN diagnosis. DNA-HPV viral load in anal cells could be a new tool to be included in anal cancer screening programs.

Cytology and HPV qualitative and quantitative determination in HGAIN-HIV infected patients

	HGAIN, n=11	NO HGAIN, n=45	p
Abnormal Cytology, n (%)	7 (63.6)	4 (8.9)	<0.001
High Risk HPV, n (%)	11 (100)	37 (82.2)	0.33
HPV 16, n (%)	8 (72.7)	16 (35.6)	0.04
HPV 18, n (%)	3 (27.3)	7 (15.6)	0.39
Other HR-HPV, n (%)	8 (72.7)	32 (71.1)	1
HPV-VL 16, p50 (IQR)	864 (80–3941)	40 (2–693)	0.09
HPV-VL 18, mean (SD)	1712±45.6	2223±5622	0.90
HPV-VL 16, n (%) >195 cop./cells	5 (71.4)	4 (26.7)	0.07
HPV-VL 18, n (%) >1121 cop./cells	2 (100)	1 (14.3)	0.08

Tests characeristics to detect HGAIN biopsy

	Sensitivity	Specificity	PPV	NPV	p-value	Kappa
Abnormal cytology	63.6	91.1	63.6	91.1	<0.01	0.547
DNA HR-HPV	100	17.8	22.9	100	0.33	0.078
DNA HPV-16	72.7	64.4	33.3	90.6	0.04	0.257
DNA HPV-18	27.3	84.4	30	82.6	0.39	0.121
Abnormal cytology + DNA HR-HPV	63.6	91.1	63.6	91.1	<0.01	0.547
Abnormal cytology + DNA HPV-16	45.5	95.6	71.4	87.8	<0.01	0.475
Abnormal cytology + DNA HPV-18	18.2	95.6	50	82.7	0.17	0.181
VL-HPV 16 >195 cop./human-cells	71.4	73.3	55.6	84.6	0.07	0.416
VL-HPV 18 >1,121 cop./human-cells	100	85.7	66.7	100	0.27	0.727

PE24/15

Primary prophylaxis against Pneumocystis jirovecii Pneumonia may be effective in preventing severe bacterial pneumonia in HIV-positive patients: findings from a large Italian center

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Purpose: We aimed to determine if HIV-infected patients taking trimethoprim-sulfamethoxazole (TMP-SMZ) or aerosolized pentamidine (AP) as primary prophylaxis for Pneumocystis jirovecii Pneumonia (PJP), presented a lower risk of developing bacterial pneumonia compared to others who don't.
Method: We retrospectively evaluated a monocentric cohort of HIV-positive patients, all of whom presented a CD4+ cell count under 200/mm^3. Follow-up was censored when CD4+ cell count became >200/mm^3 or in the event of a diagnosis of bacterial pneumonia (based on clinical, microbiological and/or radiological findings). Chi-square test and logistic regressions were used to compare parameters and assess predictors.
Results: We analyzed 1053 patients: 745 were males (70.8%), with a median age of 39 years (IQR 12–84). Full patents' characteristics are available in Table 1. Six-hundred and fifty patients (61.7%) took TMP-SMZ while 116 (11%) took AP as prophylaxis against PCP. During 1438 Patient-Years of Follow-up, there were 49 diagnoses of bacterial pneumonia requiring hospitalization, with a median duration of hospital stay of 12 days (6–31). Overall, prophylaxis against PCP was negatively associated with developing pneumonia (Odds Ratio 0.54, 95% CI 0.30–0.97, p=0.045), after adjusting for age and the presence of a previous AIDS-defining event. In a dedicated sub-analysis, we observed that prophylaxis against PCP resulted protective against pneumonia in patients with a previous AIDS event (p=0.036), while its association was not significant in patients without a previous AIDS-defining event (p=0.672). In patients with over a year since HIV diagnosis, only TMP-SMZ resulted protective against pneumonia (p=0.025) compared with AP, whose association was not significant (p=0.152).
Conclusion: Our study seems to suggest that the use of prophylaxis against PJP may have a role also in preventing bacterial pneumonia, a potentially life-threatening event in immunocompromised patients. Other studies, with larger sample size, are needed to properly assess the matter.

Patients' characteristics at baseline

Age (years), median (IQR)	39 (34–47)
Males, n (%)	745 (70.8)
CDC Stage C, n (%)	502 (47.7)
HIV Risk Factor, n (%): 1. MSM 2. Heterosexual 3. IDUs 4. Other/Unknown	1. 447 (42.5) 2. 291 (27.6) 3. 244 (23.2) 4. 71 (6.8)
Nadir CD4+ cell count (cell/mm^3), median (IQR)	67.5 (28.0–129.3)
Zenith HIV-RNA (log10 copies/mL), median (IQR)	5.12 (4.37–5.56)
Cases of severe Bacterial Pneumonia, n (%)	49 (4.7)
Patients taking TMP-SMZ, n (%)	650 (61.9)
Patients taking AP, n (%)	116 (11.0)
Time from HIV diagnosis (months), median (IQR)	16.4 (3.9–73.2)

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PE24/16

HHV-8 salivary shedding in individuals with different HIV status and sexual behaviour

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Human gammaherpesvirus 8 (HHV-8), the etiological cause of Kaposi sarcoma, multicentric Castleman's disease and primary effusion lymphoma, is mainly sexually transmitted. However, saliva is suggested to play an important role in transmission of the virus.

Objectives: To determine the frequency of HHV-8 salivary shedding in HIV-infected (HIVpos) and non-infected (HIVneg) individuals with different sexual behavior in Russia.

Methods: The study involved 165 patients: 120 male и 45 female with the median age of 36 (20–66) years. Four groups were formed: HIVpos men who have sex with men (MSM/HIVpos), MSM/HIVneg, HIVpos heterosexual men and women, HIVneg heterosexual men and women. The HHV-8 DNA in saliva was detected by quantitative real time PCR assay. Fisher's exact Test was used to evaluate the association between HHV-8 persistence and HIV status and sexual behavior, as well as Odds Ratio was calculated to assess risk for HHV-8 salivary shedding in different groups.

Results: HHV-8 DNA was detected in saliva in 5.5% (9/165) cases. The prevalence was found among MSM/HIVpos - 31.8% (7/22), MSM/HIVneg - 4.0% (2/50) cases. The concentration of viral DNA was 3.78–6.18 (median 4.98); 2.00 and 3.11 lg GE HHV-8/ml, respectively. HHV-8 in saliva was not found among heterosexual individuals. MSM are at higher risk of HHV-8 salivary shedding than heterosexual men and women, OR=27.97 ($p<0.05$, CI 95% 1.59–489.33). HIV-infected individuals also have an increased risk of HHV-8 persistence in saliva, OR=5.91 ($p<0.05$, CI 95% 1.19–29.42). Both factors significantly enhance the risk of HHV-8 shedding, OR=48.87 ($p<0.05$, CI 95% 2.64–405.03).

Conclusions: This is the first data on prevalence of HHV-8 in saliva among Russian individuals with different HIV status and sexual behavior. HHV-8 was found in saliva of 2.0% non-HIV-infected and 10.8% HIV-infected persons. The highest prevalence of HHV-8 in saliva was found in HIV-infected MSM (31.8%).

PE24/17

Insights into syphilis reinfection in HIV patients: predictors and role of serofast condition

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Purpose: An increasing proportion of cases of syphilis in people living with HIV (PLWHA) worldwide are reinfections, mainly in men who have sex with men (MSM). The objectives of this study were: to describe the occurrence of laboratory confirmed cases of syphilis reinfections among PLWHA observed from 2000 to 2019, analyze cofactors of reinfection, identify the impact of serological response in reinfection.

Method: All PLWHA in a single clinical center with a 1st episode of syphilis infection were included. Reinfection was serologically defined according toCDCdefinitions. Treatment failures were not included. Kaplan-Meier survival curves were generated to describe the cumulative incidence and time to first reinfection. Factors independentely associated to the probability of reinfection were identified by Cox regression analysis.

Results: 751pts had a 1st diagnosis of serological syphilis; 173(23%) had a reinfection. Median age at reinfection was 42 years (IQR37–50) compared to 46 (IQR37–54) of those without reinfection; 168 pts (97.1%) were males; 75.7% MSM; 85.5% Caucasian. Median CD4cell count at first reinfection was 581/mmc, median HIV-RNA1.5 log c/mL. Median time of follow-up: 6.3 years (IQR2.4–10.6) and 3.4 years (IQR1.7–6.6) at reinfection. Probability to be reinfection-free after5y from the first episode was 83% (±0.3). Serofasts' proportion was similar (4.6%vs4.5%) in those who presented a reinfection and those who didn't (p=0.944). Factors associated with reinfection were being MSM (p=0.004, AHR 1.668), Caucasian (p=0.005, AHR1.864), younger age ($p<0.001$,AHR 0.969), higher CD4 nadir (p=0.026,AHR1.001) (Table 2). At 1st reinfection, 122(70.5%) patients presented with an early or late latent syphilis, while 29.5% were symptomatic. 48(28%) of the cases presented with a 2nd reinfection (median time of reinfection 7.4y:IQT 4.3–10.3), while 23% had a 3rd reinfection.

Conclusion: Caucasian young MSM seem more likely to experience a syphilis reinfection. Serofast condition seems to be not related to reinfection occurrence. A great proportion of people who presented a reinfection were asymptomatic, suggesting a need for increasing routine syphilis test in order to reduce the potential chances of onward transmission.

Table 1. Descriptive analysis of all syphilis cases according to reinfection

	N=751 (%)	No reinfection N=578 (%)	Reinfection N=173 (%)	p
Males, n (%)	692 (92.1)	524 (90.7)	168 (97.1)	0.006
MSM/bisexual n (%)	486 (64.7)	355 (61.4)	131 (75.7)	0.006
Caucasian, n (%)	598 (79.6)	450 (77.9)	148 (85.5)	0.027
Serofast, n (%)	34 (4.5)	26 (4.5)	8 (4.6)	0.944
Median age (IQR)	46 (37–54)	46 (37–54)	42 (37–50)	0.028
CD4, median (IQR)	447 (265–660)	442 (245–684)	456 (300–607)	0.993
Log Viral load, median (IQR)	2.8 (1.7–4.7)	2.5 (1.7–4.6)	3.8 (1.7–4.8)	0.021
At first reinfection CD4, median (IQR)	581 (392–778)			
At first reinfection Log Viral load, median (IQR)	1.5 (0.9–1.70)			

Table 2. Cox regression analysis of determinants of reinfection

	Univariate			Multivariate		
	HR	CI 95%	p	AHR	CI 95%	p
Gender M vs F	3,945	1.620–9.605	0.003			
Risk factor MSM vs other	1,817	1.283–2.575	0.001	1,668	1.176–2.367	0.004
Caucasian	1,496	0.979–2.286	0.062	1,864	1.205–2.885	0.005
Age	0,968	0.956–0981	<0.001	0,969	0.955–0.983	<0.001
Nadir	1,001	1.001–1.002	<0.001	1,001	1.000–1.002	0.026

PE24/18

Infective endocarditis, a current health problem in Romanian injecting drug users

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Purpose: The use of new injectable psycho-stimulant drugs (NPS) in the last decade led to an increased risk of invasive bacterial infections, including infective endocarditis (IE). The aim of our study was to assess risk factors, clinical characteristics and survival in injecting drug users (IDUs) diagnosed with IE in a Romanian tertiary care facility.

Method: Retrospective study on IDUs hospitalized with IE at "Victor Babes" Hospital, Bucharest, between January 2008 and December 2018. Statistical analysis was performed using SPSS vs. 20.0.

Results: A total of 112 IE were diagnosed in 101 IDUs (55 IE in HIV-positive, 57 in HIV-negative IDUs). The majority were males (80.1%), from urban areas (95.0%), with a median age of 30 years (IQR 28, 34), 99% co-infected with HCV. IDUs were NPS (55.4%), opioids (20.7%) and mixed (22.7%) abusers. Right-sided IE was diagnosed in 78.5% cases. Staphylococcus aureus was isolated in 70.4% cases (42.8% MSSA, 27.6% MRSA), followed by Streptococcus spp (2.6%). Eleven cases of IE reinfections occurred, more often in NPS users (p=0.02), after a median period of 1.9 years (IQR 0.6, 4.1). IE was more frequent in HIV-positive IDUs between 2013–2018 compared to

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2008–2012 (69.7% vs 36.2%) (p=0.001). IE in HIV-positive patients was associated with multiple risk factors (Table 1). Median CD4 cell count/μl and HIV-RNA (log10 copies/mL) at IE diagnosis were 299 (IQR 141, 440) and 5.47 (IQR 4.51, 5.97), respectively. The overall mortality and early mortality rates were high, especially in patients with multivalvular IE (Table 2). Shorter survival was associated with HIV infection (p=0.043) (Figure 1), multiple valve involvement (p=0.012), reinfections (p=0.001) and CD4 cell count <200/μL (p=0.017).

Conclusion: Prevalence of IE among HIV-infected IDUs was high, especially in the last years of the study. There is an urgent need to focus on preventive interventions and intensify local harm-reduction strategies.

Table 1. Risk factors in IDUs diagnosed with IE

		Total* n=112	HIV-positive n=55	HIV-negative n=57	p value
Age at drug use initiation	median (IQR)	30 (28, 34)	29 (26, 33)	31 (28, 34)	0.005
Use of NPS	n (%)	68 (61.6)	41 (74.5)	27 (47.3)	0.001
History of alcohol abuse	n (%)	23 (20.5)	13 (23.6)	10 (17.5)	<0.0001
Imprisonment	n (%)	14 (12.5)	11 (20.0)	3 (5.2)	0.010
Homelessness	n (%)	17 (15.1)	15 (27.2)	2 (3.5)	0.002

*5 IDUs with IE being HIV-negative at first IE infection and HIV-positive at reinfection.

Table 2. Mortality rates and survival in IDUs with IE

			Infective endocarditis		
	Total n=112	Right-sided n=88	Left-sided n=14	Multiple valve involvement n=10	p value
Mortality rate n (%)	37 (33.0)	25 (28.4)	7 (50.0)	7 (70.0)	0.068
Early mortality rate n (%)	30 (26.7)	19 (21.5)	5 (35.7)	6 (60.0)	0.030
Survival (months) median (IQR)	15.1 (2.0, 59.1)	26.6 (5.1, 73.5)	12.5 (3.0, 27.8)	1.95 (0.4, 3.9)	0.012

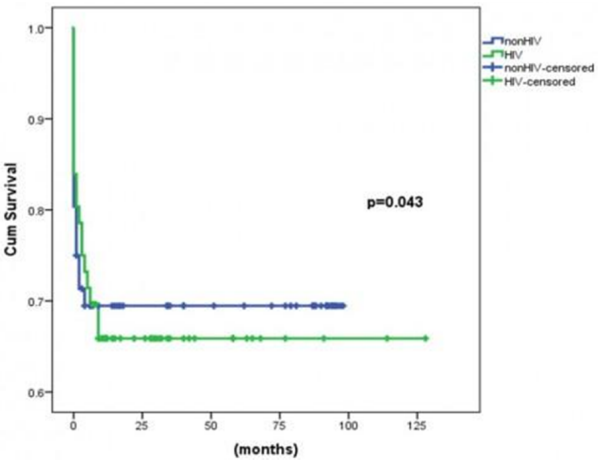


Figure 1. Kaplan Meier curve for survival in IDUs diagnosed with IE, depending on HIV status

PE24/19

Preventable risk factors and predictors of hepatic and non-hepatic co-morbidities among PLHIV

O Odukoya[1,2], E Odeghe[3], F Ogunsola[4] and Epigenetic Markers of HIV Associated Cancers

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Purpose: Nigeria has the third highest burden of HIV/AIDS in the world. We sought to identify the preventable hepatic risk factors, and the prevalent hepatic and non-hepatic co-morbidities among people living with HIV (PLHIV).
Method: HIV-positive patients aged 18 years and above were consecutively enrolled. Descriptive statistics and logistic regression analyses were conducted to determine the pattern and predictors of hepatic and non-hepatic comorbidities
Results: One hundred and twenty-four HIV positive patients were enrolled. Four patients (3.23%) had at least one form of hepatic disease, primarily hepatocellular cancer (100%). None had alcoholic or fatty liver disease. Majority (83.8%) had at least one risk factor for liver disease. The most predominant risk factors were current alcohol use (23.8%), herbal drug use and hepatitis B virus co-infection, both 16.1% and current tobacco use (5.7%). None had concurrent HCV co-infection. Only 3.3% and 0.81% had ever received vaccinations for HBV and HAV respectively. The proportion of respondents with at least one HBV risk factor was 68.6%. The most predominant HBV risk factor was high-risk sex (62.5%). Other HBV risk factors present in the population were an MSM sexual orientation, injecting drug use & previous blood transfusion with 6.6% each and prenatal exposure (1.6%)
Only 7.3% of the patients had a non-hepatic co-morbidity; primarily obesity (4.1%) and diabetes mellitus (1.6%). None had chronic kidney disease, previous renal transplant, coronary heart disease, dyslipidaemia, lung disease or any other non-hepatic malignancy. The only statistically significant predictor of having a hepatic co-morbidity was current tobacco use (OR: 8.1, 95% CI: 0.6–15.4) while the only statistically significant predictor of having a non-hepatic co-morbidity was increasing age (coeff: 0.22, 95% CI: 0.06–0.37)
Conclusion: Preventable risk factors for liver disease are prevalent among these PLHIV. Integrating the prevention of these risk factors into HIV care is recommended.

PE24/20

Incidence of asymptomatic HAV infection among MSM living with HIV in South-Western Poland

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Objectives: Poland was the country with the highest increase of acute hepatitis A incidence during an outbreak in 2016–17 in Europe according to ECDC reports. Despite the lack of country-wide epidemiological data MSM seemed to be the most affected population. The aim was to assess the rate of asymptomatic HAV seroconversion among HIV-infected MSM in HIV care center in Wroclaw, Lower Silesia region.
Method: Retrospective, single-center analysis of epidemiological and serological data concerning HAV infection and other STI among MSM living with HIV. Total anti-HAV were tested in two timepoints: at baseline before the significant increase of hepatitis incidence in Poland (till the beginning of 2017) and after the end of 2017. Patients with history of acute hepatitis A, vaccinated or with unclear history of HAV vaccination were excluded.
Results: Among 485 MSM under care 159 individuals were included, median age 34 years (range 21–65). 133 patients were anti-HAV total negative at baseline. In 14 cases (10.53%) anti-HAV total turned positive at the second timepoint, without any symptoms, signs or biochemical markers of acute hepatitis between two tests. Median CD4 at baseline was 594 (IQR 413–743), nadir CD4 was 336.5 (IQR 234–437). All patients were on cART during the observation period except 3 individuals who had interrupted therapy. In 87

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patients at least one past and current episode of other STI (eg. syphilis, gonorrhea, chlamydiosis, genital warts, acute hepatitis C) was reported, in 41 cases - more than 1 episode. No statistically significant correlation of HAV seroconversion with age, current CD4, CD4 nadir, neither episodes of current or past other STI was found.
Conclusion: Asymptomatic HAV infection rate among HIV-infected MSM was relatively high, although not related to other STI as markers of risky sexual behaviours. The proper access to anti-HAV vaccines is strongly needed in the vulnerable MSM population.

PE24/21

Behavioural patterns to identify key populations for syphilis prevention

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Purpose: Clustering HIV-positive men who have sex with men (MSM) by unsupervised machine learning based on their consistency of condom use revealed groups with dissimilar behaviour over time (Salazar-Vizcaya et al., CID2019). However, the association between these behavioural clusters and sexual disease transmission is yet to be characterised. As syphilis transmission in MSM has sharply increased in Switzerland in the last decade, we assessed this association by analysing prevalence and incidence of syphilis among behavioural clusters in the Swiss HIV Cohort Study (SHCS) between 2005 and 2018.
Method: We included 2494 MSM enrolled in the SHCS reporting condomless anal intercourse with non-steady partners (nsCAI) at least once, with at least two years of follow-up and at least two syphilis tests between 2005 and 2018.

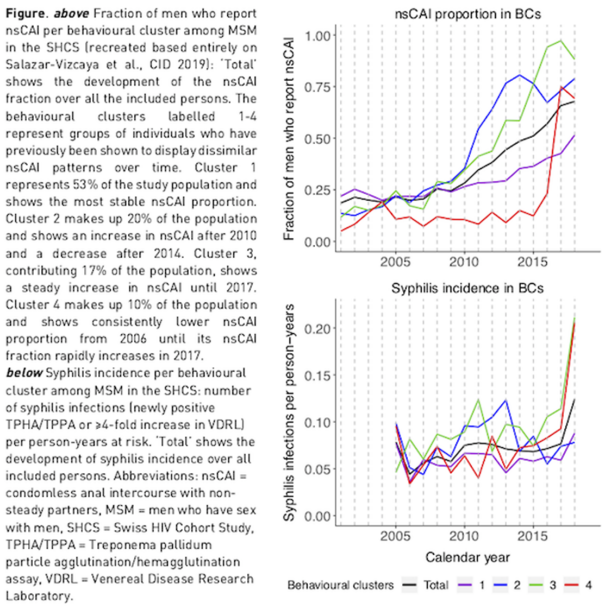


Figure. ***above*** Fraction of men who report nsCAI per behavioural cluster among MSM in the SHCS (recreated based entirely on Salazar-Vizcaya et al., CID 2019): 'Total' shows the development of the nsCAI fraction over all the included persons. The behavioural clusters labelled 1-4 represent groups of individuals who have previously been shown to display dissimilar nsCAI patterns over time. Cluster 1 represents 53% of the study population and shows the most stable nsCAI proportion. Cluster 2 makes up 20% of the population and shows an increase in nsCAI after 2010 and a decrease after 2014. Cluster 3, contributing 17% of the population, shows a steady increase in nsCAI until 2017. Cluster 4 makes up 10% of the population and shows consistently lower nsCAI proportion from 2006 until its nsCAI fraction rapidly increases in 2017. ***below*** Syphilis incidence per behavioural cluster among MSM in the SHCS: number of syphilis infections (newly positive TPHA/TPPA or ≥4-fold increase in VDRL) per person-years at risk. 'Total' shows the development of syphilis incidence over all included persons. Abbreviations: nsCAI = condomless anal intercourse with non-steady partners, MSM = men who have sex with men, SHCS = Swiss HIV Cohort Study, TPHA/TPPA = Treponema pallidum particle agglutination/hemagglutination assay, VDRL = Venereal Disease Research Laboratory.

nsCAI proportion and syphilis incidence in behavioural clusters

We estimated prevalence and incidence of syphilis infections (newly positive TPHA/TPPA or ≥4-fold VDRL increase) for each of the four previously inferred clusters and compared it to their respective proportions of men reporting nsCAI.
Results: Incidence of syphilis increased from 0.08 infections per person-years in 2005 to 0.12 in 2018. Overall syphilis prevalence differed significantly between clusters. This finding was consistent with differences in average nsCAI proportion among clusters (OR:6.0, p<0.0001). Trajectories of syphilis incidence over time differed between clusters (Figure): Clusters with increasing nsCAI proportion also exhibited recent increases in syphilis incidence. However, increases in syphilis incidence were delayed compared to those in nsCAI proportion. The increase in syphilis incidence was particularly pronounced for clusters 3 and 4, two groups characterised by recent nsCAI increases. In 2018, these clusters contributed over half of the syphilis cases while making up less than one third of the population.
Conclusion: Our preliminary results suggest that syphilis incidence over time differs between behavioural clusters and that specific clusters could be targets for potential interventions to prevent syphilis infections.

PE24/22

Evaluation of a systematic sexually transmitted infections screening pilot programme in HIV-positive men who have sex with men (MSM)

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Purpose: To describe prevalence of asymptomatic sexual transmitted infections (STI) in a cohort of MSM-HIV+ and risks factors associated; to assess the effectiveness of a risk-reduction counselling intervention and an enhanced partners management strategy.
Method: 100 MSM-HIV+ attending an HIV outpatient-clinic in Barcelona were evaluated at baseline (BL), month 6(M6) and month 12(M12), between December 2017-June 2019. Study visits included: STI screening; self-administered questionnaire about sexual behavior; risk-reduction counselling intervention. STI screening included serologic tests (Syphilis-HCV-HBV), RT-PCR for *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) in urine (U) rectal (R) and pharyngeal (P) samples. Sexual partners (SP) notification/contact strategies included written information delivered by patients and software tool-based phone messages by health professionals.
Results: Median (IQR) age was 40 years (34–47), CD4-count 752/µL (543–975), 90% on ART. Median number of SP (last year) was 8(3–20), 74% reported condomless sex, 58% recreational drugs use, and 32% chemsex use (3% slamming).
A total of 54 STI were diagnosed in 40 subjects. At baseline, 20% had at least one positive result: syphilis 10%, CT 7% (R 7%, P 1%), NG 7% (R 3%, PH 5%).
A non-significant decrease in STI prevalence was observed during the follow-up (BL 20%, M6 19%, M12 17%; p=1). No risk factors were significantly associated with STI, although a higher percentage of chemsex use was observed (24.5% vs 39.5%, p=0.222).
An increasing trend in condom use was observed overtime (BL 26% vs M12 36%, p=0.14), without differences in recreational and chemsex drugs use and number of SP.
Although subjects with STI reported a total of 2385 SP, only 61(2.5%) could be notified and 7/61(11.5%) attended our clinic.
Conclusion: Prevalence of asymptomatic STI in this MSM-HIV+ population was high. Systematic periodical screening and counselling was not effective to reduce significantly STI prevalence. Greater efforts are needed to control STI in this high-risk population, to promote safe sex and to improve partners management.

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PE24/23

Chemsex in Barcelona: a descriptive approach about men who have sex with men (MSM) who use recreational drugs in a sexual context

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Purpose: "Chemsex" refers to the intentional use of recreational drugs to enhance sexual experience in MSM. Little is known about this phenomenon in the city of Barcelona; the aim of this study is to characterize a Chemsex users cohort from our city, by analyzing socio-demographical and clinical characteristics, sexual behaviors, type of drugs and pattern of consumption and sexually transmitted diseases (STDs).
Methods: Cross-sectional study of a series of MSM patients Chemsex users. Patients were recruited between March 2018 and May 2019, at the Hospital Clinic of Barcelona. Clinical and epidemiological characteristics were evaluated based on the information obtained from the clinical history and a questionnaire answered by the patient. Likewise, screening for HIV, HCV and STDs was carried out.
Results: 161 MSM and transgender patients were included. 48% were Latin-Americans. 94% were HIV positive and 36% of them were HCV positive (24% had detectable HCV-RNA). The median of sexual partners was 20 (IQR 10; 30). 95% reported unprotected anal sex. 50% were polydrug users and 20% reported slamming. The individual frequency of drug use and the most prevalent drug combinations are reported in graphic 1 and graphic 2. The screening of asymptomatic STDs reported 91 positive PCR: *Neisseria gonorrhoeae* (55%), *Mycoplasma genitalium* (28%) and *Chlamydia trachomatis* (17%). 13% of HIV patients had detectable viral load. 70% were concerned about drug use in this context and 60% would like help to address this issue.
Conclusions: High prevalence of unprotected sexual risk practices, polydrug use and slamming are found in our MSM chemsex users cohort. The prevalence of HCV and other asymptomatic STDs is very common in this population. Specific risk reduction strategies are necessary in this population

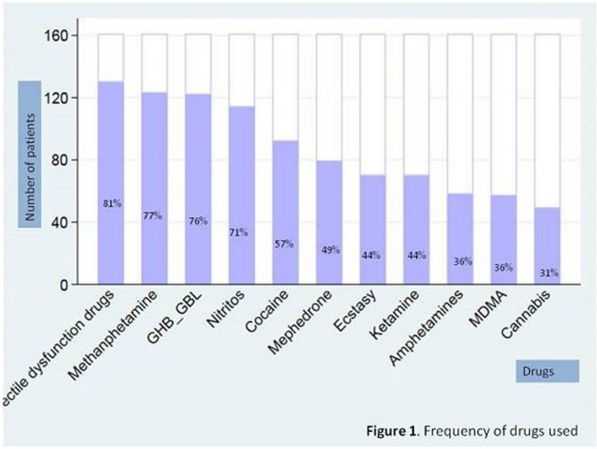


Figure 1. Frequency of drug use

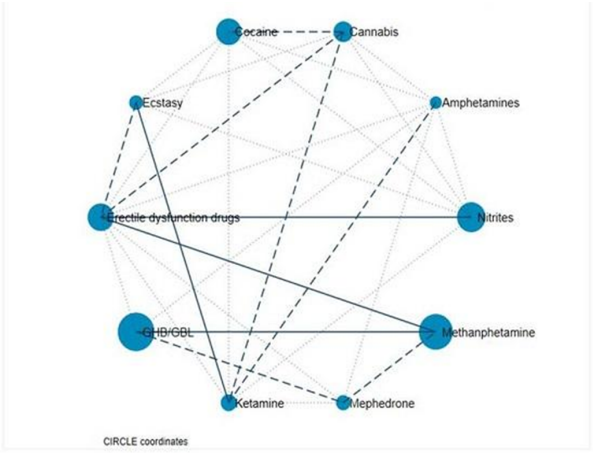


Figure 2. All drugs combinations

PE24/24

Analysis of serum metabolite changes in early syphilis patients with or without serologic response after treatment

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Purpose: The treatment success of syphilis depends on 4-fold decrease of rapid plasma reagin (RPR titer) according to current treatment guideline. However, the change of RPR titer is not sensitive. We aim to screen treponemal metabolomics response of early syphilis after treatment among HIV-infected and HIV non-infected patients.
Method: Adult patients aged 20 years or older who presented with early syphilis (primary, secondary and early latent syphilis) with RPR titers of 4 or greater were included. The serum was collected in week 1, 2, 3, 4, 8, 12 after treatment with 2.4 MU benzathine penicillin G. Serologic response was defined as decline of RPR titre by 4-fold or greater at each time point compared with baseline. We used a combined liquid chromatography MS/MS assay and direct flow injection assay for the metabolomics analyses of the samples.
Results: Total 24 patients were included between January 2015 and March 2018 while 18 subjects had HIV infection. The median baseline RPR titer were 1:128 among HIV-uninfected patients while 1:256 among HIV-infected patients. We found higher lysosome levels in HIV-infected patients than HIV-uninfected ones. After treatment, 19 patients achieved serologic response after treatment within 12 weeks and 13 of them were HIV-infected. In the metabolomic analysis, two metabolites were identified with significant changes according to the treatment response that SDMA were significantly lower and taurine had early decline change in those who had achieved treatment response.
Conclusion: In our study, we found that lower SDMA level and early decline of taurine level were associated with the treatment response of Treponemal pallidum. Further larger scale analysis should be done to identify the potential role of these metabolites as markers to evaluate treatment success of syphilis.

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PE24/25

Stable transmission of amoebiasis among newly diagnosed HIV-positive patients in Taiwan, 2009–2018

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Purpose: *Entamoeba histolytica* infection is an emerging sexually transmitted disease among men who have sex with men in the Asia-Pacific region. This study aims to investigate the overall and temporal change of the seroprevalence of amoebiasis among HIV-positive patients in Taiwan and its associated factors.
Method: We reviewed medical records of newly diagnosed HIV-positive patients who received HIV care at five medical centers across Taiwan between 2009 and 2018. Patients who had tests for indirect hemagglutination antibody (IHA) within 6 months before or after their HIV diagnoses were included for analyses. The trend of IHA seropositivity over time was tested by chi-square test for trend. The demographics, clinical presentations, and baseline laboratory test results were analyzed for the association with positive IHA (defined by an IHA titer ≥1:32) in multivariable regression models.
Results: Among 3539 newly diagnosed HIV-positive patients in the 10-year study period, 2122 (60%) had IHA titers determined. Overall, 202 (9.5%) patients tested positive for IHA and 83 (3.9%) had clinical diagnoses of invasive amoebiasis. The annual seroprevalence of IHA fluctuated, ranging from 5.9 % in 2012 to 16.5% in 2009, without a statistically significant trend from 2009 to 2018 (p=0.276). The IHA seropositivity was associated with positive rapid plasma reagin (RPR) titers ≥4 (adjusted odds ratio [aOR] 1.07, 95% confidence interval [CI] 1.04–1.11), an older age (aOR 1.002, 95% CI 1.000–1.003) and symptoms of diarrhea (aOR 1.20, 95% CI 1.16–1.24).
Conclusion: Seropositivity for *E. histolytica* infection was not uncommon among newly diagnosed HIV-positive individuals in Taiwan and the seroprevalence remained stable over the past 10 years. To facilitate early diagnosis and treatment of amoebiasis and to prevent further transmission, IHA testing should be included in the routine HIV care of HIV-positive patients in Taiwan, particularly those who present with diarrhea and RPR titers ≥4.

PE24/26

Mycoplasma genitalium resistance against macrolide antibiotics in the Berlin MSM cohort tested with the Allplex MG & AziR Assay (SeeGene)

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Purpose: Due to the high rate of sexual transmitted infections (STI) there is a rise in awareness and in STI-testing. *Mycoplasma genitalium* (MG) is one important cause of non-gonococcal urethritis and emerging macrolide resistance is a major concern. A standardized real-time-PCR test is the favoured method for this hard to culture bacterium in routine diagnostics. We tested here the Allplex MG&AziR Assay on MG positive samples.
Method: Screening MSM for MG from mainly urethral/anal swabs or urine was performed with the Hologic Panther system (Aptima MG Assay target capture and isothermal amplification TMA). Total nucleic acid extraction from left-over material from 96 MG positive samples was done with the Abbott M2000sp system, followed by testing for macrolide resistance with the Allplex™ MG&AziR Assay in a RUO version. This test differentiates the SNP mutations A2058C/G/T and A2059C/G/T of the 23S rRNA-gene region-V of MG.
Results: 69.8% (N=67) of MG positive screened samples were also positive in the Allplex™ MG&AziR Assay. In a very high proportion of these samples (80.6%, N=54) resistance mutations could be detected. A2059G was the mutation detected with the highest frequency (74.1%; N=40) followed by A2058G (24.1%; N=13). One sample had an A2058T mutation. No sample showed an A2058C or A2059C/T mutations.
Conclusion: As expected not all Aptima assay positive samples tested positive with the Allplex assay due to the known very high sensitivity of the TMA test. Of 80.6% resistant MG detected, 74% showed resistance against Azithromycin and Josamycin and 26% against Azithromycin alone. Usual second line option in Germany is Moxifloxacin despite increasing numbers of reported clinical resistance (flourchinolone resistance assay Seegene launch in summer, first data will be added). Resistance guided therapy is crucial for sufficient treatment success and addition of molecular resistance testing against Fluoroquinolones is an additional requirement.

PE24/27

Predictors of ureaplasma urealyticum urinary colonization in HIV+ pregnant women: a pilot study

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Purpose: Our objective was to identify eventual HIV-related risk factors for *U. urealyticum* urinary tract colonization in HIV+ pregnant women.
Methods: Retrospective study of 83 HIV+ women attending the University of Modena and Reggio Emilia Infectious Disease Unit outpatient clinic from January 2011 to September 2018. At baseline an monthly all subjects were evaluated for HIV-viral load, CD4+ count and urine cultures, if positive for bacterial growth a urine culture was performed after treatment. Logistic regression analyses, age adjusted, were run to evaluate eventual predictors of *U. urealyticum* urinary tract colonization. Chi-square tests were performed to assess statistically significant differences in prevalence of colonization according to CD4+ count and detectable viremia.
Results: 48 (57.8%) subjects had a positive urine cultures for *U. urealyticum*, 37 (77%) of them were African. 46 (96%) of isolates acquired resistance to azithromycin at first urine culture after treatment. 26 out of 33 (79%) with detectable viremia and CD4+ <500 cell/mmc at baseline showed positive growth of *U. urealyticum* on urine samples. Pearson's Chi-square test showed a statistically significant difference in prevalence of urinary tract colonization by *U. urealyticum* between subjects with detectable and undetectable viral load (69.9 % vs 29.1%, p<0.05) and CD4+ < or >500 cell/mmc (74.4% vs 25.4%, p<0.05). Predictors of asymptomatic bacteriuria at multivariate logistic regression (age adjusted) analyses were: detectable viremia at baseline (HIV-VL >40 copies/mL) [OR=3.513 IC=1.391;8.871, p=0.008] and CD4+ <500 cell/mmc [IC=1.526;9.857, p=0.004].
Conclusions: Our findings suggest that HIV-Viral load >40 copies/mL and T-cell CD4+ count <500 cell/mmc at first visit after pregnancy diagnosis are associated with higher prevalence of *U. urealyticum* urinary tract colonization in HIV + women.

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PE24/28

No indication of decreased syphilis susceptibility with repeated syphilis episodes in HIV-infected men who have sex with men: a multicentre prospective cohort study on risk factors and the potential role of syphilis immunity

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Purpose: Syphilis is re-emerging globally in general and HIV-infected populations and repeated syphilis episodes may play a central role in syphilis transmission among core groups. Besides sexual behavioural factors, little is known about determinants of repeated syphilis episodes in HIV-infected individuals — including the potential impact of preceding syphilis episodes on syphilis susceptibility, which may inform current vaccine developments. We therefore aimed to identify risk factors for syphilis incidence and in particular for repeated syphilis episodes.
Method: In the prospective Swiss HIV cohort study with routine syphilis testing since 2004, we analysed HIV-infected men who have sex with men (MSM). Our primary outcome was first and repeated syphilis episodes. We used univariable and multivariable Andersen-Gill models to evaluate risk factors for incident syphilis.
Results: Within the 14-year observation period, we included 2,023 HIV-infected MSM with an initially negative syphilis test. Crude incidence rates of repeated syphilis episodes in MSM increased with the number of previous syphilis episodes — ranging from 69 episodes per 1,000 person-years in MSM with one previous episode to 538 episodes per 1,000 person-years in MSM with six previous episodes. In the univariable and multivariable analysis (figure), the number of prior syphilis episodes (adjusted HR [aHR] per one-episode increase, 1.17; 95% confidence interval [CI], 1.00 to 1.36), having occasional sexual partners with or without condomless anal sex (aHR, 4.99; 95% CI, 3.96 to 6.28; and aHR, 2.48; 95% CI, 2.01 to 3.06), and being currently on antiretroviral therapy (aHR, 1.57; 95% CI, 1.16 to 2.14) were associated with incident syphilis.
Conclusion: To our knowledge, this is the largest prospective cohort study investigating the partial syphilis immunity concept among HIV-infected individuals. In HIV-infected MSM, there was no indication of decreased syphilis susceptibility with repeated syphilis episodes.

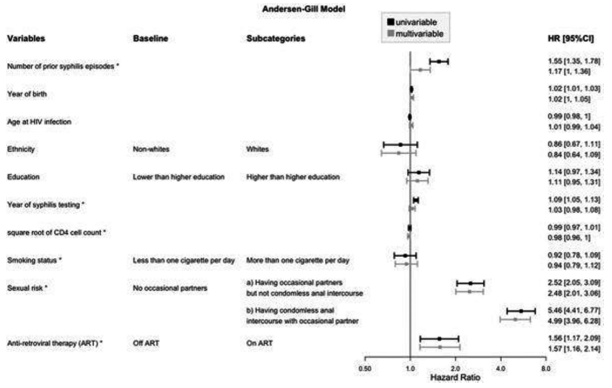


Figure: Risk factors for repeated syphilis episodes in HIV-infected men who have sex with men

PE24/29

The prevalence of high-risk anal HPV in HIV-positive MSM in Lebanon

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Purpose: Infection with HPV is associated with ano-genital cancers and potentially preventable through vaccination. 90% of anal cancers are related to HPV16 and HPV18. Concomitant infection with HIV doubles the risk of anal malignant transformation in affected MSM. To our knowledge, this is the first study to examine the prevalent anal HPV strains and anal STIs among asymptomatic HIV-positive MSM in a Middle Eastern country.
Methods: We performed a cross-sectional study at a well-established HIV clinic in Beirut. 38 participants were included; they were all men who had sex with men, asymptomatic at recruitment. EuroArray STI kits were used for screening STIs by PCR and EuroArray HPV kits for HPV PCR determination and typing.
Results: The median age of the participants was 30 (range 20–71). 82.35% of them had an undetectable HIV viral load. Only 28.95% had prior HPV vaccination; 13.15% had prior anal Pap smear testing. 75% were not aware of the association between HIV, HPV and anal dysplasia and cancer. 34 participants (89.47%) tested positive for any type of anal HPV, among them, 91.17% harbored high-risk HPV (HR-HPV) strains distributed as such: 55.8% HPV16, 26.32% HPV56 and 23.68% HPV18. The majority of participants (81.58%) had multiple HPV types (median of 4 types) and 34.21% had at least one concomitant STI, most of which were Mycoplasma species.
Conclusion: We found a high rate of HR-HPV anal infections but a low rate of HPV vaccination among this young HIV-positive population. HPV56 was the second most common high-risk strain, a finding not reported from other regions; HPV56 is not included in the 9-valent HPV vaccine. The prevalence of asymptomatic rectal carriage of Mycoplasma species was elevated. It is crucial to explore the epidemiology of anal HPV and STIs among HIV-positive MSM in this region to guide future cancer prevention efforts.

Table 1. Patient characteristics

Age, median (IQR)	30 (27–33)
History of HPV vaccination	11 (28.95%)
Currently on ART	36 (94.74%)
Duration of ART, median (IQR)	3 (1.875–3.5)
Current CD4 count, mean (SD)	641.8 (335.91)
Nadir CD4 count, median (IQR)	305 (189–448)
Current undetectable HIV VL	28/34 (82.35%)

Table 2. Results

Any HPV type	34/38 (89.47%)	
High risk HPV	31/34 (91.17%)	HPV 16 :19/34 (55.8%)
		HPV 18 : 9/34 (23.68%)
		HPV 56 : 10/34 (26.32%)
Multiple HPV (n=34)	31/34 (91.17%)	Number of HPV, median: 4 (2–6)
Any STI (n=38)	13/38 (34.21%)	
	Mycoplasma species	10 (26.31%)
	Ureaplasma urealyticum	7 (18.42%)
	Chlamydia trachomatis	1 (2.63%)
	Neisseria gonorrhea	3 (7.89%)

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Paediatric, adolescent

PE25/1

Effect of cluster of differentiation (CD4) on viral respiratory infection in children, between 0–5 years of age. A study conducted in Kwazulu-Natal, South Africa

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Purpose: Viral respiratory tract infections (RTI) contribute significantly to morbidity and mortality among children in resource-poor countries. Cell mediated immunity plays a central role in disease modification and viral clearance and individuals with defective cellular immunity are likely to have prolonged viral shedding and increased frequency of infections. Human immunodeficiency virus (HIV) infected children are likely to have higher incidence of RTI than HIV negative children.
Method: A retrospective data analysis of respiratory specimens results of children between 0–5 years of age collected between 1st January 2011 and 31st July 2015 from hospitals. Respiratory specimens were tested for viral pathogens using multiplex polymerase chain reaction (PCR) and non-viral pathogens using appropriate culture media. HIV testing was performed either by serological or PCR methods. The objectives were to analyze respiratory pathogens isolated from specimens of both HIV Positive and HIV negative and to determine the role cluster of differentiation (CD4%) plays in RTI.
Results: Out of 1264 respiratory results, 621 (49.1%) were viral isolate positive. Respiratory syncytial virus was the most detected pathogen 218 (35.1%). HIV results were available for all 621 (100%) with 122 (19.6%) HIV positive. There was statistically association between HIV infection and RTI ($p<0.05$) and also an association between CD4% and RTI, indicating the effect HIV infection or low CD4 has on RTI.
Conclusion: This study identified the common respiratory viral and non-viral pathogens detected among children. The study highlighted the difference in prevalence of viral and non-viral RTI between HIV negative and HIV positive children and it further showed the effect CD4% has on susceptibility to RTI. Upscaling the HIV treatment will likely have an impact on RTI in children. The study outcome has implications for the rational design of public health programs. Further studies is needed in understanding respiratory infection in children.

PE25/2

Adolescent HIV and asymptomatic malaria parasitemia (AMP) co-infection

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Purpose: In this study, we sought to determine the prevalence of AMP in a population of Adolescents HIV positive patients on antiretroviral therapy (ART). We also seek to know the correlation of this co-infection on the %CD4 and HIV viremia of the study population.
Method: 153 adolescents on ART at the APIN Laboratory of the Jos University Teaching Hospital (JUTH) in Plateau State, North Central Nigeria, participated in this study. The mean age of the participants was 14(±4) years. Participant's venous blood were drawn; with two (2) thick blood smears made and air-dried for each participant. The slides were stained with Giemsa and Field stains for malaria microscopy. %CD4 of the study population was analyzed using the Partec® Cyflow Counter II; while the separated plasma was assayed for HIV viral load using the Roche® Cobas Ampliprep/Cobas Taqman 96 System. Collected data analysis was done using a simple percentage.
Results: Of the 153 participants in this study, 66% (101/153) were virally suppressed (<1,000 copies/mL); while 34% (52/153) were virally unsuppressed (>1,000 copies/mL). 65% (99/153) of the study population have AMP. 54% (55/101) of the virally suppressed population have AMP; with a mean %CD4 value of 28%, while the virally suppressed population without AMP (46/101) have a mean %CD value of 30%. 85% (44/52) of the virally unsuppressed population have AMP; with a mean %CD4 value of 19%, while the virally unsuppressed population without AMP have a mean %CD4 value of 16% respectively.
Conclusion: This study shows that there is a high prevalence of AMP among adolescent HIV patients (65%). The high prevalence of AMP among the virally unsuppressed population (85%), with a mean %CD4 value of 19%, points to the fact that malaria parasitemia in HIV infection fosters increased plasma HIV viremia and a dysregulated immune response to this co-infection.

Table 1. Respiratory multiplex respiratory viruses with HIV and CD4 results.

Variables (total number of specimens) 1264, median age 3 months									
Gender (Total=1264)	Male=687 (54.4%)	Female=562 (44.5%)	Gender not stated 15 (1.2%)						
Isolated non viral pathogen total =394	Klebsiella pneumonia=143 (36.3%)	Staphylococcus aureus=76 (19.3%)	Acinectobacter baumanni=70 (17.8%)	Candida albicans=35 (8.9%)	Pseudomonas aureginosa=41 (10.4%)	Streptococcus pneumonia=29 (7.4%)			
CD4 results linked to non viral results ≤25% Total =55 (51.9%)	25	5	8	11	6	0			
CD4 results linked to non viral results ≥25% Total=51 (48.1%)	7	8	5	5	3	2			
Total=85	32	13	13	16	9	2			
p values	<0.05	<0.05	<0.05	<0.05	0.9908	<0.05			
Viral respiratory pathogens Total=621	Respiratory syncitial virus=218 (35.1%)	Adenovirus=151 (24.3%)	Human rhinovirus=78 (12.6%)	Para influenza3=60 (9.7%)	Influnza A=33 (5.3%)	Enterovirus=17 (2.7%)	Human boca virus=11 (1.8%)	InfluenzaB=26 (4.2%)	Others=27 (4.3%)
CD4 results linked to viral respiratory results ≤25% Total =66 (65.3%)	8 (p value= 0.0001)	15 (p value= 0.0001)	11 (p value= 0.0001)	13 (p value= 0.0001)	0 (p value= 0.0001)	3 (p value= 0.0001)	1 (p value= 0.0001)	2 (p value= 0.0001)	13
CD4 results linked to viral respiratory results ≥25% Total=35 (34.7%)	8	8	4	4	2	1	2	5	1

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PE25/3

Clinical features of viral diarrhea in the children of HIV

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Purpose: To study was to investigate the clinical features of viral diarrhea in children with HIV.
Method: The study involved 30 children aged between 1 and 18 years who were treated at the Republican AIDS Center. Clinical, virological, bacteriological, serologic (PCR) methods were used.
Results: The study showed that viral diarrhea is more prevalent in children under the age of 3 years with HIV. 21 (70%) of the 30 children with diarrhea have been diagnosed with viral etiology. Viral diarrhea was caused in 16 children (76.2%) by rotavirus while normal diarrhea with normal Herpes type 2 (9.5%) and adenovirus diarrhea 1 (4.76%), 2 (9.5%) patients had mixed etiologic viral diarrhea. The most severe diarrhea was rotavirus diarrhea, with strong symptoms of intoxication and symptoms of multiple vomiting in children. Catarrhal signs in the rotavirus diarrhea were more susceptible to adenovirus diarrhea. The body temperature rose slowly and reached 39.1°C until 4–5 days before the onset of the disease. In the diarrhea clinic with a normal herpes virus, multiple seizures (more than 10 times) occurred suddenly on the background of sub-febrile body temperature. The return was 5.2±1.8 days, the fecal matter was fluid and was observed 1–2 times a day.
Conclusion: Thus, according to the results of the study, ethylogically rotavirus was the leading cause of viral diarrhea in HIV-infected children. Diarrhea syndrome prevailed over vigor and vomiting.

PE25/4

High rate of rubella seronegativity in perinatally-infected HIV women of childbearing age: a case-control study

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Purpose: Rubella infection is a vaccine preventable disease. Maternal infection during pregnancy may lead to congenital infection and severe foetal malformations. Nowadays, perinatally HIV-infected women (PHIV) have better prognosis and are frequently experiencing pregnancy at a young age. We aimed at evaluating the rate of rubella seronegativity in a cohort of PHIV of childbearing age.
Methods: Perinatally-infected women of childbearing age with a documented rubella serological testing were retrospectively identified and age-matched to HIV-positive non-perinatally infected women (nPHIV). Vaccination history with the measles-mumps-rubella vaccine (MMR) was retrieved from the hospital files in the PHIV group. Conditional logistic regression was used for comparison between the PHIV and nPHIV subjects.
Results: Twenty-nine PHIV (cases) and fifty-eight nPHIV (controls) were identified. There was no significant difference between cases and controls considering country of birth (Belgium vs. outside Belgium), proportion of Sub-Saharan African origin, ART proportion, CD4+ T cell count >350 cells/μL and HIV viral load <50 copies/mL at time of rubella testing and CD4+ T cell count nadir >200 cells/μL. Median duration of living in Belgium was significantly different in the two groups: 15.9 years vs. 2 years for the nPHIV group (p value <0.01). A high rate of seronegativity was found in the PHIV group as compared to nPHIV group (34.5% vs 6.90%, p<0.01). MMR administration before rubella testing was identified in 75.8% of PHIV women (22/29) with a mean of 2 doses (range: 1–3 doses).
Conclusions: High rubella seronegativity rate was found in PHIV with high MMR vaccine coverage, reflecting defective vaccine-induced immunity. This is of particular concern for the ongoing rubella eradication strategy. We recommend that perinatally HIV-infected women of childbearing age should be regularly screened for rubella immunity.

PE25/5

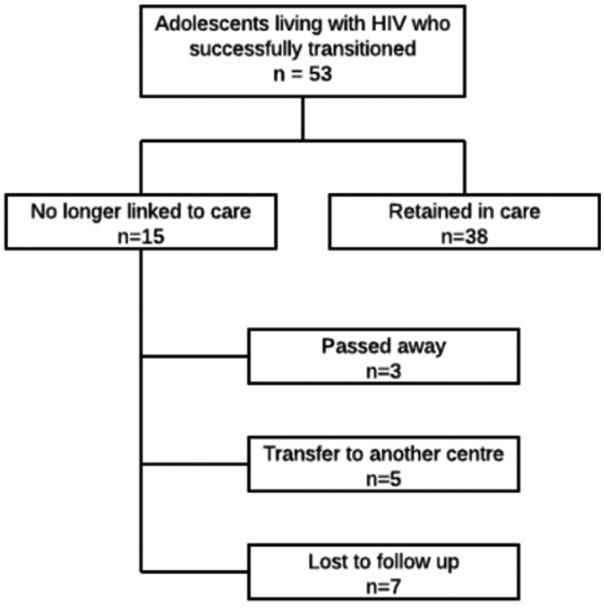
Health outcomes in adolescents and young adults living with HIV before and after transition to adult care in Barcelona

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Purpose: To describe the demographic and HIV related data of patients who transferred from paediatric to adult care in two centres of Barcelona and compare the quantitative health outcomes before and after the referral process.
Method: An observational, prospective study with retrospective data collection was conducted with 53 adolescents living with HIV who had transitioned from Hospital Sant Joan de Déu (HSJD) to Hospital Clínic (HCB) in Barcelona between 2006 and 2017. Data was collected from clinical records before transition, right after it and at the last control visit. Risk factors for detectable viral load were evaluated with a regression model that included sex, socioeconomic status, absence of virological failure during adult care and low educational level.
Results: 53 patients successfully transitioned from HSJD to HCB during the time of the study. 15 (28.3%) of them were no longer linked to care (3 deaths, 5 transferred to another centre and 7 lost-to-follow-up). Most of the patients (75%) with undetectable viral load during paediatric care were found to remain undetectable during adult care. Importantly, the results obtained with the multivariable regression model showed that low educational level was found to carry a 27-fold increase in the risk of having a detectable viral load in the last visit (aOR of 27.39 with a 95% CI of 1.5–487.48), while the absence of virological

Table 1. CD4 count and VL data of adolescents living with HIV transitioning from paediatric to adult care in a Barcelona cohort.

During paediatric care CD4 count (cells/μL) at transition (n=53)	n (%)	During adult care CD4 count (cells/μL) at last visit (N=50)	n (%)
<200	3 (5.7)	<200	5 (10)
200–499	12 (22.6)	200–499	11 (22)
≥ 500	38 (71.1)	≥ 500	34 (68)
Virological status at transition (n=29)	n (%)	Virological status at last visit (n=49)	n (%)
Undetectable	28 (57.1)	Undetectable	34 (69.4)
Detectable	21 (42.9)	Detectable	15 (30.6)



Graph 1. Linkage of care of the cohort

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failure during adulthood could be a potential protective factor, as it reduced the risk of being detectable by 88% (aOR of 0.12 with a 95% CI of 0.001–0.170).
Conclusion: While not showing a clear impact of the transition process on the health of this cohort, these findings align to those reported in similar studies. Patients with virological failure during adulthood and low educational level should be followed up more closely.

PE25/6

Correction of lipid abnormality by integrase inhibitor among children taking ART

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Objectives: Boosted PIs are milestones of HIV management in pediatric practice. Long-term ARV treatment is associated with lipid abnormalities. The statins and fibrates are routine co-medications for adults but its are not alloyed in pediatric practice. The purpose of the study was to estimate a possibility of correction laboratory abnormalities (increased level of cholesterol and/or triglycerides in blood of HIV-positive children) by switch the boosted PI to HIV integrase inhibitor (Raltegravir).
Methods: The retrospective study was conducted in group of 58 HIV-positive children (less 18 years). Inclusion criteria were hypercholesterolemia (>5.0 mM) and/or the hypertriglyceridemia (>2.3 mM) on ART with boosted PI. The ART scheme was changed for all children (n=58). Boosted PI was replaced by integrase inhibitor (RAL). RAL formulation (chewable tablets, 25 mg and 100 mg) used accordingly weight. Time horizon of observation and laboratory assessment after switch was 24 months.
Results: Lab abnormalities in study group (n=58) after switch to RAL were corrected: reliable decrease of level of cholesterol ($p<0.01$), triglycerides ($p<0.001$), viral load ($p<0.001$) and growth CD4 count ($p<0.05$).
Conclusion: Boosted PI switch to integrase inhibitor is providing long-term and effective HIV management and improvement of lipid abnormalities among children.
Key words: HIV positive children, HIV treatment of children, lipid disorders among children, lipids management, adverse events during ART among children.

Table 1. Patient Demographics and Baseline Characteristics, n=58

Characteristic	M±m	95% CI
Age of ART start, years ± SD	2y 5 m±3 m	2y 2 m–2y 8 m
Average time to II switch, years ± SD	3y 10 m±3 m	3y 7 m–4y 1 m
Average time of hypercholesterinemia, years ± SD	3y 7 m–4y 1 m	3y 7 m–4y 1 m
Average time of triglyceridemia, years ± SD	2y 3 m±2 m	2y 1 m–2y 5 m
Average cholesterol, mM	5.95±0.15	5.8–6.10
Average triglyceride, Mm	1.99±0.15	1.84–2.14
Average VL, copies/mL	400.55±224.61	175.94–625.16
Average CD4, cells	963.91±84.34	879.57–1048.25
AE on PI boosted schemes, %	17.24	

Table 2. 24 months lab assessment after boosted PI switch to integrase inhibitor, n=58

Characteristic	Boosted PI (95% CI)	Integrase inhibitor (95% CI)	p
Cholesterol, mM	5.95 (5.8–6.10)	4.1 (3.87–4.33)	0.01
Triglyceridemia, Mm	1.99 (1.84–2.14)	0.99 (0.76–1.22)	0.001
VL, copies/mL	400 (175–625)	40 (<40)	0.001
CD4, cells	963 (879–1,048)	1276 (1,094–1,458)	0.05

PE25/7

Increasing contribution of sexually-transmitted HIV diagnoses in adolescents in Spain

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Purpose: A specific approach of HIV in adolescents is of global concern. Data about new HIV diagnoses in adolescents is scarce. Describing this population will contribute to better approach this problematic situation.
Method: Description of HIV new diagnoses in patients 12–20 years-old included in CoRIS (adult) and CoRISpe (pediatric) Spanish cohorts until end 2017. Demographic, clinical, biological data and way of transmission were analysed.
Results: For 357 adolescents, new HIV diagnosis was made; 75.4% were male. Median age at diagnosis was 18.7 years. Middle-adolescents (15–17 year-old) significantly increased, from 2003–2007 (16.4%) to 2013–2017 (25.2%, p=0.030). In 275 cases (77%) way of infection was sexual (53.5% men who have sex with men, MSM; 23.5% heterosexual contact), 54 (15.1%) drug users, 10 (2.8%) vertical transmission and 6 (1.7%) hemoderivates receivers. Sexual transmission and MSM increased significantly over time to 95.5% and 74.8% respectively in 2013–2017 (figure 1).
The proportion of adolescents from total new HIV diagnoses in Spain significantly increased from 2005 (figure 2).
Regarding the origin, 131 (36.7%) adolescents were born outside Spain; 71% of them in Latin-America. For Latin-American, in 93.5%, transmission was sexual vs 72.0% for other origins (p=0.0002).
Late diagnosis (CD4<350/mm^3 or AIDS at diagnosis) was made for 123 adolescents (34.5%). This was more frequent for transmission by heterosexual

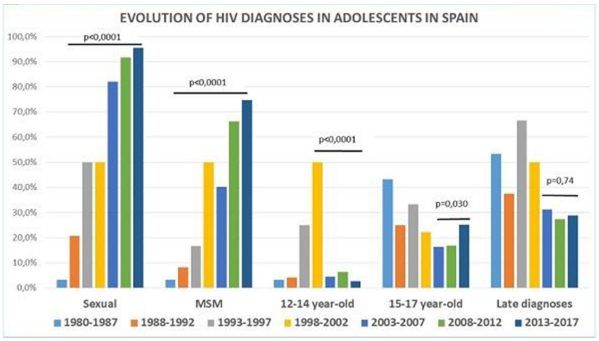


Figure 1. New HIV diagnoses in adolescents in Spain over time

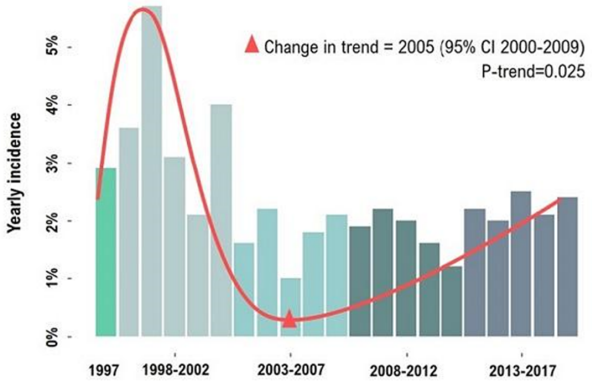


Figure 2. Trend change HIV diagnoses in adolescents from total diagnoses in Spain

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contact (41.7%) than MSM (23.0%, p=0.0023). Late diagnoses among adolescents decreased over time but not in last 15 years: 21/67 (31.3%) in 2003–2017 vs 32/111 (28.8%) in 2013–2017 (p=0.74).
Conclusion: There is an increasing contribution of sexual transmission and MSM in new HIV diagnoses in adolescents. HIV-newly infected adolescents are younger, with a growing rate of 15–17 year-old. More than 1/3 present late diagnosis and did not decrease in last 15 years. This emphasizes the vulnerability of this population and the need to develop more effective preventive actions.

PE25/8

Factors associated to late presentation of HIV newly diagnosed adolescents in Spain

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Purpose: Adolescents represent a growing share of new HIV diagnoses. Late presenters (LP) is a universal challenge that also affects adolescents. Nevertheless, data are scarce.
Method: Retrospective study of LP (<350 CD4/uL or AIDS-defining events at diagnosis) in HIV newly diagnosed adolescents (12 to <20 years-old) included in CoRIS and CoRISpe Spanish cohorts until end 2017. CoRIS enrols HIV-naïve patients from adult units and CoRISpe from pediatric units. Demographic, clinical data and way of transmission were analysed.
Results: From 357 HIV newly diagnosed adolescents, 123 (34.5%) were late presenters with a median CD4 rate of 235/μL at diagnosis. LP were mainly male (69.9%) and median age was 18.7 years, similar to general cohort. The main way of infection in LP was sexual (64.2%; 35.8% men who have sex with men (MSM) and 28.4% by heterosexual contact), 21.1% were injection drug users, 7.3% vertical transmission, 3.3% hemoderivates receivers. LP was significantly more frequent for heterosexual transmission (41.7%) than for MSM (23%), p=0.0023. Regarding the origin, 30.4% of MSM born outside Spain were LP vs 18.4% of Spanish MSM (p=0.0757). Foreign women with heterosexual transmission was a vulnerable group with 50% of LP vs 18.4% in Spanish MSM (p=0.0006). Despite mainly behaviourally transmission and younger age, LP rate for middle adolescents (15–17.9 years-old) was as high as for late adolescence (18–19.9 years-old): 34.6% vs 32%; p=0.684. LP among adolescents decreased over time but not in the last 15 years: 34.3% in 2003–2007 vs 28.8% in 2013–2017 (p=0.504).
Conclusion: More than 1/3 of HIV newly diagnosed adolescents were late presenters, with no decline in last 15 years. Adolescents with heterosexual transmission, foreign MSM and heterosexual foreign women presented higher LP rates. Specific approaches are needed to tackle this situation.

PE25/9

Comparison of antiretroviral treatment initiation in HIV newly diagnosed adolescents in Spain

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Purpose: Adolescents represent a growing share of new HIV diagnoses. However, data about antiretroviral treatment (ART) and viral suppression in this population is scarce.
Method: Description of HIV new diagnosed patients 12–20 years-old included in CoRIS (adult) and CoRISpe (pediatric) Spanish cohorts between 1996 and 2017. Comparision of time to initiation of ART and viral suppression depending on sociodemographic and clinical data was performed.
Results: 270 HIV newly diagnosed adolescents were included, 75.6% were male and median age was 18.8 years-old. The way of infection was essentially sexual (89%), in men who have sex with men (61%), mainly born in Spain (58%) and Latin America (29%). 86.3% of adolescents were initially followed up in adult units, while 12.5% in pediatric ones. 88.9% have ever received ART; the rest being mainly early loss of follow-up. Time to ART initiation from diagnosis significantly decreased over time according to evolution of guidelines, but remained 55 days from 2014, period of universal treatment. Median time from ART indication to initiation was significantly lower in early adolescents (12–14 years-old) than older patients (11 vs 26 days, p=0.025), but was similar if followed up in pediatric or adult units.
Globally 88.8% achieved first viral suppression, having the rest short follow-up. Time to suppression from ART initiation significantly decreased over study period, but remained 117 days from 2014, in a mostly behaviorally transmitted cohort. Median time from ART initiation to viral suppression was significantly longer in early adolescents than in older ones (188 vs 115.5 days, p=0.044), due to higher initial viral loads. This time did not differ if followed up in adult or pediatric units.
Conclusion: Despite being a challenging population, adolescent almost achieved 90% in treated and 90% in first viral suppression in our cohort. Younger patients started treatment earlier but achieved suppression later.

PE25/10

Oral self-testing for adolescents and young adults absent or declining to test during home-based HIV testing – a mixed-method study embedded in a cluster-randomized trial in Lesotho (ADORE study)

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Purpose: Home-based testing, widely used in sub-Saharan Africa, fails to reach high coverage among adolescents and young adults (AYA). ADORE (ADolescent ORal tEsting) is a mixed-method nested study, embedded in a cluster-randomized trial, measuring effectiveness and acceptability of secondary distributed oral HIV self-tests in Lesotho.
Methods: In intervention village-clusters, self-tests were left for absent/declining household members during home-based testing. One present household member was trained on self-test use. Distributed self-tests were followed up by village health workers (VHW). The quantitative outcome was testing coverage among AYA (age 12–24) within 120 days, defined as a confirmed HIV test result or known status, using adjusted random-effects logistic regression. Qualitatively, we conducted in-depth interviews among AYA who did (control-interviews) or did not (case-interviews) use the self-test, following the concept of saturation, coded and analyzed according to the Framework Method. Trial registration: NCT03598686.
Results: 1,065 consenting households with 2,685 AYA were enrolled (intervention arm: 56 clusters; 572 households; 1,447 AYA; control arm: 47; 538; 1,236). In the intervention arm, 937 AYA were absent or declined. Self-tests were left for 790 eligible AYA, and 487 (62%) were returned. In the control arm, 860 AYA were absent or declined; 7 (1%) subsequently tested at a health-facility. Coverage after 120 days was 1083/1447 (75%) in the intervention versus 469/1236 (38%) in the control (odds ratio 5.21 [95% confidence interval 3.83–7.09]; p<0.001). The intervention effect was greater in males (70% versus 24%; 7.94 [5.55–11.37]) than females (79% versus 50%; 3.96 [2.81–5.59]; p-interaction <0.001). 11 case- and 10 control-interviews were performed. In-person assistance during and after self-testing, and convenience of testing emerged as key qualitative themes.
Conclusion: Secondary distribution of oral self-tests among AYA increased HIV testing coverage by >35%, and was particularly successful among males. Training of a present household member and the VHW on self-testing is key.

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PE25/11

Preterm births in women living with HIV in Switzerland: a 13-year evaluation

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Purpose: Combined antiretroviral treatment (cART) and advanced HIV infection are associated with negative pregnancy outcomes, particularly preterm birth. About 10 years ago, we identified a prematurity rate of 24–26% in women with HIV under cART. Here we assess the recent years during more than a decade to identify changes.
Method: We analysed all pregnant women included in the Swiss Mother and Child HIV Cohort Study (MoCHiV) and the linked Swiss HIV Cohort Study (SHCS) from 2005–2017. Preterm births by elective cesarean section were excluded. Gestational age (GA) was available in weeks and additional days within the following week, e.g. GA 37+0 which is equivalent to a term birth.
Results: We evaluated a total of 798 pregnancies in 581 women including 16 twins that were counted separately. 78% (621) of the pregnancies achieved at least GA ≥ 24. 86% (536) of them were exposed to the same cART regimen for at least 90 days. Over time, this rate increased from 70% in 2005 to 93% in 2017. 156 pregnancies ended before GA 24, of which 38% (59/156) were spontaneous abortions and 37% (58/156) pregnancy terminations (see *Figure 1*). 70% (557/621) of neonates were term born. The rate of preterm birth was 10% (64/621) whereof 63% (40/64) were late preterm deliveries (GA 34+0 to 36+6). We observed a reduction of preterm deliveries since 2005 from 14.3% in 2005 to 7.3% in 2017 (p=0.04, see *Figure 2*).
Conclusion: The rate of preterm births has decreased compared to our previous analysis in 2010 and is now close to the rate in the total population of Switzerland, which declined from 7.4% in 2007 to 7.0% in 2017. It is thus necessary to identify determinants that explain changes in preterm birth, such as e.g. modifications in cART regimens.

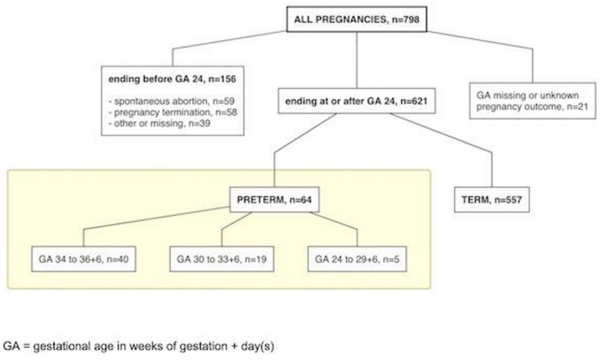


Figure 1. Overview of pregnancy outcomes

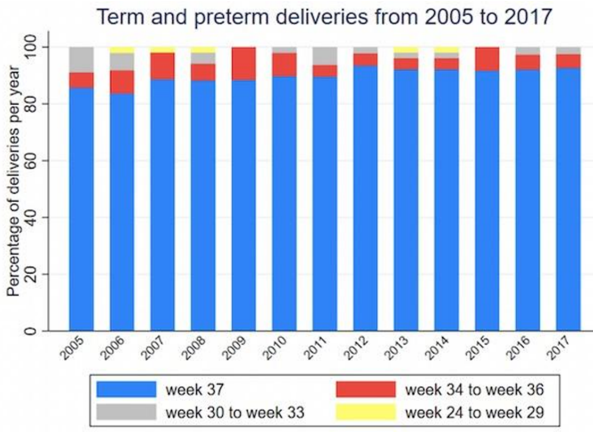


Figure 2. Gestational age of live born infants from mothers with HIV 2005–2017

PE25/12

Poor clinical outcomes in HIV-infected children who start antiretroviral therapy at an older age

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Purpose: The current standard of care in pediatric HIV is to start antiretroviral therapy (ART) as soon as possible after diagnosis. However, this strategy was only recently implemented in Tanzania and many children in care were started on ART based on clinical or immunological criteria.
Method: A retrospective chart review was performed among children (0–19 years) on ART and attending an HIV clinic in Mbeya, Tanzania from 2015–2018. Children were grouped according to age at ART-initiation and comparison was made of clinical characteristics on their last clinic visit with labs as well as their status by the end of 2018.
Results: This study included 1,813 children (Table 1). Those who initiated ART at earlier ages were currently younger (p<0.0001) and children who initiated ART by 6 months of age were on ART for less time (p=0.00075) and were more likely to be on a protease inhibitor (p<0.00001). Average VL was higher in the <6-month category than the 1–5-years category (p=0.038727) and on multivariable analysis, the >5-year category had lower odds of having VL>1000 (AOR, 0.4 [95% CI, 0.2–0.9]). CD4 counts and percentages were lower in the >5-years category (p<0.0001). More children initiating ART later had both a WHO stage 3/4 condition at initiation (p=0.000499) and a WHO T-stage (current WHO stage) of 3/4 (p=0.011239) plus lower odds of having WHO stage 1 at initiation (AOR, 0.2 [95% CI, 0.1–0.5]). Older age groups were found to have worse clinical outcomes (lost to follow-up or death) (p=0.009529).
Conclusion: Children starting ART later were more likely to have severe clinical disease both at initiation and at time of clinic visit. They were also more likely to have greater immunosuppression and worse clinical outcomes. VL alone may not be a good indication of the clinical status of children on ART.

Table 1. Client characteristics

Group (age at initiation)	<6 months	6–12 months	1–5 years	>5 years	p-value
Number	102	86	560	1065	
Female (%)	57 (44)	49 (57)	289 (52)	565 (53)	0.724023
Age in years	4.56	5.72	8.14	15.11	<0.0001
Months on ART	50.6	58.8	65.5	62.2	0.00075
VL in copies/mL	70,435	36,770	13,844	32,520	0.038727
CD4 in cells/mm^3 (#)	1539 (66)	1464 (64)	1139 (401)	656 (756)	<0.0001
CD4% (#)	34.9 (65)	37.7 (64)	34.7 (391)	27.5 (738)	<0.0001
WHO stage 3 or 4	72 (71)	75 (87)	462 (83)	805 (76)	0.000499
Outcome LTFU or death	2 (96)	1 (76)	3 (508)	12 (237)	0.009529

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PE25/13

Prevalence and predictors of unintended pregnancies among HIV positive young adults (14–24 years) attending an urban HIV clinic in Uganda

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Purpose: To assess the predictors of unintended pregnancies among HIV positive young adults attending an urban HIV clinic.
Method: The Infectious Diseases Institute (IDI) adults' HIV clinic provides care and treatment to over 8,000 patients about 400 of which are young adults. We abstracted data from electronic medical records of all young women aged between 14 and 24 years enrolled at the IDI sexual and reproductive health clinic from January 2012 to December 2018. Descriptive statistics were used to explore baseline characteristics and a logistic regression model was fit at the multivariate analysis to assess factors associated with unintended pregnancies.
Results: A total of 255 women were included in the study. The prevalence of unintended pregnancy was 37.7%. Median (IQR) age, parity and duration on ART was 22 (21–24), 2 (1–2) and 8 (0–28) months respectively; majority of the women were married or cohabiting 160/255 (62.8%); on a first line ART regimen 174/255 (68.2%) and had attained above secondary level education 100/255 (39.2%). At the multivariate level adjusting for age, parity, duration on ART, marital status and education level, young women who were widowed or separated had increased odds (OR=2.9; 95% CI=1.09–7.54; p=0.03) of unintended pregnancy compared to single women. Young women on Efavirenz based regimen had increased odds (OR=1.6; 95% CI=0.95–2.80; p=0.07), with a borderline statistical significance. Age, duration on ART, ART regimen, and education level were not associated with unintended pregnancies.
Conclusion: The prevalence of unintended pregnancies among HIV positive young adults is lower than that in the general population of adolescents in Uganda with those who are not in committed relationships being more likely to have unintended pregnancies. Efforts to encourage family planning use need to be focused on this category of women.

PE25/14

Microbiota richness and diversity in a cohort of underweight HIV-positive children aged 24–72 months in Cape Town, South Africa

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Introduction: Elements of the human gut microbiome have been found to impact on a range of pathologic conditions.Human immunodeficiency virus (HIV) infection disturbs the microbiota-mucosal immune system balance and disrupts the stable microbiome which results in inflammation and chronic HIV pathogenesis.Globally there is a 68.7%prevalence of malnutrition amongst children who are HIV positive.
Limited data exists on microbiome diversity of underweight, HIV-infected children in developing countries.This study describes the microbial diversity within a cohort of underweight children on Antiretroviral therapy (ART) & highlights implications for practice.
Methods: This data forms part of a larger randomized control trial of which HIV-positive children aged 24–72 months were recruited from high disease burden areas within Cape Town.Fecal samples, anthropometric data (weight&height) and venous blood (CD4) were collected at baseline and at follow-up visits. Only baseline data was analysed for this abstract.The microbiota was analysed by culture and molecular-based methods. Anthropometric data was converted to percentiles. Biomedical raw data was exported to STATA for statistical analyses.
Results: More than half the cohort were on the 5th percentile WFA (52%; p=0.03). 65% of children had a CD4 >1,000 cells/μL (p=0.02).The microbiota was enriched with *Bacteroides, Clostridium Perfringes, Bifidus, Enterobacteria, Enterocoque* and *Lactobacilus*.Nine children had *Fungi* growth, indicative of bacterial microbiota disruption.Diminished growth of *Clostridium Perfringes* and increased growth of *Enterobacteria* was shown, which is common in the HIV adult population due to inflammation.*Enterobacteria* has been linked to immune activation and pathogenic activities.Compared to studies of healthy children, this cohort had low diversity of microbiota.Firmicutes, a Bacterial Phyla that is commonly depleted in the HIV population was reasonably well represented in this cohort, which is possibly associated with ART, as ART has been shown to allow for recovery of the microbiota in the HIV adult population.
Conclusion: The potentially pathogenic microbiota contributes to ongoing mucosal inflammation resulting in microbiome changes&disease progression.Microbiota manipulation can reduce inflammation, improve absorptive capacity of the GIT&overall health of the child which will reduce morbidity and mortality.

PE25/15

Influence of maternal parameters on birth outcome in HIV-exposed newborns – 11 year observation

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Purpose: The perinatal status of neonates is affected by a range of conventional and HIV-infection related risk factors. Therefore, to study the correlation, we reviewed information on maternal parameters during pregnancy and neonatal parameters at birth.
Method: HIV Out-Patient Clinic of the Hospital for Infectious Diseases in Warsaw is providing integrated gynecological and HIV care since its constitution in 1994. In collaboration with Department of Children's Infectious Diseases, we reviewed all pregnancies and neonates occurring between 2006 and 2017 in the clinic. Data on neonates were collected from medical documentation analysis.
Results: In the investigated period, there were 187 pregnancies. Of 159 with known birth outcome, 18 (11.3%) were preterm births, only 1 neonate was very preterm. Median mother's age at delivery was 31 (IQR: 27.5–34) years, median gestation week at delivery was 38 (37–39). Of 148 children with known HIV status, one patient born in term was HIV-positive (0.7%). In the group of newborns with birth weight <10 percentile (defined as intrauterine growth restriction), the median last CD4 count in women during pregnancy was lower, 318 (113–800) compared to 488 (37–1254) in neonates >10 percentile (p=0.0008). There was a tendency towards a higher risk of neonatal birth weight <10 percentile in the older mothers (p=0.077).
Conclusion: Insufficient maternal immune status is a risk factor for intrauterine growth restriction. Advanced maternal age at delivery may have a probable effect on birth weight. Due to limited study sample, further investigations should be considered.

Pathogenesis and immunopathogenesis

PE26/1

SHIV162P3 transmission by semen leukocytes is efficiently inhibited by a combination of broad neutralizing antibodies

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Background: The semen of HIV-1 infected subjects contains either free infectious virus or cell-associated virus (infected leukocytes). Although transmission by cell-cell contacts has been shown to be a more potent and efficient means of virus propagation than infection by cell-free virus particles, transmission by seminal leukocytes has been overlook in studies of cell-cell transmission and related inhibitory factors.
Methods: Semen leukocytes and splenocytes were collected from a SHIV162P3 infected Cynomolgus macaque at the peak of blood viremia. The

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ability of a combination of bNAbs to protect from SHIV162P3 cell-cell transfer by semen leukocytes was tested *in vitro* in a TzmBL assay. To confirm the data and to extend the panel of bNAbs, neutralization assays using TzmBL and PBMC as target cells were developed using infected splenocytes as surrogate of semen cells.
Results: A combination of 1st generation bNAbs 2F5+2G12+4E10 inhibited cell-cell transmission with equal efficiency when both semen leukocytes and splenocytes were used as donor cells in a TzmBL assay. Protection was highly reduced when the same bNAbs were used in double combination or individually. Interestingly, a series of the so-called "2nd generation bNAbs" (10–1074, PGT128, PGT151 and N6) even when used individually, revealed to be as efficient against cell-cell transmission as the triple combination of the 1st generation bNAbs. Moreover cell-free infection inhibition was achieved with 1 log lower IC50 values compared to cell-associated transmission, whatever it was the bNAb used.
Conclusion: A subset of bNAbs could efficiently prevent cell-cell transmission by semen infected leukocytes, and this property should be considered an important characteristic defining antibody potency for therapeutic or prophylactic antiviral strategies.

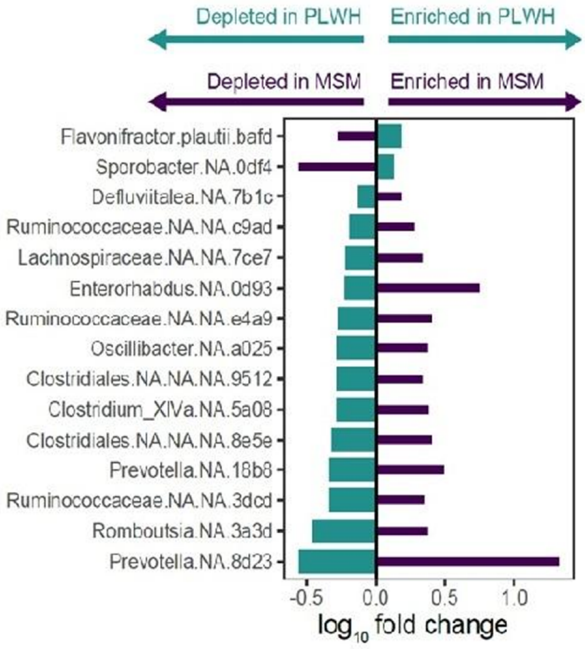
PE26/2

Colonic microbiota exhibits disparate associations with HIV-infection and sexual practices

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Purpose: Effective antiretroviral therapy (ART) has prolonged survival and shifted the morbidity spectrum for people living with HIV (PLWH) from AIDS-associated opportunistic infections and malignancies towards age-associated noncommunicable comorbidities (AANCCs), with these being more prevalent in PLWH compared to in age-matched HIV-uninfected individuals. A key contributor to the current disease spectrum includes HIV-associated inflammation and immune activation, the etiology of which in PLWH remains incompletely defined. Gut microbial dysbiosis is thought to be a potential important contributor, but data thus far are conflicting regarding the role that lifestyle factors, including sexual orientation and behavior, and HIV-infection itself have on gut microbial dysbiosis.
Methods: Using 16S rRNA gene sequencing, we profiled the microbiota from fecal samples of PLWH with suppressed viremia on ART and HIV-uninfected controls participating in the AGEhIV Cohort Study. PLWH were selected to include 40 men having sex with men (MSM), 20 men having sex with women (MSW) and 20 females (F) matched 1:1 by age, sex, sexual orientation, BMI, birth country, and smoking status with HIV uninfected controls.
Results: HIV-infection was associated with alterations in the gut microbiota including an enrichment in Enterobacteriaceae and Desulfovibrionaceae members and a depletion of short chain fatty acids-producing bacteria such as Lachnospiraceae and Ruminococcacea. Furthermore, comparisons between MSM and non-MSM males revealed a unique MSM-associated microbiome signature characterized by an enrichment particularly in Prevotellaceae members (figure), which was independent of HIV-infection. Finally, practicing receptive anal intercourse, regardless of condom use, was linked to a specific bacterial community variance independently of sex, which may explain the Prevotella-rich microbiome in MSM.
Conclusions: Our data provide unique evidence that colonic microbiota exhibit disparate associations with HIV-infection and sexual practices.



Abundance trends differs significantly in both comparison of MSM vs. MSW and PLWH vs. HIV-negatives.

PE26/3

Zonulin indicates loss of intestinal integrity and microbial translocation in HIV+ patients

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Purpose: Damage of the gastrointestinal (GI) mucosa in HIV infection leads to microbial translocation and immune activation, which in turn contributes to non-infectious comorbidities. Combined antiretroviral therapy (cART) leads to only partial restauration of this gut damage. Several biomarkers of the epithelial barrier have been identified, however, some are not specific and others are impacted by cART. Zonulin is a modulator of epithelial tight junctions. Some studies reported an increase of Zonulin in the blood during HIV infection while others reported a decrease. We quantified Zonulin and compared it to inflammatory markers and the viral reservoir in blood, ileum and rectum from HIV patients and controls.
Methods: Biopsies from terminal ileum (TI), rectum (R) and blood (PB) were collected from 5 treatment naïve ($HIV+_{NAïVE}$) and 10 cART-treated ($HIV+_{cART}$) HIV+ individuals and 11 controls (CTRL). Median time on $ART_{[years]}$ was 6 (9–10). ELISA (Immundiagnostik) was used to measure Zonulin in serum. CD4+ T cells and total HIV DNA was quantified in PB, TI and R. Ultrasensitive digital ELISA (Simoa; Quanterix) was used to measure IFN-α in serum and tissue supernatants.

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Results: The median CD4+T cell count [cells/μL] in HIV+$_{NAÏVE}$ was 70 (30–255) versus 426 (293–787) in HIV+$_{cART}$. Zonulin levels [ng/mL] were highest in treatment-naïve HIV+when compared to cART-treated HIV+(p=0.04) or CTRL (p=0.0087; HIV+$_{NAÏVE}$>HIV+$_{cART}$>CTRL). Similarly, HIV+$_{NAÏVE}$ showed higher IFN-α and HIV-DNA levels in PB when compared to HIV+$_{cART}$ (IFN-α: p=0.0390; HIV-DNA: p=0.0420). Zonulin was correlated negatively to CD4+ T cell frequencies (r=−0.58, p=0.04) and positively to IFN-α (r=0.65, p=0.05) in the TI.
Conclusion: Zonulin was highest in HIV+$_{NAÏVE}$ patients. In addition, its levels in blood were associated with loss of intestinal CD4 T cells and increased inflammation in the gut, suggesting that increased levels of systemic Zonulin correlate with intestinal damage.

PE26/4

Distinct pro-inflammatory and cardio-protective effects of antiretroviral drugs in vascular endothelial cells

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Purpose: Studies have linked cardiovascular disease (CVD) in people living with HIV (PLWH) with certain antiretroviral drugs (ARVs); however, a causative link has not been established. CVD is driven by inflammation of the vascular endothelium leading to increased leukocyte/platelet adhesion and pro-coagulant activity. In addition, the endothelium has cardio-protective, anti-thrombotic properties. Our objective was to compare the effects of different ARVs upon endothelial inflammatory responses to better understand the causes of increased CVD in PLWH.
Method: Human umbilical cord vein endothelial cells were treated with ARVs and inflamed with TNF-α. Inflammation was evaluated as cell adhesion molecule (intercellular adhesion molecule [ICAM]-1) and coagulation factor (tissue factor [TF]) expression by flow cytometry. We also determined the ability of endothelial cells, via the release of microparticles, to affect platelet activation by real-time flow cytometry. Endothelial cardio-protective properties were measured as expression of anti-thrombotic CD39/CD73, which degrade the platelet activator adenosine diphosphate (ADP). Statistical significance was determined by one-way ANOVA with Tukey's multiple comparison test.
Results: Abacavir sulphate (ABC) increased ICAM-1 and TF expression compared to both tenofovir disoproxil fumarate (TDF, +46.1% and +15.4%, p<0.05) and tenofovir alafenamide (TAF, +46.2% and +14.0%, p<0.05). Microparticles isolated from ABC-treated endothelium significantly enhanced collagen-evoked platelet activation (integrin activation and α-granule release). The ability to breakdown the platelet activator ADP was enhanced by TDF and TAF (+44.4% and +46.0%, p<0.05) but ABC had no significant effect.
Conclusion: ABC, TDF and TAF differentially impact the endothelial inflammatory response. ABC induces effects that are pro-inflammatory and would be expected to increase CVD, whereas TDF and TAF have anti-thrombotic and therefore potentially cardio-protective effects. Further work is required in more relevant cell types and in clinical settings with licensed ARV combinations to establish whether these inflammatory changes elucidate mechanisms by which ARVs may affect CVD in PLWH.

PE26/5

Bacterial translocation kinetics in HIV-1 infection: from acute to chronic stages

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Purpose: In acute HIV infection (AHI), viral load (VL) increases and the virus reaches gut, where intestinal epithelial barrier disruption occurs, resulting in bacterial translocation (BT) and the following immune activation. The aim of this study is to evaluate the BT kinetics during the different AHI stages (defined by Fiebig classification).
Method: In this retrospective study, 10 subjects diagnosed during AHI (4 in Fiebig II, 3 in Fiebig III and 3 in Fiebig IV) were included (8/10 were male with a median age of 22 years at the time of diagnosis). In addition to these 10 plasma samples, other 39 plasma samples were analysed from diagnosis until antiretroviral therapy (ART) and VL suppression. 40 samples from ART-suppressed late-chronic (LC) infected subjects were analysed as control. Days post-infection were estimated according to Fiebig stage at the time of diagnosis. sCD14, IFABP and LPS BT biomarkers were measured on all plasma samples by ELISA.
Results: sCD14 levels were higher in Fiebig III stage (median: 5.99 μg/mL), LPS levels were higher in Fiebig IV stage (median: 6.25 EU/mL) while IFABP levels were higher in Fiebig VI stage (median: 0.86 ng/mL) than in other Fiebig stages (Table1). IFABP had highest levels at 26–80 days post-infection (p=0.04), sCD14 levels were higher at 15–30 days post-infection (p=0.001), while LPS showed similar trend to sCD14 (p=0.51). sCD14, IFABP and LPS medians of LC infected subjects are showed in Table1.
Conclusion: sCD14 and LPS have the highest values during the first stages of infection. While LPS decreases along time, sCD14 shows similar dynamic to LPS, but finally increases at LC infection. Moreover, we show that IFABP increases along time and establishes at LC infection. These results suggest that BT occurs in large-scale at the first term of infection and is stable at LC stage, independently of an increase of other inflammation biomarkers (as sCD14).

Table 1. Samples median and IQR values

	Fiebig II	Fiebig III	Fiebig IV	Fiebig V	Fiebig VI	LC
N samples	4	3	3	25	14	40
N subjects	4	3	3	9	7	40
Log VL	6.64 (6.61, 6.75)	7 (6.73, 7)	6.80 (6.58, 6.90)	2.93 (2.13, 4.94)	1.73 (1.70, 1.96)	<1.5
CD4 (cell/μL) (N=28)	586 (577, 595)	NA	NA	618 (463, 750)	564 (489, 702)	727 (598, 978)
CD8 (cell/μL) (N=28)	940 (875, 1004)	NA	NA	954 (816, 1185)	771 (693, 860)	860 (631, 1098)
sCD14	2.92 (2.81, 3.24)	5.98 (4.73, 6.69)	3.13 (2.78, 3.73)	2.41 (2.28, 3.16)	2.44 (2.26, 2.59)	4.52 (3.55, 7.05)
IFABP	0.33 (0.15, 0.48)	0.30 (0.25, 0.34)	0.17 (0.16, 0.42)	0.83 (0.31, 1.09)	0.86 (0.65, 1.03)	0.55 (0.33, 1.12)
LPS	2.52 (1.95, 3.75)	3.06 (2.47, 3.66)	6.25 (5.88, 6.62)	2.99 (2.36, 5.35)	3.22 (2.28, 4.26)	0.96 (0.69, 1.47)

*NA: not available

PE26/6

Mitochondrial antioxidants attenuate In vivo liver fibrosis in chronic treated HIV

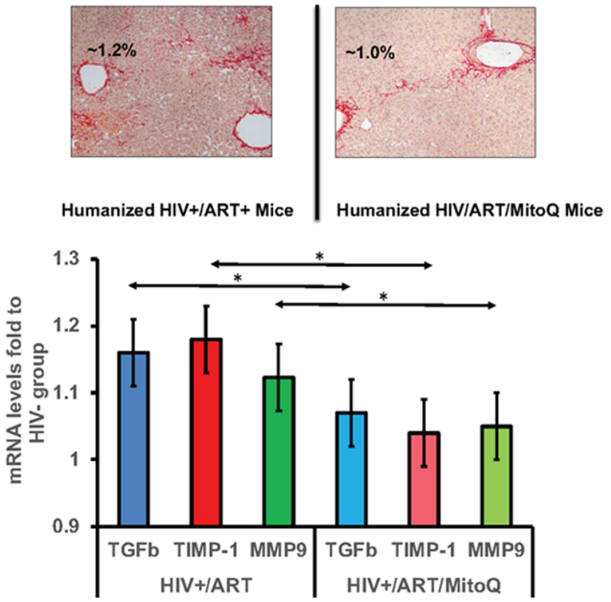
S Sen Roy, A Kossyvakis, R Heymans, P Hamid, S Beaven and T Kelesidis
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Purpose: Elucidating mechanisms of HIV-related liver fibrosis will set the basis for therapies that can lessen its impact including cirrhosis and mortality. As mitochondria are the main source of cellular oxidative stress, the mitochondrial antioxidant MitoQ may target HIV-related liver fibrosis. We used a physiologically relevant humanized mouse model of chronic treated HIV to study whether MitoQ attenuates *in vivo* HIV- and/or ART-driven liver fibrosis.
Method: The C57BL/6 *Rag2−/−γc−/−CD47−/−* Bone Marrow/Liver/Thymus mice do not develop early graft versus host disease and thus HIV- and/or ART-driven changes on liver fibrosis can be dissected in vivo. After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, mice (n=20) were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. MitoQ was given in water at 250 μM daily. The groups were: A (n=5): uninfected (HIV-); B (n=10): HIV+, ART; C (n=10): HIV+/ART/MitoQ. Liver fibrosis was assessed histopathologically by Picrosirius red staining of fibrotic mouse liver. Real time PCR was used to determinate mRNA levels of key mediators of liver fibrosis (TIMP-1, TGF-beta, MMP-9). Results are described as mean+ SEM and t-test was used for statistical analysis.
Results: Potent ART suppressed viremia within 4 weeks. HIV+ mice exposed to HIV/ART for 12 weeks demonstrated a ~12-fold increase in fibrosis (Figure).

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In the liver of HIV+/ART+ mice there was a mean 22%, 16%, 18% and 12.3% increase in Picrosirius Red signal, TGF-b, TIMP-1 and MMP-9 mRNA levels, respectively, compared to uninfected mice ($p<0.05$). MitoQ attenuated HIV/ART-induced increase in Picrosirius Red signal, TGF-b, TIMP-1 and MMP-9 ($p<0.05$).

Conclusion: MitoQ attenuated HIV/ART-driven increase in collagen content and molecular mediators of fibrosis in the liver. Further studies are needed to determine whether MitoQ can be a novel therapeutic strategy for liver fibrosis in chronic treated HIV.



Figure

PE26/7

Mitochondrial antioxidants attenuate In vivo mitochondrial dysfunction and exhaustion in T cells in chronic treated HIV

S Sen Roy, A Kossyvakis, R Heymans, P Hamid and T Kelesidis

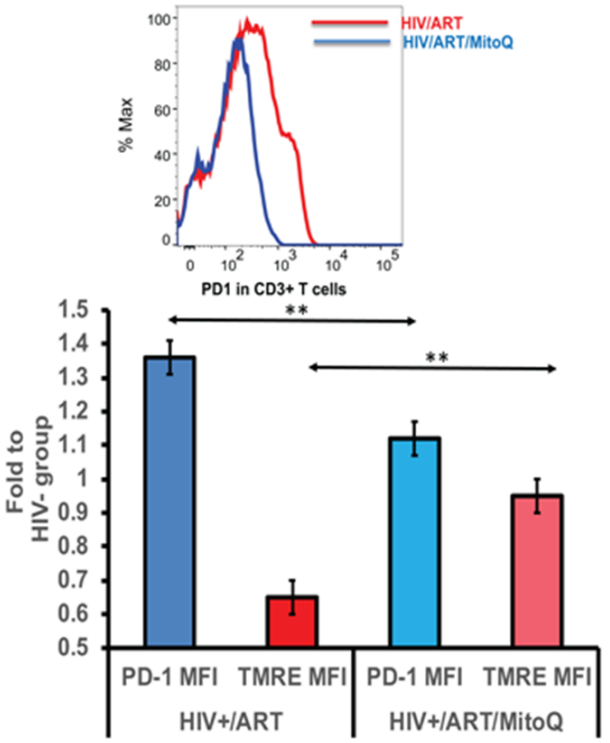
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Purpose: Elucidating how oxidative stress and mitochondrial dysfunction contribute to T cell impairment in chronic HIV infection despite potent antiretroviral therapy (ART) could provide new therapies to reduce aging of the immune system related to morbidity and mortality. Oral MitoQ has successfully been tested in vivo (animals, clinical trials) for oxidative damage-related states and T cell exhaustion in chronic viral infections such as hepatitis. We used a physiologically relevant humanized mouse model of chronic treated HIV to study whether MitoQ attenuates *in vivo* HIV- and/or ART-driven mitochondrial and T cell dysfunction (exhaustion).

Method: After 4 weeks of infection with the dual-tropic 89.6 HIV-1 virus, C57BL/6 *Rag2−/−γc−/−CD47−/−* Bone Marrow/Liver/Thymus humanized mice (n=20) were treated with daily emtricitabine (200 mg/kg), tenofovir (208 mg/kg), raltegravir (80 mg/kg) for up to 12 weeks. MitoQ was given in water at 250 μM daily. The groups were: A (n=5): uninfected (HIV-); B (n=10): HIV+, ART; C (n=10): HIV+/ART/MitoQ. Multicolor flow cytometry was used to assess human T cell (CD3+) exhaustion (PD-1) and Mitochondrial membrane potential (MMP) (staining with the fluorochrome TMRE). Reduced fluorescence signal of TMRE suggests reduced MMP and mitochondrial dysfunction. Results are described as mean+ SEM and t-test was used for statistical analysis.

Results: Potent ART suppressed viremia within 4 weeks. HIV+ mice exposed to HIV/ART for 12 weeks demonstrated a mean 36% increase in PD-1 expression and a mean 35% reduction in MMP in CD3+ T cells compared to uninfected mice (Figure) ($p<0.05$). MitoQ attenuated HIV/ART-induced increase in PD-1 MFI and decrease in TMRE MFI in CD3+ T cells ($p<0.01$).

Conclusion: MitoQ attenuated HIV/ART-driven increase in exhaustion and mitochondrial dysfunction in T cells. Further studies are needed to determine whether MitoQ can be a novel therapeutic strategy for immune dysfunction in chronic treated HIV.



Figure

PE26/8

Inhibition of caspase 1 reduces viral load, CD4 T cell depletion and immune activation in HIV-1 infected humanized mice

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Purpose: HIV-1 infection results in the activation of inflammasome involving IFI16, NLRP3, caspase-1 and release of IL-1 β and IL-18. Early inflammasome activation may facilitate viral spread and establishment of viral reservoirs. We evaluated the effect of the caspase-1 inhibitor VX-765 on virological and immunological parameters after HIV-1 infection in humanized mice.

Method: NSG mice engrafted with human CD34+ hematopoietic stem cells were infected with HIV-1 JRCSF. 15 mice were first sacrificed serially to investigate kinetics of the HIV-1 related inflammasome activation. Infected mice (n=24) were then treated daily injected with VX-765 or vehicle from day 1 post infection on, for 21 days. Blood and organs were collected at different time points and analysed for inflammasome genes expression, cytokines levels, viral load and CD4 cell count.

Results: HIV-1 RNA disseminated within 3 days post-infection in different organs, in concommittance with increased expression of NLRP3 and IL1-β such as in lymph nodes (fold change of 3.1 and 1.64) and bone marrow (fold change of 2.74 and 4.96), respectively ($p<0.001$). IFI16 expression peaked at D24 in lymph nodes and Bone marrow (fold change of 1.49 and 1.64, $p<0.05$) and coincides with increased IL-18 levels in plasma (6.89 vs. 83.19 pg/mL, $p=0.004$). Treatment with VX-765 significantly reduced TNF-α at day 11 (0.47 vs. 2.2 pg/mL, $p=0.045$), IL-18 at day 22 (7.8 vs 23.2 pg/mL, $p=0.04$), CD4 + T cells (44.3% vs 36.7%, $p=0.01$) and the CD4/CD8 ratio (0.92 vs 0.67, $p=0.005$) after 21 days of infection in plasma. Importantly, viral load and total HIV DNA were decreased in VX-765-treated mice (4.26 vs. 4.89 log 10 copies/mL, $p=0.027$).

Conclusion: We report early inflammasome activation associated with HIV replication in tissues. Inhibition of the inflammasome activation early upon infection with HIV-1 improves CD4+ T cell homeostasis, viral loads as well as immune activation.

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PE26/9

Effect of early initiation of ART on alterations in natural killer cells in HIV infected pediatric patients

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Purpose: HIV disease progression is faster in children. According to the recent NACO guidelines, all children diagnosed HIV-1 positive and below the age of two should be initiated on ART therapy, irrespective of their CD4 counts. However, on antiretroviral therapy, the viruses in the infected individuals develop resistance mutations, as is observed in the ART non-responders. Whether early initiation of ART helps to preserve immune cells like NK cells, which play a key role in inhibiting viral replication and also in regulating the host adaptive immune response to HIV infection from early loss or promote their recovery is yet not known and therefore it is important to assess the effect of early initiation of ART on the immune responses in the HIV-1 infected children (ART responders and non-responders). .
Method: In a longitudinal study on 30 HIV infected pediatric patients (≤5 years) and uninfected pediatric healthy controls, alterations in NK cell subset along with their activating, inhibitory and cytotoxic receptor were enumerated and functionally characterized by flow cytometry and correlated with CD4 count, viral load, neutralization response and plasma ADCC activity before and after early initiation of ART at every 6 month follow-up .
Results: Circulating NK cells were significantly increased after first follow up of ART initiation and the activating (NKG2D, NKG2C), cytotoxic (NKp30, NKp44, Nkp40) and inhibitory receptor (NKG2A, KIR) of NK cells were also restored to the normal level. The CD4 counts were increased and viral load decreased as compared to the ART naive patients. Neutralization response and plasma ADCC activity is improved after 6 months of ART initiation
Conclusion: Our study suggest that early initiation of ART is beneficial to the patients, since our study is a longitudinal study results will be further confirmed after a long follow ups.

PE26/10

HIV-DNA levels, HLA-B*27 and HLA-DRB1*13 among LTNPs, ECs and HIV controllers

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Background: The aim of this study was to determine the association of HLA-B*27 and HLA-DRB1*13:03 with HIV-DNA in Elite Controllers, Long-Term Non-Progressors, HIV Controllers, ART-naïve and ART treated patients (pts).
Methods: We evaluated 231 HIV-1 pts from the ICONA and the Elvis Cohorts categorized in 5 distinct groups: 20 EC (ART-naïve pts, always with HIV-RNA <50 cps/mL); 35 Long term non Progressors (LTNP; ART-naïve pts for ≥8 years, with VL>1,000 cps/mL and CD4+ ≥500 cells/μL); 17 HIV controllers (ART-naïve pts, always with HIV-RNA 50–1000 cps/mL); 122 ART-naïve (pts who started ART, with HIV RNA >50 cps/mL and CD4+ <500 cells/μL); 37 pts under suppressive ART (HIV-RNA<50 cps/mL). Total HIV-DNA was extracted from PBMCs by droplet digital PCR (ddPCR) and classified as undetectable if below the detection limit. HLA-B*27 rs4349859 and HLA-DRB1*13:03 rs424232 genotypes were determined. Multivariable linear regression was performed to assess SNPs association with HIV-DNA values.
Results: rs 4349859 GG genotype was found in 16%, 6%, 14%, 8% and 9% of EC, HIV-controllers, LTNP, ART-naïve and ART-treated pts, respectively (p=0.819; Table 1).
Undetectable HIV-DNA was found in 60%, 31%, 35%, 17% and 19% EC, HIV-controllers, LTNP, ART-naïve and ART-treated pts with rs4349859 AG genotype, respectively (p=.004) and in 67%, 100%, 40%, 22% and 0% of EC, HIV-controllers, LTNP, ART-naïve and ART-treated pts with GG genotype (p=.231).
After adjusting for patients' group, age, gender, years of infection, nadir CD4+, zenith HIV-RNA, CD4+ cell count, CCR5Δ32, IL28B rs12979860 genotypes and rs4349859, lower HIV-DNA levels were associated with higher nadir CD4+(p=.015), rs4349859 GG genotype (p=.049); a marginal association was also observed for CCR5 heterozygous genotype (Table 2). No significant association was found between HIV-DNA values and HLA- DRB1*13:03 rs424232.
Conclusion: Lower values of HIV-DNA were found to be associated with the presence of HLA-B*27 rs4349859 GG genotype.

Table 1 - Characteristics at HIV-DNA determination of unmatched HIV-1 infected subjects

Characteristic		EC (n=20)	HIV-CONTROLLER (n=17)	LTNP (n=35)	NAIVE (n=122)	ART-TREATED (n=37)	p-value
Age (years)		49 (40-56)	38 (29-48)	47 (38-51)	36 (30-48)	51 (44-55)	<.0001
Male gender		13 (65%)	7 (41%)	26 (74%)	86 (72%)	25 (68%)	0.153
Italian nationality		18 (90%)	11 (65%)	29 (83%)	83 (68%)	30 (82%)	0.068
Years since HIV diagnosis		12.7 (5.0-17.00)	1.76 (0.87-4.38)	9.26 (5.00-13.0)	0.20 (0.01-2.0)	17.5 (9.0-22.0)	<.0001
CD4+ nadir (cells/μL)		527 (442-644)	472 (423-592)	546 (484-672)	405 (302-513)	220 (74-306)	<.0001
CD4+ (cells/μL)		700 (548-1088)	655 (506-717)	739 (626-934)	473 (345-666)	647 (462-891)	<.0001
CD8+ (cells/μL)		761 (529-1335)	812 (668-1120)	1040 (783-1464)	865 (659-1258)	681 (449-1200)	0.208
HIV-DNA (log_{10} copies/10^6PBMC)		0 (0-2.09)	2.22 (0-2.54)	2.16 (0-2.97)	2.75 (1.99-3.24)	2.13 (1.80-2.55)	<.0001
	Undetectable	11 (55%)	6 (35%)	12 (34%)	22 (18%)	7 (19%)	0.003
	Detectable	9 (45%)	11 (65%)	23 (66%)	100 (82%)	30 (82%)	
IL28B rs12979860							0.011
	CC	3/18 (17%)	6/17 (35%)	14/34 (41%)	54 (52%)	10 (28%)	
	TC	14 (78%)	7 (41%)	14 (41%)	31 (29%)	19 (53%)	
	TT	1 (6%)	4 (24%)	6 (18%)	22 (22%)	7 (19%)	
Presence of HLA-B5701		2/5 (40%)	3/7 (43%)	1/12 (8%)	8/91 (9%)	0/21 (0%)	0.004
CCR5Δ32							0.027
	HT	3/17 (18%)	4/17 (24%)	10/34 (29%)	10/105 (10%)	0/10 (0%)	
	WT	14 (82%)	13 (76%)	24 (71%)	95 (90%)	10 (100%)	
HLA-B*27rs4349859							0.819
	AA	1/19 (5%)	0/17 (0%)	1/35 (3%)	7/116 (6%)	1/35 (3%)	
	AG	15 (79%)	16 (94%)	29 (83%)	100 (86%)	31 (89%)	
	GG	3 (16%)	1 (6%)	5 (14%)	9 (8%)	3 (9%)	
HLADRB1*13:03 rs424232							0.495
	CC	5/16 (31%)	3/16 (19%)	10/31 (32%)	37/105 (35%)	8/30 (27%)	
	CT	11 (69%)	12 (75%)	16 (52%)	59 (56%)	17 (57%)	
	TT	0	1 (6%)	5 (16%)	9 (9%)	5 (17%)	

Results described by median (IQR) and frequency (%).
Comparisons among groups performed by Kruskal-Wallis test (continuous variables) or chi-square/Fisher exact test (categorical variables).

Table 1. Characteristics at HIV-DNA determination of unmatched HIV-1 infected subjects

Table 2 - Multivariable linear regression: factors associated with HIV-DNA.

Characteristic	Category	Adjusted mean HIV-DNA (95%CI) (log_{10} copies/10^6PBMC)	Slope of HIV-DNA (95%CI)	p-value
Age	Per 1-year older		-0.005 (-0.027, 0.017)	0.674
Gender				
	F	1.828 (1.042, 2.614)	0.444 (-0.110, 0.997)	0.115
	M	1.384 (0.768, 2.000)	Ref	-
Patients' group				0.244
	EC	1.070 (-0.357, 2.496)	-0.784 (-2.219, 0.651)	0.280
	HIV-CONTROLLER	1.954 (0.976, 2.932)	0.100 (-0.917, 1.116)	0.846
	LTNP	2.227 (1.232, 3.221)	0.373 (-0.666, 1.411)	0.477
	NAIVE	1.854 (1.274, 2.434)	Ref	Ref
	ART-TREATED	0.926 (-0.329, 2.181)	-0.928 (-2.058, 0.202)	0.106
Years HIV infection	Per year longer			0.611
CD4+ nadir	Per 100-cells/μL higher		-0.257 (-0.462, -0.052)	0.015
Zenith HIV-RNA	Per log_{10} copies/mL higher		0.134 (-0.181, 0.449)	0.400
HLA-B*27 rs4349859	GG	1.217 (0.312, 2.122)	-0.778 (-1.556, -0.0003)	0.049
	non-GG	1.995 (1.423, 2.567)	Ref	-
CCR5Δ32	HT	1.246 (0.317, 2.130)	-0.720 (-1.495, 0.054)	0.068
	WT	1.966 (1.364, 2.567)	Ref	-
IL28B rs12979860				0.683
	CC	1.633 (0.944, 2.322)	0.191 (-0.446, 0.827)	0.553
	CT	1.743 (1.022, 2.464)	0.300 (-0.381, 0.982)	0.384
	TT	1.442 (0.629, 2.256)	Ref	-
CD4+ cell count	Per 100-cells/μL higher		0.149 (-0.0005, 0.298)	0.051

Table 2. Multivariable linear regression: factors associated with HIV-DNA.

PE26/11

Macromolecule uptake across intestinal epithelia in HIV infection

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Purpose: Increased serum levels of microbial macromolecules are associated with chronic immune activation, disease progression and comorbidity in HIV infection. Although they have been attributed to a pathological influx across the gut mucosa, it is unknown how these microbial components cross the intestinal mucosal barrier. Prior studies demonstrated an increased permeability to small solutes such as electrolyte or monosaccharides.

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Therefore, the mechanisms described cannot be attributed to the mucosal translocation of macromolecules. In this study, we quantified macromolecule translocation across the gut mucosa of HIV infected patients and performed mechanistically studies on the translocation processes involved.
Methods: Epithelial barrier function and transmucosal transport of macromolecules (FITC-Dextran 4000 (FD4, 4 kDa) and horseradish peroxidase (HRP, 44 kDa)) were quantified by means of Ussing chamber experiments on duodenal and colon mucosa endoscopically obtained from HIV-infected individuals and uninfected controls. The contribution of epithelial apoptosis and transcytosis to macromolecular translocation was investigated by transwell flux measurements in monolayers of cultured intestinal cells (T84) using inducers and inhibitors of apoptosis at 37 °C and 14 °C. Epithelial apoptosis was quantified by the SensoLyte© Homogeneous AFC Caspase-3/7-Assay.
Results: FD4 and HRP fluxes across the mucosa as well as epithelial apoptoses were increased in untreated HIV+ patients compared to controls but tended to normalize in patients on antiretroviral therapy. In cultured epithelial cells, induction of apoptosis increased permeability to both macromolecules. Inhibition of active transcytosis at 14 °C revealed a reduction in translocated HRP in both control as well as treated T84 cells.
Conclusion: For the first time, an increased mucosal macromolecule translocation has been directly demonstrated in intestinal mucosa obtained from HIV-infected patients. Our data indicate that epithelial apoptoses represent an unselective translocation pathway for both, medium and large size macromolecules, whereas large size macromolecules seem to predominantly translocate via active transcytosis.

PE26/12

Immune cell activation as a risk factor for hypertension in people living with HIV in Sub-Saharan Africa using the recent American Heart Association and American College of Cardiology Guidelines

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Purpose: This study was aimed at determining factors associated with hypertension and the role of immune activation in People living with HIV (PLWH) using the new hypertension guidelines by the American Heart Association (AHA) and the American College of Cardiology (ACC) in Sub-Saharan Africa.
Methods: We conducted three cross-sectional, one systematic and one prospective study. The World Health Organization Stepwise approach to Surveillance (WHO STEPs) and the international physical activity questionnaire (IPAQ) were used to collect data for cross-sectional studies while Preferred reporting items for Systematic reviews and meta-analyses was employed for the systematic study. FlowJo for flowcytometry analysis and Statistical evaluations were employed to elucidate relationships between hypertension and response variables.
Results: Factors significantly associated with increased odds for developing hypertension among 226 PLWH after adjustments in multivariate logistic regression were waist circumference, sedentary lifestyle, age, body mass index, employment status, fasting blood sugar, table salt consumption and moderate physical activity respectively ($p<0.05$). 94% had uncontrolled blood pressure. The new AHA/ACC criteria for hypertension shifted 26% of the originally normotensives into hypertension category. Hypertension was associated with higher neutrophil, white blood cell counts and neutrophil lymphocyte ratio ($p<0.05$).
IL-6 and IL-10 were associated with hypertension in a carefully selected age-sex matched group (n=38) of PLWH ($p<0.05$). Interleukin (IL)-17A, interferon (IFN)-γ, and higher $CD4^+$ T cell counts were associated with hypertension in antiretroviral treated participants in 45 carefully selected studies from 13 unique African countries. High salt intake was associated with increased Innate immune cell activation markers (CD86+, CD80+) and hypertension.
Conclusion: Targeting modifiable risk factors and adaptive immune activation could provide improved care for hypertensive PLWH, however, further research is needed to characterize the inflammatory milieu contributing to hypertension in PLWH especially in African populations where the burden of HIV is the highest.

PE26/13

Increased level of plasma Galectin-9 is associated with microbial translocation in perinatally HIV-infected children

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Purpose: Perinatal HIV infection is distinct from chronic HIV infection in adults in terms of rapid disease progression, higher viral load and increased depletion of CD4+ lymphocytes. Galectin-9 (Gal-9) is a component of the first waves of cytokine storm in acute HIV infection that remains elevated in antiretroviral therapy (ART)-suppressed HIV-infected individuals. The elevated levels of Gal-9 in chronic HIV infection despite viral suppression in adults suggest that it may contribute to ongoing inflammation. Here we seek to investigate the levels of Gal-9 in treated and untreated HIV-infected children compared to healthy controls and its role in microbial translocation and inflammation.
Method: Gal-9 and soluble CD14 (sCD14) were measured in the plasma of 15 treated and 15 untreated HIV-infected children, and 10 healthy controls by sandwich ELISA. The effect of rGal-9 on tight junction proteins, Claudin-4 and ZO-1, was studied in gut epithelial cell-line HT-29, using immunofluorescence and qRT-PCR.
Results: Increased levels of Gal-9 were found in treated (Median=10.7 ng/mL) and untreated (Median=13.6 ng/mL) HIV-infected children as compared to healthy controls (Median=6.7 ng/mL). Plasma levels of Gal-9 showed a strong positive correlation (Spearman $r=0.64$, $p<0.0001$) with sCD14, a marker of microbial translocation, both in treated and untreated HIV-infected children. Immunofluorescence revealed disruption of Claudin-4 tight junctions after 24 h of stimulation of HT-29 cells with 500 nM rGal-9. qRT-PCR results also showed 4 folds downregulation of Claudin-4 ($p=0.03$) and ZO-1 ($p=0.01$) tight junctions.
Conclusion: Elevated levels of Gal-9 in perinatally HIV-infected children sustain even during ART. The demonstrated loss of tight junction integrity by rGal-9 along with elevated sCD14 suggest the role of Gal-9 in microbial translocation and chronic inflammation observed in ART-treated children. Targeting Gal-9 either by exploiting its secretory pathways or competitive blockade may serve as novel therapeutic approach to control HIV-driven inflammation that persists during ART.

Pharmacology, pharmacogenomics and drug interactions

PE27/1

Efficacy and safety of artemether-lumefantrine as treatment for **Plasmodium falciparum** uncomplicated malaria in adult patients on efavirenz based antiretroviral therapy in Zambia: an open label non-randomized interventional trial

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Purpose: HIV-infected (HIV+) individuals on antiretroviral therapy (ART) require treatment with artemisinin-based combination therapy (ACT) when infected with malaria. Artemether-lumefantrine (AL) is the most commonly-used ACT for treatment of *Plasmodium falciparum (Pf)* malaria in Africa but there is limited evidence on the safety and efficacy of AL in HIV+ individuals on ART, among whom drug-drug interactions are expected. We assessed the day 42 adequate clinical and parasitological response (ACPR) and incidence of adverse events (AEs) in HIV+ individuals on efavirenz-based ART with uncomplicated *pf* malaria treated with AL.

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Method: We conducted a prospective open label non-randomized interventional clinical trial at St Paul's Hospital, in northern Zambia involving 152 patients aged 15–65 years with uncomplicated *pf* malaria who were on efavirenz-based ART. They received a 3-day directly-observed standard treatment of AL and were followed up until day 63.
Results: Enrolled patients had a baseline geometric mean (95% CI) parasite density of 1,108 (841–1,463). 16.4% (25/152) of the participants had a recurrent malaria episode by day 42. PCR data was available for 17 of the patients with recurrences and demonstrated re-infection in all making the PCR-adjusted day 42 ACPR 100% in the 144 patients who could be evaluated. Even when patients with missing PCR data were considered very conservatively as failures, the day 4 ACPR was over 94%. None of the participant, disease or treatment characteristics, including day 7 lumefantrine concentations, predicted the risk of malaria recurrence by day 42. AL was well tolerated following administration.
Conclusion: AL was well tolerated and efficacious in treating uncomplicated *pf* malaria in HIV co-infected adults on efavirenz-based ART. However, a fairly high proportion of participants experienced a recurrent malaria infection which highlights the need for additional malaria prevention measures in this sub-population after treatment with AL.

PE27/2

Ritonavir-boosted darunavir plus two nucleoside reverse transcriptase inhibitors versus other regimens for initial antiretroviral therapy for people with HIV infection: a systematic review

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Background: Darunavir is a second-generation protease-inhibitor used with ritonavir (DRV/r) and two nucleoside reverse-transcriptase inhibitors as an option in first-line antiretroviral treatment (ART).
Methods: We systematically reviewed randomized controlled trials (RCTs) of DRV/r versus other regimens in patients initiating ART. We searched five bibliographic databases and other key resources. We had no language limitations. We assessed bias risk with the Cochrane tool and used GRADE to assess evidence quality. We report findings in terms of risk ratio (RR) with 95% confidence intervals (CI).
Findings: Three RCTs met inclusion criteria. In plasma viral load suppression, DRV/r outperformed ritonavir-boosted lopinavir at 48 weeks (RR 1.13, 95% CI 1.03–1.25), 96 weeks (RR 1.11, 95% CI 1.02–1.21), and 192 weeks (RR 1.20, 95% CI 1.07–1.35). DRV/r was similar to dolutegravir at 48 weeks (RR 0.96, 95% CI 0.87–1.06) but less effective at 96 weeks (RR 0.84, 95% CI 0.75–0.93). At 96 weeks, DRV/r underperformed raltegravir (RR 0.94, 95% CI 0.88–0.99) but was similar to ritonavir-boosted atazanavir (RR 1.02, 95% CI 0.96–1.09). Overall bias risk was moderate. Evidence quality was also moderate. Interpretation. Initial ART regimens using DRV/r should be considered in future World Health Organization guidelines.

PE27/3

Towards individualization of antiretroviral therapy – more cost-effective than dose intensification in patients

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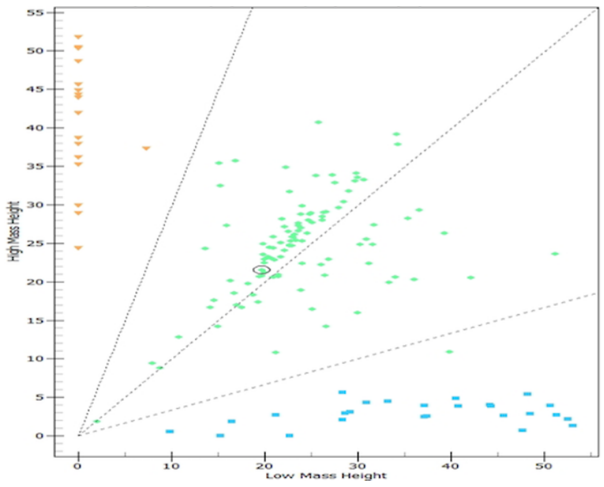
Background: As a result of the policy shift to "test and treat", an exponential increase in the number of people receiving ART may be expected in the near future. Moreover, there is no pharmacogenetic algorithm strategy for decreasing the quantity of active pharmaceutical ingredients required to cover the need of ART regimens.
Objectives: To explore the role of gene polymorphisms in drug metabolism enzymes and drug transporters in ART associated adverse toxicities in HIV patients in India. To measure plasma ART concentration in patients using HPLC and its correlation with genotypes.
Method: Sixty-six HIV-1 patients on Zidovudine and hundred on Tenofovir based combinational therapy were enrolled from the KEM Hospital in Mumbai. Genotype analysis was performed with the SEQUENOM MassARRAY iPLEX pro PGx 74 panel. ART drug levels were quantified by HPLC. The Olerup SSP was used for HLA typing. Odds ratios (OR) with 95 % confidence intervals were calculated to assess patient's increased risk of developing rash in comparison with Tolerant.
Results: Patients with allele G in ABCB1 gene whereas allele T in CYP2B6 gene is associated with EFV toxicity like neuropathy. CYP2B6-516 G/G, G/T and T/T genotypes were found in 68%, 21% and 11%, respectively. (Fig. 1). The median EFV plasma concentration was 3,238 ng/mL. 10 (10%), 72 (72%) and 18 (18%) had an EFV concentration <1,000 ng/mL, 1,000–4,000 ng/mL and >4,000 ng/mL, respectively. (Fig. 2) The NVP/EFV rash risk appears to depend on the presence of the predisposing alleles HLA-DRB1*14, HLA-DQB1*05 and HLA-DQB1*02 (Table.1). Also, alleles HLA-A*11, HLA-B*56:01:01:01, HLA-B*52:01:01:01 and HLA-C*12 may play a protective role in EFV/NVP hypersensitivity reaction (Table.2).
Conclusion: The various genetic factors will aid in designing effective dosing/treatment strategies. The strong association between HLA alleles and ART induced hypersensitivity reaction can be utilized to avoid life threatening consequences in HIV infected patients in India.

Association of MHC Non-classical markers in Tolerant and Non-tolerant groups

MHC Non-classical markers	Tolerant	EFV/NVP Rash	p value	odds ratio
HLA-DRB1				
*14	0/17	6/16	0.03	9.6
*01	1/17	3/16	0.33	3.69
*10	2/17	4/16	0.045	2.5
HLA-DQB1				
*05	3/17	11/16	0.005	10.267
*02	1/17	6/16	0.03	9.6

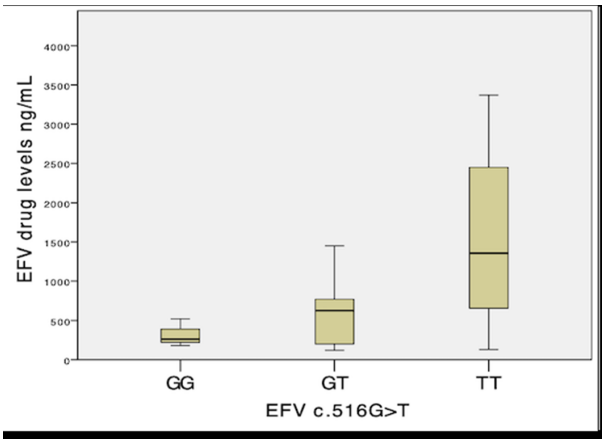
Association of MHC classical markers in Tolerant and Non-tolerant groups

MHC Classical marker	Tolerant	EFV/NVP Rash	p value	odds ratio
HLA-A *11	7/17	0/16	0.039	0.09
*29	0/17	3/16	0.33	3.69
*03	0/17	3/16	0.33	3.69
HLA-B*7	3/17	5/16	0.43	2.12
*56:01:01:01	3/17	0/16	0.60	0.31
*52:01:01:01	2/17	0/16	0.48	0.001
HLA-C				
*12	9/17	0/16	0.001	0.001
*03	1/17	4/16	0.17	5.33



CYP2B6- 516 genotype cluster analysis using MassARRAY

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Median efavirenz (EFV) plasma concentrations, by CYP2B6- 516 genotype

PE27/4

The valproic acid – dolutegravir drug-drug interaction is based on displacement of protein binding and unlikely to be clinically relevant

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Purpose: Previous literature suggests that there is a drug-drug interaction (DDI) between dolutegravir (DTG) and valproic acid (VPA) that leads to >80% decreased DTG plasma concentrations[1]. Possible explanations include induction of DTG's metabolizing enzymes by VPA, impaired DTG absorption due to complexation of DTG by excipients in VPA, or competition for binding sites on plasma proteins. In this pharmacokinetic (PK) sub study, we evaluated DTG-PK in HIV-infected subjects on DTG-containing regimens participating in the "LRAs United as a Novel Anti-HIV strategy" (LUNA) study.

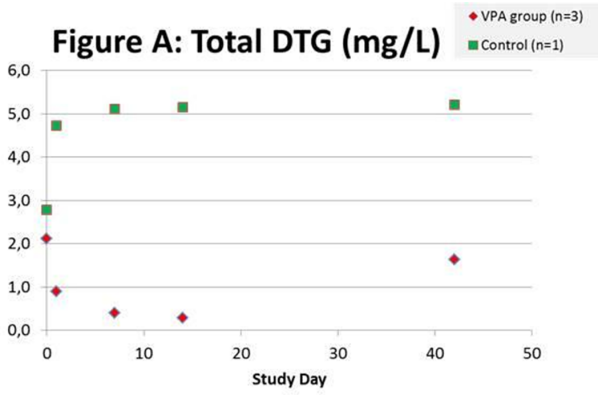
Methods: Intrasubject comparisons were made for DTG PK (50 mg QD) with and without co-administration of VPA (30 mg/kg BID for 14 days). Trough samples for total DTG, free DTG, and DTG-glucuronide plasma concentrations were taken on Day 0 (upon start of VPA and after 6 h), on Day 1, 7, 14, and finally 28 days after VPA was stopped on Day 42 (table 1). Subjects in study arms without VPA served as controls.

Results: Ten subjects on DTG were included six of whom received VPA. Preliminary results of four subjects (three on VPA) showed total DTG trough levels (geometric mean (GM)) prior and after VPA of 1.8 mg/L on Day 0 and 1.5 mg/L on Day 42. During VPA administration total GM DTG levels decreased sharply to 0.79, 0.33 and 0.24 mg/L on Day 1, 7 and 14, respectively (figure A). We observed a parallel increase in the free fraction of DTG: 0.53–0.69% during VPA administration *vs* 0.29–0.30% without VPA administration (figure B). All free DTG concentrations were above the proposed in vitro EC_{90} value for unbound DTG of 0.9 microg/L[2] (not shown).

Conclusion: Our data confirm the reported decrease in total DTG plasma concentrations after addition of VPA. It can be explained by displacement of protein binding of DTG by VPA. This DDI is probably not clinically relevant.

Table 1. DTG sampling

	Day 0	Day 1	Day 7	Day 14	Day 42
Valproic acid administration	Yes	Yes	Yes	No	No
Dolutegravir trough sample	Yes (pre dose)	Yes	Yes	Yes	Yes
6-hour sample	Yes				



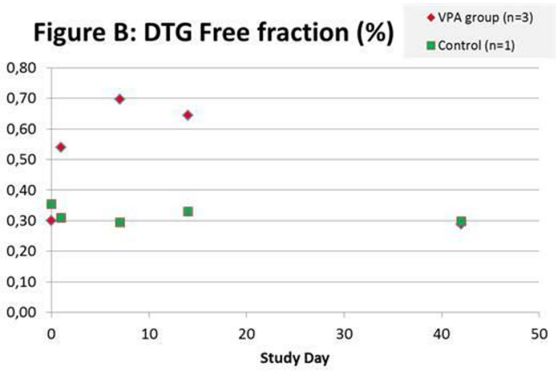


Figure A. Total DTG (mg/L); **Figure B.** DTG free fraction (%)

PE27/5

BESIDE – clinical relevance and implications for management of antiretroviral therapy due to recreational drug use in PLWH in Germany

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Recreational drug use among PLWH in Germany is common [EACS 2017]. This puts patients at risk for drug-drug interactions potentially leading to adverse events and/or loss of efficacy of antiretroviral therapy (ART). Here, we assessed the clinical relevance of illicit drug consumption and potential implications for management of ART.

BESIDE was a cross-sectional study, evaluating the prevalence of concomitant diseases and co-medication including OTC and illicit drugs in PLWH on ART. Regional distribution of study sites (n=20), consecutive recruitment and age-stratified sampling ensured a representative sample of the PLWH population in Germany. Data on recreational drug use were gathered via anonymized patient questionnaires.

Between 09/2016 and 12/2018, centers collected data of 453 PLWH on ART. A high proportion of patients with data available (76%; 223/293) consumed recreational drugs, 21% (47/223) to stimulate sexual activities. 71% (207/293) of patients had been asked about drugs by their doctors and 66% (194/293) had been educated on potential risks and interactions. However, no more than 29% (65/223) of patients seeked consultation with their doctor about their drug use and only 7% (15/223) saw a problem in the use of drugs in combination with ART. Strikingly, 39% (86/223) of patients had undergone medical treatment and 36% (81/223) had been hospitalized due to their drug consumption, with even more concerning numbers in patients aged <30 years

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(medical treatment: 60%, 12/20; hospitalization: 65%, 13/20). This was consistent with a high number of patients who had problems with their ART (31%, 70/223; <30 years: 60%, 12/20) or needed to switch it (28%, 62/223; <30 years, 60%, 12/20) due to recreational drug use.
These data demonstrate the high clinical relevance of recreational drug use in PLWH and the need for pro-active education on potential risks and drug-drug interactions with ART by treating physicians, especially of younger patients.

PE27/6

Drug-drug interactions between antiretrovirals and carbamazepine or oxcarbazepine: a real-life investigation

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Purpose: Carbamazepine and oxcarbazepine are strong inducers of metabolic enzymes. For this reason, potential drug-drug interactions (DDIs) may take place between these two drugs and antiretrovirals. Here, we aimed to assess the relevance of these DDIs in real life clinical settings.
Methods: Patients treated concomitantly with carbamazepine or oxcarbazepine and contraindicated antiretrovirals for at least three months were considered. Data on therapeutic drug monitoring (TDM) of both antiepileptic and antiretrovirals trough concentrations were collected and compared with those from HIV-positive patients regularly followed in our hospital not taking antiepileptic drugs.
Results: Eleven HIV-positive patients given carbamazepine or oxcarbazepine were identified (8 men, 3 women, mean age 52±8 years). These patients were given oxcarbazepine or carbamazepine from 3,126±2,267 days for idiopathic epilepsy (n=6), post-infection epilepsy (n=2), post ischemic stroke epilepsy (n=1), and trigeminal neuralgia (n=2),
The TDM evaluations for carbamazepine and oxcarbazepine resulted within the therapeutic ranges, a task reached by wide distribution in the daily drug doses (Figure 1). Tenofovir trough concentrations measured in HIV-infected patients given concomitantly one of the two antiepileptics with tenofovir disoproxil fumarate (49±13 vs. 109±62 ng/mL; p=0.115) or with tenofovir alafenamide (11.4±3.5 ng/mL vs. 17.8±7.8; p=0.246) showed drug concentrations comparable with values usually measured in the overall population of HIV-infected patients routinely followed in our hospital. The same trend was found also for darunavir (2,301±1,195 vs. 2,837±1,937 ng/mL in patients given or not given concomitantly carbamazepine or oxcarbazepine; p=0.512) Conversely, the trough concentrations of atazanavir (190±91 vs. 546±380 ng/mL; p<0.001) and dolutegravir (191±78 vs. 1,096±510 ng/mL; p<0.001) resulted significantly lower compared with values usually measured in HIV-infected patients not treated with antiepileptic drugs.
Conclusions: Coadministration of carbamazepine or oxcarbazepine with atazanavir or dolutegravir should be avoided; for these two drugs, the adoption of TDM is strongly advisable, eventually combined with increased antiretroviral doses.

Drug	Drug TDM (n)	Drug concentrations	Therapeutic range
Oxcarbazepine, mg/L	10	19.5 ± 4.3	10 – 35
Carbamazepine, mg/L	22	7.4 ± 1.8	4 – 12
Tenofovir (TDF), ng/mL	10	49 ± 13	40 – 180
Tenofovir (TAF), ng/mL	12	11.4 ± 3.5	Not established
Atazanavir, ng/mL	8	190 ± 91	150 – 800
Darunavir, ng/mL	9	2301 ± 1195	>500
Dolutegravir, ng/mL	7	191 ± 78	>100
Raltegravir, ng/mL	7	849 ± 1184	>40
Rilpivirine, ng/mL	2	<20, 35	>25
Elvitegravir, ng/mL	2	<25, 160	>45

TDF: tenofovir diproxil fumarate; TAF: tenofovir alafenamide; TDM: therapeutic drug monitoring

Figure 1

PE27/7

Drug-drug interactions between dolutegravir (DTG) and immunosuppressant drugs (IS) in HIV-infected patients with solid organ transplantation (SOT): a single-arm clinical trial (DTGSOT)

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Purpose: Dolutegravir (DTG) is a non-boosted integrase inhibitor, metabolized primarily by UGT1A1, playing CYP3A a minor role, neither inducer nor inhibitor of cytochrome P450 or glucuronidation. Therefore, DTG could avoid drug-drug interactions (DDI) with calcineurin and mTOR inhibitors, although a potential DDI could exist with mycophenolic acid (MPA) which also is glucuronidated (UGT1A9). However, there is limited information in the transplantation setting. The aim was to know the pharmacokinetic (PK) profiles of IS and DTG (plus two NRTIs) in HIV-infected SOT recipients
Method: Single-arm trial including 12 consecutive HIV-infected SOT adult recipients on stable and effective ART who were switched from RAL-based to DTG-based ART. Patients maintained the same doses of IS drugs during the study period. The areas under the concentration-time curve (AUC), maximum (Cmax) and trough concentrations (Cmin) of DTG and RAL were determined by UPLC/MS/MS and HPLC/Fluorescence detector methods, respectively. The same PK parameters were analyzed for tacrolimus, cyclosporin and MPA prior to and two weeks following ART switch, using standard immunoassays. ClinicalTrials.gov Identifier:NCT03360682
Results: There were six kidney, five liver and one cardiac HIV-infected transplant recipients. One kidney recipient left the study due to neurocognitive DTG side effects. Median (IQR) age was 57 (51–60) years. Six were males (64%). Renal function (creatinine, glomerular filtration) was stable in all cases during the PK studies. RAL and DTG PK studies were in the normal range (data not shown). Results of IS drugs are depicted in the table. There were no changes in tacrolimus levels, whereas there was a non-significant increase in the MPA Cmax (+39%), Cmin (+34%) and AUC (+14%) and a decrease of the Cmax (-37%) and AUC (-53%) of cyclosporin levels
Conclusion: DTG-based ART was safe and did not significatively change tacrolimus and MPA PK profiles in HIV-infected SOT recipients. More data is needed with cyclosporine

PE27/8

Abacavir hipersensivity reaction (HSR), associated to baseline false negative HLAB5701 screening, in antiretroviral treatment naive HIV-1 patient

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Background: Patients with HIV infection, generally, perform at enrollment a pharmacogenetic test for detection of HLAB5701 allele, that is related to abacavir (ABC) hipersensivity reaction (HSR).
Aim: Describing a rare case of HSR to ABC in *antiretroviral treatment naive* HIV-1 patient with baseline false negative HLAB5701 test.
Material and Methods: This case report is about a Ukrainian woman,40 years old, with HIV infection.She arrived at our Unit since November 2017 and first baseline exams showed CD4+ 460 cell/μL, HIV-RNA 1030 copies/mL, no viral resistances, no B and C viral hepatitis, negative Mantoux test, no alcohol intake, no other drugs or addiction, normal liver enzymes, classified as CDC A1.Baseline HLAB5701 screening, performed by cytofluorimetric assay, resulted negative.
Results: Patient started antiretroviral treatment (ART) with ABC+3TC+Dolutegravir, but after 2 weeks, began to show fever, articular pain, nausea, stomach cramps.ART was early stopped and exams were performed showing elevate liver enzymes.Other causes of hepatitis were analyzed, but all resulted negative (Table 1). After 1 month from stopping ART, patient showed CD4+ 394 cell/μL, HIV-RNA 713 copies/mL, no viral resistances and normal liver enzymes.In January 2018, she began a new co-formulated regimen with Elvitegravir/Cobicistat+Emtricitabina+Tenofovir Alafenamide.showing, after 1 month, good efficacy and tolerability, with

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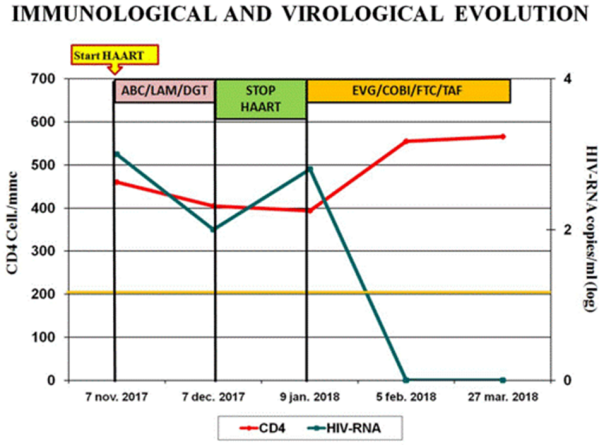
Pharmacokinetic parameters of immunosuppressors before and two weeks after the change to dolutegravir.

	Tacrolimus before	Tacrolimus after	p-value*	MPA before	MPA after	p-value*	Cyclosporin before	Cyclosporin after	p-value
No. of cases	7	7		7	7		2	2	
Cmax	14.4 (10.8–18.3)	16.4 (12.1–18.7)	1,0000	6.3 (3.8–10.7)	10.3 (5.3–12.9)	0.1763	825 (686–964)	299 (120–478)	NA
Cmin	6.2 (5.2–8.9)	4.4 (4.3–8.5)	0.2359	1.9 (1.5–2.5)	2.9 (1.7–4)	0.3980	86.5 (83–90)	98.5 (65–132)	NA
Tmax (h)	2 (1–2)	2 (1–2)	0.7751	2 (0.5–4)	1 (0.5–2)	0.6392	1 (1–1)	0.75 (0.5–1)	NA
AUC (ng/µg·h/mL)	113.1 (78.6–166.3)	103.5 (59.2–171.1)	0.6121	35.8 (23.7–43.9)	41.4 (33.9–47.7)	0.3105	2649.6 (2307.3–2991.8)	1407.5 (900.1–1914.9)	NA
Doses (mg/day)	5 (3–5)	4 (4–5)	0.3173	720 (500–1000)	720 (500–1000)	1,0000	125 (100–150)	125 (100–150)	NA

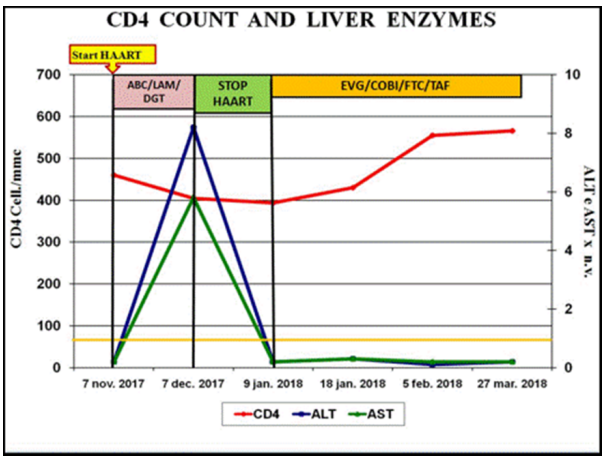
All data expressed as median (IQR)
Tacrolimus and cyclosporin are expressed in ng/mL and MPA in µg/mL
*Wilcoxon signed-rank test; NA=Not applicable

persistent normal liver enzymes (Fig. A/B).In September 2018, in the suspect of baseline false negative HLAB5701 test, screening was repeated, but this time using a PCR assay, that resulted positive.This test so clarified that patient had developed an HSR to ABC, due to a baseline false negative HLAB5701 test.This screening, performed by 2 different assays, had given discordant results, therefore it was repeated for the third time, using again a cytofluorimetric assay that resulted doubt.

Conclusions: HSR to ABC is a rare dangerous condition and so the screening is important to avoid drug intolerance and false negative tests. Data of literature show that cytofluorimetric or PCR assay have the same high sensitivity to detect HLAB5701 allele, avoiding false negative tests.Cytofluorimetric is generally preferred for baseline screening, being less expensive. In contrast with these data, our case report shows a discrepancy between 2 assays, underlying that in rare cases, it is possible to obtain a false negative test, performing cytofluorimetric test.



Immunological and virological evolution



Cd4 count and liver enzymes

Screening for Hypertransaminasemia

IgM anti HAV	Negative
HBsAg/Anti HCV	Negative
IgM/IgG anti HEV	Negative
HCV-RNA	Negative
HBV-DNA	Negative
CMV-DNA	Negative
EBV-DNA	Negative
ANA, AMA, ASMA	Negative
HOMOCISTEINE	Normal values
LIVER ULTRASONOGRAPHY	Negative

PE27/9

Central nervous system penetration of antiretroviral drugs in HIV-positive patients with neurocognitive impairment, assessed from paired plasma-CSF concentrations

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Purpose: Whilst modern antiretrovirals (ARVs) have dramatically reduced the occurrence of neurocognitive impairment (NCI), the penetration of ARVs into the brain and cerebrospinal fluid (CSF) has been incompletely examined. This study aimed at evaluating factors associated with CSF passage of ARVs.

Method: In addition to multidisciplinary clinical examination, all patients seen at the Lausanne University Hospital Neuro-HIV Platform since 2013 undergo therapeutic drug monitoring (TDM) in both plasma and CSF. We examined CSF/plasma ratios in consecutive patients examined over 6 years at their first plateform visit. Linear models were used to identify factors affecting ARVs CSF penetration and to correlate it with NCI.

Results: Since 2013, 197 TDM measurements in paired plasma and CSF samples were performed in 68 patients (median age 49, 54% men, 50% Swiss). Plasma and CSF HIV RNA was undetectable in 87% and 85% of them, respectively. Emtricitabine was the most frequently prescribed ARV (40% of patients), followed by ritonavir-boosted darunavir (28%), dolutegravir (22%) and etravirine (19%). CSF to plasma ratios were highly variable (CV 612%). Univariate analyses revealed that drug molecule, free fraction (retrieved from summary of product characteristics) explained respectively 88%, 44% of overall variability ($p<0.001$). In addition, CSF/plasma ratio slightly increases along dosing interval by 4% per hour, explaining 3% of overall variability

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(p=0.017). Neither gender, age, body weight nor CSF albumin level correlated with CSF/plasma ratio. CSF penetration was not significantly associated with the presence of NCI.
Conclusion: CSF/plasma ratio markedly varies between ARVs. Free fraction is an imperfect proxy for CSF concentration. The impact of ARVs' CSF penetration on the development of NCI is inconclusive.

PrEP

PE28/1

Establishment of the service system of HIV pre-exposure prophylaxis/post exposure prophylaxis (PrEP/PEP) in a certain area of Southern Taiwan

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Purpose: Establish the service system of HIV pre-exposure prophylaxis/post-exposure prophylaxis (PrEP/PEP) in a certain area of Southern Taiwan, in order to reduce the HIV infections and decrease prevalence in Taiwan.
Method: Our hospital has been collaberated with the Department of Health, Kaohsiung City Covernment since 2017 July. In order to improve the HIV prevention in Kaohsiung City and respond to the trend of "Treatment as Prevention,Tasp," the Kaohsiung City Government supoorts citizens at high risk of HIV whose current residence or mailing address is located at Kaohsiung City with NTD$ 286,125 to offer "HIV pre-exposure/post-exposure oral prophylaxis." This could improve the accessibility of medication.
Results: People at exposure risk could ask for consultation at the one-stop healthcare center or ER in our hospital. Rapid HIV test is required if needed. People with HIV negative and qualified with the medication guidelines of CDC could immediately receive the PrEP/PEP medication. Form Nov 28th, 2017 to Dec 2018, 131 people received PrEP/PEP. 39% of them chose to take medication from ER. This medication process has become the pioneering work of HIV prevention inf the world.
Conclusion: Our hospital sets up the twenty-four hours nPEP/PrEP clinic and ER and the HIV prevention surveillance in order to assist people at sexual risk to be able to receive the fast, safe, precise, and the most effective treatment as soon as possible.

PE28/2

Systematic review of post-migration HIV acquisition within Europe: the case for PrEP interventions for migrants

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Background: Migrants bear a disproportionate burden of HIV in Europe. Despite the common assertion that infection in this group is acquired prior to migration, there are no reliable estimates for post-migration HIV acquisition (PMHA) that could inform practice for HIV prevention interventions, such as expansion of pre-exposure prophylaxis (PrEP). This review aimed to estimate PMHA as a proportion of all HIV cases in migrants within Europe, by undertaking a systematic review of the literature, and explore the feasibility of PrEP as a prevention intervention for PMHA in Europe.
Methods: Eight databases were searched and studies investigating PMHA in long-term migrants in Europe were included. Two independent reviewers screened titles and abstracts and quality assessment was performed on all included records. PMHA was analysed by host country, region of origin, gender and sexuality. No meta-analysis was undertaken due to the heterogeneity of the data.
Results: Eighteen articles, including a total population of 22,064 migrants in 11 European countries, were included in the analysis. Data was highly heterogeneous. Overall PMHA was found to be 37.5%, ranging from 13.3% to 68.9% in Italy and the Netherlands respectively.
PMHA was higher in men who have sex with men (MSM; 62.2%) than in heterosexuals (30.8%). There was a lower proportion of PMHA in African migrants (29.9%) than in European migrants (58.1%). Knowledge and potential uptake of PrEP as an HIV prevention intervention was found to be poor across all migrant groups.
Conclusions: A large proportion of HIV cases in migrants within Europe are likely acquired post-migration, but improvements in data collection are required to improve estimates. The proportion of PMHA found in this review indicates that effective prevention services, such as expanded PrEP, must be improved in this population if it is to be considered a feasible prevention intervention.

PE28/3

Self-reported STI history and associated factors among German PrEP users

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Purpose: People taking HIV pre-exposure prophylaxis (PrEP) have a high risk for contracting other sexually transmitted infections (STI). The objective was to describe and analyze the STI history of current PrEP users in Germany.
Method: From 24th July to 1st November 2018 (wave 1) and from 1st April to 15th June 2019 (wave 2) we recruited PrEP users on geolocation dating apps for MSM, community-based HIV testing sites, and a community website in Germany for an anonymous online survey. The investigated outcome was self-reported history of STIs. Risk factors were assessed with logistic regression adjusting for age, sex, number of partners, and condom use. Participants in wave 2 were excluded if they indicated previous participation in wave 1.
Results: We recruited 5,004 current PrEP users (wave 1: 2,118; wave 2: 2,886). Median age was 37 years (IQR: 30-45). 85.6% identified as cisgender male and 1.6% as not cisgender-male (missing 13.0%).
Among 3,488 participants providing information on their STI history, 73.2% ever tested positive for an STI. Gonorrhea, chlamydia, and syphilis were the most common STI diagnoses regarding "ever being diagnosed" and "last diagnosis during PrEP use" (Table 1). The results were comparable between waves 1 and 2. Most viral diagnoses occurred before starting PrEP. 25 participants (0.7%) reported 2 HCV episodes and two participants indicated >2 HCV episodes.
Factors associated with testing positive for any STI were: having >10 partners within the last 6 months (OR=2.6, 95% CI 2.0 - 3.3) and using condoms half the times or less (OR=1.5, 95% CI 1.1 - 2.0).
Conclusion: German PrEP users had a high burden of STI including gonorrhea, chlamydia, and syphilis indicating that PrEP is used in the right population in Germany. Future surveys will evaluate how potential changes in sexual behavior might impact STI risk.

STI history of current PrEP users in Germany

	Participants having ever been diagnosed with (n=3,488)	Last diagnosis before PrEP use	Last diagnosis during PrEP use	No information on time of last diagnosis
Syphilis	1,059 (30.4%)	574 (16.5%)	459 (13.2%)	26 (0.7%)
Gonorrhea	1,547 (44.4%)	737 (21.1%)	772 (22.1%)	38 (1.1%)
Chlamydia	1,335 (38.3%)	551 (15.8%)	751 (21.5%)	33 (0.9%)
HPV/ condyloma	804 (23.1%)	604 (17.3%)	173 (5.0%)	27 (0.8%)
Hepatitis A	131 (3.8%)	74 (2.1%)	33 (1.0%)	24 (0.7%)
Hepatitis B	169 (4.9%)	100 (2.9%)	37 (1.1%)	32 (0.9%)
Hepatitis C	103 (3.0%)	35 (1.0%)	38 (1.1%)	30 (0.9%)
Mycoplasma	276 (7.9%)	70 (2.0%)	185 (5.3%)	21 (0.6%)
Other	62 (1.8%)	30 (0.9%)	30 (0.9%)	2 (0.1%)

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PE28/4

PrEP implementation among MSM in Ukraine: results of pilot project in Kyiv

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Issues: According to latest bio-behavioral study in 2018, HIV prevalence among MSM in Ukraine is 7.5%; condoms are constantly used by only 58% MSM. MSM is the only group in which, increase in the incidence is observed, especially among hard-to-reach subgroups/cross-groups. Therefore, there was a very high need for the implementation of a pilot project on PrEP introduction among 100 MSM in Kyiv.
Project: A pilot project was implemented among such cross-groups as sex workers and MSM. All participants had HIV-negative status, clients aged 18 years and older, signed an informed consent, the clients practiced sex without a condom during the last 6 months with other men, the participants had previously been diagnosed for STI/hepatitis and/or received of PEP. Mode of PrEP use: daily. Attraction of clients to PrEP was done through mobile dating apps for MSM, social networks and among regular clients of our organization.
Lessons learned: 148 MSM, among them positive results for: HIV 8; HBV 5; HCV 4; syphilis -21 (6 newly discovered); gonorrhea and chlamydia 19. Received PrEP 124 persons. The number of HIV infections when receiving PrEP: 1 ("window" period). The number of refusals from PrEP after joining to the program 24. There was gradual reduction in the use of condom by clients during the program - about 40% of the total; % of their sexual partners - MSM/PLWH or with unknown status:75-82%; the average number of sexual partners per month-5.
Next steps: 1) Developed and launched an All-Ukrainian information campaign to promote and receive of PrEP among MSM and launched a new website www.prep.com.ua
2) Longer-term client's involvement in the program.
3) Maximum decentralization of services (transfer of all possible services from medical institutions to NGOs)
4) Advocacy of PrEP inclusion to the basic package of HIV prevention services for MSM financed from the state budget starting from 2020.

PE28/5

Emergency post-exposure prophylaxis (PEP) seeking behaviors among men who have sex with men (MSM) with recent HIV risk exposure in Thailand

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Contrary to the widely advocated pre-exposure prophylaxis (PrEP) HIV prevention tool, post-exposure prophylaxis (PEP) should only be used as an emergency intervention, is not intended for frequent use and does not replace condoms. However, PEP demand is alarmingly high in Thailand. We aimed to understand PEP seeking behaviors among Thai men who have sex with men (MSM).
Qualitative interviews were conducted among MSM seeking HIV risk assessment, PEP linkage and adherence support over Adam's Love (www.adamslove.org) platforms to elicit the reasons for PEP uptake, PEP seeking behaviors and future PrEP use intentions.
Between October 2017-November 2018, Adam's Love provided PEP eCounseling to 370 MSM, and 32 (8.6%) participated in the qualitative study. Being under influence (substance/alcohol) and having unprotected sex with unknown status partner were reasons for accessing PEP. "I sniffed poppers, it went up through my nose and after that I couldn't control myself", shared a 29-year-old MSM. Long-tail Google keyword-searches yielded Adam's Love PEP webpages and directed MSM to eCounselors. "I had risk around 2 am and immediately searched for emergency HIV medicine and contacted Adam's Love", noted 23-year-old MSM. Primary barriers to accessing PEP included high drug costs "Medicine cost is an obstacle. If I didn't have money, I would have decided not to take PEP" (21-year-old MSM) and clinic hours "I had sex on Saturday but clinic was closed on Sunday so contacting provider was difficult" (26-year-old MSM). Except one participant who discontinued PEP due to side-effects, all 31 participants completed 28 days PEP regimen and were highly-satisfied with daily PEP reminders. Low self-perceived risk, anticipating lower perceived probability of future risks, and prior PEP side-effects were reasons for majority's (23/31) lack of interest in PrEP.
Surge in PEP demand and PEP-taker's lack of interest in PrEP calls for greater emphasis on provider-initiated tailored counseling interventions.

PE28/6

The back side: Lymphogranuloma venereum in PrEP-users and PLWH

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The introduction of PrEP, improved treatment options for PLWH and mobile dating apps have significant impact on the sexual behaviour of MSM. Berlin with a population of 3.72 Mio has an estimated population of 300.000 MSM of which 14.900 are estimated to be PLWH. Not only is there an increasing incidence of STD, most likely due to a decreased use of condoms, we also see a qualitative change of STD. *Chlamydia trachomatis* has various serotypes of which serotypes L1-L3 cause *Lymphogranuloma venereum*, a condition that beyond the typical genital manifestations of STD causes a complex of severe symptoms with lymphadenitis, fever and disintegration of lymphatic tissue leading to bleedings, cramps and severe manifestations of proctitis.
Our clinic, based in urban Berlin is specialized on the treatment of STD, predominately in sexually highly active MSM. We analysed the incidence of *C. trachomatis* infections in rectal PCR swabs and performed a further analysis of serotypes in positive samples. An additional analysis of risk-factors was performed to identify potential groups at risk.
Out of the 789 samples we tested from January 2018 until April 2019, 6.9 % (n=55) were positive for *C. trachomatis*. In 29 % (n=25) Serotypes L1-L3 were identified, in 8% of cases a further identification wasn't feasible. While incidence rates of around 7 % are in line with other urban samples, the high incidence of serotypes L1-L3 are surprisingly high. All patients tested positive for LGV were either using PrEP or were PLWH.
Lymphogranuloma venereum is a severe subtype of *C. trachomatis* infection that requires a prolonged treatment. Regular differentiation of serotypes is uncommon in most settings. High incidence rates in our samples demonstrate a need for regular testing, subdifferentiation of serotypes and change of treatment patterns which also should be considered for future PrEP and HIV-treatment guidelines.

PE28/7

Awareness and interest in pre-exposure prophylaxis (PrEP) among MSM population in Serbia

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Purpose: Pre-exposure prophylaxis (PrEP) has become a routine in many countries, with a high percentage of MSM population using it. In Serbia a drug has been registered recently for PrEP but still there is no standardized procedure how a person can obtain the drug and there is no standard on the follow up of a person using it.
Method: The study was conducted to assess the knowledge, accessibility, feasibility and obstruction of taking PrEP among the MSM population. Research has involved 700 people age ranged between 17-60 yrs. They were surveyed through online questionnaire on a MSM dating website.
Results: Our study found that 39.8% of the participant use condom regularly, while 14,6% of participant admitted to never using a condom. One third of responders tested for the HIV in the last 6 months, while almost one third (28.5%) of participants never tested for HIV. Two thirds of the participants were familiar with the concept of PrEP, but only 4.5% of participants ever used it. Most of the participants took "event based" PrEP (60%). Information on how to take the drugs was mostly based on friend's advice (60%), some found the information online (25%) and only 3 persons (15%) got the information on

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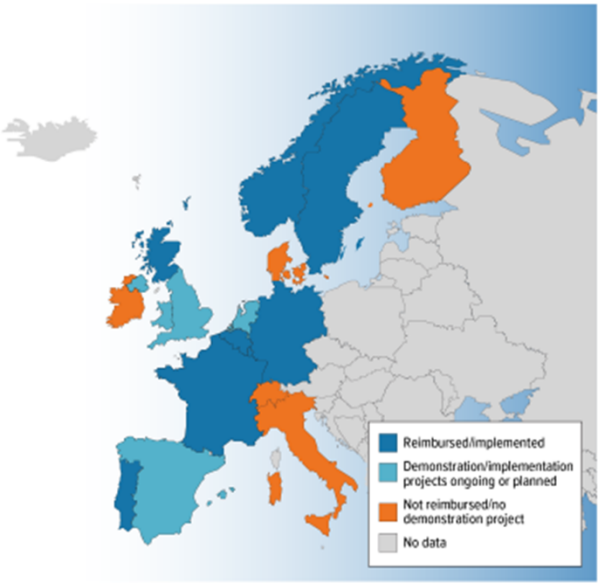
PrEP from their physician. The survey showed that the main reason for not using PrEP was the price of the drug (39%), insufficient knowledge on PrEP (30.8%) and its possible side effects (2%).
Conclusion: HIV testing and information on PrEP are at an unsatisfactory level in Serbia. There are also concerns regarding high price and the lack of standardized PrEP prescription and follow up. There is an interest from the MSM population about PrEP which should encourage further activities to set up easily accessible information and care for people willing to use it.

PE28/8

PrEP reimbursement and access in Europe: 2019 update

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Purpose: To describe the current state of the reimbursement and access of pre-exposure prophylaxis (PrEP) for people at high risk of HIV infection in European countries.
Method: A review of published literature, as well as desktop research of websites of European national governments, advocacy groups and HIV-related associations on PrEP reimbursement and availability was conducted.
Results: In 2016, the European Medicines Agency approved once-daily oral tenofovir disoproxil and emtricitabine (TDF/FTC) as PrEP in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high-risk. A total of 7 European countries (Belgium, France, Germany, Norway, Portugal, Scotland, Sweden) currently reimburse PrEP through their national health systems. PrEP is available free of charge in the Netherlands and England through implementation/demonstration trials with a limit on participation, and in Wales and Northern Ireland through pilot projects. In other countries, PrEP can be purchased out of pocket through some pharmacies, health clinics, and through the internet.



Early 2019 Status of PrEP Reimbursement and Implementation in Europe

France and England have the largest number of PrEP users (>10,000 each). In France, out of >626,000 men who have sex with men, 32,000 (~5%) are considered high-risk, and >10,100 (32% of high risk) were using PrEP as June 2018. PrEP users are constantly increasing as demonstrated by reports from France, Belgium, Scotland and England. Studies in London and Paris have attributed the reduction of new HIV diagnoses to the introduction of a HIV prevention strategy that includes PrEP.
Conclusion: PrEP reimbursement and access in European countries is increasing, but there are still several countries in Central and Eastern Europe that have no or very limited PrEP access. It is too early to determine the real PrEP impact in the at-risk population. Further investigation of PrEP use in real-world settings is needed to understand its true impact on HIV epidemiology.

PE28/9

Users' perspective of an ideal service model for delivering pre-exposure prophylaxis (PrEP) to men who have sex with men

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Purpose: Pre-exposure prophylaxis (PrEP) is an effective means of HIV prevention in the high-risk populations, the engagement of whom is however a challenge in public health practice. This study described the views regarding PrEP delivery among users in Hong Kong, and explored the facilitators contributing to an ideal service model for PrEP delivery in the longer term.
Method: We conducted individual in-depth interviews with 13 men who have sex with men (MSM), who received PrEP service at a university hospital via a pilot study, from March to June 2019. All interviews were audio-recorded with prior consent sought. They were transcribed verbatim, manually coded, and thematically analyzed using a grounded theory approach.
Results: We identified three key characteristics of a PrEP service delivery system which were viewed favorably by the MSM: (1) requirement of adherence monitoring along with regular testing for HIV and sexually transmitted infections (STI) as part of the PrEP service, (2) ease and comfort of collection of biological specimen for HIV and STI testing at the clinic, and (3) regular consultation with professional healthcare providers with non-judgmental attitudes. Operationally delivering PrEP with government commitments at affordable price, accessible and gay-friendly settings combined with community education to remove PrEP-related stigma, were perceived as facilitators of an ideal service model. Integrating PrEP in the routine HIV care service in the public sector was not uniformly supported for fear of being labelled as HIV positive by others.
Conclusion: Our study revealed some positive views and experiences among MSM regarding existing PrEP delivery mechanism, indicating their recognition of the importance of testing services and consultation, although challenges persist in overcoming PrEP-related stigma. The results also highlighted the lack of affordability as a major barrier in accessing PrEP in Hong Kong.

PE28/10

Assessment of the trough concentrations of tenofovir in HIV-negative subjects on pre-exposure prophylaxis: a single center, real-life experience

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Purpose: In most countries, branded and generic formulations of tenofovir disoproxil fumarate (TDF) are interchangeably used as PrEP for HIV prevention. Here, we measured tenofovir plasma trough concentrations in MSM taking PrEP using different TDF formulations.
Methods: This retrospective, observational study considered all MSM subjects who performed a blood test for the measurement of tenofovir plasma concentrations during PrEP. Tenofovir trough concentrations were stratified according to way of PrEP administration and type of TDF formulation.
Results: Sixty-six MSM subjects were enrolled (mean age 39±10 years, body weight 75±11 kg). They had normal kidney function (serum creatinine 0.9±0.1 mg/dL) and started PrEP therapy 144±121 days before the assessment of tenofovir concentrations. A wide distribution in the tenofovir trough concentrations was observed, with values ranging from 17 to 243 ng/mL (coefficient of variation 47%). No significant differences were found on tenofovir trough concentrations (105±62 vs. 110±59 ng/mL; p=0.331) when comparing patients given PrEP daily (n=49) or on demand (n=16). Only 2 out of the 66 subjects was using the branded TDF formulation, whereas the remaining were on treatment with a generic formulation purchased at the

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community pharmacy (n=20, referred as TDF DOC), on a secure website (Ricovir EM:10, Tenvir-EM:20, Lupin:1, Tenof-EM:4, Mylan: 2), or purchased on unchecked websites (n=7; referred as generic online). A not significant trend for different tenofovir trough concentrations was observed when comparing the TDF generic formulations (Fig. 1). 25% of the enrolled subjects were concomitantly treated with other drugs.
Conclusions: A wide inter-individual variability in the tenofovir trough concentrations was observed in HIV-negative MSM on PrEP. The type of drug administration (daily vs. on demand) did not significantly impact on tenofovir exposure. The possibility that the observed variability in tenofovir concentrations could have been significantly affected by the type of TDF formulation cannot be presently ruled out.

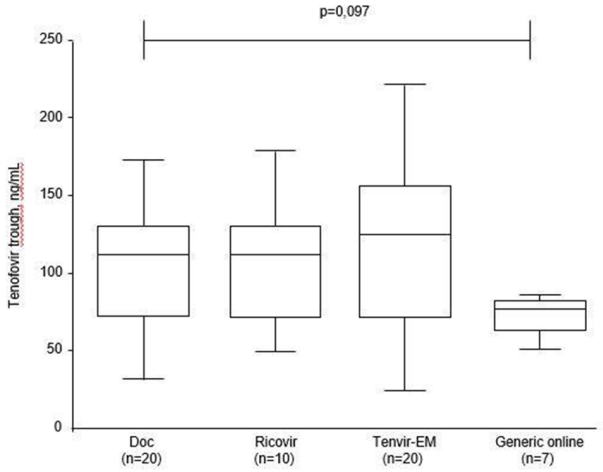


Figure 1

PE28/11

No new HIV infections, but high incidence of syphilis among Pre-exposure Prophylaxis (PrEP) users in Georgia

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Purpose: A number of studies showed an increased incidence of sexually transmitted infections (STIs) following HIV Pre-exposure Prophylaxis (PrEP) initiation. We studied incidence of HIV and syphilis among PrEP users in Georgia.
Method: : Georgia initiated PrEP program in October 2017 for high risk men who have sex with men and transgender women. PrEP users were screened for HIV using 4th generation Ab/Ag test at baseline, at month 1 after starting PrEP and then at 3-monthly intervals. Screening for syphilis was performed at baseline and 6-monthly thereafter. Analysis included all persons initiating PrEP between October 2017 and March 2019, who were followed until June 15, 2019 or until their last documented visit Incidence rates per 100 person-years of follow-up were calculated as number of new infections divided by total person-years of follow-up contributed to the observation period.
Results: Of the 154 enrollees, the median age was 26 (IQR: 19-52) years, 90 (63.8%) identified themselves as gay men, 41 (29.0%) - as bisexual and there were 4 transgender women (2.8%). At baseline examination, 5 enrollees (3.2%) were anti-HCV positive and 46 (29.8%) had evidence of syphilis. A total of 108 persons were evaluable for incidence of syphilis, among them 5 persons seroconverted over follow-up with cumulative Incidence of 4.6% over 1.5 years and incidence rate of 13.07 new cases per 100 person-years of follow-up (95% CI: 4.24, 30.49). 154 persons were evaluable for incidence of HIV, with no new case of HIV infection were documented over follow-up (incidence rate: 0 new cases per 100 person-years, 95% CI: 0 - 6.62).
Conclusion: Georgian PrEP users continue to engage in high risk sexual behaviours as evidenced by high incidence of syphilis. While PrEP is effective in protecting from HIV, better strategies are needed to control STIs.

PE28/12

Feasibility and acceptability of an oral pre-exposure prophylaxis (PrEP) program against HIV targeting female sex workers in Belgium

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Purpose: Being a female sex worker (FSW) is associated with a relative risk ratio of 13, compared to the general population. This makes FSW a target population for better prevention of HIV and other sexually transmitted infections (STI). However, FSW are often not aware of the new prevention methods against HIV, such as PrEP; moreover, they are underrepresented amongst those accessing sexual health counselling. Unmet needs in this area should be addressed by studies investigating the efficacy of PrEP in FSW.The purpose of this study is to evaluate the feasibility and acceptability of PrEP amongst FSWs and to understand its limitations in a wealthy country such as Belgium.
Method: FSW aged more than 18 years declaring themselves HIV-negative were included. A survey containing 50 questions was submitted to the subjects of the study, and completed during a semi-directive interview. The questions looked into the subjects' lifestyle, HIV and STI knowledge, sexual behavior in their private life and at work, knowledge of prevention methods and their interest for PrEP.
FSW were contacted by phone via an internet-site offering priced sex or face-to-face at sites of street and showcase prostitution.
Results: 46 FSW were included in the study. 80.4% were not aware of the existence of PrEP but 71.7% were interested in it. 34.8% had 1-5 condom breaks during the last 12 months, only 4.3% used post-exposure prophylaxis (PEP). 67.4% were in a stable relationship but 47.8% declared never using condom with their partner.
Conclusion: Our study demonstrated a real need and great interest for PrEP amongst FSWs in Belgium, in spite of a lack of information about the different prevention methods and HIV screening. Promoting access to sexual health centers, providing a better social status and strengthening prevention campaigns could therefore be crucial in the future management of FSW's sexual health.

PE28/13

First results after 52 weeks of informal PrEP use in a cohort of MSM in Southern Spain

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Despite Southern Spain has similar HIV incidences than Eastern Europe, PrEP use is unavailable. Between January- December 2018, a sample of 167 MSM with high risk practices has been included in a cohort of informal PrEP users in Seville, the PrevenPrEP program offers counselling, follow ups and regular checkouts for HIV and other STIs.to make safer the use of on line PrEP
The educators first evaluate the real risk of the different potential prevenPrEP users. Those selected, were tested for HIV/STIs using PCR technology and they were required a general blood analytic from their GPs to evaluate the kidney and liver function.
A total of 167 MSM were included in the program. All of them showed a normal biochemistry parameters and no initial HIV/STIs infections. The general characteristics of our PrevenPrEP users was similar to those shown by previous studies; an MSM of 34 years, 58% with a university degree. 85% of users showed previous HIV tests, with an average of 9 times per user. Regarding anal sex, 78.4% never used condoms during sexual intercourse with an average of 32 different sexual partners in the last 6 months, 15.6% of them were chemsex users. Finally, regarding HIV, no infection was detected in this cohort and 6.6% of them were reactive for Chlamydia, 5.4% Gonorrhoea, and 1.2% Syphilis.
There has not been HIV seroconversions in this cohort during follow up. The percentage of STIs diagnosed was approximately 50% lower than those people tested in our community center who are not using PrEP, showing the importance of STIs monitorization and counselling to prevent new infections. Community centers as SevillaCheckpoint have the capacity to offer proffessional advise and monitoring services to informal PrEP users and prove to be strong candidates to offer these services when PrEP will be implemented by the Spanish Government.

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PE28/14

Clinical outcomes of pre-exposure prophylaxis from clinical center in Warsaw, Poland

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Purpose: HIV epidemics in Poland is expanding among MSM populations. Despite that, pre-exposure prophylaxis (PreP) is not funded by national programs, being only available via private centers.This study aims to present clinical experience related to PreP use, including baseline characteristics and 6 months of follow-up.
Method: Data of 103 men-who-have-sex-with-men (mean age 36.4 ±6.6 years) followed at clinic Chmielna Express in Warsaw, Poland were analyzed at baseline and 6 months of follow-up. Clinical data including chem-sex use, estimated glomerular filtration rate, STI frequency, proteinuria, patient-reported adverse effects were collected. Number of condom protected intercourses was calculated for the last 10 sexual contacts.
Results: Median time from the last unprotected sexual intercourse to PreP initiation was 6(IQR:2-8) weeks with 27(26.21%) cases previously on HIV post-exposure prophylaxis. Chem-sex was reported by 51(49.51) patients. History of prior gonorrhea or syphilis was found in 33(32.03%) and 39 (37.86%) cases, respectively, with new gonorrhea or syphilis infections after six months of PreP observed in 2(1.94%) and 19(18.44%) of cases, respectively. Additionally, at baseline 30(29.12%) cases were PCR positive for asymptomatic chlamydia (n=23, 22.33%) or gonorrhea (n=17, 16.5%). No patients were HCV positive at PreP initiation, however 9(8.73%) acute HCV infections occurred after 6 months of follow-up. Glomerular filtration rate remained stable between baseline (mean 91.07±13.34) and 6 month visit (mean 90.40±11.26), p=n.s, with observed proteinuria being numerically less frequent after 6 months than at baseline visit (n=24, 23.3% vs. n=27, 26.2%, respectively). Estimated frequency of condom use decreased notably from mean 7.47±1.97 to 5.49±2.77 per 10 intercourses, p=0.001. The most common PreP AEs were gastric, reported by 25 24.27%) users, followed by vertigo (n=13, 12.6%) and decreased libido (n=4, 3.88%).
Conclusion: Pre-exposure prophylaxis may be successfully introduced in the private setting, however STI surveillance, including HCV epidemiologically is vital for the optimal patient safety.

PE28/15

Where are we with PrEP use in Central and Eastern Europe? - data from the ECEE Network Group

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Purpose: Pre-exposure prophylaxis (PrEP) for HIV infection is an important intervention to stop HIV epidemic. Central and Eastern European (CEE) countries experience increasing incidence of new HIV cases. Therefore we investigated the change over time in PrEP use in this region.
Method: The Euroguidelines in Central and Eastern Europe (ECEE) Network Group was initiated in February 2016 to compare standards of care for HIV and viral hepatitis infections in the region. Data about access to PrEP were collected through on-line surveys. Respondents were ECEE members from 25 countries from the region. We performed two surveys, in March 2017 (76 respondents from 23 countries) and in October 2018 (28 respondents from 22 countries).
Results: In 2017, 34.2% of respondents stated that tenofovir/emtricitabine (TDF/FTC) was licenced in the country, while in 2018, this was the case in 66.7% of respondents (p=0.02). PrEP was recommended in national guidelines in 39.5% of responses in 2017 and 40.7% respondents in 2018 (p=0.378). 70.7% of respondents were aware of "informal" PrEP use in 2017, while 66.6% of respondents were aware of it in 2018 (p=0.698). In 2018 in CEE region there were 53 PrEP offering centres (with the highest number in Poland and Romania). In six countries there were no PrEP offering centres. The estimated number of HIV-negative patients on PrEP in 2018 in the region was about 4500. Generic TDF/FTC costs (in Euro) ranged from 10 (in Romania) to 275 (in Slovakia), while brand TDF/FTC costs (in Euro) ranged from 60 (in Albania) to 853 (in Finland).
Conclusion: There has been some improvement in licensing processes of TDF/FTC for PrEP, but this has yet not been reflected in guidelines nor has it lead to a decrease of "informal" use of PrEP. PrEP remains rarely used method of prevention in CEE countries.

PE28/16

Sexual risk and HIV preventative behaviours among men who have sex in men in London in the era of HIV pre-exposure prophylaxis, 2019

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Purpose: HIV prevention in gay, bisexual, and other men who have sex with men (MSM) remains a public health priority in England, and especially London. Implementation and scale-up of HIV combination prevention, including increased repeat HIV testing, treatment as prevention, and the use of HIV pre-exposure prophylaxis (PrEP), is attributed to continued national HIV incidence declines; however, numbers of sexually transmitted infections (STIs) in MSM have continued to increase. The Gay Men's Sexual Health Survey (GMSHS), a serial cross-sectional, self-administered survey in London commercial venues (e.g. clubs, pubs, bars, saunas) will provide a 2019 monitoring update of sexual risk and HIV preventative behaviours in a community sample of MSM during a period of greater PrEP availability in England.
Method: London venues primarily frequented by MSM have been approached to take part (n=81). At participating venues, men aged ≥18 are asked to self-complete a sexual health questionnaire and, if willing, provide an oral fluid sample for anonymous HIV antibody testing. Recruitment commenced 8th June and continues through 17th August 2019. Descriptive analyses examining HIV prevalence; accuracy of self-assumed HIV status; HIV/STI test frequency; sexualised drug-use; condom-less anal sex; self-reported STI diagnoses; and awareness, uptake, and source of PrEP in self-identifying MSM will be conducted.
Results: Thus far (8th–29th June 2019), 775 men have been approached in 25 London venues; 463 (60%) agreed to participate and 319 (69%) provided oral fluid samples for antibody testing. Full analyses will be performed when data collection and laboratory testing concludes. Data on PrEP utilisation and other sexual risk and HIV preventative behaviours will be available for presentation.
Conclusion: The GMSHS 2019 will provide insight to sexual risk and HIV preventative behaviours, especially PrEP use, in a community sample of MSM within a changing landscape of HIV/STI epidemiology and evolving HIV prevention options in England.

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PE28/17

Chemsex and mood disorders under HIV pre-exposure prophylaxis

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Purpose: To assess the prevalence of Chemsex and anxious-depressive disorders among subjects on HIV pre-exposure prophylaxis (PrEP).
Method: Between Jan 2018 and March 2019, all consecutive adults presenting for PrEP renewal in 6 health care centres from the South of France were enrolled in this cross-sectional study. Participants completed a questionnaire including questions about Chemsex (defined by use of any psychoactive drug during sex) practises. Anxious-depressive disorders were assessed using the Hospital Anxiety and Depression (HAD) scale. We adapted the Assist score to assess Chemsex addiction.
Results: The 236 participants enrolled were mainly men (99.6%) with a median age of 36 years [IQ_{25-75} : 30-46]. PrEP was use daily (64.5%) or on-demand (26.9%) for a median 7.6 months [IQ_{25-75} : 3.3-12.5]. Over the last 3 months, 94 subjects (39.8%) reported the practice of Chemsex, including 9 participants (9.5%) reporting psychostimulants injections. The main psychoactive substances (PS) consumed during Chemsex were synthetic cathinones (74.6%), gammahydroxybutyrate (GHB, 66.3%) and psychostimulants (60%, incl. cocaine, amphetamines), with poly-drug use (≥ 2 PS) reported by 38.1% of participants. Using the HAD scale, anxious disorders (HAD ≥11 meaning definite presence of symptoms) were more frequent among participants having practiced Chemsex over the last 3 months than others: 18.1% versus 8.0%, respectively (p=0.042). The median Assist test score was 8 [IQR25-75: 3-15]; 67.8% of participants had a score between 4 and 26 justifying a brief intervention, and 4.4% had a score ≥ 27 justifying a referral to an addict. In multivariable analyses among chemsexers, alcohol consumption during Chemsex and higher assist test score were associated with anxiety: OR 3.13; 95% CI 1.04-9.44, and OR 1.13; 95% CI 1.05-1.12, respectively.
Conclusion: Chemsex is very frequent among PrEP users. It is associated with anxiety disorders, justifying systematic screening, management and implementation of risk reduction strategies.

PE28/18

Pre-exposure prophylaxis one year after implementation in Portugal – the reality of a central hospital

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Introduction: HIV Pre-Exposure prophylaxis (PrEP) is available in Portugal since May 2018. It is important to evaluate PrEP implementation and outcomes.
Objective: To characterise people who initiated PrEP between May 2018 and June 2019.
Methods: We included all patients that started PrEP. This is a retrospective cohort study and data was obtained by clinical records review. Statistical analysis was performed using *IBM SPSS25*®.
Results: We included 108 PrEP users, of which 22 have stopped PrEP. The 86 active PrEP users had a mean age of 46 yo (min. 19, max 65), and were mostly (98.8%) men that have sex with men. Sixty patients were Portuguese, 15 Brazilian and 11 had other nationalities. Sixty-eight patients (79.5%) were highly educated. Seventy-six (88.4%) patients had multiple sexual partners and twenty (23.3%) admitted the use of drugs. Post Exposure Prophylaxis had been prescribed previously in 14 users and 10 had used PrEP before mainly by online purchase. Fifty-four (62.8%) users had a past sexually transmitted disease (STD). Three (3.5%) had comorbidities: one patient with hypertension and two with type 2 diabetes mellitus.
Eighty-four users started PrEP daily and two on demand. Mean duration of PrEP was 115 days (min. 12, max. 370). Only six (6.9%) users were diagnosed with STD on the follow-up.
Twenty-two users stopped PrEP: 13 were lost to follow-up, three had moderate to severe adverse effects, two users seroconverted, two were transferred to other hospitals and two had no longer increased risk behaviour and stopped PrEP.
Conclusion: The majority of PrEP users are MSM with high educational background. Adherence to PrEP consultations (88%) and follow up were high and the seroconversion rate was 1.8%. It is important to inform the general population about PrEP and make it accessible to other groups that also have increased risk for HIV infection.

PE28/19

DISCOVER in Europe: a sub-analysis of the phase 3 randomized, controlled trial of daily emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV pre-exposure prophylaxis (PrEP)

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Objectives: Primary DISCOVER trial results were reported, establishing the non-inferiority of F/TAF (200/25 mg) to F/TDF (200/300 mg) for PrEP in 5,387 cis-men and trans-women who have sex with men, are at risk of sexual HIV acquisition, and were at least 18 years of age. Analyses of data from the 9 European country sub-population are reported here.
Methods: In this randomized (1:1), double blind, active-controlled study, the primary endpoint was the HIV incidence rate (IR) when 100% completed 48W and 50% completed 96W. HIV testing was conducted at each study visit, 3 anatomic sites were evaluated for sexually transmitted infections, and adherence was assessed by pill count, self-report, and TFV-DP levels in dried blood spots (DBS).
Results: Among 1807 adults enrolled in EU sites with 2885 person-years (PY) of follow-up, there were 5 HIV seroconversions; F/TAF n=4 and F/TDF n=1 for an incidence rate (IR) of 0.275 (95% CI 0.075-0.705) and 0.070 (95% CI 0.002-0.389), respectively. All 5 participants had TFV-DP levels that were undetectable or in a low pills per week range. The 5 HIV diagnoses were reported in Spain (3), UK (1), and Germany (1).

Table1. DISCOVER HIV Infections and Incidence Rates, EU and Overall

	F/TAF EU Only	F/TDF EU Only	F/TAF Overall	F/TDF Overall
N	908	899	2670	2665
Person years of follow up	1453	1433	4370	4386
# of HIV infections	4	1	7	15
HIV Infection rate/100PY	0.275	0.070	0.16	0.34
95% CI	0.075–.705	0.002–0.389	0.064–0.330	0.191–0.564

Table 2. DISCOVER STI Incidence by arm, EU and Overall

		F/TAF EU Only	F/TDF EU Only	Total EU Only	F/TAF Overall	F/TDF Overall	Total Overall
Any Gonorrhea, Chlamydia, or Syphilis	# of events (IR per 100 PY)	1917 (132)	1794 (125)	3711 (129)	4340 (99)	4227 (96)	8567 (98)
	# of participants (%)	634 (70)	652 (73)	1286 (71)	1590 (60)	1643 (62)	3233 (61)
Rectal Gonorrhea	# of events (IR per 100 PY)	486 (34)	451 (32)	937 (33)	943 (22)	900 (21)	1843 (21)
	# of participants (%)	318 (35)	312 (35)	630 (35)	651 (24)	662 (25)	1313 (25)

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Bacterial STIs (gonorrhea, chlamydia or syphilis) were reported in 71% of participants with an IR of 129/100 PY. Rectal gonorrhea was reported in 35% of participants with an IR of 33/100 PY. IRs were not different between arms. Spain had the highest IR (158/100PY) and the UK the lowest (109/100PY).
Conclusion: Among participants at European sites in the DISCOVER study, HIV incidence was low and HIV infection was associated with poor adherence to PrEP. The study population had high rates of STIs indicating ongoing high risk for HIV infection.

PE28/20

The Good and Bad of PrEP: a 14 month follow up on awareness, adherence, efficacy and sexually transmitted diseases at Hospital de Curry Cabral

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Introduction: Pre-exposure prophylaxis for human immunodeficiency virus (HIV) in adults is a preventive strategy that might reduce new infections by as much as 90%. In 2018, we have started a PrEP appointment, at Hospital de Curry Cabral's Infectious Diseases Department.
Objectives, materials and Methods: Laboratory, clinical and epidemiological evaluation of 319 adults started on PrEP between May 2018 and June 2019, by retrospectively reviewing their charts.
Results: We have registered 389 first appointment requests of which 77.7% were Portuguese nationals. Of these, 297 (93%) have started prophylaxis with tenofovir disoproxil fumarate/emtricitabine daily and 22 (7%) on demand. Twenty-five individuals (27.2%) are awaiting evaluation to start PrEP, fourteen (15.2%) abandoned follow up appointments and the remaining fifty-three (42.4%) did not meet criteria. Out of 319 individuals, 95.6% were males, 3.1% females and 1.3% transgender. Men who have sex with men are the majority comprising 90.6%. In all first observations *Neisseria gonorrhoeae* infections, *Chlamydia trachomatis*infections and syphilis were screened and in 30.7% cases at least one of them was present. In subsequent screenings, performed during follow up, of the 69.3% originally negative 13.8% became positive for one of the infections screened.
Regarding drug use, sixty-eight individuals (21.3%) reported regularly using drugs during sexual relations.
Three patients were diagnosed with HIV while waiting to be started on PrEP and only one individual became positive while on PrEP.
Conclusions: Our results show that migrants and women might still be under using this resource. This maybe due to unawareness and/or fear of stigma, which might have a limiting impact on the benefits of PrEP in preventing HIV transmission. Furthermore, we are witnessing a possible increase in sexually transmitted infections diagnosis, rendering PrEP an educational role and facilitating health care access, adequate treatment and, therefore, an impact on public health.

PE28/21

PrEP for life: new challenges and barriers in PrEP uptake among men who have sex with men (MSM) and transgender people (TG) in Kyiv, Ukraine

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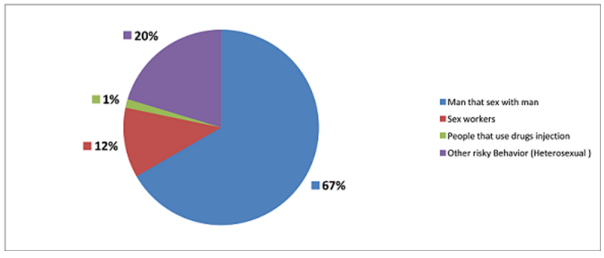
Background: Kiev has initiated a clinic-based PrEP program. Although a modest correlation between risk behavior and preference for PrEP has been established, there is a little knowledge about how PrEP medication's cost, side effects, adherence, and daily or 'on-demand' regimens affect PrEP use. The purpose of this study was to identify perception of and barriers to PrEP use among MSM and TG people in Kyiv.
Methods: Face-to-face structured interviews were used to assess attitudes towards cost, side effects, and alternative prevention methods. Descriptive statistical and factor analysis was conducted.
Results: 184 participants completed the survey. 6.0% of them had at some point taken PrEP. 173 participants who had never used PrEP included in the analysis.
The often reasons for a lack of interest in PrEP are: need for daily administration (83.2%); concerns about side effects (78.4%); risk of other STIs (71.2%); and out-of-pocket costs (65.6%). Factor analysis found: the first factor included concerns about expenses, regular medical examinations, effectiveness of PrEP and bad attitudes of other people; second factor included confidence in absence of need for PrEP; third factor included concerns about daily regimen, side effects and risk of STIs, and fourth factor - concern this would reduce their condom use.
ver 0.0%) of them had t program;
Among barriers: side effects (63.8%), cost expenses (60.3%) and necessity of a daily regimen (52.6%). PrEP should be free of cost (53.2%) or partly free (35.8%), and best delivered in LGBT-centers (50.9%) or through pharmacies (19.7%).
Conclusions: Daily administration, potential side effects, risk of STIs and cost were major barriers to PrEP uptake. Expanded efforts to increase community awareness of PrEP safety and efficacy, as well as more research to determine on-demand PrEP regimen as a second viable strategy for MSM and TG in Kyiv, are urgently needed.

PE28/22

Analysis of the need for pre-exposure prophylaxis of HIV among people that have high risk to be infected

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Background: In 2018, PrEP pilot project for 100 MSM and TG was implemented in Kyiv, Ukraine. After the pilot project, the program was extended to the whole territory of Ukraine, the dispensing of drugs began in May 2019. Currently number of annual courses composes 2806. It was decided to provide an opportunity to get daily PrEP for free to anyone who has high risk of infection. Patients and their physicians identified risk and need in adherence to daily regime of PrEP. In our opinion, the possibility of dispensing the drug not only with key populations has helped to reduce the stigma and self-stigma of PrEP in communities.
Methods: Estimation of the total number of participants in PrEP program according to the medical information system.
Comparison of absolute data: numbers of PrEP users and convert them into percentages.
Processing by stratification method.
Results: 561 PrEP clients during 4 months took pills at least 1 time 374 clients identificate them for doctors like MSM, which is 67%; 114 clients are heterosexual people that have high risk of infection (20%); 64 clients include semself to SW (women) (12%) and 8 clients- people that use drugs injection (1%).
Conclusions: PrEP is popular among MSM, this group also shows the higher awareness and readiness to PrEP;
Also we can see high interes in PrEP among people that not identificate themselves with KP, they are heterosexual man and women, that identificate their risk like high. This figure may also be high, as not all KP representatives report their affiliation with them;
A low percentage of sex workers may also indicate stigma and out-of-state status.



Distribution of PrEP-clients to different groups of people that have high risk of HIV infection

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PE28/23

Lesson learnt from a combined HIV prevention using HIV self-testing and oral pre-exposure prophylaxis (PrEP) demonstration project in the United Republic of Tanzania

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Purpose: Despite remarkable progress in HIV treatment, new infections continue to occur especially among KVPs. Intensified efforts to implement biomedical combination HIV prevention are essential to achieve HIV epidemic control. We implemented a demonstration project with the aim of generating data on the implementation models, uptake, feasibility and acceptability HIV self-testing and PrEP through community services provision. Target populations were key and vulnerable populations (KVP).
Methodology: We used observational cohort for HIVST and longitudinal open cohort for PrEP among KVP at substantial risk of HIV were identified through HTS. The project duration was 21 months; 3 months for site preparation and training, 12 months for implementation and data collection, and 6 months for data analysis and dissemination. It was implemented in regions with pre-existing combination prevention programs for KVP in 10 regions from January 2018-April 2019. All clients attending routine HIV prevention services, including HIV testing, were assessed for eligibility.
Results: Total of 24,674 (94.1%) clients were included in data analysis. 7,332 of PrEP clients and 21,585 number of HIVST client ware entered in the database and analyzed. The two interventions were provided through facility led community outreach services and facility only services. 83% of clients received HIVST and PrEP services through facility led community services while 17% was facility based only. Around one thousand clients were able to be enrolled into PrEP after HIVST tests confirmation. Majority of clients enrolled were FSW 65%, AGYW 15%, 4% PWIDs, MSM 3% and clients of sex workers 13%. 54% of study participants aged 20-29, followed by 30-39, 32%. The younger KPs 15-19 were least represented, 8.1%.
Conclusion: Uptake of both HIVST and PrEP among the study population was high. The demonstration project ended in April and a scale up plan is under way after successful implementation of the program.

Prevalence, incidence and dynamics of HIV epidemics

PE29/1

Monitoring rates and accessibility of HIV and STI's testing, HAV and HBV vaccination among men who have sex with men in Slovenia

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Purpose: The aim of this study was to examine HIV testing rates, accessibility to testing and to HAV and HBV vaccination among MSM who answered the online survey between October 2017 and end of January 2018. Study was part of European study EMIS 2017.
Method: This large internet based study enrolled men who had been involved in sexual contact with another man in the last 12 months. Respondents were recruited via different online gay dating websites and mobile applications. Structured questionnaires were self-administered by participants (N=685).
Results: Monitoring levels of HIV and other STI testing gave us the following results;
7% of MSM reported to have full STI screen in last 12 months: HIV, blood test, anal swab + urethral swab.
2.5% reported to be diagnosed with syphilis in last 12 months.
One half of them has been tested for HIV in the last 12 months (49.8%). Almost a third (32.4%) used community-based HIV-testing for/at their last HIV test. 6.3% of respondents were diagnosed with HIV (among tested). 100% of those diagnosed reported to had their infection monitored (linked to care).
Monitoring vaccination rates for HAV and HBV; Almost one third (32.6%) reported of full course of HAV vaccination. 40% reported of full course of HBV vaccination.
Conclusion: Study showed very important and relevant data: that only one half of MSM are getting tested and should be encouraged to be tested even more, to be tested earlier, and more regularly. Data also showed that almost 28% of respondents were never tested for HIV. Data suggest that MSM should have access to testing in gay venues. The most important result is that it was once more confirmed that we have MSM concentrated HIV epidemic in Slovenia and as such should no longer be considered as low HIV prevalence country.

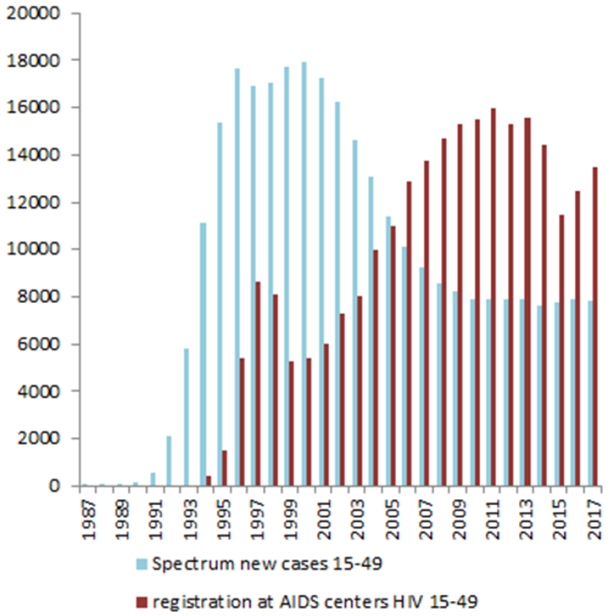
PE29/2

Data triangulation to re-shape interventions to improve the HIV response: compering data from estimates, case reporting, and sentinel surveillance in Ukraine

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Purpose: Strategic Information is core for program management. Recently Ukraine is experiencing the difficulties with reaching "first 90"- 90% of people knowing HIV status. HIV surveillance is well developed and includes various types of data from 1998. Study was aimed at locking on different aspects of HIV epidemic which could be potentially used for better program management.
Method: Study implies the secondary analysis of data from three sources: HIV case reporting for 1987-2017, HIV estimates for 2017 produced by Spectrum, and IBBS among key populations conducted in 2017.
Results: HIV case registration system captured substantial amount of HIV cases occurred among all adult sub-populations since 1887 - 87% (247692 of estimated 285067 cases, Graph 1). The majority of under detected HIV cases might be hidden among the population aged 50 y.o. and above. According to the Spectrum estimates, 40% of new HIV cases occurred in this population (190 thousands of cases), while routing surveillance captured only 8% of them. Spectrum may overestimate the number of HIV cases in the population 50+, however, routing surveillance data shows that HIV epidemic is getting older in Ukraine: the number of HIV cases detected and registered in 50+ populations has been increased significantly from 261 cases in 2005 to 2068 cases in 2017. According to IBBS among PWIDs and MSM, HIV prevalence



New HIV cases (15-49) in Ukraine from 1987 to 2017: estimated and officially registered

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among those who are 50+ is significantly higher than those younger: 28% Vs. 22% among PWID and 10% Vs.7% among MSM. Additionally, estimated and IBBS data suggest that the majority of unidentified HIV cases are among current and former drug users and MSM.
Conclusion: Available data is substantial to understand current HIV trends. Data discussion and triangulation exercises are crucial to get national consensus on PLHA estimates and prioritize strategies to find remaining underdiagnosed HIV cases and improve treatment uptake in al sub-populations.

PE29/3

The impact of frequent cannabis use on injection drug use patterns among people who use drugs in a Canadian setting

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Purpose: People who inject drugs (PWID) are 22 times more likely to acquire HIV than the general population and an estimated 25% of new HIV infections outside of sub-Saharan Africa are attributed to injection drug use. Preliminary evidence suggests that cannabis use may have the potential to reduce drug-related harm among PWID, including the frequency of illicit drug use and accidental overdose. We sought to expand this evidence by evaluating the impact of frequent cannabis use on the frequency of injection drug use and injection cessation among PWID in Vancouver, Canada.
Method: The data for this analysis were collected from three prospective cohorts of PWID in Vancouver, Canada, between September 2005 and May 2018. At baseline and semi-annually, participants completed an interviewer-administered questionnaire that collected data including socio-demographic information, substance use patterns, HIV risk behaviours and engagement with health and social services. Generalized linear mixed-effects models and extended Cox regression models with time-updated covariates were used to analyze the impact of daily cannabis use on injection frequency and injection cessation.
Results: Among the 2,390 participants included in the analysis, daily cannabis use was associated with decreased frequency of injection drugs use (Adjusted Odds Ratio [AOR]=0.81, 95% confidence interval [CI]: 0.73-0.89), and increased rates of injection cessation (adjusted hazard ratio [AHR]=1.17, 95% CI 1.04-1.33).In both subanalyses, the effect of cannabis use on frequency of injecting and injection cessation was restricted to opioid use and the association between cannabis use and stimulant use was not significant.
Conclusion: Our findings describe longitudinal reductions in the frequency of illicit opioid injection associated with high-intensity cannabis use. Experimental research is needed to identify the mechanisms by which cannabis use and specific cannabinoids (e.g., THC and CBD) may mitigate the harms of injecting illicit drugs.

PE29/4

Predicting early loss to follow-up on ART: a retrospective review of clients' retention on ART in North-western Nigeria

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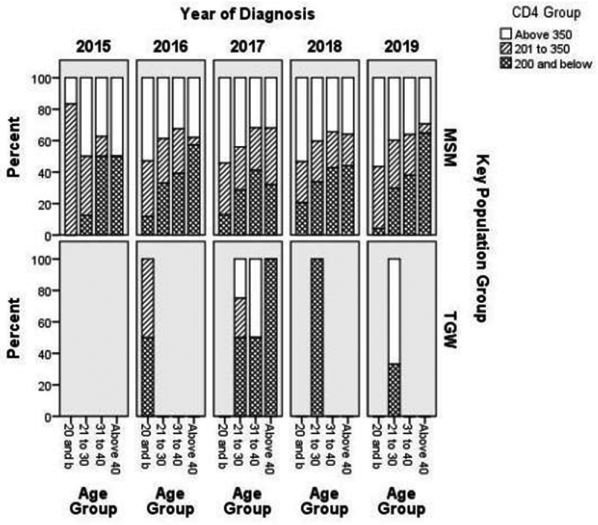
Purpose: Retaining patients on ART is as important as initiating them into ART. Only clients who are retained in ART can achieve viral suppression. Loss-to-follow-up (LTFU) remains an important cause of ART attrition, apart from death and discontinuation of treatment especially in resource-poor settings. Earlier researches in Nigeria have studied rates and factors responsible for LTFU. The objective of this study was to evaluate early loss to follow-up on ART and factors associated with it.
Method: The facility paper-based ART registers in one secondary and one tertiary ART centers containing data of clients enrolled into ART between Jan 1 2013 to Dec 31 2016 were reviewed. The study focused on clients lost to follow-up within 12 calendar months of initiation into ART. Sociodemographic and other clinical data were extracted, entered into Microsoft Excel, and exported into SPSS version 21 for bivariate and multivariate logistical regression analysis.
Results: Of the 279 LTFU clients studied, 146 (52.3%) were females, 159 (57.0%) were from the tertiary ART center, and 150 (53.8%) lived within 15 km from their ART center. The median age of the study population was 34 years (IQR: 26-40). Within 6-months of initiation into ART, 85.7% (239/279) of the loss to follow-up occurred. Accessing ART in the secondary center (AOR=2.7, CI: 2.2-3.3, p<0.001) and initiating ART at CD4-count greater than 180 (AOR=1.9, CI: 0.9-2.4, p<0.002) were associated with higher risk of being lost to follow-up within 6-months of ART initiation. Statistically, there was no relationship between early loss to follow-up and the distance from the ART center.
Conclusion: More than three-quarter of LTFU events occurred less than 6-months after ART initiation. Clients accessing ART in the secondary center were more likely to be lost earlier. Intensive pre-treatment preparation may be required to decrease early loss to follow-up on ART.

PE29/5

The increasing number of late HIV diagnosis among men having sex with men and transgender women in a key population-led HIV testing and treatment facility and its societal implication in the Philippines

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Purpose: There is sustained increase in the incidence rate of HIV infection among the youth, MSM, and TGW in the Philippines. Since there is known benefit in early diagnosis and treatment, efforts are made to achieve this. The objective was to estimate the temporality of the diagnosis from time of infection and analyse its implications.
Method: LoveYourself is a key population-led organisation operating clinics providing HIV and STI testing and treatment free-of-charge. Among the 3,425 MSMs and 21 TGW who tested reactive to HIV antibody using 3rd Gen EIA rapid testing, CD4 count measurement were obtained. CD4 count was used to assess the timing of diagnosis. Data analysis was done using SPSS.



CD4 counts at diagnosis among MSM and TGW in a key-population led healthcare facility

Results: The median CD4 at diagnosis is 296 cells/μL. Among the MSMs, CD4 count at diagnosis is significantly higher among 20 and below (374.62±173.5 cells/μL) compared to the older age groups 21 to 30, 31 to 40, and above 40 years old (315.7±213.0 cells/μL, p=.001, 284.3±230.0 cells/μL, p=.000, 266.4±234.0 cells/μL, p=.000, respectively). There is no significant difference in the CD4 count at diagnosis through the years and in terms of whether being a MSM or TGW (p=.840, p=.073, respectively); half of those aged 20 years and below were diagnosed late (47%) and more than half of those aged above 20 (58.4%, 66.4%, and 65.6%). Among the TGW, most cases were diagnosed late.
Conclusion: Despite a significant increase in HIV testing, data suggest that more than half of the newly diagnosed cases were seen late. Late diagnosis in

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the younger age group suggests early infection; late diagnosis in the older age group corresponds to late treatment leading to longer persistence of possible transmission among the key population. Both is a manifestation that there are barriers to early diagnosis and treatment which is key to maximising the benefits of ART.

PE29/6

HIV transmission network in a cohort of subjects with primary infection in a single clinical center in Rome

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Purpose: To analyse transmission dynamics in a cohort of individuals with primary HIV infection (PHI) presenting to the largest HIV clinic in Rome, Italy, from 2013 to 2018.
Methods: For individuals with PHI linked to care, we collected epidemiological, clinical, viro-immunological and therapeutic data, and performed transmission clusters (TCs) analysis at diagnosis with HIV pol sequences, using Maximum-Likelihood and Bayesian methods (threshold of 1.5% genetic distance). Among factors possibly associated with TCs, we investigated by univariate analysis: gender, age, nationality, transmission risk, year of diagnosis, Fiebig stage, CD4 count and viral load at diagnosis, HIV subtypes, transmitted drug resistance, and time to virological suppression.
Results: Of 227 PHI, 218 were linked to care, with a median follow-up of 136 weeks (IQR 68-192); median (IQR) age was 38 (31-47) years; 94.9% were males; 86.6% Italians; 83.3% were men having sex with men (MSM). We compared sequences from 216 individuals (sequencing was not successful in 2). Acute infections (Fiebig II to IV: 50.5%) had a higher HIV-1 viral load than recent infections (Fiebig V-VI) [log_{10} copies/mL, median (IQR), 6.15 (5.4-7.0) vs 5.0 (4.2-5.5), $p<0.001$)]. Of 216, 92.1% started treatment soon after diagnosis (median [IQR] 4 [2-8] days), with 2NRTI+DRV/b+RAL, or (from May 2015) 2NRTI+DTG. Those for whom treatment was delayed (15/17) were diagnosed in 2013-2014. Median (IQR) time to virological suppression was 16 (8-28) weeks. HIV-1 B subtype was predominant (56.5%). Sixty-four individuals (29.6%) grouped into 18 TCs (median size 3, range 2-9). A less recent year of diagnosis was the only factor significantly associated with TC inclusion.
Conclusions: Data show that TCs among PHI continue to occur. These involve predominantly Italian males and MSM, suggesting local transmission networks in this risk group. Early treatment with antiretrovirals, especially those determining a rapid viral load decay, could reduce TCs over time.

Characteristic	Overall N=216	In cluster N=64 (29.6%)	Out of cluster N=152 (70.4%)	P value*
Male, n (%)	205 (94.9)	62 (97.0)	143 (94.1)	0.39
Age (years), median (IQR)	38 (31-47)	37 (30-43)	38 (31-48)	0.19
Year of diagnosis, n (%)				
2013-2014	78 (36.1)	31 (48.4)	47 (30.9)	**0.01**
2015-2016	76 (35.2)	18 (28.1)	58 (38.2)	0.13
2017-2018	62 (28.7)	15 (23.5)	47 (30.9)	0.32
Nationality, n (%)				
Italians	187 (86.6)	59 (97.2)	128 (84.2)	0.12
Foreigners	29 (13.4)	5 (2.8)	24 (15.8)	
Risk factor, n (%)				
Heterosexual	33 (15.3)	7 (11.0)	26 (17.1)	0.25
MSM	180 (83.3)	56 (87.5)	124 (81.6)	0.28
IV drug addict	3 (1.4)	1 (1.6)	2 (1.3)	0.89
Fiebig stage, n (%)				
II-IV	109 (50.5)	33 (51.6)	76 (50.0)	0.83
V-VI	107 (49.5)	31 (48.4)	76 (50.0)	
CD4 cell count (cell/mm³), median (IQR)	563 (390-720)	575 (370-747)	560 (394-709)	0.89
Viral load (log_{10} copies/mL), median (IQR)	5.5 (4.6-6.3)	5.6 (4.6-6.6)	5.4 (4.6-6.2)	0.52
Subtype[1], n (%)				
B	122 (56.5)	38 (59.4)	84 (55.3)	0.58
Non B	94 (43.5)	26 (40.6)	68 (44.7)	0.65
Transmitted drug resistance, n (%)				
Any drug class	23 (10.6)	4 (6.3)	19 (12.5)	0.17
Time from diagnosis to virological suppression (weeks), median (IQR)[2]	16 (8-28)	20 (11-32)	16 (8-24)	0.14

*By Mann-Whitney test (for quantitative variables) and Chi-squared test or Fisher's exact test (for categorical variables), as appropriate. P values <0.05 were considered as statistically significant.
[1]10 B clusters (2-9 individuals) and 8 non-B clusters (2-6 individuals)
[2]199 individuals treated shortly after diagnosis (median [IQR] 4 [2-8] days)
Abbreviations: MSM, Men who have sex with Men.

Characteristics of Primary HIV Infections possibly associated with Transmission Cluster inclusion

PE29/7

Evaluation of a multiassay approach for determination recent HIV infection in the Russian Federation

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Purpose: Information on the rate of new infections is critical to monitoring the HIV epidemic. Differentiating recent from established HIV infections is possible due to the evaluation of HIV-specific immune response development and viral markers measurement. Recent Infection Testing Algorithm (RITA) is an approach that allows differentiating recent and established HIV infection. Laboratory tests include detection of antibody titer, avidity index, viral load, and CD4-count. The aim of this study was to assess the effectiveness of RITA for determination of recent HIV infection in Russian patients.
Method: Plasma samples (n=291) was obtained from ARV-naïve HIV patients: 122 samples from patients with infection duration up to 6 months (recent infection) and 169 samples from patients with duration more than 6 months (established infection). The duration of infection was determined on the last negative and first positive ELISA tests. Determination of antibody titers was carried out with DS-EIA-HIV-Ab-TERM kit (Diagnostic Systems, Russia) and antibody avidity was estimated by Architect HIV Ag/Ab Combo kit (Abbott, USA).
Results: On the first step, all samples were analyzed by the antibody avidity and sensitive-less sensitive assays. The concurrence of Architect HIV Ag/Ab Combo results and epidemiological data were obtained for 222 of 291 samples; this index for DS-EIA-HIV-Ab-TERM was 238/291 samples (Table 1.). For using RITA in addition to serologic assays the following criteria have been defined for recent infection: CD4-count >200 cells/mm^3; viral load >400 copies/ml; the absence AIDS-defining illness. RITA classified 78.69% of diagnoses in accordance with epidemiological data and correctly identified recent infection in 73.77% of cases.
Conclusion: Study results showed that serological tests (Abbott and DS) correctly identified the duration of HIV infection in 76.29% and 81.79% respectively. However, the use of RITA reduces the number of false recent results, which is more significant for statistics and determining the level of incidence.

Table 1. Distribution of samples according to test results.

	Architect HIV Ag/ Ab Combo	DS-EIA-HIV-Ab-TERM	RITA
true recent (<6 months)	101/122 (82.79%)	109/122 (89.34%)	90/122 (73.77%)
false recent	48/169 (28.40%)	40/169 (23.67%)	30/169 (17.75%)
true established (>6 months)	121/169 (71.60%)	129/169 (76.33%)	139/169 (82.25%)
false established	21/122 (17.21%)	13/122 (10.66%)	32/122 (26.23%)
total number of correctly determined samples	222/291 (76.29%)	238/291 (81.79%)	229/291 (78.69%)

PE29/8

Ongoing spread of HIV subtype A in Tel Aviv, Israel

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Purpose: HIV-1 A, B and C were identified as the major subtypes in Israel. This study evaluated the pattern of subtype A among HIV-1 treatment-naïve patients in Tel Aviv from 2010 to 2018.

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Method: We retrospectively analyzed sequences of subtype A viruses from plasma drawn from treatment-naïve patients for routine resistance testing obtained at admission to the Crusaid Kobler AIDS Clinic between 2010-2018. Phylogenetic reconstruction was inferred by means of pol sequences.
Results: 251 sequences of subtype A viruses were obtained. Intravenous drug users (IVU) accounted for 37% of the patients, heterosexuals for 34% and MSM for 16%. Between 2010-2013, IVU accounted for 46% of the subtype A virus population, 29% of the heterosexual patients ($p<0.05$) and 16% of the MSM . Between 2014-2018, 41% of the viruses were from heterosexuals ($p=0.05$ compared to IVU), among whom 66% were women. IVU accounted for 27% of all the viruses and for 17% of the MSM. Among the IVU, heterosexuals and MSM, 82%, 87% and 23%, respectively, were born in the FSU. Among the MSM, IVU and heterosexuals, 65%, 13% and 11%, respectively, were born in Israel.
Phylogenetic analysis of subtype A showed one cluster in a group of IVU during an outbreak of acute HIV infection, suggesting a single source of infection, and a few clusters among MSM, including clusters with drug-resistance mutations.
Conclusion: This study of subtype A revealed complex transmission dynamics and evidence of ongoing spread and diversification. We observed a shift of the incidence in subtype A infection from IVU to heterosexuals originating from the FSU and a spread to the MSM born in Israelin a cluster pattern. The phylogenetic analysis is important for understanding patterns of transmission among the various risk groups.

PE29/9

Simple clinical and laboratory based score may identify HIV infection recency and subsidize HIV surveillance in low and middle-income countries (LMIC), Santo André/Brazil experience

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Purpose: Identification of acute/recent HIV infection is also important for surveillance purposes. We evaluated, with known laboratory markers of HIV recency, a simple protocol to identify recent infections.
Method: Newly diagnosed patients (2011-2017) were classified as recent (RI) or established (EI) infection according to two definitions: i) Definition-A: RI=Seroconversion <365 days or avidity Index <40% (Bio-Rad, USA) vs EI=avidity≥80% or CDC1993_C; ii) Definition-B: RI=seroconversion <365 days or [avidity <40% and CMIA <500 (Architect 4th generation, Abbott, USA) and ambiguity index at polymerase sequence <0.5% and CD4 >200 cells/mm³] vs EI=CDC1993_C or [avidity≥80% and CMIA≥500 and ambiguity≥0.5% and CD4 <500cells/mm³]. A score was proposed considering HIV-1 RNA viral load (VL) $\log_{10}$ (5 to 6= +5; 6 to 7= +6; ≥7 = +7 points) + CD4 (CD4 <100cells/mm³=-7; CD4 100 to 200 cells/m=-3; CD4 200 to 350 cells/mm³ =-2 points) + 7 points if clinical symptoms compatible with acute retroviral syndrome were observed in the last 365 days prior to diagnosis The score was evaluated for the two definitions using ROC analysis.
Results: 204 cases were included, with avidity analyzed in 181, CMIA in 137, ambiguity in 181, CD4 in 200 and VL in 203. 103 cases were classified as RI and 68 EI at definition-A and 76 RI and 25 EI using definition-B (Table 1).
A score of 4 points had a 62% sensitivity and a 76% specificity, with area under the curve (auc) of 0.75 (95% CI 0.68-0.82, p<0.001) for definition-A and 66% sensitivity and 84% specificity (auc 0.83, 95% CI 0.74-0.92, p<0.001) for definition-B (Fig. 1).

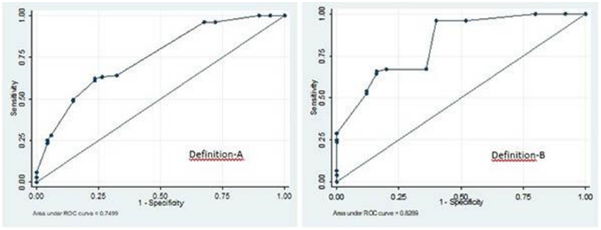


Figure 1. Receiver Operating Characteristic (ROC) curve for a score based on clinical and laboratory

Conclusions: Using data from patient interview and laboratory tests (CD4&VL) at admission, a simple algorithm may allow a surveillance definition of HIV recency that may be useful in monitoring the epidemic, subsidizing LMIC AIDS program.

PE29/10

Clinical, epidemiological & virological features of primary HIV-1 infection in an HIV reference center in Brussels: a ten years' review

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Purpose: Early diagnosis of HIV is critical in order to limit viral transmission in the community and from patient perspective decrease the size of reservoirs and diminish damage on immune system.

Table 1. Age, sex and laboratory markers of recency in definition A and B

		Definition-A (n=171)			Definition-B (n=101)		
	All (n=204)	RI (n=103)	EI (n=68)	p	RI (n=76)	EI (n=25)	p
Median age (years) (n=204)	27 (23-34)	24 (21-30)	30 (24-39)	p=0.0001	n=76 24 (21-24)	n=25 31 (24-40)	p=0.0001
Male/MSM (n=204)*	178/145	103/94	68/57	p=0.15	76/71	25/22	p=0.41
Avidity (n=181)**	73% (21%-100%)/ 37%	n=92 22 (8-54)/71.7%	n=67 100 (98-100)/1.5%	p<0.0001	n=65 24 (11-77)/60%	n=24 100 (97-100) 4%	p<0.0001
CMIA (n=137)***	578 (242-907)/43%	n=71 252 (108-577)/72%	n=47 935 (704-1106)/ 6.4%	p<0.0001	n=53 250 (103-547)/74%	n=18 1007 (759-1218) 6%	p<0.0001
Ambiguity (n=181)****	0.20 (0.00-0.60)/69%	n=97 0.09 (0.00-0.36)/ 83%	n=52 0.58 (0.29-0.99)/ 40%	p<0.0001	n=70 0.09 (0.00-0.39) 79%	n=24 0.78 (0.59-1.23) 13%	p<0.0001
CD4 cells/mm³ (n=199)	528 (353-769)	617 (452-837)	377 (136-643)	p<0.0001	n=71 570 (436-825)	n=25 134 (39-224)	p<0.0001
Viral Load (log10) (n=203)	4.67 (4.06-5.19)	4.73 (4.15-5.34)	4.70 (4.00-5.17)	p=0.33	n=76 4.73 (4.12-4.73)	n=25 5.11 (4.47-5.47)	p=0.17

Recent infection (RI); Established Infections (EI); *MSM: men who have sex with men; **Avidity index for Bio-Rad-Avidity assay serology test (CEPHIA protocol)/% of cases with Avidity index lower than 40% (surrogate for recent infection); ***Chemiluminescence microparticle immunoassay (ARCHITECT HIV Ag/Ab, Abbott, USA)/% of cases with index below 500 (surrogate for recent infection); ****Ambiguity index as the number of nucleotide mixtures (excluding unresolved four nucleotides) divided by the total number of nucleotides analyzed/% of cases with index below 0.5 (surrogate for recent infection); Continuous variables described as median and percentile 25th-75th (IQR). Mann-Whitney test was used to compare variables by recency group except proportion of MSM (Fisher).

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We aimed at characterizing clinico-epidemiological and virological features of patients diagnosed at primary infection during the last 10 years along with their outcome.
Method: Monocentric, retrospective, epidemiological study including patients diagnosed at primary infection between 2007 and 2017. Primary HIV infection definition: positive HIV test with negative ELISA in the previous 180 days, positive ELISA with positive P24 antigen and negative or indeterminate Immunoblot, positive HIV test with known risk and/or symptoms in the last 180 days. Data collected from database or medical files.
Results: 127 patients were diagnosed at primary infection between 2007 and 2017. The proportion of such patients on total new HIV diagnosis in our center significantly increased from 2007 (0.6%) till 2017 (12.5%) p=0.01. Median age was 34.7 years, 116-(91.3%) were males, 102-(80.3%) were MSM, 65-(51.2%) were non-Belgian born, 72.1% were symptomatic and 13.2% were hospitalized at diagnosis. HIV testing was mainly performed by general practitioners (36.2%). Main viral subtypes were B (63.3%), CRF02-AG (10%) and F1 (8.8%). Time from diagnosis to treatment shortened significantly from 2007 till 2017 (300 versus 14.5 days p=0.01). Non-Belgian born patients had lower rate of treatment initiation (90.7% vs 100% p=0.02) and higher rate of lost to follow-up (7% vs 2.3%, p=0.08 NS). 90.7% of treated patients had undetectable viral load (<50copies/ml) after 1 year of treatment.
Conclusion: During those 10 years, early diagnosis of primary HIV infection increased while delay from diagnosis to treatment initiation significantly shortened. When compared to Belgian epidemics data, early diagnosis concerned mainly the MSM population. Non-belgian born patients could benefit to targeted intervention in order to improve treatment uptake and retention to care.

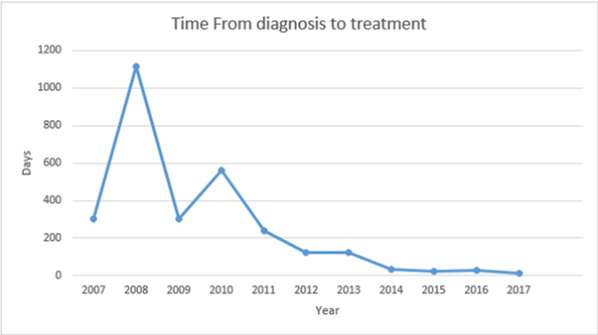


Figure 1.

PE29/11

Current trends in HIV genetic diversity in Russia: increase of the unique recombinants prevalence

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Purpose: During the last two decades, HIV-1 has been spreading rapidly in the Russian Federation with subtype A (sub-subtype A6) dominating in almost all territories. In 2005-2010, the genetic diversity of HIV-1 in Russia began to increase. Subtypes B, C, and recombinants CRF02_AG, CRF63_02A1 have also been identified. This phenomenon created the conditions for the new unique recombinant forms (URFs) emergence as an important component of the HIV-infection epidemic. The purpose of this study was to make first estimates of the prevalence of HIV-1 unique recombinant forms in Russia.
Method: Laboratory database of nucleotide sequences obtained during 2011-2018 was used as a source of 1839 HIV-1 *pol* gene fragments sequences from different regions (Moscow, Krasnoyarsk, Krasnodar, Yuzhno-Sakhalinsk, Cherepovets and Barnaul) of Russia. Genotyping and recombinant analyses were carried out using the tools COMET HIV-1, REGA HIV-1 Subtyping Tool (V 3.0), RIP and jpHMM. 330 additional HIV-1 *pol* sequences from Tomsk, Kemerovo and Krasnoyarsk were taken from Genbank (http://hiv-web.lanl.gov) and included into analysis.
Results: The results of genotype analysis revealed that 74.0% (1606/2169) of the sequences studied belonged to sub-subtype A6, 11.4% (247/2169) - CRF63_02A1, 5.7% (123/2169) - URFs, 5.5% (120/2169) - subtype B, the remaining subtypes accounted for 3.4%. The prevalence of URFs in the regions studied in 2011-2012 was 3.5%; in 2013-2014 - 5.1%; in 2016 - 5.8%; in 2017 - 6.9%; 2018 - 10.7%. The URFs were represented by the following variants: URF_AB, URF63_02A1, URF_02AG and composite patterns (URFA6_02AG, URFB_02AG, URF63_02A1/A6, URF03_AB/A6).
Conclusion: The study results point to the increasing genetic complexity of the HIV-1 epidemic in Russia, including due to the frequent emergence of URFs. There is a tendency to increase the prevalence and genetic diversity of URFs. The results can help to better understand and predict the future trends of the HIV epidemic in Russia.

PE29/12

Analysis of risk factors in HIV/AIDS patients

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Purpose: The epidemic of HIV is increasing in our country while decreasing in the world. In order to understand the cause of this increase and to prevent the epidemic, it is important to examine the transmission route of HIV-infected cases. The aim of this study was to evaluate the risk factors for transmission of infection in HIV/AIDS patients followed up in our outpatient clinic.
Method: The files of HIV/AIDS patients who applied to our clinic between January2008-December2017 were evaluated retrospectively.
Results: Of 520 HIV/AIDS patients, 463(89%) were male, the meanage 37.1 (17-79 years). The initial mean number of CD4 was 384/mm^3(0-2522), the mean HIV-RNA was 1761571 IU/mL (211-46969526). 221(42.5%) were married, 55(10.5%) were single, 45(8.6%) were widowed, 32(6.1%) had fixed partners. While no HIV infection was detected in 126(49.8%) of the fixed partners ofthepatients, 73(28.8%) were infected withHIV. The transmission route was shown in table1. The increase in the ratio of those who did not give information about the transmission route between 2013-2017 suggested that there were those who preferred to hide themselves due to stigmas. Stimulant and druguse are known to cause an increase in HIV transmission. According to OECD data, smoking rates decreased from 32% to 23.8% between 2000-2015. However, smoking rates were higher among our patients (mean rate 42.5%) and did not demonstrate the similar decrease. Alcohol consumption rates among patients were shown intable2. The prevalence of lifetime substance use in the general population was 2.7% in a research of Turkey Monitoring Center for Drugs and DrugAddiction in 2011. Drug use in our patients was quite high (mean rate 6.8%) compared to the general population.
Conclusion: Unlike UNAIDS'statement that HIV epidemic in the world decreasing, thereis a rapid increase in HIV incidence in Turkey. Epidemiological Dynamics should be followed to determine the causes of this increase and preventive actions/training programs may be applied.

Distribution of transmission path within years

Transmissionroute	2008-2012	2013-2017
Heterosexualcontact	97 (51.3%)	108 (32.6%)
Homosexual/bisexualcontact	64 (33.8%)	120 (36.2%)
Sexualcontact -unspecified	2 (1%)	7 (2.1%)
Blood transfusion	3 (1.5%)	2 (0.6%)
Others (IVdruguse, Needlesinking. . .)		5 (1.5%)
Unknown	23 (12.1%)	89 (26.8%)
Total	189 (100%)	331 (100%)

Change in alcohol consumption within years

	2008-2012	2013-2017
Alcohol free	70 (37%)	119 (35.9%)
Socialdrinker	48 (25.3%)	90 (27.1%)
>21 units for men >14 units for women	18 (9.5%)	15 (4.5%)
Quitted	9 (4.7%)	4 (1.2%)
Unknown	44 (23.2%)	103 (31.1%)
Total	189 (100%)	331 (100%)

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PE29/13

Tracing the first HIV-1 epidemics in the Milan area

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Purpose: The aim of study was to investigate the origin and the dynamics of first HIV cases in Milan area to understand future trends of the epidemics in term of intermixing among risk categories.
Methods: We analyzed 110 *pol* sequences collected between 1997 and 1999 at 'L.Sacco' Hospital of Milan from patients who have first HIV-positive test ranging from 1982 to 1998.The transmission networks were identified by MrBayes.Dated phylogeny was performed using Beast program considering two separate datasets,the first including IDUs (n=44) and the second involving subjects with sexual risk (n=53).
Results: Male were 74%;IDUs,HEs,MSM and bisexual were 42.8%,27.5%,18.3% and 5.3%,respectively.Two patients with non-B subtypes were excluded from the analyses.Based on tree topology we identified 13 significant epidemiological networks that included 2 to 9 sequences.No differences were observed in the distribution of risk categories; males were significantly more present in clusters than females (28.3% vs. 9.7%, p=.011).For sexual transmission,the dated phylogeny showed that the root of the tree dated back 27 years (95%HPD:22.9-31.6) and the median tMRCA of significant clusters was 10.5 years (95%HPD:1-27) before 1999.IDUs dataset showed a tMRCA of 21 years for the root (95% HPD:17.5-24.5);the median tMRCA of significant clusters was 17.4 years (95% HPD:12.9-21.5) before 1999.The estimated mean grow rate for IDUs was 1.2(range:0.02-2.57) resulting in an estimated R_0=12.8 considering doubling time of the epidemics of 7 months.These parameters were 0.5(range:0.0014-1.15),R_0=6 and 15 months of doubling time for sexual transmission.The Bayesian Skyline plot showed that cases of sexual transmission exponentially grew from the beginning until 1980;the IDUs started their exponential grow until reaching the plateau in 1990.
Conclusions: Our study indicated an early introduction of the virus at the end of 70s.We observed initial multiple penetration events related to sexual modalities of infection followed by the spread among IDUs,characterized by a highest R_0 and doubling time of infection that explains their role in fueling the epidemic.

PE29/14

Analysis of the local HIV-1 epidemic in Vologda region, Russia: predominance of CRF03_AB and rapid expansion of URFs

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Purpose: The distribution of HIV-1 subtypes between Russian regions is no uniform. Although sub-subtype A6 is responsible for about 80% of HIV-1 infections in Russia, the CRF03_AB recombinant is widespread in Vologda region (along with Kaliningrad region). At the beginning of the epidemic, this recombinant was responsible for more than 75% HIV-1 cases in the region, primarily due to the rapid growth of infection among injecting drug users (IDUs). In the context of Russia's transition from "IDUs" epidemic to "sexual" epidemic, we can expect the spread of CRF03_AB among other risk groups. Our studies were aimed at studying the current state of the HIV-1 diversity in Vologda region, and reconstruct the spatial-temporal dynamics of the CRF03_AB recombinant.
Method: Maximum likelihood and Bayesian coalescent-based analyses of time-stamped data were performed on HIV-1 pol sequences generated from PMBC collected from 79 individuals as part of a molecular monitoring in Vologda region during 2016-2018.
Results: In general, sub-subtypes A6 (51.9%) prevailed, followed by CRF03_AB (33%), B (6.3%), URFs (5%) and "other" subtypes. Most of the CRF03_AB sequences belonged to HIV-infected patients from Cherepovets city (n=52), where this recombinant dominated (48%). The proportion of CRF03_AB among heterosexuals increased from 22% in 2008 to 54% in 2017. Phylogenetic reconstruction showed that most of CRF03_AB viruses were introduced into the epidemic cluster that appeared in 1999 [1998-2000]. Phylogeography analysis indicated a genetic flow between Cherepovets and Kaliningrad city (BF=15), Ekaterinburg city (BF<10) and Saint-Petersburg city (BF<10), which is consistent with previous epidemiological data.
Conclusion: This study provides a new understanding of the HIV-1 epidemic in Vologda region, which is becoming increasingly complex, including due to the emergence of URFs. According to our data, the recombinant CRF03_AB entered the region around 1999, most likely from the Kaliningrad IDUs.

PE29/15

Identification of first near full length recombinant genome of HIV-1 in Korea

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Purpose: Human immunodeficiency virus (HIV)-1 subtype B was a predominant variant in Korea. Korean clade B subtype (Korean B), a unique strain of HIV-1 subtype B, was over 80% of subtype B infection cases in Korea since 1990. However, full genome sequencing and analysis of the viral variants have not been conducted. We were to get the recombinant form of near full-length HIV-1 sequence.
Method: We performed near full-length genome sequencing, phylogenetic, and recombination analyses with 50 plasma of the men who have sex with men (MSM) with HIV-1, which obtained from Korea HIV/AIDS cohort study. Viral genomes were amplified in two overlapping fragments of 5.5 kb and 3.7 kb. The sequences were subtyped using REGA version 3.0, RIP and jpHMM. Phylogenetic trees were inferred with MEGA 6. We estimated the prevalence and patterns of antiretroviral drug resistance mutations using Stanford drug susceptibility algorithm.
Results: Of 50 plasma, we obtained thirteen near full length sequences and the near full length sequences determined with NGS and Sanger sequencing. Nine (69.2%) of thirteen HIV-1 near full length sequences were subtyped as pure HIV-1 subtype B. Four (30.8%) of 13 HIV-1 sequences were characterized recombinant. The recombinants were composed; A1 and G subtype region in a subtype B backbone, four of A1 subtype regions in a subtype G backbone, AE subtype region in a subtype B backbone, and C subtype regions in a subtype B backbone, respectively.
Conclusion: This is the first recombinant near full length sequences of HIV-1 in Korea. To further understand the pattern of viral recombination and recombinant site, it is necessary to constantly monitor of near full length genome analysis.
(REGA; subtyping tool, RIP; Recombinant Identification Program, jpHMM; jumping profile Hidden Markov Model)
Keyword: HIV-1 recombinant, near-full length genome, Men who have Sex with Men, HIV/AIDS cohort, NGS, Korea

PE29/16

Characteristics of HIV infection among children in Georgia, 1989–2018

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Purpose: Since 2005 Georgia ensured universal access to PMTCT services, which includes free HIV test during the first trimester of pregnancy and free antiretroviral therapy (ART) for those positive. We aimed to study peculiarities of HIV in children less than 15 years old diagnosed in Georgia in 1989-2018.
Method: A retrospective data of all registered HIV patients less than 15 years of age was extracted from the national HIV/AIDS health information system operated by infectious Diseases, AIDS and Clinical Immunology Research Center.
Results: The data of 111 HIV positive children less than 15 years old was analyzed. The median age was 4.4 years, 71 (63.9%) of patients were boys. 105 (94.6%) was infected through mother to child transmission, 4 (3.6%) through blood transfusion and the route of HIV transmission is unknown for 2

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(1.8%) patients. 106 from registered 111 HIV positive children was registered since implementation of HIV program in Georgia in 2005. HIV positive status of mother was detected before delivery for 6 (5.6%) child, from them 5 was register at the final week of pregnancy and one left the country. 60 (54%) child were registered at AIDS stage. 28 (25.2%) child died during first year after registration, 18 (64.3%) death was associated with AIDS related complications: meningitis, tuberculosis and pneumonia. 94 (84.6 %) of registered children were receiving ART. Currently 21 (19%) child grew up older than 15 years.
Conclusion: Most of HIV infections among children in Georgia are due to the missed opportunities to diagnose women during pregnancy, resulting in high rates of late presentation and mortality in children. Repeated HIV screening of pregnant women is warranted to prevent new pediatric infections.

PE29/17

HIV infection in older patients

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Purpose: Focusing the characteristics of people diagnosed whit HIV infection at an older age (over 50 years old)
Method: we performed an observational retrospective study including patients who had a new diagnosis of HIV infection attending Perugia Infectious Diseases Clinic; data refer to period from January 2008 to December 2018 and are derived from clinical records.
Results: among the 511 HIV+ patients visited at our centre during that period, we found 101 people that were >50 years old (19.7%). This percentage increased in the last years rising to 34.5% in 2018.
Demographic and clinical characteristics are reported in Table 1.
HIV diagnosis was late in the majority of patients (73.2%) and 35.6% were affected by AIDS-defining diseases at the time of diagnosis. In contrast, HIV general population who received diagnosis in the same period in Umbria showed AIDS-defining diseases in 23%.
Non-infective co-morbidities were present in 69.3% (Table 2). Most patients (71%) received other therapies apart from ART, and >5 drugs in 20%. The choice of ART, so, is fundamental to avoid drug interactions: 51.5% of our sample of patients received PIs as starting treatment but in the last 3 years the percentage fell down to 16.6% in favour of INIs (70%).
Conclusion: Our study shows the increasing number of people seroconverting HIV at an older age as the result of a lower perception of sexual risk in elderly people. This is the main way to acquire HIV among them and explains the frequency of STDs. Besides, the advanced stage of HIV infection at the time of diagnosis implies a slower immunological recovery. Moreover, the frailty typical of this population, due to multi-morbidity, is a predictor of care complexity and polypharmacy that rises risks of pharmacological interactions and increases the cost of clinical management.

Table 1

Age (years)	Mean value: 58.96 Range: 50-77
Sex (%)	89 (M) - 11 (F)
Nationality (%)	92.86 (Italians) - 7.14 (Foreigners)
Main transmission route (%)	52 (sexual risk factor)
Sexually transmitted diseases (STDs) n. (%)	Syphilis 26 (44.8) HPV infection 7 (12) Both 5 (8.6) HBV 24 (41.3) HCV 8 (13.8) Co-infection HBV HCV 2 (3.4)
CDC stage (%)	46.5 (A) - 13.7 (B) - 35.6 (C)
CD4 nadir (cells/mmc)	Mean value: 222.49 Range: 3-860
Antiretroviral therapy (ART) 2008-2018 (%); Antiretroviral therapy (ART) 2016-2018 (%)	Protease Inhibitors (PIs) 51.5 Integrase Inhibitors (INIs) 39.6; Protease Inhibitors (PIs) 16.6 Integrase Inhibitors (INIs) 70
CD4 count after 1 year of ART (cells/mmc); based on CDC stage A - B - C	Mean value: 404.07 Range: 65-1205; 225 - 302 - 121
Viral suppression after 1 year of ART (%)	79

Table 2. Non-infective co-morbidities (%)

Hypertriglyceridemia	52.5
Hypertension	22.2
Hypovitaminosis D or Osteopenia	22.2
Diabetes mellitus	19.2
Depression or cognitive impairment	13.8
Non-AIDS defining cancer	13.1
Cardiopathy	10.1
Renal failure	5

PE29/18

Seroincidence of the human herpesvirus 8 (HHV 8) infection among HIV-positive patients in Taiwan, 2016–2019

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Purpose: Because of shared transmission routes, HIV-positive patients are more likely to be infected with the human herpesvirus type 8 (HHV-8) than HIV-negative counterparts. In this study, we aimed to estimate the seroprevalence and incidence rate of HHV-8 infection among HIV-positive patients seeking care at a university hospital from 2016 to 2018.
Method: From 2016 to 2018, 627 HIV-positive patients were included who had archived blood samples for serial determinations of antibodies for HHV-8 with the use of the ELISA kit (Abbexa, UK).
Results: The overall HHV-8 seroprevalence was 5.7%, 2.7%, and 6.3% in 2016, 2017, and 2018, respectively. Patients testing seronegative for HHV-8 and those testing seropositive for HHV-8 had similar clinical characteristics in terms of age, sex, CD4 count (351 vs 381 cells/mm^3), HIV viral load (4.4 vs 4.2 $\log_{10}$), syphilis, HBsAg positivity (3.3% vs 8.3%), and anti-HCV positivity (0% vs 10.%). During the study period, 504 included patients had follow-up until April 2019 to estimate the incidence rate of seroconversion for HHV-8. In total, 41 patients acquired HHV-8 infection during a total duration of 782.3 person-years of follow-up (PYFU), giving an overall incidence rate of 5.24 per 100 PYFU. The rate was 1.16, 3.31, 7.56 and 5.50 per 100 PYFU from 2016 to 2019. In case-control study, 1 case patient with HHV-8 seroconversion was matched for 4 controls who had no HHV-8 seroconversion in terms of age, sex and the first date of seeking care. In multivariate logistic regression analysis, the only factor associated with HHV-8 seroconversion was baseline CD4 count >200 cells/mm^3 (AOR 2.98; 95% CI, 1.00, 8.85).
Conclusion: We found that the baseline HHV-8 seroprevalence among HIV-positive patients in Taiwan remained low; however, an increasing trend of HHV-8 infection has occurred during the follow-up, which appeared to be associated with a higher baseline CD4 count.

PE29/19

Risk factors for late presentation for HIV care in 2019 in Ukraine

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Purpose: The aim of the study was to assess factors associated with late presentation for HIV care among newly diagnosed people who live with HIV in 4 big cities (Kyiv, Odessa, Kherson, Mykolaiv) in Ukraine in 2017-2019.
Method: We analysed data from records of 208 newly diagnosed PLHIV in 4 Regional HIV Centres, located in big cities: Kyiv, Odessa, Kherson and Mykolaiv (Ukraine). Descriptive analysis was performed to assess the prevalence and characteristics of late presenters. Biological and behavioral factors that might increase the risk for late presentation for HIV care were analyzed. Multivariate analysis was used to assess the association of each factor with late diagnosis of HIV infection.
Results: The study included 208 patients (73 females and 135 males) aged from 20 to 77 years (mean age 44.9 years) with new diagnosis of HIV-infection. 65 (31.3%) acquired HIV by injection drug use, 114 (54.8%) by heterosexual and 20 (13.9%) by homosexual contact. 144 patients (69.2%) were late presenters with CD4 ≤350 cells/μL or AIDS-defining condition regardless of the CD4 cell count at time of diagnosis. In this group there were 90 (62.5%) males and 54 (37.5%) females. The median CD4 cell count in group of late presenters was 145.6 (IQR 1-332) cells/μl. We analyzed biological and

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behavioral factors that might increase the risk of being diagnosed late: gender (and pregnancy status in women), age, marital status, educational level, mode of transmission. The results are shown in Table 1.

Table 1. Risk factors for late presentation for HIV care in Ukraine

Factors	Study group, People who live with HIV (N=208)			
	Late presenters (N=144)	Non-late presenters (N=64)	χ2	p
Male gender, N (%)	90 (62.5%)	45 (70.3%)	1.187	p>0.05
Pregnancy, N (%)	4/54 (7.4%)	7/19 (36.8%)	9.515	p<0.05
Age ≥ 40 years, N (%)	78 (54.2%)	20 (31.3%)	9.339	p<0.05
Marital status: not married, N (%)	70 (48.6%)	25 (39.0%)	1.628	p>0.05
School level of education, N (%)	64 (44.4%)	22 (34.4%)	1.853	p>0.05
Transmission mode: IDU, N (%)	41 (28.5%)	24 (37.5%)	0.195	p>0.05
Transmission mode: heterosexual, N (%)	95 (66.0%)	28 (43.8%)	9.054	p<0.05
Transmission mode: MSM, N (%)	8 (5.6%)	12 (18.8%)	0.207	p<0.05

Increased risk of late presentation was seen in individuals aged older than 40 years, non-pregnant women, people who acquired HIV by heterosexual contact.

Conclusion: The following groups have been identified as groups of increased risk for late presentation for HIV care in Ukraine: individuals older than 40 years, non-pregnant women and individuals who acquired HIV by heterosexual contact.

PE29/20

Incidence of hepatitis C virus infection among people living with HIV (PLHIV): an Egyptian Cohort Study

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Purpose: Hepatitis C virus (HCV) infection is a major public health problem in Egypt with an estimated prevalence 11.9% among the general population. However,a little is known about the epidemiology of HCV among people living with HIV (PLHIV). Our aim was to determine the incidence of HCV infection among PLHIV in Egypt.

Method: Demographic data,self-reported injection drug use (IDU),history of risky sexual activities,HCV antibody (Ab) test results were collected from a total of 460 HIV-infected patients attending Imbaba Fever Hospital, Cairo, between January 2016 and March 2019. HCV testing was done by using fourth-generation HCV Ag-Ab enzyme-linked immunosorbent assay (ELISA). We determined incidence of HCV infection among HIV patients with a baseline negative HCV serology and at least 1 more HCV antibody test. The person-time incidence rate was calculated as the number of seroconversion events divided by person-time at risk . Multivariable regression analysis was used to identify the independent risk factors of HCV seroconversion.

Results: Out of 460 patients who were screened for HCV,146 (31.7%) had a positive HCV Ab result. A total of 218 patients had an initial negative HCV Ab test result and at least 1 subsequent HCV Ab test result,contributing >443 person-years. Eighteen (8.3%) seroconverted, with overall incidence of 4.06 cases per 100 person-years (95% CI:3.87-4.24). Mean age at seroconversion was 42 years,83% were males and 5.6% had history of risky sexual activities (p value 0.302).Seroconversion was associated with IDU (83.3% of seroconverters reported IDU history vs 47.2%% of nonseroconverters; p 0.005), whereas 16.7% of seroconverters reported no IDU (incidence 7.08 cases per 100 person-years among IDUs).

Conclusion: High incidence of HCV infections in the HIV-infected patients was mainly associated with IDU .This highlights the importance of annual HCV testing for HIV-infected patients especially higher-risk groups to allow for early HCV diagnosis and treatment .

PE29/21

High HIV prevalence following screening of subjects with HIV indicator conditions in a hospital setting

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Purpose: In Europe, approximately half of new HIV diagnoses are identified with CD4+ T-cell counts <350/uL. European recommendations suggest that subjects presenting with medical conditions associated with HIV prevalence >0.1% (HIV Indicator Conditions, HIV-ICs) should be tested for HIV. Aim of the present study is to verify the feasibility of offering HIV testing to individuals suffering from one or more HIV-ICs during hospital admittance.

Method: We organized a screening campaign to detect undiagnosed HIV infections in subjects presenting HIV-ICs admitted in hospital wards, from

HIV-Indicator Conditions (HIV-ICs)	Number of HIV-ICs screened in the total 492 patients on study (%)	Number of HIV-ICs in subjects tested HIV-positive (%)
Pregnancy	256 (52)	0 (0)
HBV Infection (acute/chronic)	56 (11.4)	2 (3.6)
HCV Infection (acute/chronic)	23 (4.7)	2 (8.7)
HAV Infection	22 (4.5)	0 (0)
Mononucleosis-like syndrome	45 (9.1)	3 (6.7)
M. tuberculosis infection (pulmonary and extrapulmonary)	20 (4.1)	0 (0)
Pneumonia (<50 years of age)	20 (3.9)	3 (10.5)
Recurring pneumonia (> 2 episodes in12 months)	3 (0.6)	0 (0)
Syphilis	23 (4.7)	2 (8.7)
Gonorrhea	6 (1.2)	1 (16.7)
Esophageal Candidosis	2 (0.4)	0 (0)
Herpes zoster (<60 years of age)	3 (0.6)	1 (33)
Dementia (<60 years of age)	4 (0.8)	1 (25)
Cerebral Lesions	2 (0.4)	0 (0)
Hodgkin's Lymphoma	2 (0.4)	0 (0)
Non-Hodgkin's Lymphoma	5 (1)	0 (0)
Total	**492 (100)**	**14/492 (2.8)**

Table 1. Study population according to HIV-indicator conditions

Patient	Age	Sex	Nationality	HIV Indicator Conditions at HIV Screening	Risk Factor for HIV	CD4 cells/uL	CD4%
1	32	F	Nigeria	Pneumonia (<50 years of age)	heterosexual	176	9
2	47	M	Italy	Pneumonia (<50 years of age, diagnosed as PJP)	heterosexual	1	5
3	23	M	Morocco	Pneumonia (<50 years of age); HBV and HCV infection	Intravenous drug use	1100	25
4	45	F	Ethiopia	Dementia (<60 years of age)	heterosexual	31	5
5	40	M	Italy	Gonorrhoea; Syphilis	unknown	unknown	unknown
6	36	M	Perù	Mononucleosis-like syndrome (diagnosed as acute HIV infection)	homosexual	119	5
7	42	M	Italy	HBV infection	Intravenous drug use	21	8
8	54	F	Italy	Herpes zoster (<60 years of age)	heterosexual	224	20
9	34	F	Italy	Mononucleosis-like syndrome	heterosexual	27	8
10	42	M	Italy	Mononucleosis-like syndrome	undisclosed	117	16

Table 2. Details of the 10 patients diagnosed with HIV during hospital stay for HIV indicator Condi

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January 2019 to June 2019. All patients provided informed consent for the collection of demographic and clinical data.
Results: 462 subjects suffering from a total of 492 HIV-ICs were tested (Table 1). The most frequently screened HIV-IC was pregnancy (Table 1). 435/462 (94%) presented with 1 HIV-IC, 24/462 (5.2%) presented with 2, and 3/462 (0.6%) with 3. 155 subjects (33.5%) were males, with median age of 33 (27-43) years. The majority (307, 66.5%) were Caucasian, with 272 (58.9%) Italians.
10 patients were diagnosed with HIV (Table 2). Overall HIV prevalence in our hospital setting was 2.2%; excluding pregnancies, HIV prevalence was 4.9%. Among the 10 HIV+ patients, 6 were Italian, 3 African and one was Latin American. Median age was 41 (34-46) years. Median CD4 T-cell absolute count and percentage were 117(24-200)/uL, and 8% (5-18) respectively. One patient (#3) died during hospital stay because of severe clinical complications despite minimal immunological impairment.
Conclusion: Prevalence of HIV infection in a hospital setting was relatively high, supporting the implementation of HIV-ICs screening. Most subjects presented with low CD4+ T-cell counts and 30% with AIDS-defining events, suggesting that this strategy may not serve as a useful tool for implementation of early HIV diagnosis. Nevertheless, opt-out strategy at least in case of several conditions might favour HIV diagnosis.

PE29/22

First decrease in new HIV diagnoses in 2018 among men who have sex with men (MSM), in the East PACA (Provence Alpes Côte-d'Azur) area in France

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Purpose: The objective of the study is to describe the trend of the number of new HIV diagnoses among patients attending HIV clinical centers between 2016 and 2018 in the East PACA area, a territory characterized by one of the highest HIV prevalence among MSM in France.
Method: We collected data from clinical centers using a common electronic medical record for the follow-up of HIV infected adults and patients on Pre-Exposure Prophylaxis (PrEP). This database covers 80 % of people living with HIV (PLHIV), and more than 90 % of patients followed on PrEP. Clinical and biological data are collected in real time since 2009. Those data, confirmed by the French healthcare system, were used to produce robust epidemiological indicators of follow-up. Sexual behavior was also available and allowed to decline indicators by group risks.
Results: The number of new HIV diagnoses decreased from 91 to 60 over 2016-2018 period, accounting for a difference of 34 %. MSM are the most concerned with a decline of 49 %. In parallel, the percentage of controlled patients remains stable over 95 % since 2014 and the number of patients using Prep has tripled since 2016, increasing from 207 to 586 in 2018.
Conclusion: In accordance with our "*getting to Zero" project*, the prevention against HIV improved in the East PACA area since 2016, through an active implementation of the PrEP and the use of treatment as prevention based on an excellent virological control among PLHIV followed and treated. This synergy could explain the strong decrease of new HIV diagnoses, reaching its lowest point in 10 years, especially among MSM. Although the number of mandatory reporting is high declared (87 % in 2018), these observations will have to be confirmed by the French National Agency of Public Health data's.

PE29/23

The collision of public health interventions on HIV-1 spread in Albania by molecular epidemiology

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Purpose: The assessment of sequential alterations in human immunodeficiency virus (HIV) diffusion models can assist in illuminating the collision of preventive policies and public health guidelines.
Methods: Albanian HIV-1 subtype B and G pol genetic series were attached to worldwide reference data sets to recognize country-detailed communication clades. Bayesian birth-death patterns were applied to approximate subtype-detailed efficient reproductive numbers (Re). Discrete trait analysis (DTA) was applied to measure combination between transmission clusters.
Results: We acknowledged 4 subtype B Albanian clades (23-76 sequences) and a huge monophyletic subtype G Albanian clade (225 sequences). We projected that major shifts in HIV-1 transmission took place red around 2000 (95% Bayesian credible interval [BCI], 1998-2000) and 2001 (95% BCI, 1998-2001) for subtypes B and G, correspondingly. For subtype B, Re fell from 1.89 (95% BCI, 1.68-2.05) to 0.58 (95% BCI,.52-.72).
Conclusions: The predictable rejections in Re match with the foreword of highly active antiretroviral therapy and the increase of harm reduction for PWID. Contingent transmission occurrences across diffusion groups highlight the significance of prevention attempts for connected populations.

PE29/24

Two decades of HIV infection late diagnosis: the experience of a Portuguese Hospital

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Purpose: Evaluate late HIV diagnosis evolution in the last two decades considering two cut-off points: 200 and 350 CD4+ T-cells/μl. Compare demographic, epidemiological data, AIDS defining illnesses and mortality.
Method: Retrospective study of a cohort of HIV-infected patients diagnosed between 1998 and 2018 and followed at the HIV clinic. Excel® was used for statistical analysis.
Results: The total number of new HIV diagnosis from 1998 to 2018 was 1114; 55% (N=616) were late presenters and, from these, 81 were excluded due to lack of data. From the final 535 patients, 65% presented with less than 200 (group A) and 35% with 200-350 CD4+ T-cells/μl (group B). Demographic and epidemiological characterization revealed (A vs B): male predominance 80% vs 68%; age at diagnosis less than 50 years 66% vs 77%; heterosexual transmission 55% vs 53%. At presentation, 45% of patients with less than 200 CD4+ T-cells/μl had an AIDS defining illness - most common was tuberculosis. From 2009 to 2013, the percentage of patients presenting as very late presenters (<200 CD4+ T-cells/μl) was 37% and from 2014 to 2018 this decreased to 27%.Analysis of mortality showed a death rate of 29% in group A versus 19% in group B with a shorter average number of days from HIV diagnosis to death in group A (2208 vs 2939).
Conclusion: This study evidenced a high rate of late presenters in our setting. The percentage of very late presenters was high which still has serious implications for individual prognosis and for HIV transmission. Increased testing is necessary to improve HIV care and is important to eliminate missed opportunities for screening and diagnosis in health care settings especially among high-risk groups.

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PE29/25

Characterization of HIV patients followed in a specialist consultation at a tertiary and universitary centre

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Background: In 2014, UNAIDS launched the 90-90-90 targets; the aim was to diagnose 90% of all HIV-positive persons, provide antiretroviral therapy (ART) for 90% of those diagnosed, and achieve viral suppression for 90% of those treated by 2020.
Aim: To describe and characterize the current cohort of HIV patients followed in our tertiary and university hospital centre.
Methods: An observational longitudinal cohort study of HIV patients, between 2013 and 2019. We reviewed clinical records of 3634 patients.
Results: Of 3634 patients, 367 were lost to follow-up, 268 died, 83 were transferred to other hospitals and 38 emigrated. 2920 HIV patients are currently being followed at our hospital.
Of these, the majority are men (73.9%), the mean age being 48 years (8-90 years), with about a quarter of patients (25.9%) older than 55 years. The average duration of the disease is less than 5 years in 17.1%, 6-10 years in 18%, 11-20 years in 47.2% and more than 20 years in 17.8%. The main risk of transmission was heterosexual (43%), followed by MSM (21.8%), use of intravenous drugs (32.1%) and non-drug-related blood transmission (hemophiliacs, transfusions, mother-to-child) in 2.1%.
Regarding virological control, 81% have recent undetectable viral load (VL<20 copies of RNA/mL), 90.3% are suppressed (VL<50 copies RNA/mL) and only 5.4% had VL> 200 copies of RNA/mL. Only 65 patients (2.2%) are not currently on antiretrovirals. Regarding imunological control, the mean CD4+ cell count is 692 cells/mcL. Only 136 patients (4.6%) have CD4+ cell counts <200.
Conclusion: Our hospital, as well as our country, already fulfills the objectives of the 90-90-90 campaign. The highest risk of transmission is sexual, which has been growing. We have a high percentage of adherence to treatment, and more than 60% of patients have more than 10 years of disease, with good immune and virological status.

Table 1

	Virological control		
Duration of disease	VL<20 copies RNA/mL	VL<50 copies RNA/mL	VL> 200 copies RNA/mL
<5 years	79.8%	89.1%	6.1%
6-10 years	79.6%	89.5%	5.5%
11-20 years	80.6%	90.6%	5.4%
> 20 years	84.0%	91.2%	4.8%

PE29/26

Trends in epidemiology and clinical picture of late presentation among patients of the Hospital for Infectious Diseases in Warsaw

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The analysis was carried out on patients of the Hospital for Infectious Diseases in Warsaw, who were diagnosed with HIV infection from 2008-2010 and from 2016-2018.
The number of new diagnoses of HIV infection from 2008-2010 was 758, and from 2016-2018 was 953 people. In the years 2008-2010 324 patients (42.7%) were classified as LPs, 186 patients (24.5%) with advanced disease. In the years 2016-2018 the number of new diagnoses increased to 953 people, but the proportions remained comparable - 426 LPs (44.7%), 211 cases of advanced disease (22.1%).
There was a significantly higher number of men than women - in 2008-2010 676 were men (89.9%) and 82 were women (10.8%). From 2016-2018 there were 866 men (90.9%) and 87 women (9.1%).
The dominant route of infection in both periods was homosexual contact - from 2008-2010 56.2% of new diagnoses, compared to 69.8% from 2016-2018. In the second place was heterosexual contact - 18.2% and 17.2% respectively, and the third was intravenous drug use. In this case, there was a significant drop in 10 years - 9.3% respectively in the first period and 3.1% in later years. The highest percentage of late presentation was found among heterosexual men - 56% from 2008-2010, increasing to 64% from 2016-2018.
AIDS defining events were diagnosed among 55 patients from 2008-2010 and among 61 patients from 2016-2018. The median CD4 + cell count was 69 cells/μl and 100.5 cells/μl, respectively. Tuberculosis was the most frequent AIDS defining event from 2008-2010, followed by pneumocystis pneumonia and wasting syndrome. From 2016-2018 pneumocystis pneumonia became the most frequent AIDS defining event, followed by tuberculosis and Kaposi's sarcoma.
From 2008-2010, 33.8% of patients received treatment in 3 months after diagnosis compared to 89.4% in later periods. Non-treated patients accounted for 13.3% and 7.5% respectively.

PE29/27

An evolutionary insight into a growing HIV subtype A epidemic in Serbia

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Purpose: HIV epidemic in Serbia is marked by predominance of subtype B with prevalence of non B subtypes found in less than 10%. According to the recent report encompassing samples from 1997 to 2015 among non B subtypes, subtype G and subtype C were found to be the most prevalent one. However, in the latest period the number of subtype A has been significantly increased. Therefore, we performed in depth phylodynamic analysis on a growing subtype A subepidemic, in particular time scale evolutionary, demographic and transmission dynamic analysis.
Method: The dataset comprised of 17 subtype A HIV sequences collected from 2010 to 2018. Phylogenetic analyses were performed as follows: estimations of evolutionary and demographic parameters were performed employing different Bayesian approaches encompassing selection for site model, demographic model, clock model and model of viral transmission, prior to run MCMC chains.
Results: The time of the origin for subtype A subepidemic was estimated 14 years ago (2004; HPD 2001-2007). Obtained results suggest that subtype A subepidemic started 10 years after other non B epidemics and 20 years after the first introduction of HIV subtype B in Serbia. A Bayesian Skyline plot analyses showed initial stationary phase followed by exponential growth started from 2013. The estimated birth-death skyline plot showed initial decreasing value of Re in the period of 6 years followed by sharp increasing trend from 2011 reaching maximum value of 2.4.
Conclusion: The transmission dynamic analysis showed that subtype A subepidemic is in expansion, with high tendency for further growth. The complexity of the Serbian HIV-1 epidemic has been increasing during recent years, reflected in increasing prevalence of non B subtypes, linked to migration and later dispersal through local transmission networks. This result is concordant with reports derived from Balkan as well as West European countries.

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PE29/28

Change of prevalence, diseases distribution and factors associated with the risk of AIDS presentation in Italy over last decade (2009-2018)

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Purpose: Despite universal recommendations about early ART initiation, a consistent proportion of newly diagnosed HIV people continue to be diagnosed late. Prevalence and factors associated with the risk of AIDS presentation over the last decade in people seen for care at the main infectious disease clinical sites in Italy were investigated.

Method: All consecutive chronic, ART-naïve individuals in the Icona Foundation Study cohort firstly HIV diagnosed from January 2009 to December 2018 over three months preceding their enrolment were divided in: a) Patients with AIDS defining event (AIDSP); b) Asymptomatic Patients (ASP). Chi-square and Mann-Whitney test were used for comparisons and multivariable logistic regression to identify factors associated with the risk of AIDS presentation.

Results: 7,001 naïve individuals analyzed, 959 AIDSP (13.7%) and 6,042 ASP (86.3%). The main characteristics are reported in Table 1. Prevalence of AIDSP was 16.4% in 2009-2010, 14.7% in 2011-2012, 13.4% in 2013-2014, 13.8% in 2015-2016 and 11.8% in 2017-2018 (chi-square for trend=0.003). From fitting a multivariable logistic regression, older age, heterosexual and IDU transmission (compared to MSM), not-Italian origin, HBV coinfection, baseline HIV-RNA >100.000 copies/mL and having occasional jobs were all associated with a higher risk of AIDSP. More recent calendar years were associated with a

Table 1. Main characteristics of 7,001 HIV-infected naïve patients enrolled (AIDS presenters and asymptomatic).

	AIDS presenters	Asymptomatic	
	n = 959	n = 6,042	P - value
	13.7%	86.3%	
Female gender, N (%)	246 (25.6%)	1113 (18.4%)	<0.001
Age, Yrs, median (IQR)	44 (36 - 53)	38 (30 - 47)	<0.001
Nationality, N (%)			
Italian	561 (58.5%)	4599 (76.1%)	<0.001
Not Italian	255 (26.6%)	1443 (23.9%)	
Days from first HIV test to enrollment, median (IQR)	9 (3-20)	15 (5-32)	< 0.001
Mode of HIV transmission			
MSM	272 (28.4%)	2323 (38.5%)	
Heterosexual	532 (55.5%)	2989 (49.5%)	< 0.001
IVDU	45 (4.7%)	269 (4.5%)	
Other/Unknown	110 (11.5%)	461 (7.6%)	
HCV coinfection			
Positive	46 (4.8%)	313 (5.2%)	<0.001
Negative	732 (76.3%)	4940 (81.8%)	
HBV coinfection			
Positive	59 (6.2%)	214 (3.5%)	<0.001
Negative	729 (76.0%)	4929 (81.6%)	
CD4 at enrollment, median (IQR)	42 (19 - 115)	359 (193 - 544)	< 0.001
HIV-RNA, copies/mL			
< 100.000 copies/mL	220 (22.9%)	3496 (57.9%)	< 0.001
> 100.000 copies/mL	632 (65.9%)	2204 (36.5%)	
eGFR, median (IQR)	96 (75-113)	91 (75 - 109)	0.001
# of comorbidities			
0	776 (80.9%)	5380 (89.0%)	< 0.001
1	151 (15.7%)	519 (8.6%)	
2	26 (2.7%)	118 (2.0%)	
≥3	6 (0.6%)	21 (0.4%)	
Employment status			
Unemployed	143 (14.9%)	781 (12.9%)	<0.001
Employed	325 (33.9%)	2217 (36.7%)	
Self Employed	110 (11.5%)	751 (12.4%)	
Occasional	47 (4.9%)	168 (2.8%)	
Student	9 (0.9%)	252 (4.2%)	
Retired	45 (4.7%)	154 (2.6%)	
Housewife	33 (3.4%)	91 (1.5%)	
Other	38 (3.9%)	200 (3.3%)	
Level of education			
Primary education	83 (8.7%)	263 (4.4%)	< 0.001
Middle school	180 (18.8%)	847 (14.0%)	
High school/University	333 (34.7%)	2615 (43.3%)	

Table 1

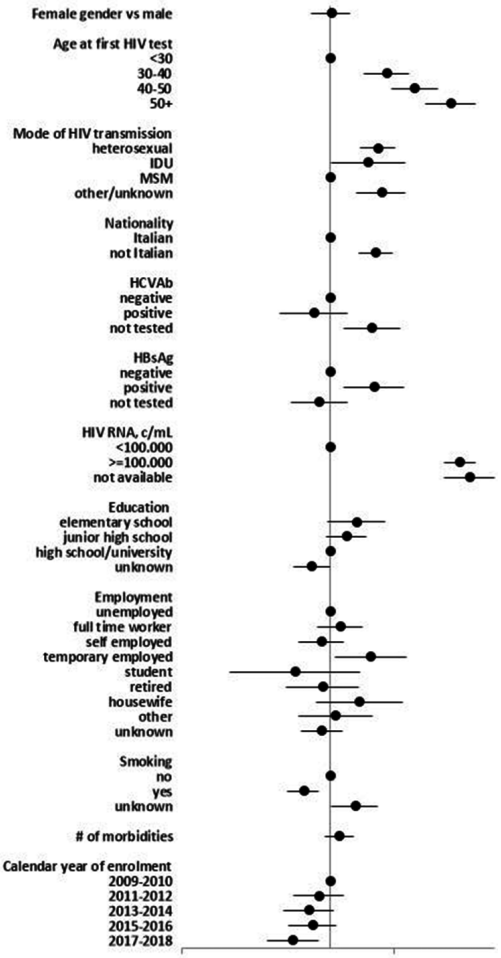


Figure 1. Factors associated to an AIDS defining event at HIV diagnosis (AIDS presenter) by fitting a multivariable logistic regression model.

Figure 1

Table 2. Prevalence and temporal trends for main opportunistic infections (OIs) and AIDS-related cancers at AIDS presentation

OIs and AIDS-related cancers	Overall N	Overall %	2009-10	2011-12	2013-14	2015-16	2017-18	Chi-Square for trend p-value
Pneumocystis pneumonia	315	32.9%	24.8%	31.8%	35.8%	34.7%	33.2%	0.16
Kaposi's sarcoma	126	13.1%	11.5%	13.1%	14.4%	12.3%	14.0%	0.73
Esophageal candidiasis	149	15.5%	20.3%	14.7%	14.4%	13.4%	17.6%	0.65
Tuberculosis	108	11.3%	12.4%	12.6%	10.2%	11.9%	9.3%	0.39
Cytomegalovirus disease	139	14.5%	16.8%	11.6%	19.3%	14.6%	11.4%	0.43
Toxoplasma encephalitis	78	8.1%	5.3%	9.1%	5.4%	11.2%	7.3%	0.40
Non-Hodgking's lymphomas	62	6.5%	7.1%	7.6%	6.4%	5.2%	6.7%	0.56
Wasting Syndrome	71	7.4%	10.6%	9.6%	9.1%	5.6%	4.2%	0.006
Non-tuberculous mycobacteriosis	29	3.0%	3.5%	3.0%	2.7%	3.4%	2.6%	0.78

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lower risk (Fig. 1). Not significant trends over time were observed for main opportunistic diseases (Table 2).
Conclusion: AIDS presentation still occurs in approximately 14% of newly HIV diagnosed individuals in Italy in the last decade, even with a slight reduction in the last years. Older age, heterosexual route, non-Italian origin and occasional employment seems to identify a socio-demographic profile of HIV people who presents for care very late. No difference of prevalence over time for main opportunistic disorders was observed. These are key data for planning focused interventions to discover unknown long-lasting infections.

PE29/29

The effect of gender on late diagnosis of HIV infection in a high incidence European population

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Purpose: HIV burden in Portugal remains one of the highest on western Europe and late presentation is a major concern. The identification of key population characteristics is an essential step to design preventive and clinical effective response. We hypothesised that gender might flag different risk clustering.
Method: HIV infected patients admitted from January/2008 to December/2017 to a tertiary-care hospital were retrospectively evaluated regarding characteristics at diagnosis. After excluding 47 cases with previously known HIV positive status, 923 patients remained for analysis. Gender specific trends and independent determinants of late presentation of HIV infection, defined as CD4 cell count at diagnosis <200/mm^3, was evaluated using logistic regression.
Results: The proportion of male patients with CD4 cell count <200/mm^3 at HIV diagnosis was 37.2%, and in female patients was 37.7%. There was a significant (p=0.009) trend in late presentation over years with lower levels in 2012-2015, particularly in man (2008-09: 47.7%; 2012-14: 28.1% and 2016-17: 43.1%, p=0.002). In a multivariate logistic regression model, adjusting for the diagnosis year, late presentation in male patients was positively associated with age (OR=5.7; 95% CI: 2.8-11.8, for those >60 years old compared with <30 years old) and being MSM was a protective factor (OR=0.5; 95% CI: 0.3-0.7). For female patients, older age (OR=4.3; 95% CI: 1.3-14.3, for those >60 years old compared with <30 years old) and being migrant (OR=3.7; 95% CI: 1.5-8.9) increased the risk of late presentation.
Conclusion: We found different factors associated with late HIV diagnosis in men and women and older heterosexual men and migrant women were identified as target populations for interventions to overcome late HIV diagnosis.

PE29/30

Two decades surveillance of HIV-1 transmitted drug resistance in Serbia

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Background: HIV-1 transmitted drug resistance (TDR) in antiretroviral-naïve individuals has a potential to jeopardize the clinical benefits associated with antiretroviral therapy (ART) and increase the risk of virological failure.
Methods: The studied data set included 377 sequences from therapy naïve patients generated from 1997 to 2018. The Stanford Calibrated Population Resistance program v6.0 was used to determine the presence of TDR mutations.
Results: The overall prevalence of SDRM was 8.8% (33/377). The most commonly identified SDRMs were M46I 2.1% (8/377) and K103N 2.1% (8/377), followed by M184V 1.3% (5/377) and L74V 0.8% (3/377). Regarding other mutations, E138A was found with the highest prevalence of 4.2% (16/377). Furthermore, while the prevalence of SDRMs in the two analyzed time periods with the comparable number of sequences (1997 to 2011 vs 2012 to 2018) was similar (8.6% vs 7.7%), the differences in the mutation patterns were significant (K103N 3.5% (7/197) vs. 0.5% (1/181); M46I 1.5% (3/197) vs 2.7% (5/181)). The frequency of mutation E138A was also different in two studied periods; 1.6% (3/181) vs 3.5% (13/377). Moreover, in the first period multiclass HIV drug resistance was predominate compared to second period in which singleclass HIV drug resistance was much more frequent.
Conclusion: Transmitted HIV drug resistance was found in around 9% of newly diagnosed patients in Serbia in twenty years studied period (1997-2018), similar to the European average. We showed a changing pattern of TDR, with different frequency of detected mutations over the two studied periods (1997 to 2011 vs. 2012 to 2018). Ongoing surveillance of SDRM is clearly needed to better understand the possible role that such mutations could play in undermining first-line treatment.

PE29/31

3M-BRiHT – Manchester Cohort. Investigation of the feasibility and acceptability of rapid HIV testing in a European Emergency Department setting

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Purpose: To investigate the feasibility of establishing unselected, rapid HIV testing with pre and post-test video counselling in 2 Manchester emergency departments (EDs).
Method: This was a prospective, randomised study of ED attendees. Rapid HIV testing and video counselling were performed, with participants randomised to a choice of 4 ethnically diverse counsellors, or a single, pre-assigned counsellor. Data were collected on HIV acquisition risks during post-test counselling. Analysis was by Chi-square tests, Mann Whitney U and logistic regression.
Results: Of 1,942 participants in the study, 81.6% (n=1584) consented to HIV testing. 46.8% were female, 53.2% were male. Median age was 41 years (IQR=24). 91.2% (n=1,771) of patients were Caucasian, 55% (n=1069) attended a GP at least once a year.
49.2% reported either never or almost never using condoms, 2.9% described >5 sexual partners in the last 12 months, and 10.7% reported a previous sexually transmitted infection. 1.65% of the population self-reported as men who have sex with men and 1.4% had previously injected drugs. 48.5% had never previously been tested for HIV, with only 0.7% testing regularly.
There were no significant differences in uptake between randomised groups (82.5% in the choice arm, vs 80.5% in the no-choice arm p<0.259). Those consenting to HIV testing were younger (median age of 39 [IQR 29 to 52] vs 50 [IQR=34 to 63]; p<0.0001), and more likely to be male (84.72% of men, 77.97% of women, p<0.0001).
Conclusion: Significant risk profiles and low rates of previous testing emphasise the role ED screening can play in reducing the burden of undiagnosed HIV, within the Manchester region.

PE29/32

HIV-1 A6 subtype: its challenging identification and Southern Russian molecular epidemiology

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In Russia and other former soviet countries, the HIV-1 "Russian A1" subtype, also referred to as "IDU-A" or "A-FSU" and now renamed as A6, is the most prevalent subtype, though robust epidemiological data are still missing.
We analyzed samples and epidemiological data from 303 patients taking care in Southern Russia. Protease/reverse transcriptase and integrase sequences

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were used for subtyping and drug susceptibility analysis. We performed phylogenetic analysis of these and A6 sequences retrieved from Los Alamos database for identification of A6 samples. Moreover, we generated an A6 consensus sequence for the *pol* region which can be used as reference for systematic identification of A6 samples in future studies.
We also performed molecular epidemiology analysis of the Southern Russian samples addressing subtype prevalence, transmission routes and presence of antiretroviral resistance-associated-mutations. Our results confirm the different characteristics of the Russian HIV-1 scenario compared to Western Europe: high prevalence of subtypes A6 (69%) and G (23%) (the latter is a special characteristic of South Russia), and the importance of drug consume (32%) and heterosexual contact (27%) for HIV-1 transmission.
Overall PI- (12.2%), NRTI- (29.2%), NNRTI- (20.2%) and INI- (3.3%) resistance was detected, with 17% of the patients displaying intermediate to high resistance to two- or three-drug-classes. NRTI- (6.4%) and PI- (8.2%) transmitted resistance was detected in therapy-naïve patients. Finally, we identified two specific resistance-associated-mutations significantly associated to A6 samples.
Conclusion: HIV Epidemiology in South Russia ist different to that in Western Europe Different routes of transmission dominate, namely heterosexual contacts, drug abuse, prostitution. The subtype distribution is dominated by A6 and in South Russia a larger cohort of subtype G occurs.

PE29/33

Neurodevelopmental assessments to screen for HIV encephalopathy in newly diagnosed infants not on ART in Mozambique

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Purpose: To evaluate neurodevelopmental signs of HIV Encephalopathy (HIVE) in HIV-infected, ART naive infants less than 12 months and determine clinical variables associated with HIVE
Method: This study is a retrospective review evaluating hospitalization data from Hospital Central de Maputo (HCM) and Hospital Central de Beira (HCB) in Mozambique. Criteria for inclusion: a) HIV-infected children aged <12 months; and b) who are not currently on ART; and c) seen between Jan 1, 2019 through June 30, 2019. Assessments of development were made using WHO Integrated Management of Childhood Illness (IMCI). All statistical analyses were performed in Excel and SPSS®.
Results: A total of 31 HIV+, ART naïve infants under 12 months were included in this study. Of the 31 patients, 3 patients were excluded from analyses due to primary neurological diagnoses. 8 out of 28 patients (28.5%) were diagnosed with presumptive HIVE. No significant differences were found in demographic variables such as sex, age, gestational age, or prior hospitalization. Maternal ART and post-natal prophylaxis were significantly associated with HIVE (p=0.03; p=0.02). Delayed milestones were observed in 67% of infants and hyperreflexia in upper or lower extremity was seen in 16%. HIVE (+) infants were, on average, delayed in 2.88 categories vs 1.15 in the HIVE (-) group. Number of unmet developmental milestones in fine motor (p=0.006), speech and language (p=0.01), and social and adaptive (p=0.023) milestone categories was significantly associated with HIVE.
Conclusion: HIVE prevalence is high in newly diagnosed infants (28.5%), particularly in those with risk factors for in-utero transmission. This highlights the need for comprehensive care that includes PMTCT, ART, and physical/occupational therapy for HIVE infants.

Prevention of horizontal transmission, cART as prevention

PE30/1

Tolerability and treatment completion of tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV) as HIV postexposure prophylaxis

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Purpose: HIV post-exposure prophylaxis (PEP) guidelines differ from one country to another; most guidelines recommend regimens favouring tolerability and adherence, such as single-tablet regimens. French guidelines recommend TDF/FTC RPV since October 2016.
Method: Prospective, observational, multicentre, open-label, non-randomized study, to evaluate treatment completion, tolerability, and efficacy of single-tablet TAF/FTC/RPV as PEP in six French HIV centres. Adults requiring PEP according to French guidelines (high risk exposure) were prescribed TAF/FTC/RPV one pill qd. TAF/FTC/RPV was either started at D1 or after a maximum of 5 days of another PEP regimen when a starter kit had been initiated in emergency room (total PEP duration was 28 days). Participants were contacted by phone at week (W) 6 to collect adherence, treatment completion and adverse events (AEs). Blood samples were prescribed at W2, 6 and 12.

Table 1. Participants' characteristics

			Sexual N=163	
	Total N=173	Occupational N=10	Heterosexual N=83	MSM N=80
Men, n (%)	127 (73.4)	4 (40)	43 (52)	80 (100)
Mean age (years, ± SD)	34.9 (11.4)	29.5 (5.2)	32.2 (10.2)	38.3 (12.3)
Born in France	141 (81.5)	8 (80)	61 (73.5)	72 (90)
Currently working, n (%) (n=144)	105 (72)	9 (90)	50 (69)	46 (73)
HBV protected*, n (%) (n=143)	88 (62)	-	-	-
History of syphilis, n (%) (n=163)	6 (3.7)	-	1 (1.2)	5 (6.3)
Positive N. gonorrhoeae PCR ≥ 1 site (n=103)	-	-	1 (2)	2 (3.8)
Positive chlamydia PCR ≥ 1 site (n=117)	-	-	2 (3.5)	4 (6.7)

Table 2. Exposure risk

			Sexual N =163	
	Total N = 173	Occupational N = 10	Heterosexual N = 83	MSM N = 80
Known HIV+ source person, n (%)	9 (5.2)	2 (20)	5 (6)	2 (2.5)
Condomless exposure, n (%) (n=159)	-	-	36 (45)	58 (73)
Sexual assault, n (%) (n=161)	-	-	21 (25)	4 (5)

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Results: Between March 2018 and March 2019, 173 participants were included. Table 1 presents subjects' characteristics and table 2 circumstances of exposure.
At W6, 21 (12.1%) participants were lost to follow-up and 17 had prematurely discontinued treatment: 10 because the source person was found to be HIV negative, 5 (3.5% of participants with confirmed indication to PEP) for AE (gastro-intestinal intolerance, n=2 at D27 and D10, fatigue, n=1 at D2, headache, n=1 at D2, cutaneous signs, n=1 at D2), and 2 for patient's decision. 88 participants (57.9%) reported at least one AE (no serious AE). Most frequent AEs were gastro-intestinal intolerance (44.6%), amongst them abdominal pain (16.7%), diarrhoea (11.9%) and nausea (9.5%); fatigue (16%); insomnia (8.9%) and headache (5.4%). No biological toxicity occurred. All 82 participants with results at W12 had a negative HIV test (100%).
Conclusion: In this first study evaluating TAF/FTC/RPV as HIV PEP, tolerability was good, with few premature cessation for AE, suggesting TAF/FTC/RPV could be a good alternative option as once-daily PEP.

Social and behavioural science

PE30/2

Priorities for behavioral interventions in a group of long term PLWHA – the experience of the Baylor Clinical Centre of Excellence in Constanta, Romania

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Purpose: Quick identification of key psychological determinants that can affect the health outcomes of PLWHA can help health psychologists and other professionals to better target their interventions in a busy clinical setting. We aimed to identify the main intervention priorities that can lead to empowering patients maintain and improve the management of their disease.
Methods: Baylor Clinic offers behavioral health interventions to approximately 1000 PLWHA. We selected the Capability-Opportunity-Motivation-Behavior theory developed by Michie et al (2011) and created a questionnaire focused on determinants of health and key health outcomes, such as adherence and quality of life. As part of usual care, 560 PLWHA were evaluated, the mean duration since their HIV diagnosis was 19.39 years, 49% were females and the mean age was 34 years old.
Results: The main determinants with low scores where interventions might be prioritized concern: medical independence (76% had low scores), behavior regulation (69%), memory and decision skills (42%) and cognitive skills (37%). Determinants regarding physical skills (4%) and social opportunity (17%) had the best scores in this sample. Medium scores were obtained for motivation (28%), treatment acceptance (28%) and knowledge (25%). In terms of outcomes, 61% report good quality of life and 79% good adherence to ARVs.
Conclusion: Our findings show that, although most patients report acceptable outcomes in terms of quality of life and adherence, the PLWHA in the care of our clinic still need support form healthcare professionals in ensuring management of their disease long term. Interventions should prioritize medical independence skill building, alongside teaching patients techniques to organize, both behaviorally and mentally, their life routines around management of their disease, including comorbidities.
While newer cases need more information and interventions focused on disclosure and acceptance of treatment, longer term care needs to empower patients in the management of their chronic disease.

PE30/3

Will HIV-infected patients taking oral ARV switch to long-acting injectable ART when It become available?

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Purpose: Cabotegravir and rilpivirine are currently being studied for use as injectable LAI (long-acting injectable) ART. We investigated awareness of, *feeling* and preference for using LAI- ART among PVVIH currently taking oral ART.
Method: A cross-sectional monocentric study recruited patients from an adult HIV clinic with experience of LAI-ART. Two outcomes were measured 1) awareness of long-acting injectable ART 2) preference for route of administration of ARV. Reasons for preference, and feeling of "stay without oral therapy" were investigated in the last half of the patients surveyed.
Results: Participants included 304 patients, of whom 71% identified as patients of color, 46% received a QD STR.
About 40% of patients had heard of LAI-ARV. Over 64% of participants stated they would be willing to use LAI-ART (injections once a month) and 76% (injections once every two months). None of the variables, age, sex, race, duration of HIV infection, duration of ART, receiving STR, was associated with preference for the injectable route.
Of the 152 patients who responded to the semi-quantitative survey, reasons for preference included most of the time « convenience » (112/152), and « afraid to forget my treatment » (58/152).
To the question about "feeling of stay without daily oral therapy", many patients talked about joy, happiness, pleasure (27/120) and relief (21/120). Moreover, 23 patients talked about "feeling not to be sick", "forget the disease", "as if I am as everybody". Eleven patients more talked about healing.
Conclusion: In this study most of participants expressed willingness to use LAI, 64% (injections monthly) and 76% (injections every two months).
Some patients evoke a feeling of healing that possibly may impact treatment adherence. Even if providers have to listen the strong willingness of their patients to reveived LAI-ART, the observance of this delivery method will have to be carefully monitored.

PE30/4

Time perspectives as predictors of depression and suicidal ideation amongst adolescents and young adults with HIV: the moderating role of resilience

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Purpose: Depression and suicidal ideation are common mental health disorders among HIV positive patients. This study investigated the influence of Time perspectives on depression and suicidal ideation in HIV patients,and the moderating role of resilience
Method: An expo-facto research design and purposive sampling technique was adopted for this study.102 participants (ages 10–36) were sampled for the study. Structured questionnaires were administered and the data was subsequently analyzed at 0.05level of significance. Four hypotheses were tested using multiple regression, and hierarchical multiple regression.
Results: Findings revealed that time perspective had a significant joint influence on depression (R^2= 0.35; (6, 81) = 7.36, $p \leq 0.001$), jointly accounting for 35% variance; present fatalistic contributed the best, followed by Past negative, and future positive. The result further revealed that past positive, past negative, present fatalistic, past hedonistic, future positive, future negative jointly predict suicidal ideation (R^2= 0.19; (6,86)= 7.36, $p \leq 0.01$), jointly accounting for 35% variance; Present hedonistic contributed the best, followed by future positive and future negative. Furthermore, the addition of moderation of the independent variables by resilience had significant joint influence on depression (R2 = 0.30; ΔR2= 0.28; (6, 81) = 7.74, $p<0.05$); contributing 30% to depression. The independent influence of the predictor variables shows that when moderated by resilience, only past positive, past negative and present fatalistic were independent and significant predictors of depression. Lastly, the addition of moderation of the independent variables by resilience have significant joint influence on suicidal ideation (R^2=0.15; ΔR^2=0.11; (6, 85) =3.31, $p<0.05$); contributing 15%. The independent influence of the predictor variables shows that when moderated by resilience, only present hedonistic and future positive were independent and significant predictors of suicidal ideation.
Conclusion: In conclusion, time perspectives predict depression and suicidal ideation, and resilience is efficacious in alleviating these mental health problems.

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Table 4.1. Table showing Zero Order correlation, Means and Standard Deviation of all variables.

Variables	1	2	3	4	5	6	7	8	9	M	SD
Past positive	1										
Past negative	.23*	1									
Present hedonistic	.28**	.31**	1								
Present fatalistic	-.00	.68	-.6	1							
Future negative	.16	.34**	.27**	.30**	1						
Future positive	.21*	.19	.54**	-.14	.94	1					
Depression	-.21*	.20	-.15	.40**	.26**	-.33**	1				
Suicidal ideation	.04	-.01	-.25*	-.03	.10	.11	.18	1			
Resilience	.44	-.02	.34**	-0.37**	-.07	.42**	-.47**	-.10	1		

P<0.05 **P<0.01

Table 4.2. Multiple regression summary table showing the joint and independent influence of Past po

Variable	R	R^2	F	β	t	p
Past positive				-0.16	-1.64	p>0.05
Past negative				0.28	2.79	p<0.01
Present fatalistic				0.28	2.85	p<0.01
	0.59	0.35	7.36			
Past hedonistic				-0.10	-0.87	p>0.05
Future positive				-0.28	-2.63	p<0.05
Future negative				0.17	1.63	p>0.05

Table 4.3. Multiple regression summary table showing the joint and independent influence of Past po

Variable	R	R^2	F	β	t	p
Past positive				0.62	2.13	p>0.05
Past negative				-0.01	0.60	p>0.05
Present fatalistic				-0.07	-0.67	p>0.05
	0.43	0.19	3.27			
Present hedonistic				-0.51	-4.12	p≤0.001
Future positive				0.33	2.80	p≤0.01
Future negative				0.22	1.97	p≤0.05

Table 4.4. Summary of Hierarchical Regression Showing the Moderating role of resilience in the infl

	Model 1			Model 2		
Predictors	B	t-value	P	B	t-value	P
Past positive	-.16	-1.64	>.05	-.20	-2.12	<.05
Past negative	.28	2.79	<.05	.24	2.40	<.05
Present fatalistic	.28	2.85	<.05	.48	3.94	<.01
Present hedonistic	-.10	-.86	>.05	-.03	-.25	>.05
Future positive	-.28	-2.63	<.05	-.18	-1.67	>.05
Future negative	.17	1.63	>.05	.16	1.61	>.05
Past positive X Resilience				-.32	-2.15	<.05
Past negative X Resilience				.38	2.61	<.05
Present fatalistic X Resilience				.32	2.66	<.05
Present hedonistic X Resilience				-.11	1.34	>.05
Future positive X Resilience				-.15	1.65	>.05
Future negative X Resilience				.09	.87	>.05
R		.59[a]			.55[b]	
R^2		.35			.30	
ΔR^2		.31			.28	
Df		6, 81			6, 81	
F-Ratio		7.36**			7.74**	

**p<.01, *p<.05,

Table 4.5. Summary of Hierarchical Regression Showing the Moderating role of resilience in the infl

	Model 1			Model 2		
Predictors	β	t-value	P	B	t-value	P
Past positive	.06	-60	>.05	.04	.38	>.05
Past negative	-.01	-.10	>.05	-.04	-.34	>.05
Present fatalistic	-.07	-.67	>.05	.07	.55	>.05
Present hedonistic	-.51	-4.12	<.01	-.47	-3.71	<.01
Future positive	.33	2.80	<.05	.40	3.23	<.05
Future negative	.22	1.97	<.05	.22	1.99	<.05
Past positive X Resilience				.06	.55	>.05
Past negative X Resilience				-.02	-.32	>.05
Present fatalistic X Resilience				-.23	-1.76	>.05
Present hedonistic X Resilience				-.56	-4.01	<.01
Future positive X Resilience				-.29	-2.11	<.05
Future negative X Resilience				.08	.29	>.05
R		.43[a]			.39[b]	
R^2		.19			.15	
ΔR^2		.13			.11	
Df		6, 85			6, 85	
F-Ratio		3.27*			3.31*	

**p<.01, *p<.05,

PE30/5

Social support and quality of life of people living with AIDS receiving ART at BPKIHS

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Purpose: HIV/AIDS leads to severe impairment in the health-related QOL for the patients. Antiretroviral therapy (ART) reduces morbidity and mortality due

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to AIDS. The objective of the study are to assess the social support and quality of life of PLWA receiving antiretroviral therapy at BPKIHS; to find out the association of Quality of life and Social Support of people living with AIDS and selected variables and to find out the relationship between Quality of life of PLWA and social support.
Methods: Descriptive cross-sectional research design was used for this study among PLWA receiving ART at ART Clinic, BPKIHS. Total 90 PLWA were selected by convenient sampling technique. Data was collected by both qualitative and quantitative method through interview questionnaire and focus group discussion. Data were analyzed using SPSS version 20.0.
Results: The study demonstrated that the mean age of respondents was 38.40 ± 8.80 and half of them (54.4%) were female. Mean score of overall QOL (62.74 ± 17.4) and social support (69.50 ± 18.50) were found to be higher .Overall QOL score was significantly associated with gender and educational status and overall social support score was significantly associated with gender and employment at 0.05 level of significance. There was significant positive relationship between overall score of social support and overall score of quality of life ($r=0.07$, $p=<0.001$) at 0.01 level of significance.
Conclusion: Based on the results, it can be concluded that more than half of the subjects had high QOL. Similarly, more than two-third of the subjects had good social support. Male sex and employed PLWA got good social support. There was positive relationship between QOL and Social Support. Thus, increase or decrease in social support tends to increase or decrease Quality of Life respectively.

PE30/6

Knowledge on the prevention of HIV and tuberculosis infection among young adults using drugs in slum area of Dhaka city, Bangladesh

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Purpose: HIV & Tuberculosis (TB) are synergistic infectious diseases. These are affecting mostly adults using drugs, especially affects the most vulnerable. Slum areas are overcrowded, poor ventilation and unhygienic living conditions coupled with acute poverty. HIV with TB can act as a deadly cocktail to push up the number of cases.
Method: A cross-sectional study design, 210 young adult participants from selected slums using drugs were enrolled in this study between May and August 2018. A structured questionnaire was used to interview the participants to collect data on knowledge on the prevention of HIV and tuberculosis infection.
Results: Majority of the participants were male (61.3%) followed by female (38.7%). 18–28 years of age group (82.7%) were mostly was the majority of the participants. More than two third (87.1%) of the respondents were Muslim followed by 8.6% of Hindus people. Majority of the participants (69.3%) indicated they haven't received information about HIV and TB infection. Majority of the respondents (68.3%) stated they don't know what the signs and symptoms of TB or any transmitting mode of HIV. Majority of participants (53.4%) indicated they disagree that TB can be prevented. However, 62.5% of them indicated good nutrition can be prevented HIV infection & TB. Majority of them 52.1% stated they have no opinion whether HIV infection or TB can be transmitted by shaking hands and 57.1 indicated they have no opinion whether HIV and TB can be transmitted by sharing foods or drinks. 7.0% stated they wish to get more information on HIV infection and TB. In the study gender (p-value 0.03) and level of education (p-value 0.007) were significantly associated with the knowledge on HIV infection and TB.
Conclusion: Knowledge about HIV and TB within the population was inadequate. Current policies on it need to be upgraded as an immediate effect.

PE30/7

Knowledge, attitudes, beliefs and HIV-related behaviour in metropolitan France: investigation in a festive place

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Purpose: This article is a follow-up to the ANRS-KAPB surveys on HIV knowledge conducted between 1992 and 2010 and similar questionnaires, offered at the Solidays festival in 2017.
Method: The ANRS-KAPB surveys were conducted by telephone on a probability sample of telephone numbers. The 2017 survey included some questions in the form of a questionnaire given to festivalgoers.
Results: A total of 1192 questionnaires were collected, with the following characteristics: 68.8% women, 31.7% men, 24 years old on average, 81.96% heterosexual, 77.2% from Ile-de-France and 62.9% with a high level of education. Ninety-eight percent of respondents knew that HIV is transmitted through unprotected sex or with the use of a used syringe, 16.7% think it is possible to become infected in public toilets (vs. 16.7% in 1994 and 16.8% in 2010) and 35% think it is possible to become infected through mosquito bites (vs. 13.9% in 1994 and 24.3% in 2010). In 2017, 53.9% of festivalgoers had a good knowledge of the modes of contamination with 100% of correct answers; 73.7% are very fearful of HIV (vs. 50% in 1994 and 21.9% in 2010); Of the 47.5% who did not use a condom, 25.2% were not in a relationship and 32.4% had never had sexual relations. Almost 40% of respondents refuse protected sex with an HIV-positive person, and 74.4% refuse it with a person on Prep, without a condom.
Conclusion: In 2017, in a population interviewed in a festive place dedicated to STI and HIV awareness, false beliefs persist and worsen regarding modes of contamination, even if the populations are not comparable. Condoms remain poorly accepted despite changes in use. This survey highlights the importance of teaching about HIV prevention methods even today.

PE30/9

Injectable long acting antiretrovirals for HIV treatment or prevention: the ANRS CLAPT study

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Purpose: In the era of well-tolerated once daily single pill regimens for HIV treatment and prevention, there will be an opportunity to provide an alternative option using potent injectable long-acting antiretrovirals (LAA) that may improve adherence and quality of life. The purpose of this study was to evaluate patients' acceptability of this new mode of administration and to identify potential user profiles.
Method: We performed a quantitative survey through self-administered questionnaires among people living with HIV and pre exposure prophylaxis (PreP) users in three Infectious Diseases units. To be included HIV-infected participants had to be well controlled on ART and PrEP users had to be treated for at least 6 months. We collected data from participants such as lifestyle, medical history, treatment experiences, perceived benefit and inconvenience of injectable LAA.
Results: Between October and December 2018, 100 HIV infected patients and 100 PrEP users were enrolled with a majority of men (76 % and 100%, in the HIV infected and prEP users groups, respectively). HIV infected participants were older (median age 50 vs 39 years), with a higher rate of comorbidities (hypertension 25% vs. 8%, diabetes 8% vs.4%, hypercholesterolemia 33% vs.2%) compared to PreP users. 49% and 53% of HIV- infected participants and PrEP users, respectively, are interested to get monthly injectable LAA. Perceived advantages and drawbacks were reflecting nuanced opinions in both groups with reluctance to receive the injection at the hospital for HIV infected patients (41%). A multiple correspondence analysis suggested a higher

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acceptance by HIV-infected participants and PrEP users without treated comorbidities and who are not smokers, alcohol or drug addicts.
Conclusion: Nearly half of HIV-infected patients and PrEP users expressed interest in monthly injectable LAA with a higher rate for every other month LAA (89%) for PrEP users. Further studies are needed to better characterize these populations.

PE30/10

Quality of life in people living with HIV: a regional survey in Flanders

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Purpose: Due to medical development, HIV has evolved into a chronical infection with an increased life expectancy. Therefore, attention is shifting toward quality of life (QOL) of people living with HIV (PLWH). Little, however, is known about QOL of PLWH living in Flanders and about coping with HIV in general.
Method: The survey questionnaire was developed in collaboration with experts and pretested in PLWH. QOL comprised the following domains: physical health, mental health (Mental Health Index-5 (MHI-5)), social support (Oslo Social Support Scale (OSS)), impact of HIV, coping with HIV and stigma (Brief Measure of Stigma of HIV (BMSH)). The survey was available online for 5 months in 3 languages. Participants were recruited using a mixed method approach.
Results: In total, 505 PLWH participated in the survey. In comparison with the Cohort of all PLWH in Flanders, this sample was representative for demographic and HIV-related characteristics. Overall, 26% of PLWH were ever diagnosed with depression and 43% had weak social support (62% in recent diagnosis). The impact of HIV was limited on professional life (15%), but pronounced on life satisfaction (40%) and sexual satisfaction (41%). Coping with HIV was rather positive, with e.g. 70% reporting to have integrated HIV in their life. With regard to stigma, 85% was very careful to disclose their status and 61% feared rejection by sexual partners. Self-image remained positive, with 75% not agreeing to be a lesser person due to HIV. Finally, 46% ever withheld from important matters and 65% ever experienced discrimination due to HIV.
Conclusions: This survey indicated that several domains of QOL in PLWH require attention: mental health and social support of PLWH are impaired, especially in recent diagnosis, and HIV-related stigma and discrimination are still widespread. On the other hand, this survey uncovered strengths of PLWH, e.g. positive coping and self-image.

PE30/11

Innovative strategies to sustain community participation in HIV vaccine trials, experience of Makerere University Walter Reed Project (MUWRP) in Kampala, Uganda

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Purpose: Active community participation is an established component of HIV vaccine trial design and implementation. Continued and meaningful community participation ensures that community expectations and/or concerns are taken care of during the design and conduct of the trial. I present innovative strategies that have been used to keep research communities engaged in HIV vaccine trials in an urban setting.
Method: At the start of every research protocol, a strategic meeting is held with the core research teams to discuss community outreach approaches that are relevant to the study design and the participants targeted.The community structure is engaged to brainstorm on specific approaches that resonate with their specific communities and support the message design.
During trial conduct, the research team convenes periodically to discuss the pros and cons of the community engagement strategies with the view of continuing with what is working well and dropping what does not work. A multi-channel community outreach package, explicitly designed in the perspective of the trial participants with flexibility to adapt to changing dynamics and participation needs of the research communities is used to reach out to the study participants.
Results: Key stakeholder engagement meetings during the planning stage sets the stage for future engagements & have been used to disseminate key trial information, learn about & plan to address the misconceptions; the use of media engagement help in triggering mass awareness & also counteracts emerging misconceptions; targeted community meetings are crucial in setting up interpersonal communication platforms that provide one on one interactions, also improves research literacy; engagement of the representatives of research communities at all stages of the trial re-enforces recruitment and retention messaging and also gives useful feedback to the researchers.
Conclusion: Community participation in HIV vaccine trials requires teams to involve the community's stakeholders at all levels in designing relevant community engagement strategies.

PE30/12

Stigma among healthcare providers towards people living with HIV/AIDS in India

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Purpose: The healthcare providers (HCPs) are the ones that are suppose to provide PLHA with medical care, psychological support and counselling. This study was done to find out the level of stigma among the HCPs in India.
Method: The study is a cross-sectional study of a convenience sample of 208 healthcare providers working in a tertiary care hospital in Coimbatore city in the state of Tamil Nadu. The data concerning the HCWs' attitudes and acts towards PLWHA were collected using a self-administered questionnaire, the Sexually Transmitted Blood Borne Infection (STBBI) Stigma Scale.
Results: A total of 208 healthcare providers participated in the study, out of which 142 (68.3%) were females, 111 (53.4%) were doctors, and 179 (86.1%) were Hindu. Notably only 13% of providers believed that they lack training required to handle HIV patients, but 37% of the providers expressed their hesitation in dealing with them. The mean score of STBBI stigma scale was 2.71 +/- SD 1.08 which suggests moderate level of stigma. The mean scores of stereotype, prejudice and discrimination sub-scales were 2.81 +/- SD 1.07, 2.57 +/- SD 1.19 and 2.78 +/- SD 1.37, respectively, suggesting that HCPs have a higher tendency of stereotyping and discriminating as compared to having prejudice against HIV patients. Male Gender, being a doctor, and having an experience of less than 5 years were significantly associated with presence of stigma. ANOVA test was used to find the association between stigma and age, and it was deduced that the age group of 25 to 29 years was significantly associated with higher stigma scores as compared to younger or older age groups.
Conclusion: A large number of HCPs demonstrated stereotype, prejudice and discrimination towards HIV patients, and this attitude can adversely affect the quality of care.

PE30/13

"I love my life, I don't want to miss a thing": motivators and Barriers to ART adherence among women living with HIV/AIDS in Iran

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Purpose: Adherence to ART plays a vital role in HIV/AIDS prevention and treatment. Iran has embarked on the fast-track strategy to end the AIDS epidemic by 2030, so it is necessary to fully understand the motivators and barriers to optimal adherence.

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Method: Using semi-structured interviews, we explored the motivators and barriers to ART adherence in 42 women (aged 27–63) who were taking medication for at least 6 months. Medication adherence was assessed by self-report of how many times they have missed their pills in the past 7 days. If it was <90%, they were considered non-adherent. These women were participating in SPASDI weekly social support sessions.
Results: Except for 6 women, everyone else was adherent. The will to live was the major motivator for adherence. Sense of belonging to family and playing the role of caretaker gave the women a reason to stay healthy. For most of the women, their children were their first and most important priority. On the other hand, family and friends were effective facilitators because they constantly reminded them to take the pills and provided psychological support in times of distress. A close relationship with doctors and counselors and believing in the efficacy of ART also enhanced the adherence. Interacting with other HIV-positive women and sharing their experiences motivated them to keep using the prescribed medications. Most women admitted that if their treatment was not free, they could not afford it. Whenever these different parts of social support network failed to function properly, non-adherence followed. Family conflicts, severe side-effects and hiding the HIV status were the main contributors to non-adherence.
Conclusion: We should never forget that the patient is part of several social networks and should always include family members, friends, peers, health-care providers and the society that surrounds him/her in programs for enhancing adherence.

PE30/14

Medical students as potential sources of information about HIV/AIDS

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Purpose: To analyze the knowledge of Ukrainian and international students of the first year of medical university regarding the problems of HIV infection.
Method: On a survey carried out amongst 78 first year medical university students (30 - Ukrainian and 48 - from other countries), the questionary included 15 questions with different options to be chosen.
Results: 80% Ukrainian students and 75% international students knew the difference between HIV and AIDS, 75% and 91% had correct information about aetiology of disease. Most of the interviewed students knew the main route of transmission the infection and possibility of its verification. Pregnancy and HIV is a question of dilemma for both group of interviewed students. The difficulties for students were the question of the immunization possibility against HIV and treatment of the disease with recovery. A half of respondents expressed fear in their everyday communication with HIV positive people, because they considered their knowledge of HIV-infective as insufficient and expressed their desire to receive reliable information on this problem. Most freshmen themselves received information about HIV most often from the Internet and television, but trusted the information from parents and health personnel. the results of the survey on knowledge of their own HIV status turned out to be interesting. So, 50% international students and 30% of Ukrainian students explored their own HIV status, while 20% international and 30% Ukrainian students do not want to do the appropriate laboratory tests.
Conclusion: Medical students should deepen their knowledge of the problem of HIV and AIDS throughout the training period in order to disseminate accurate information on the prevention of the disease.

PE30/15

Gender violence, intimate partner violence and domestic violence among HIV-positive patients in Alicante (Spain). Preliminary results of the VIHOLETA study

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Purpose: Analyse the prevalence of gender violence (GV), intimate partner violence (IPV) and domestic violence (DV) among HIV-infected adults in Alicante (Spain) and analyse if victims have worse adherence to antiretroviral therapy (ART).
Method: Observational study recruiting HIV-infected adults on ART for >1 year in three hospitals of Alicante (Spain). Abuse Assessment Screen (AAS) tool was used for violence screening and Danger Assessment (DA) questionnaire for risk level. Simplified medication adherence questionnaire (SMAQ) and medication possession ratio (MPR) were used to assess adherence. Qualitative variables were compared using the Fisher test and quantitative ones using t-student or Mann-Whitney-U. Logistic regression was used in multivariate analysis.
Results: From Feb2019 to June2019 we recruited 94 HIV-infected adults: 37.2% women, 21.3% immigrants, 39.4%HSH, 38.3% heterosex,12.8%IDU, mean age 49±10.3, median time since HIVdiagnosis= 131 months (IQR:76.4-263), median time on ART: 121.8 months (IQR:58.7-226), 89.4% undetectable VL.
Twenty-six patients (27.66%) had suffered abuse in their lifetime (table 1): 20 emotional abuse, 8 physical abuse, none sexual abuse. Four (4.3%) were currently suffering violence (3 emotional, 1 physical); one was considered at extreme risk.

Prevalence of abuse in each group

Prevalence of abuse among women	34.3% (CI95%: 19.1–52.2)
Prevalence of abuse among men	23.7% (CI95%: 13.6–36.5)
Prevalence of DV in the cohort	24.4% (CI95% 16.2–34.4)
Prevalence of IPV in the cohort	19.2% (CI95%11.8–28.6)
Prevalence of GV among women	31.4% (CI95% 16.8–49.3)
Prevalence of DV among women	34.3% (CI95% 19.1–52.2)
Prevalence of IPV among HSH	16.2% (CI95% 6.2–32)
Prevalence of DV among HSH	18.9% (CI95% 7.9–35.1)
Prevalence of IPV among non-HSH men	4.5% (CI95% 0.1–27.3)
Prevalence of DV among non-HSH men	18.1% (CI95% 5.2–40)

Mean age at abuse was 28.3±12.1. Median abuse duration: 36 months (IQR:24–81). Victim's HIV-status was considered a cause of violence by 11.5% of victims. Abuse was exercised by 13 male-partners, 3 male-ex-partners, 1 female-partner, 1 female-ex-partner, 1 father, 1 son, 3 male relatives and 4 non-family-related men. Table 2 shows bivariate analysis of factors associated with abuse.

Bivariate analysis of factors associated with abuse

Bivariate analysis	% in abused vs % in non-abused	OR (CI95%)	p	Bivariate analysis	Mean in abused vs mean in non-abused	p
Women	46.2% vs 33.8%	1.67 (0.59–4.63)	0.3412	Age (years-old)	47 vs 49	0.4918
Alcohol use	30.8% vs 39.7%	0.67 (0.26–1.77)	0.481	Nadir CD4 (cells/mm^3)	253 vs 281	0.614
Drugs consumption	42.3% vs 30.9%	1.64 (0.65–4-17)	0.336	Current CD4 (cells/mm^3)	642 vs 729	0.313
Former stay in prison	11.5% vs 13.2%	0.86 (0.21–3.44)	1			
Immigrant	30.8% vs 17.6%	2.07 (0.73–5.87)	0.172			
HSH	71.4% vs 60%	1.67 (0.45–6.14)	0.537			
Studies≤primary school	38.5% vs 39.7%	0.95 (0.38–2.4)	1			

Abused patients were more frequently non-adherent assessed by SMAQ (57.7% vs 32.4%; OR: 2.82; $CI_{95\%}$ 1.02–8.05; p=0.034) and by MPR (median MPR 92% vs 99%; p=0.032) and had more frequently a detectable VL (19.2% vs 4.4%; OR: 5.16, $CI_{95\%}$:1.14–23.44; p=0.035). In the multivariate analysis, abuse was the only factor associated with detectable VL (HR:9.88;

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CI95%:1.56–62.73; p=0.015), while both former-prison (HR: 4.07; CI 95%:1.09–15.25; p=0.037) and abuse (HR 3.08; CI95%:1.18–8.00; p=0.021) were associated with non-adherence.
Conclusion: HIV-infected patients are frequently victims of abuse and that hampers ART adherence and virological success. HIV clinicians should incorporate abuse screening tools in their routine HIV care.

PE30/16

Influence of stigma and discrimination on psychosocial health in children affected by AIDS in Nepal: a cross-sectional study

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Purpose: Children Affected by AIDS (CABA) face discrimination and have poor psychosocial condition. CABA comprise of children who have HIV-positive status either HIV positive; children with one or more HIV+ parents/caregivers; children who lost one or both parents to AIDS or children living in the house with one or more HIV+ person (s). Little is known about the influence of stigma on psychosocial condition of CABA in resource-limited settings. Therefore, the study examined the influence of stigma and discrimination on psychosocial consequences in CABA.
Method: A cross-sectional study was conducted among 468 Children aged between 2 to 14 years who were affected by AIDS from March to April 2019 in Nepal. Children's psychosocial problems were measured using questionnaires and scales developed by AIDS Psychosocial metrics. Stigma and discrimination perceived by children were measured using stigma, discrimination inventory for AIDS Affected Children. The associations between stigma and discrimination with psychosocial consequences were analyzed using multiple regression and logistic regression analysis.
Results: Of 468 children, 38% reported that they experienced any form of stigma from the community. Those who experienced stigma were more likely to have fear of isolation compared to those who did not experience stigma (AOR: 2.48, 95% CI: 1.50, 4.11, p<0.001). CABA were more likely to have lower score for support seeking for psychosocial support (β=-0.55, p=0.021) when they experienced stigma. Additionally, children were more likely to have higher scores for psychological distress if they had stigma and discrimination (β=1.30, p=0.005).
Conclusion: CABA experienced high stigma and discrimination that resulted in poor psychosocial well being and fear of isolation in Nepal. The results highlight the need of psychosocial counselling and support services to children at their school and in the mutual support groups to improve their psychosocial well-being.

PE30/17

The quality of life among people living with HIV in Taiwan in the era of STR

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Purpose: We have adopted single tablet regimen (STR) for treating people living with HIV in Taiwan in recent years. The STR has largely increased the compliance and also viral suppression rate. However, the study of impact on quality of life (QoL) is lacking in Taiwan.
Method: This is a cross-sectional study by self-administrated structured questionnaire. The people living with HIV treated in National Taiwan University Hospital (NTUH) and Yun-Lin branch, NTUH were invited to participate the web-based questionnaire of WHOQoL-HIV BREF and BSRS. We aim to analysis the participants' QoL and risk of depression.
Results: During April 1 to June 30, 2019, there were 212 participants responded the questionnaire. The mean age was 39.31±9.66 and 183(86.32%) were male. There were 126 participants were mam sex with mam (MSM), 43 heterosexual and 43 persons with injection drug use (PWIDU). The ART coverage rate, 100% adherence and viral suppression were significant different among the three risk groups (p<0.001, 0.009 and 0.01 respectively) and lowest among the PWIDU group. PWIDU also had lowest QOL, even though no statistical significantly difference among the three risk groups. There was a trend for BRBS difference (p=0.07), which is higher in the MSM group. By multiple linear regression we noted that partner relationship, income level, treatment duration, BSRS level were independent factors associated with QOL after adjusted by risk groups, adherence and comorbidities.
Conclusion: Most people living with HIV in Taiwan can achieve viral suppression under STR. The QoL among PWIDU need more attention. We suggest caregiver should still note high tendency of depression among MSM groups even while they have good viral control. Whether the partner relationship can improve after same marriage law issued since 2019 in Taiwan and improve QoL in turn warrants further study.

Table 1. The character of the participants and QOL and BSRS results

	All N=212	MSM n=126	Heterosexual n=43	PWIDU n=43	p value
Age mean (SD)	39.31 (9.66)	37.08 (9.94)	42.33 (9.78)	42.84 (6.49)	<0.001
ART Tx. Years mean (SD)	6.74 (5.83)	6.57 (5.83)	8.94 (7.09)	5.01 (3.31)	0.0062
ART-coverage	72.48%	80.48%	78.70%	42.81%	<0.001
100% Adherence	111 (55.22%)	69 (54.76%)	28 (68.29%)	14 (32.56%)	0.009
Viral suppression	175 (82.55%)	111 (88.10%)	35 (81.40%)	29 (67.44%)	0.01
QoL_sum	82.89 (12.17)	83.71 (12.08)	83.16 (12.73)	80.22 (11.77)	0.27
BSRS_sum	5.62 (4.58)	6.16 (4.67)	5.33 (5.18)	4.33 (3.32)	0.07

Table 2. Multiple linear regression for factors associated with Quality of Life

Variable	Coef.	95% CI	p value
Partner relationship	1.089	0.25–1.92	0.01
Income level	2.191	0.85–3.53	0.002
Risk groups (MSM)	(reference)		
Heter	-0.627	[-3.76- 2.51]	0.69
IDU	-2.760	[-6.29- 0.77]	0.13
Hx years	-0.275	[-0.53- -0.02]	0.04
Comorbidity	-1.276	[-2.59- 0.04]	0.06
Adherence	1.007	[-0.51- 2.52]	0.19
BSRS	-1.761	[-2.02- -1.49]	<0.001

PE30/18

Experiences of and factors influencing physical activity in people living with HIV: a qualitative systematic review

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Purpose: Despite proven benefits of physical activity (PA) for physical, mental and social wellbeing to people living with HIV, and in preventing co-morbidities, uptake of PA in this population remains low. Understanding the reasons is critical to effecting behaviour change. This systematic review of qualitative research aimed to synthesise evidence of experiences, barriers, and facilitators of PA in people living with HIV using the Theoretical Domains Framework (TDF) for behaviour change.
Method: A systematic search of six electronic databases. Screening of results by two independent reviewers with adjudication by a third reviewer. Qualitative and mixed methods studies that reported perceptions and/or experiences of engaging with PA were included. Two quality appraisal tools

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were used to assess risk of bias in individual papers and judge confidence in review findings. Study findings were extracted to populate the TDF domains and then condensed and summarised.
Results: 22 studies were included. 33 factors related to 13 of the 14 TDF domains were identified. Confidence in findings was judged high or moderate for 27 of the 33 factors. Most commonly reported barriers to PA, with at least moderate confidence, were; lack of knowledge about types of exercise and how to access them, low motivation resulting from depression or fatigue, and low confidence and perceived physical limitations. The most common facilitators to PA, with at least moderate confidence, were support from friends and family, group settings, buddy systems, and experiencing the potential benefits of PA in terms of prevention or delay of symptoms and co-morbidities.
Conclusion: This systematic review indicates the key barriers and facilitators to uptake of PA reported by people living with HIV. Incorporating these findings into development and delivery of interventions could improve uptake and continuation of PA, potentially increasing the likelihood of effectiveness, and contributing to improved health outcomes in this population.

PE30/20

Perception of condom use in the era of pre-exposure prophylaxis (PrEP): a qualitative analysis

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Purpose: Risk compensation by reducing condom use has become a new focus of considerable concern in the course of delivering pre-exposure prophylaxis (PrEP) for preventing HIV infection. The development of effective PrEP programs will require an understanding of perception of condom use that can be explained by how high-risk individuals perceive their personal risks. This study aimed to explore the perceptions of early adopters of PrEP towards condom use in Hong Kong.
Method: This is part of a larger study involving in-depth interviews with men who have sex with men (MSM) between March and June 2019. All were PrEP users attending a pilot PrEP service in Hong Kong. Audios were transcribed verbatim, manually coded, and categorized with themes emerged using inductive approach.
Results: A total of 13 MSM between 22 and 59 year-old were interviewed. Four themes arose from self-reported data: (1) "Condoms provide better protection than PrEP to prevent HIV" among those perceiving relatively unchanged level of risk due to poor PrEP adherence; (2) "Condoms are less essential" among those perceiving substantial decreased risk resulted from good PrEP adherence, coupled with personal preference for condomless sex; (3) "Condoms are still essential" among those emphasizing the need to respect partner preferences for condom use, and those perceiving irregular sexual encounter as a higher-risk behavior than regular sexual encounter; and (4) "Condoms are actually essential" among those who wanted better protection after diagnosis of sexually transmitted infections (STIs) during the study.
Conclusion: The estimation of self-perceived HIV risk based on an MSM's views towards PrEP's efficacy, relationship status with partner, and experiences of STIs, strongly influences perception of condom use. While HIV risk has been redefined varying from individual experience, advice on risk assessments through risk-reduction counselling would need to be tailored to the changing behavioral practices in PrEP users.

PE30/21

Recommendations for enabling timely pregnancy disclosure to clinical staff of women living with HIV

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Purpose: The Baylor clinic in Romania initiated a quality improvement program, starting from the observation that several women living with HIV (WLH), enrolled into care for longer than 12 months, have not informed the clinical staff about the ongoing pregnancy, endangering both their health and their infants. We aimed to identify improvement areas in the clinic operations, based on lessons learnt from interviews with WLH.
Method: WLH were interviewed about their experiences regarding pregnancy disclosure and subsequent care received in the clinic (n=39, 14% did not disclose, 86% disclosed). Three independent coders classified responses facilitators and barriers using the RQDA software. Quality improvement recommendations were inferred from the barriers listed by patients.
Results: The WLH had mean age 30 and were from 53% rural area. Recommendations to overcome barriers include: ensuring communication of roles and responsibilities of all staff especially to newer patients; displaying and communicating guaranteed confidentiality, to decrease apprehension about negative consequences; shortening and streamlining duration of service delivery to affect less patients' schedule; improving personnel's attitude, towards a more neutral and judgement-free, to increase discussions on difficult topics, such as abortions or casual sex encounters; clarifying patients' roles in shared decision making.
Conclusion: The willingness to disclose pregnancy is dependent upon favorable external circumstances. To positively alter the clinic circumstances, we plan to create information-education-communication materials for WLH to encourage patients disclose and anticipate their journey in case of pregnancy. Ways of effectively communicating roles and responsibilities of staff in the clinic need to be assessed and deployed. Healthcare providers' communication skills will be diversified with other tools, such as the teach back technique and it's use in clinical encounters will be assessed regularly. Communication around confidentiality and patients rights, including reproductive rights, will be prioritized among WLH, regardless of number of years since enrollment into care.

PE30/22

Health-related quality of life in a single center cohort of people living with chronic diseases: comparison between HIV and other clinical conditions

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Purpose: To perform a comprehensive assessment of patient's reported outcomes measures (PROMs) among PLWH and patients affected by other chronic conditions (OC) such as diabetes mellitus type 1, rheumatoid arthritis, breast cancer in hormonal therapy and to investigate factors associated with different PROMs outcomes.
Methods: Cross-sectional observational study. Questionnaires investigating quality of life (Medical Outcomes Study Short Form 36-item Health Survey), work productivity (WPI), adherence (Morinsky), health status (Eq-5D-3L), treatment satisfaction (TSQ) were administered to pts consecutively observed at a single Universitary Hospital during a 2 month-period (march-may, 2019). Inclusion criteria: age<70 y, history of chronic disease> 1 y, being in a stable therapy>6 months, clinician-based life expectation >2 y, absence of main functional impairment (IADL>5).
Logistic regression analysis was used to analyze the association between disease group (HIV vs OC) and PROMs.
Results: 132 patients were enrolled (51 PLWH, 81 OC). Mean age: 49 y (SD 11), mean time of disease 12y (10), 96% were Caucasian, 35% assumed polypharmacy, 42% of male were PLWH vs 16% OC (p<0.001), 19% PLWH vs 6% OC had clinical complications (p<0.001). Differences in specific PROMs means are reported in figure 1. PLWH showed greater values in all domains considered. At multiple regression analysis after controlling for variables in the legend, older age, polypharmacy and HIV infection were independently associated with most of domains. In particular, HIV infection was associated with all except for mental health and work productivity.

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Conclusions: In this cohort of patients with chronic conditions followed within the same health setting, PLWH showed better self-reported health outcomes compared to other chronic conditions considered as a whole, with comparable characteristics of chronicity. The independent detrimental role of older age and polypharmacy in most outcomes suggests the need of longitudinal assessment of PROMs in clinical practice

PROMs	variable	b	SE	p
SF-36				
Physical health	Age*	-0.38	0.14	0.008
	HIV**	-19.43	3.13	<0.001
Mental health	Polypharmacy#	-9.28	3.31	0.006
Bodily pain	HIV**	-18.8	3.06	<0.001
General Health	Polypharmacy#	-8.91	3.75	0.01
	HIV**	-20.78	3.47	0.001
Physical role functioning	Age*	-0.45	0.16	0.007
	HIV**	-12.9	3.7	0.001
Vitality	Polypharmacy#	-10.25	3.31	0.002
	HIV**	-10.77	3.24	0.001
Social role functioning	HIV**	-11.02	3.94	0.006
Work productivity	Age*	-0.01	0.00	<0.001
Health status (EQ-5D)	Polypharmacy#	-9.90	2.64	<0.001
	HIV**	-7.09	2.58	0.007

*other variables in the model: gender, ethnicity, time from chronic condition diagnosis, presence of complication related to chronic condition
*For each year older: **vs other condition: # any drug other than drugs for primary chronic condition

Significative correlations between PROMs and sociodemographic and clinical characteristics

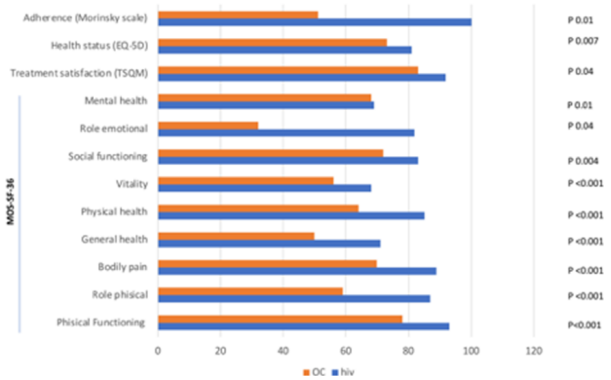


Figure 1. Mean values of PROMs according to chronic conditions (HIV vs OC)

PE30/23

Experiences of Dutch obstetric healthcare providers with HIV-positive pregnant women: a qualitative study

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Purpose: HIV-related stigma is still present among healthcare providers, which potentially endangers the quality of care for all HIV-positive people. In case of pregnancy, this stigma negatively influences mental health during pregnancy, and during and after birth. The aim of this study is to assess the experiences of Dutch obstetric healthcare providers in providing care to HIV-positive pregnant women, and the role of HIV-related stigma in that.
Method: This was a qualitative study. Semi-structured individual interviews and duo-interviews were conducted with 16 Dutch obstetric healthcare providers, varying from cleaner to gynaecologist.
Results: Through thematic analysis, five themes emerged: transmission, knowledge, assumptions based on society's view, compassion with HIV-positive pregnant women, and culture differences as source for conflicting values. The first two themes belong to 'care for yourself as healthcare provider', while the resting themes belong to 'care for pregnant women'. A frequently mentioned motif was extra awareness to prevent HIV transmission, which was related to not having adequate knowledge about HIV. There seems to be a difference in level of knowledge among the healthcare providers, where the gynaecologist and midwives had the highest level of up to date knowledge. Besides, healthcare providers struggled with non-disclosure of HIV-status of the pregnant women to their partner, where contrasts with other perceived cultures took a central place. Another recurrent theme was the perspective of the partner, including the rights of the father. Overall, healthcare providers reported behaviour that arose from certain negative connotations related to considerations about HIV, which can be considered as unintended stigmatizing behaviour resulting from existing stigma.
Conclusion: This study provides insight into the experiences of obstetric healthcare providers in providing care to HIV-positive pregnant women. These findings suggest a need to increase knowledge about HIV among obstetric healthcare providers, and to increase culture comprehension in healthcare settings.

PE30/24

Evaluation of knowledge, attitudes and practices among HIV positive pregnant women and their partners in four healthcare facilities in Malawi

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Purpose: In Malawi, HIV prevalence in the adult population is one of the highest in the world, especially in young women (11.7% vs 7.4%-UNAIDS). Understanding knowledge, attitudes and practices (KAP) is crucial to plan proper interventions to reduce the spread of HIV and overcome cultural barriers.
Method: HIV+ pregnant women accessing 4 health DREAM facilities in Malawi (Machinjiri, Chileka, Blantyre and Balaka) were invited to answer a KAP questionnaire with their partners on the PMTCT process. A KAP questionnaire (27 questions) was developed exploring the level of knowledge about HIV (route of transmission, modes of prevention and treatment), of attitude (way of being and of taking care of HIV+ people) and of practices (behaviours).
Results: 79 subjects from 4 DREAM centres (Balaka 8, Blantyre 2, Chileka 23, Machinjiri 46) participated; 48.1% were female. Regarding knowledge of HIV, (14 questions) males showed a higher number of correct responses than women (13±0.3 vs 11.6±0.3, p=0.001), on attitude (7 questions) male and women reported similar number of positive answers (5.7±0.2 vs 5.4±0.2,ns) whereas risky practices were more often reported by women (68.4% vs 42.5%, OR 2.9 [1.15–7.40]), with significant differences on condom use (36.8% vs 60.0%, p=0.046) (ns). Associations of knowledge with attitudes and practices (logistic regression): with increasing knowledge scores responders were likely to have positive attitudes (OR=1.06, p=0.001) and safe practices (OR= 1.04, p=0.045). Moreover, distinguishing by gender, the association between knowledge and attitude was significant both in male (OR=1.08, p=0.02) and female respondents (OR=1.06, p=0.02), but the association between knowledge and practices was significant only in males (OR=1.08, p=0.03).
Conclusion: Rates of knowledge and attitudes are still particularly poor in HIV+ patients in Malawi, especially women. The scarce association between KN and practices in female patients underscores the need for a deeper understanding of behavioural mechanisms in HIV+ patients in Malawi, especially women.

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PE30/25

Towards the 4th 90, measuring multi-dimensional quality of life in people living with HIV in Aquitaine, France: psychometric properties of the French version of the WHOQOL-HIV BREF

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Purpose: To assess the psychometric properties of the French version of the WHOQOL-HIV BREF instrument in adults living with HIV-1 (PLWH) in Nouvelle Aquitaine.

Method: We conducted a cross-sectional study nested within the ANRS CO3 Aquitaine cohort. From July 2018 - May 2019, participants were consecutively enrolled at their HIV-consultations and completed a web-based (n=402) or paper self-administered questionnaire (n=181). The mean, s.d., floor and ceiling effects for items and domains were computed. We assessed internal consistency (Cronbach's alpha coefficients per domain) and construct validity by Confirmatory Factor Analysis (CFA) in STATA 15. Concurrent, convergent and discriminant validity were assessed with Pearson's correlations. We explored known-group validity based on CDC clinical categories.

Results: 583 PLWH were enrolled: median age 56, 73% male, 85% French descent, 99% currently treated and 91% virally suppressed. Floor effects were found for 1 item and ceiling effects for 11/31 items. The personal beliefs domain had the highest mean score (15.04 ± 3.35) and the psychological health domain had the lowest (13.70 ± 2.78). 4 of 6 domains demonstrated adequate internal consistency (Table 1).

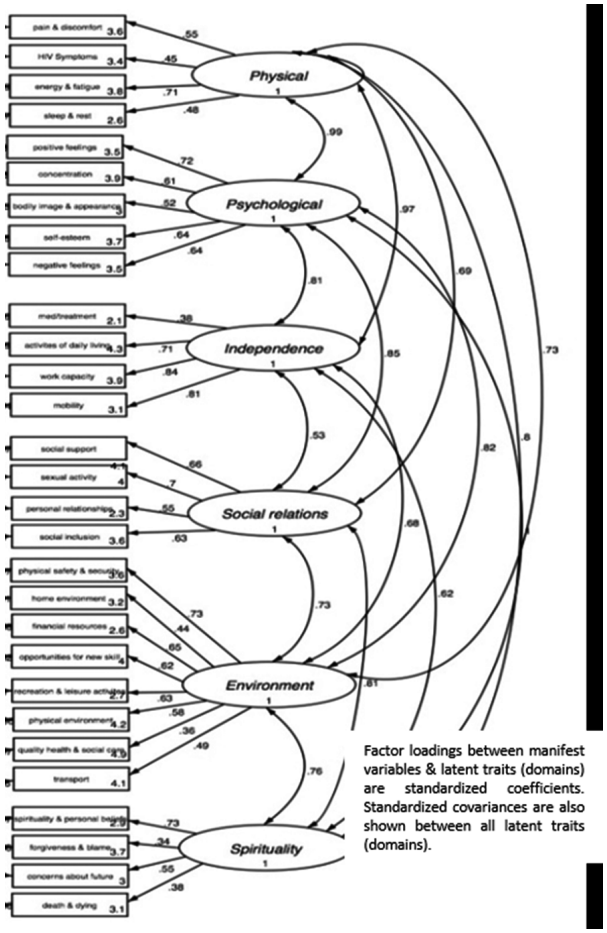


Figure 1. The structure of the French version of the WHOQOL-HIV BREF based on CFA

Table 1. Internal consistency of the French version of the WHOQOL-HIV BREF]

Domain	N	Mean	SD	Range (Min)	Range (Max)	Cronbach's α Coeff.
I. Physical health	571	14.15	2.97	4	20	0.63
II. Psychological health	566	13.70	2.78	4.8	20	0.76
III. Level of independence	557	14.65	3.49	4	20	0.72
IV. Social relations	554	13.91	3.03	4	20	0.70
V. Environmental health	554	14.37	2.58	6	20	0.79
VI. Spirituality/personal beliefs	567	15.04	3.35	4	20	0.64

The CFA results (Figure 1) showed that the six-domain structure of the WHOQOL-HIV BREF produced an acceptable fit to the data (CFI= 0.833; RMSEA= 0.071 (90% CI 0.067 - 0.075)). Items were correlated with their domain (r= 0.45 - 0.82). All but one item were more highly correlated with their respective domains. Scores were higher among asymptomatic compared to symptomatic participants but no differences were detected between B and C categories (Table 2).

Conclusion: The French version of the WHOQOL-HIV BREF in an older, treatment-experienced but virally suppressed population showed adequate internal consistency for four/six domains. The CFA showed the original structure produced an acceptable fit to the data. It showed good concurrent, convergent and discriminant validity and evidence of known-group validity.

Table 2. Known-groups validity of the WHOQOL-HIV instrument according to CDC clinical categories for HIV infection (N=583)

Overall QoL & Health	A (N=330)		B (N=136)		C (N=117)		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	*F*
General QoL	3.79	(3.70–3.87)	3.57	(3.44–3.71)	3.50	(3.35–3.36)	7.46**
General Health Status	3.67	(3.57–3.77)	3.36	(3.19–3.53)	3.43	(3.25–3.60)	6.46**
I. Physical health ‡	14.56	(14.25–14.87)	13.61	(12.73–13.68)	13.63	(13.06–14.20)	7.13**
II. Psychological health ‡	13.97	(13.67–14.28)	13.21	(12.73–13.68)	13.51	(12.99–14.02)	3.94*
III. Level of independence ‡	15.18	(14.81–15.55)	13.92	(13.26–14.57)	14.00	(13.38–14.62)	8.73**
IV. Social relations ‡	14.12	(13.79–14.46)	13.43	(12.89–13.96)	13.88	(13.35–14.41)	2.47
V. Environmental health ‡	14.68	(14.42–14.94)	14.05	(13.57–14.52)	13.86	(13.33–14.39)	5.55**
VI. Spirituality/ religion and personal beliefs ‡	15.30	(14.95–15.66)	14.53	(13.95–15.11)	14.90	(14.26–15.55)	2.64

PE30/26

Body size modifies the relationship between internalized HIV stigma and pain in people with HIV in the Southeastern USA

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Purpose: Pain and obesity have emerged as common co-morbidities with HIV. Meanwhile, HIV-related stigma poses a significant barrier to improving health for people with HIV (PWH). Research supports an association between stigma and pain. Obesity is also associated with pain, but may interact with other variables. In the present analysis, we investigated the role of body size as a moderator of the association between internalized HIV stigma and acute pain.

Method: Participants (N=180 PWH not currently using substances) completed measures at a HIV primary care clinic in Birmingham, Alabama.

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Internalized HIV stigma was measured using the revised HIV Stigma Scale, self-stigma subscale. Height and weight measures were collected. BMIs were categorized as "Healthy" (BMI=18.5–24.9), "Overweight" (BMI=25–29.9), and "Obese" (BMI=30+). Current pain was reported one week following initial study measures using a numerical rating scale from 0: "none," to 10: "worst imaginable." Covariates included age, sex, race, sexual orientation, socioeconomic status, and months on antiretroviral medications.
Results: Participants included 31% with healthy range BMI, 39% with overweight range, and 30% with obese range. Both internalized HIV stigma and BMI category were positively associated with pain. The interaction of stigma with weight category was significant (B=-1.02, SE=0.45, 95% CI [-1.90, -0.13]). Upon examination of simple slopes, among PWH with lower BMIs internalized HIV stigma was positively associated with pain (B=1.48, SE=0.55, 95% CI [0.40, 2.56]). Internalized HIV stigma was not associated with pain for PWH in the overweight range (B=0.46, SE=0.36, 95% CI [-0.24, 1.17]), or the obese range (B=-0.55, SE=0.60, 95% CI [-1.73, 0.62]). Significant covariates included female sex, and lower socioeconomic status.
Conclusion: Findings support HIV stigma relates to greater perceptions of pain. The association may depend on body size. Research is needed to understand individuals' body size and composition perceptions in relation to HIV stigma, which can inform health communication for PWH managing their weight or pain.

Standard of care

PE31/1

Exploring the attitudes of HIV-positive patients on single-tablet antiretroviral regimens towards generic de-simplification

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Purpose: The majority of HIV-positive outpatients attending the Mater Hospital in Ireland are prescribed single tablet antiretroviral regimens (STRs). However, generic equivalents of the most commonly-prescribed STRs are not yet available. In order to switch to generic antiretrovirals, the majority of patients on STRs would therefore be required to 'de-simplify' their regimen. Although the potential exists to realise substantial medication cost savings through generic de-simplification, barriers to its widespread adoption include potential effects on adherence and quality of life. The study aim was to establish the perspectives of patients on STRs regarding generic de-simplification.
Method: A questionnaire was completed by 287 Mater Hospital outpatients on STRs. IBM® SPSS® was used for further analysis. Descriptive statistics were used to summarise participants' characteristics and non-parametric tests were used to test for statistical significance between groups.
Results: The highest proportion of participants were non-Irish national, employed males with a college degree or higher (n=66, 23%). The majority of participants were on antiretrovirals 1–4 years (n=114, 39.7%). Of those on treatment less than 1 year, 77.3% (n=17) were always on a STR, compared with 20% (n=16) of those on treatment 10 years or longer. Thirty two percent (n=91) were open to a proposed switch to two tablets daily. This rose to 46.1% (n=132/286) and 59.1% (n=169/286) when participants who were unsure, or unwilling, were asked if generic de-simplification would be acceptable to them for cost saving reasons or re-investment into HIV care respectively. Having excess medication bottles was the main reason for reluctance to switch at 53.6% (n=105/196), followed by adherence concerns (n=85/196, 43.4%).
Conclusion: It appears the majority of participants would not oppose generic de-simplification for the benefit of society or HIV care. Patient engagement and effective communication may aid acceptance. Generic de-simplification could result in significant cost savings without compromising patient care.

PE31/2

Comparison of Immunological and virological response to cART between HIV-1/O and HIV-1/M patients followed-up in France: the ANRS ORIVAO and COPANA studies

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Therapeutic outcomes for patients infected by genetically divergent HIV-1/O are not well-known, due to scarce data and lack of comparison with patients infected by pandemic HIV-1/M. Our aim was to compare the response to cART between HIV-1/O and HIV-1/M patients followed-up in France.
All naïve HIV-1/O subjects initiating cART in France in the ANRS-ORIVAO study were compared to naïve HIV-1/M initiating cART in the ANRS-COPANA cohort. Piecewise linear mixed-effect models and Kaplan-Meier survival curves were used to analyze immunological and virological response to cART, in the overall population (n=65 HIV-1/O vs 279 HIV-1/M), and in two subpopulations: patients originating from sub-Saharan Africa (African population), as most HIV-1/O patients are of Cameroonian origin, and patients initiating 2INTI+1IP/r (IP/r population).
In the overall population, baseline plasma viral load (pVL) was 0.7 log_{10}copies/mL lower in HIV-1/O than in HIV-1/M patients (p=0.003), but no difference was found for occurrence of pVL<200 cp/mL after cART initiation (log-rank test, p=0.57). Baseline median CD4 count was lower in HIV-1/O (179/mm^3) vs. HIV-1/M (248/mm^3) (p=0.002). Between baseline and 4 months, CD4 increase did not differ (p=0.87), but was significantly lower for HIV-1/O after 4 months of treatment (p=0.04).
The African population showed no difference between HIV-1/O vs HIV-1/M for baseline pVL, occurrence of pVL<200cp/mL and CD4 increase. For the IP/r population, baseline pVL was 1 log_{10}copies/mL lower in HIV-1/O vs. HIV-1/M patients (p=0.003), leading to occurrence of pVL<200cp/mL significantly faster for HIV-1/O vs.HIV-1/M (log rank test: p<0.001), but immunological response to cART was similar.
pVL differences between HIV-1/O and HIV-1/M existed at baseline, in the overall population and IP/r population. However, HIV-1/O and HIV-1/M immunological and virological responses to cART did not differ when patients' geographical origin was taken into account. In France, treating HIV-1/O following HIV-1/M defined criteria leads to similar therapeutic outcomes.

PE31/3

From HIV diagnosis to antiretroviral therapy initiation in Croatia from 2013 to 2018

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Purpose: We describe where the HIV diagnosis was made, linkage to care and the time from HIV diagnosis to antiretroviral therapy (ART) initiation in Croatia, 2013 to 2018.
Methods: Croatia has a centralized system of care and all HIV patients are treated at the University Hospital for Infectious Diseases (UHID) in Zagreb. Data on persons entering care were extracted from the electronic database at UHID. Included were the persons that were nationals or residents of Croatia that have previously not been in care elsewhere.
Results: Overall 587 patients entered care from 2013 to 2018. The first HIV-positive test was done at: hospitals (other than UHID) in 150 (25.6%) persons, voluntary counselling and testing settings in 147 (25.0%), UHID in 103 (17.5%), community-based settings in 85 (14.5%), other places in 62 (10.6%) and unknown sites in 40 (6.8%) persons. For the period 2014–2018, linkage to care among those who entered care, was within 7 days of the first HIV-positive test in 53%, within 14 days in 78% and within one month in 91% persons. The median CD4+ cell count at entry into care ranged from 255/μL in 2017 to 341/μL in 2018. It was very low when HIV was diagnosed in hospital settings (median, 84/μL) and highest when HIV was diagnosed at community-

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based settings (median, 413/μL). In 2017 and 2018 ART was initiated within 24 hours from the first clinical visit in 78% and 71% persons respectively, whereas in 2014–2016 it was initiated in 36–62% persons.
Conclusion: Community-based HIV testing contributed to earlier HIV diagnosis. Linkage to care was very good and rapid ART initiation is currently a common practice in Croatia. Expanding community-based HIV-testing accompanied by prompt linkage and early ART might contribute to the decrease of new HIV-infections in Croatia.

PE31/4

Effective management of symptoms – a nursing intervention

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Purpose: Effective symptom management is considered an essential component of nursing care practice for different clinical conditions, but it is particularly important in chronic diseases (Sidani, 2001), as is the case with HIV infection.
Method: Thus, the purpose of this research was to develop a nursing intervention program that demonstrates its effects on symptom management and consequently adherence to antiretroviral therapy in the person with HIV infection.
Results: This is a study who the sample was 73 participants with symptoms of anxiety, fatigue, fear, depression and headaches. The majority of participants (95.9%) reported never having failed the therapy, 24.7% took the therapy as they learned, "every time", 57.5% reported adhering to instructions, 91.8% said didn't forget, 28.8% reported "never having stopped". As for the reason for not taking, at 15% was simply forgetting. Regarding evaluation pre and post intervention of the manual of symptom management strategies use, by the Wilcoxon test, the differences were shown to be statistically significant in the symptoms anxiety, fear and fatigue confirming the theoretical construct that the use of the manual improved these three symptoms. On the other hand, the use of the manual helped to reduce the failures in antiretroviral therapy, with statistically significant differences.
Conclusion: Nursing consultation as a care context, where nursing intervention has contributed to a better management of symptoms and adherence to antiretroviral therapy in the person with HIV infection, should receive greater attention at the hospital level, but also, and especially at the level of the organization of primary health care. The study showed that symptom management is a sensitive indicator of nursing care, where the intervention of the nurse, wherever it takes place, privileges the quality of communication and relation with the sick person and helps to improve the management of its symptoms, as well as adherence to antiretroviral therapy.

PE31/5

Tetanus seroprotection in HIV-positive subjects living in Belgium: risk factors for seronegativity, evaluation of medical history and a rapid dipstick test

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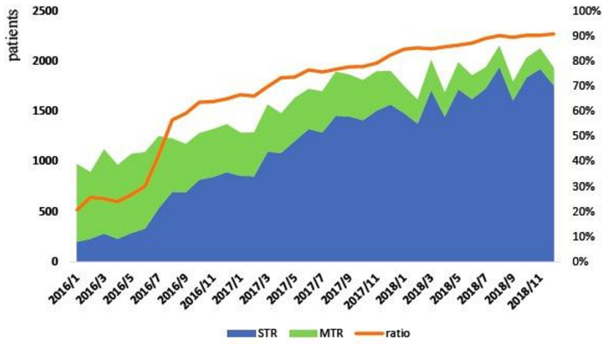
Purpose: Tetanus is a deadly but vaccine preventable infectious disease. The objectives of this work are, in a population of HIV-positive patients: 1) Determine the prevalence of tetanus-toxoid (TT) seroprotection, 2) identify the risk factors for TT seronegativity and 3) evaluate the accuracy of vaccination history and a rapid dipstick test.
Methods: HIV-positive patients attending the outpatient clinic of Saint-University Hospital AIDS Reference center were recruited between 04/01/2018 and 15/02/2019. TT-specific antibodies were measured by ELISA and a level >0.15 IU/mL was considered protective. The Tetanus Quick Stick (TQS), a rapid bedside immunochromatographic test, was evaluated in a subgroup of patients. A questionnaire was used to collect risk factors associated with seronegativity: socio-demographics features, education level, insurance data, current and nadir CD4+ T cell count, viral load & ART use. Fisher's exact test was used for categorical variable univariate hypothesis testing and logistic regression for multivariate hypothesis tests. The Mann Whitney test was used to compare continuous variables. A p-value <0.05 was considered statistically significant.
Results: Three hundred forty-four patients were included. TT seroprotection rate was 84.9%. After multivariate analysis, two factors were independently associated with TT seronegativity: being born outside Europe (OR: 3.02, 95% CI (1.35–6.76)) and education level lower or equivalent to high school (OR: 2.35, 95% CI (1.14–4.85)). Vaccination history report was shown to be unreliable (Sensitivity 43.79%, Specificity 76.47%, Positive predictive value 91.37% and Negative predictive value 19.31%) while TQS performance was good (Sensitivity 86.42%, Specificity 96.00%, Positive predictive value 99.29% and Negative predictive value 52.17%).
Conclusion: HIV-positive patients born outside Europe and those with a lower education level should be prioritarily targeted for TT booster. As in the general population, vaccination history is not reliable and TQS could represent a useful tool for screening.

PE31/6

The prevalence of virologic failure and resistance associated mutations in single and multi-tablet HIV treatment regimens

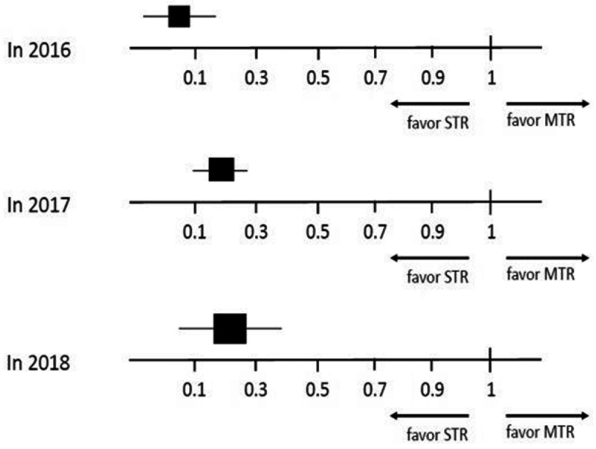
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Purpose: The availability of once-daily fixed dose single tablet regimen (STR) would benefit 2nd and 3rd goals of 90 in population with HIV. This study aims to evaluate the prevalence of virologic failure and resistance associated mutations in patients taking STR.
Method: We conducted a retrospective study to compare virologic outcomes of STR and MTR since January 2016 to December 2018, and 1861 HIV-infected patients ever took combination antiretroviral therapy (cART) more than 6 months. There were TDF/FTC/EFV, TDF/FTC/RPV, TAF/FTC/EVG/c and ABC/3TC/DTG in single-tablet HIV regimens in the study site. Virologic failure was defined as plasma viral load (PVL) ≥200 copies/mL after 6 months of cART or confirmed PVL ≥200 copies/mL after achieving PVL <50 copies/mL. Population sequencing was retrospectively performed to detect emergent resistance associated mutations (RAMs). RAMs were interpreted using the International AIDS Society-USA 2016 mutations list.
Results: The proportion of patients on STR was significantly increased from 20.7% (202/977) to 91.0% (1759/1934) (p<0.001) since 2016 to 2018. (Figure 1) However, 4.3% (53/1232), 4.3% (73/1701) and 1.5% (27/1861) of patients were diagnosed virologic failure in 2016, 2017 and 2018, respectively. Moreover, 56.5% (30/53), 41.1% (30/73) and 63% (17/27) of patients were detected RAMs. Patients on STR had significantly less virologic failure when compared to patients on MTR in 2016 (odds ratio [OR]: 0.07 [95% CI: 0.03, 0.18], p<0.001), 2017 (OR: 0.17 [95% CI: 0.1, 0.28], p<0.001) and 2018 (OR: 0.17 [95% CI: 0.08, 0.38], p<0.001), respectively. (Figure 2) Of 201 patients diagnosed virologic failure, patients on STR had similar risk of being detected RAMs when compared to patients on MTR (OR: 0.57 [95% CI: 0.3, 1.11], p=0.1).
Conclusion: These findings may help healthcare authority and physicians to plan for optimal HIV disease management when the choice of both STRs and MTRs are available.



The proportion of patients on STR

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Patients on STR with less virologic failure

PE31/7

Development and validation of a risk score for predicting non-adherence to antiretroviral therapy

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Purpose: Despite factors influencing ART-adherence are known, a practical tool to predict non-adherence at ART initiation is lacking.
Method: A model to predict non-adherence to ART was developed and validated using a cohort of people living with HIV (PLHIV) starting or resuming ART at Hospital del Mar, Barcelona, in 2012–2015 (derivation cohort) and in 2016–2018 (validation cohort). Adherence was evaluated bimonthly by pharmacy refills and self-reports. Non-adherence was defined as taking <90% of prescribed dose and/or ART interruption >one week. Predictors of non-adherence were identified by logistic regression. β coefficients were used to develop a predictor model. Optimal cut-offs were identified through bootstrapping methodology and performance was evaluated through C statistic.
Results: Overall, 574 patients were enrolled, including 349 and 225 in the derivation and validation cohorts respectively. 104/349 patients in the derivation cohort (29.8%) were non-adherent. Non-adherence predictors included: alcohol use (adjusted OR (aOR) 5.53; 95% CI 2.44–12.55) (20 points); current substance use (aOR 2.43; 95% CI 1.16–5.21) (11 points); language barrier (aOR 7.44; 95% CI 2.78–19.95) (24 points); unstable housing (aOR 3.11; 95% CI1.43–6.77) (13 points); ART prejudgment (aOR 11.05; 95% CI 1.81–67.53) (28 points); missed appointments (aOR 10.50; 95% CI 4.36–25.31) (28 points); psychiatric disorder (aOR 2.10; 95% CI0.96–4.61) (9 points) no factor (6 points). A score cut-off of 26.3 points identified non-adherence (sensitivity 0.87, specificity 0.86, positive predictive value (PPV) 0.73, and negative predictive value (NPV) 0.94, C statistic 0.86 (0.82–0.94)). In the validation cohort, 78/225 (34%) were non-adherent. The model predicted non-adherence with a sensitivity, specificity, PPV and NPV of 0.87, 0.86, 0.77, and 0.93 respectively (C statistic 0.91 (0.86–0.95)).
Conclusion: This easy-to-use highly sensitive and specific tool could be used at ART initiation to identify patients in need of higher resources to achieve optimal treatment goals.

PE31/8

Measles seroprevalence among HIV infected patients in central part of Poland – vaccination proposal

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Purpose: In 2018, there was 5x increase in measles in Poland with 335 cases confirmed. The majority of measles cases in Europe were reported in Ukraine (bordering with Poland), with more than 54 000 cases. The aim of study was to check the presence of measles antibodies in HIV-infected patients and establish local vaccination recommendations in this group of persons.
Method: HIV(+) patients with no prior history of measles vaccination or with one dose of measles-containing vaccine (MCV) in the past were tested for measles IgG antibodies (IgGAb) between March and May 2019. They were divided into two groups: Group I - patients born before 1975 (before the introduction of measles vaccine in Poland) and Group II - patients born in 1975–1990 (received only 1 dose of MCV). Medical documentation of epidemiological data (age, sex, vaccination) and laboratory tests (CD4 and VL HIV) were analyzed.
Results: Measles IgGAb were analyzed for 161 patients (84%male), median age 41[36, 49] with VL HIV<40 (94%). In Group I - 63 patients - never vaccinated measles IgGAb were found in 56 (89%) people, after natural infection. In Group II, 98 patients, vaccinated with 1 dose of MCV in childhood, specific IgGAb were found in 36 (37%) subjects. 11 (16%) persons without measles immunity were vaccinated with MMR vaccine. Table1.
Conclusion: Among patients who received only one dose of MCV, the presence of measles IgGAb is quite low, only 37%. Such group of patients should be vaccinated without prior specific IgGAb testing. In group of older patients over 45 years the measles seroprevalence is high, about 90%; vaccination should be considered after testing for specific antibodies.

Patient characteristics associated with IgG measles

Measles antibodies	HIV(+) patients N (%)			Gender Male N (%)	last CD4 c/uL median [IQR]	MMR vaccination N (%)
	Group I	Group II	p			
Measles IgG (+)	6 (89%)	36 (37%)	<0.0001	78 (85%)	644 [503,1013]	0
Measles IgG (-)	7 (11%)	62 (63%)	<0.0001	52 (75%)	534 [392,838]	11 (16%)

PE31/9

Nurse-led annual health review – one year follow up

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Objectives: People living with HIV require an annual health monitoring and assessment according to BHIVA guideline, to improve the quality of care. We developed an annual health pro-forma in 2018, for nurses to assess and monitor the prevalence and outcomes of co-morbidities in patients attending the nurses-led clinic. With this audit, we evaluated the cardiovascular, renal, bone, emotional, sexual and women's health for 55 patients aged 31–87.
Methods: We conducted an audit of 55 PLWHIV attending a large South-East London HIV clinic in the UK, all selected via our annual health Nurse-Led clinics in June 2019. A retrospective case note review was undertaken to evaluate the annual health pro-forma the nurses introduced in July 2018.
Results: 55 patients were identified (65% male and 35% Female; median age 50 years [IQR 44–55]; 56% Black, 38% white and 5% mixed ethnic background).

- 42/47 (90%) had a 10-year Q-Risk3 assessment, 7/47 (15%) assessed scored ≥ 10% and 5/7 (71%) require an ART review.
- 32/55 (58%) patients on TDF base regimen are currently receiving ARVs associated with nephrotoxicity (TDF, LPV, and ATV), however 5/32 (13%) did not have yearly urinalysis as per BHIVA guidelines.

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Table 1. Annual health review in 2018

Annual Health Review		Assessment conducted (n=55)	BHIVA Target % (Achieved)	Outcome : No Issues	Outcome : Sign-posted	Outcome : Referred
Cardiovascular	BMI (kg/m^2)	51 (93%)	90% (Y)	25%	50%	25%
	Blood Pressure (mm/Hg)	55 (100%)	90% (Y)	68%	36%	32%
	10-year CV risk (QRisk3)[1] (n=47)	42 (90%)	90% (Y)	48%		16%
Renal health	Renal profile – bloods	55 (100%)	100% (Y)	87%	None	13%
	Urinalysis	47 (85%)	100% (N)	None	None	None
Bone health (n=28	FRAX score calculated[2]	26 (93%)	90% (Y)	93%	•None	7%
Emotional health	Adapted GAD/ PHQ	51 (93%)	90% (Y)	89%	5%	6%
Woman Health (n=19)	Informal woman health discussed	18 (95%)	95% (Y)	95%	5%	None
Sexual Health		55 (100%)	95% (Y)	31%	67%	2%
Alcohol		54 (98%)	95% (Y)	91%	7%	2%
Smoking		51 (93%)	90% (Y)	85%	15%	None
Recreational Drugs		48 (87%)	90% (N)	96%	2%	2%

[1]CV risk preform to patient over 40 years old.
[2]FRAX score was done to all patients over 50 years old.

Table 2. Presence of co-morbidities and high-risk indicators

Co-morbidities		Number of patients and N (%)	High risk
Cardiovascular BMI (kg/m^2) (n=51)	≤18.5 kg/m^2	1 (2%)	≥25 Kg/m^2: 38 (74%)
	18.5 to 24.9 kg/m^2	12 (24%)	
	25 to 29.9 kg/m^2	25 (49%)	
	30 to 39.9 kg/m^2	13 (25%)	
	Systolic BP (mm/Hg) (n=55)	9 (16%)	>140 mmHg
		9 (16%)	>90 mmHg
	Diastolic BP (mm/Hg) (n=55)	11 (20%)	N/A
	Receiving anti-hypertensive (n=55)		
	10-year CV risk (QRisk3)	20 (43%)	>10%; 9 (21%)
	3 (n=47)	15 (32%)	
	≤ 4.9%	7 (15%)	
	≥ 5% to 9%	5(10%)	
	≥ 10%		
	Not assessed		
	Smoking (n=55) o Current o Never o Ex-smoker	1 (2%)	N/A
		49 (89%)	
		5 (9%)	
	Recreational drugs (n=55) o Current o Never o Ex-user	1 (2%)	1 (2%)
		49 (89%)	
		5 (9%)	
Renal health	CKD stage (CKD EPI)4 (n=55)	48 (87%)	eGFR <60; 7 (13%) uPCR ≥ 15 mmol/L
		7 (13%)	
	Normal>60 mmol/L (CKD1 and 2)	0	
	30–60 mmol/L (CKD3)		
	<30 mmol/L		
	Urinalysis - proteinuria present (n=55)	10 (18%)	
		27 (84%)	
	Urinalysis on TDF (n=32)	4 (7%)	
	Urinalysis - not done but required (n=55)		
Bone health	FRAX score (n=26) o Norma o Abnormal	24 (92%)	2 (8%) hip fracture
		2 (8%)	

3 Over 40 years old; 4eGFR was corrected for black ethnicity

- Of those with normal blood pressure, 11/55 (20%) are receiving anti-hypertensive, however 5/11 (45%) have uncontrollable blood pressure (≥140/90 mmHg).

Introducing the annual health review has enabled the majority of the BHIVA target attainment except for urinalysis and recreational drugs, however overall results has improved over 30%.

Conclusion: One year on, the uptake of the annual health review has dramatically improved. We identified high prevalence of comorbidities and psycho-social issues using the Nurse-led annual pro-forma, and they were referred and addressed appropriately. Due to the high complexity of care, urinalysis and recreational drugs falls short of the BHIVA target which is being addressed by the multi-disciplinary team.

PE31/11

Viral hepatitis in HIV-positive patients – testing, prophylaxis and treatment in Central and Eastern Europe

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Objectives: Because of shared routes of transmission hepatitis C (HCV) and hepatitis B (HBV) are the most common co-infections in people living with HIV (PLWH). All PLWH should be vaccinated against HBV and hepatitis A virus (HAV) and treated for HBV and HCV due to increased risk of developing end-stage liver disease. We aimed to describe testing, prophylaxis and treatment of viral hepatitis in PLWH in Central and Eastern Europe.

Method: Data was collected from 18 countries of Euroguidelines in Central and Eastern Europe Network Group (ECEE): Serbia, Turkey, Bosnia and Herzegovina, Romania, Bulgaria, Croatia, Estonia, Ukraine, Hungary, Greece, Albania, Armenia, Czech Republic, Georgia, Belarus, Slovakia, Lithuania, Poland, four countries had information from two centers.

Results: In total 21 of 22 (95%) centers in ECEE screen all PLWH for HCV antibodies and for HBsAg. In 20 centers (91%) HCV testing is free of charge either covered by governmental programs (five centers (23%)) or by health insurance (15 centers (68%)), in two centers (9%) PLWH have to pay. All centers have access to DAAs but only six centers (27%) have no limitations for treatment access. HbsAg testing is covered by governmental programs in four centers (18%), by health insurance in 15 centers (68%), in three centers (14%) HBsAg screening is available as paid service. 13 centers (59%) vaccinate all PLWH against HBV, it is free of charge in 11 centers (50%). In HIV/HBV co-infected patients 20 centers (91%) use tenofovir-based regimen. Only 12

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centers of 22 (55%) screen for HAV IgG, and three centers (14%) vaccinate all PLWH against HAV, vaccination is free of charge in six centers (29%).
Conclusion: Testing for viral hepatitis in PLWH in ECEE is sufficiently good, however, vaccination against HBV especially against HAV has room for improvement, also HCV treatment access needs rectification in entire ECEE.

PE31/12

Evaluating a national pilot process for reviewing late HIV diagnoses in England and Wales

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Purpose: Late HIV diagnosis is associated with significant mortality in people living with HIV (PLWH) and high numbers of missed opportunities (MOs) for earlier testing have been identified. A pilot of a national late diagnosis review process (LDRP) was undertaken in 15 HIV services evaluating the feasibility and effectiveness.
Method: 15 HIV services across England and Wales participated in the pilot between July and December 2018. All patients presenting to HIV service with CD4 count <200 cells/mm^3 at diagnosis were included. Healthcare attendances within 5 years were reviewed for MOs, and safety reviews and feedback to external services where MOs occurred undertaken if MOs and patient harm was identified. A structured survey was completed by service leads evaluating the pilot.
Results: Of 127 very late diagnoses identified, 40 (31.5%) had 79 possible or definite MOs identified for earlier testing. Clinical indicator conditions were present in 58.2% of MOs episodes. PLWH with MOs were more likely to be white, UK-born (Table 1), have lower CD4-counts and AIDS-defining conditions and suffer significant harm at diagnosis (Table 2). There were no differences in age, gender, and route of HIV acquisition between those with MOs or without (Table 1).

Table 1. Summary of patient characteristics

	Very late diagnoses without MOs (n=87)	Very late diagnoses with MOs (n=40)	p-value
Mean age (SD)	44.1 years (± 12.1)	46.9 years (± 12.6)	0.238
Male gender	60 (69%)	31 (77.5%)	0.367
Female gender	26 (29.9%)	9 (22.5%)	
Transgender	1 (1.1%)	0 (0.0%)	
White ethnicity	41 (47.1%)	28 (70%)	0.016
Non-White ethnicity	46 (52.9%)	12 (30%)	
Country of birth - UK	26 (29.9%)	23 (57.5%)	0.003
Country of birth - Outside the UK	61 (70.1%)	17 (42.5%)	

Table 2. Summary of disease characteristics at HIV diagnosis

	Very late diagnoses without MOs (n=87)	Very late diagnoses with MOs (n=40)	p-value
Mean CD4 count at diagnosis (SD)	101.4 cells/uL (± 78.2)	61 cells/uL (± 64.5)	0.003
Mean HIV viral load at diagnosis (SD)	1 043 498 copies/mL (±3 565 733)	733 471 copies/mL (±1 655 354)	0.506
AIDS-defining conditions at diagnosis	28 (32.2%)	26 (65.0%)	0.001
Grade 3 or worse harm	30 (34.5%)	29 (72.5%)	<0.0001
Deaths	1 (1.1%)	2 (5.0%)	-

Only 1 of 11 leads who contacted external services where MOs occurred reported positive engagement with the feedback process to enable earlier testing. 73.3% of services agreed the LDRP was sustainable. One site reported three deaths linked to MOs, leading to organisational learning following safety review and creation of a task force to implement universal testing.

Conclusion: This pilot demonstrates feasibility and effectiveness of a national case review process for patients with late HIV diagnoses in identifying MOs for earlier testing. Challenges remain to engage other services, but expansion of this process nationally may encourage earlier testing and reduce rates of late HIV diagnoses.

PE31/13

GESIDA quality of care indicators for PLWH: report from two Spanish hospitals 2009–2017

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Purpose: To analyze the GESIDA Quality of care (QOC) indicators and describe its fulfillment in two spanish hospitals during the 2009–2018 period.
Method: Observational retrospective study that included adult HIV-infected patients followed-up at the Son Espases (HUSE) and Son Llátzer (HSLL) hospitals in Palma de Mallorca between 1/1/2009 and 12/31/2017. Required data for analysis of the QOC indicators was collected from proprietary software (eVIHa) using an automated process.
Results: 2931 patients were included with a mean age of 48 years. Main characteristics at diagnosis are presented in Table 1. The epidemiological characteristics (average age, sex, risk group of acquisition of HIV infection were similar in both hospitals). We appreciated some differences in the uptake of patients (median days, percentage of patients with late diagnosis).
The percentage of patients on ART was very high in both centers, with an increase in the % of patients on ART at 90 days of diagnosis (but still with low percentages of 55–40%). Other indicators of kidney function evaluation process, cardiovascular risk, vaccination against pneumococcus were performed regularly in both centers (Table 2). The outcome indicators were

Table 1. Characteristics at diagnosis

	2009	2010	2011	2012	2013	2014	2015	2016	2017
Patients included - HUSE - HSLL	1645	1676	1715	1746	1807	1834	1852	1904	1952
	677	742	731	832	865	904	911	945	979
Mean age (y) - HUSE - HSLL	44.	44	45	45	46	46	47	47	48
	43.	43	44	45	45	45	46	47	47
Median Time diagnosis- first visit	56	74	73	43	40	29	40	34	49
(d) - HUSE - HSLL	52	68	51	45	42	34	28	33	45
CD4 <350 at diagnosis (%) -	45.87	50.42	41.73	39.86	40.14	39.42	33.33	33.60	27.91
HUSE - HSLL	39.44	38.46	45.56	53.62	50.65	39.02	50.88	30.43	34.18
Patients receiving ART in the first	18.42	25.0	18.68	25.53	25.74	32.88	42.86	51.14	55.41
90d since diagnosis (%) - HUSE	26.92	21.0	24.14	33.33	27.78	43.86	46.34	36.73	40.74
- HSLL									
Patients without ART (%) - HUSE	9.56	8.33	6.89	7.52	7.27	5.80	3.84	2.42	1.02
- HSLL	9.94	9.23	7.86	8.0	7.93	7.26	3.98	4.55	0.89

Table 2. GESIDA Quality of Care indicators

	2009	2010	2011	2012	2013	2014	2015	2016	2017
GESIDA 23 (pneumococcal	71.18	72.7	76.36	77.79	78.13	80.76	85.27	86.51	88.64
vaccinated) % HUSE	7.73	21.95	44.78	60.98	61.31	67.12	65.31	64.92	65.63
HSLL									
GESIDA 17 (eGFR and urinalysis)	75.76	94.09	97.96	95.45	96.80	97.83	97.81	96.55	98.69
HUSE	77.23	96.42	98.23	99.56	98.89	99.72	99.72	97.80	99.55
HSLL									
GESIDA 56 (Cadiovascular risk	0.08	41.19	83.48	86.20	87.47	86.49	85.0	83.13	84.11
estimation, FHS) HUSE	0	75.22	95.64	95.28	94.62	96.25	96.04	93.37	95.72
HSLL									
GESIDA 57 (Patients requiring	9.83	8.20	5.58	5.25	6.65	5.74	5.14	4.14	4.04
admission) HUSE	7.45	4.90	9.04	6.81	6.82	5.03	3.70	4.41	3.73
HSLL									
GESIDA 40 (ART switch during	37.33	54.05	19.48	23.88	31.65	30.30	25.93	19.59	18.18
first year) HUSE	64	51.06	52.38	39.58	20.41	23.19	23.91	35.90	18.52
HSLL									
Mortality HUSE	0.74	1.08	0.98	0.95	0.62	0.94	0.53	0.17	0.28
HSLL	0.41	0	0.39	0.89	0.56	0.14	0.28	0.29	0.15

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very similar between both hospitals: CV <50 in weeks 24 and 48 of the start of ART, changes in ART in the first year, mortality rate and percentage of patients requiring admission.
Conclusion: - Although improved in the last years, the pecentage of late diagnosis is still high in the included centers. An improve in the delay of ART start was also observed.
- Both centers comply with GESIDA QOC indicators of follow-up including renal function measuring, pneumococcal vaccination and cardiovascular estimation.

PE31/14

Late presentation and barriers to the early HIV diagnosis in Central part of Ukraine

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Ukraine has the second-largest HIV epidemic in Eastern Europe and Central Asia with high prevalence of late presentation - to 55–59% every year.
Purpose: To explore predictors for late HIV diagnosis and barriers to the early HIV diagnosis.
Method: We conducted interviews with 325 HIV-infected patients registered in Poltava regional AIDS center in 2016–2018. Barriers to early HIV diagnosis were analyzed in 128 health workers (physicians and nurses) of regional center. Nadir CD4 count <350 cells/mL or AIDS-defining illness defined late presenters. Binary or multinomial logistic regression models were used to identify the predictors for late HIV presentation.
Results: Among 325 HIV-infected patients, 182 (56.0%) were late presenters. Main predictors of late presentation identified male sex (78%, p=0.001), drug using (55.6%, p<0.05), age >40 years (43.2%, p<0.05). Most late presenters visited of medical clinics with symptoms during last year preceding HIV test (76.8%, p=0.001) and obtained first HIV-test following a doctor's recommendation (62.9%, p<0.05). The main barriers to the early HIV diagnosis in health workers were pre-test and post-test counseling (82.1%), writing consent (92.7%) and social problems with testing patients from not key groups («It is not convenient») (71.3%).
Conclusion: This study suggests association between the male sex, age>40 years, drug using and late presentation of HIV. Implementation of new HIV testing strategies and enhanced HIV-testing in medical clinics are urgently needed.

PE31/15

Operational research of barriers and facilitators to harm reduction services for intravenous drug users (including female IDUs)

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Purpose: Harm Reduction programs have been operating in Georgia since 2005 with the aim to reduce the health, social and economic harms of substance use to individuals, communities and societies. The aim of the study was to evaluate barriers and facilitators to HR programs and develop recommendations for improving quality of services and overcoming those barriers.
Method: Qualitative study using in-depth interviews was conducted during September-November 2017; the study participants were providers and beneficiaries of harm reduction services. Overall 12 providers and 35 IDUs participated in the study.
Results: The study results showed that stigma and discrimination is one of the leading barriers to harm reduction services, which is even much greater against female IDUs. Anonymity and confidentiality are among the most important factors for IDUs when using harm reduction services. Existing strict drug policy considerably limits access to NSP services. The issue concerning the take away dosages was named as an important barrier for joining as well as for retaining in OST programs. The study revealed that there is a geographical accessibility barrier to all harm reduction services in regions. There is a lack of awareness of NSP while awareness of OST programs is very high among IDUs. The leading factor encouraging IDUs to get harm reduction services is a free service that was common for all programs. User-friendly environment is another facilitator to the services.
Conclusion: Results of this study shed additional light on some social, structural, individual and environmental factors hindering IDUs' access to harm reduction services. Overcoming these barriers and addressing IDUs' needs is an important prerequisite for effective implementation of preventive programs. The study results serve as a bases for key policy recommendations for improving measures of HIV response in Georgian.

PE31/16

A seven-month prospective review of HIV admissions to a regional infectious disease unit in Manchester, UK

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Background: North Manchester General Hospital (NMGH) is home to a tertiary Regional Infectious diseases unit (RIDU) in the North West of England. It is the largest HIV centre outside of London in the United Kingdom, caring for around 2500 people living with HIV (PLWH). It is also the primary HIV inpatient unit for the Greater Manchester region specialising in all aspects of HIV patient care from disease complications to opportunistic infections (OI). It additionally provides specialist advice to healthcare professionals in the region with regards to assessment, management of PLWH and their holistic care.
Method: A prospective analysis of all patients admitted to RIDU was undertaken over a 7-month period (1st Nov 2017 - 1st Jun 2018). Each patient who required inpatient admission was assessed for patient demographics, referral method (whether from primary or secondary care), presenting complaint and whether their 18 month end-diagnosis was related or independent of their HIV diagnosis
Results: Of 1053 admissions to the Regional Infectious Disease Unit in Manchester, 12% (123/1053) of all admissions were due to HIV related disease. From the patients with an HIV related admission, 50% (61/123) were due to " Complications of HIV infection", 31% (38/123) were "HIV patients with OIs and 19% (24/123) were "New HIV diagnosis" who required inpatient admission.
There were multiple OIs in 20 patients, PCP in 14 patients, Mycobacterial infection in 9 patients and Respiratory infection in 26 patients. Sui generis end-diagnoses comprised of leishmaniasis, falciparum malaria, schistosomiasis, limbic encephalitis, CD8 encephalopathy and immune reconstitution inflammatory syndrome secondary to progressive multifocal leukoencephalopathy.
Conclusion: The RIDU in Manchester admits a significant number of people with HIV who require inpatient care due to the complexity of their condition. The unit manages People living with HIV due to a large diversity of reasons including a variety of opportunistic infections.

PE31/17

Annual health review for people living with HIV – an evaluation

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Purpose: To better standardise our documentation and to meet national standards we introduced an annual health review form from early 2019. The annual form is in two parts, one completed by the patient and one by an HIV nurse. The purpose of this audit was to evaluate the completion of the proforma and documented outcomes of people living with HIV.
Method: We reviewed completeness and outcome of the annual review form process after 6 months of implementation. We interrogated documentation of physical comorbidities such as bone health, cardiovascular risk, general physical health and frailty. The Patient health question-2 (PHQ2) and Generalised anxiety disorder2 (GAD2) scales were used to screen for anxiety and depression and AUDIT C for alcohol consumption.
Results: A total of 68 annual review forms were analysed: 18% female; 76% white or not stated, 21% black, 3% Asian ethnicity; mean age 56 years (IQR 51–63).
According to BHIVA guidelines 84% (57/68) needed cardiovascular risk assessment, of which 51/57 (89%) occurred. Almost all 67/68 (99%) had a FRAX® score recorded and all patients >50 years (n=54) had frailty assessed.

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The GAD2 was completed on 100% and 98% had a PHQ2 documented with 21% and 17% respectively triggering consideration of onward referral to psychology support services. Almost all had alcohol consumption assessed with 13% scoring 5 or higher. Onward referrals arising from annual review is presented in Table 1.

Conclusion: Our annual form has improved documentation and identified a significant proportion of medical comorbidities triggering further investigation and intervention. Involving the wider clinical team in this process has helped improve detection of otherwise missed comorbidity, facilitated onward referral, and better supported the delivering of holistic, person-centred HIV care.

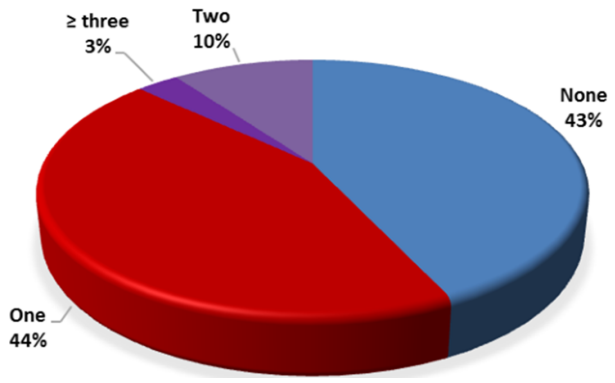
Referrals to specific services following annual health review (N=68)

Referral Type	n (%)
Frailty Clinic	17 (25%)
Psychology Services	7 (10%)
Peer Support	2 (3%)
In-house Support hub	9 (13%)
Community Nurse Specialist	2 (3%)
Cardiology Clinic	8 (12%)
AIN (anal) Screening	6 (9%)
DEXA screening	9 (13%)

Annual Health Assessment

Assessment	Number (%)
PHQ2 Score[1]	
0	36/68 (53%)
<3	20/68 (29%)
≥3	11/68 (17%)
Not recorded	1/68 (1%)
GAD Score[2]	
<3	54/68 (79%)
≥3	14/68 (21%)
FRAX® Score	
≥10%[3]	7/68 (11%)
<10%	60/68 (88%)
Not recorded	1/68 (1%)
Qrisk®2	
Not recorded	6/68 (9%)
Not required	11/68 (16%)
Performed	51/68 (75%)
Audit-C Score	
≥5 or more[4]	9/68 (13%)

[1]Scored ≥3, suggesting some degree of depression, prompting further discussion and/or onward referral.
[2]Scored ≥3, suggesting some degree of depression, prompting further discussion and/or onward referral.
[3]Required intervention following our local guidelines.
[4]Positive screening - prompting further discussion and/or onwards referrals.



Onward Referral to other services following annual health review

PE31/18

Analysis of adherence to HIV-positive quality of care indicators and their impact of service quality perceptions in patient: a Spanish cross-sectional study

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Purpose: The objective was to evaluate compliance with current quality indicators of care and analyze their influence on satisfaction with patient-perceived healthcare.

Method: All HIV patients attended in a Spanish hospital between 2011 and 2017 were included for compliance with HIV quality indicators proposed by GeSIDA (Spanish AIDS Study Group).To assess patient satisfaction, the *SUCE* (User Satisfaction of External Consultations) questionnaire was given between February and November 2017 to those who signed the informed consent. This questionnaire was specifically designed and validated to understand the satisfaction of patients at outpatient clinics hospital. It consists of 12 items with a response scale of 1 (worst rating) to 10 (best). Through ROC curves, 6.3 was selected as value to discriminate satisfied/unsatisfied patients.

Results: Compliance with 47 indicators was calculated in the 334 patients attended. The satisfaction of 163 patients was assessed: 93 were excluded for loss of follow-up, transfer or decease, 43 for illiteracy or declined to participate. Of the 198 surveys delivered, 26 were not returned, 8 were delivered unanswered and 6 were invalid.74.46% of the quality indicators evaluated were met. The average satisfaction score was 9.04 out of 10 (95% CI: 8.90–9.20). 98.16% patients were satisfied. The response rate was high (86%).

The indicators whose compliance was most related were 16-*Periodicity of visits* [difference of averages CI 95%: 0.62 (0.13–1.11)], 21-*Vaccination against Hepatitis A* [difference of averages CI95%:1.14(0.16–2.12)] and 23-*Vaccination pneumococcal infection* [difference of averages CI95%:0.74 (0.10–1.38)]. Those who met the indicator of 26-*Assessment of alcoholic intake* had a lower satisfaction [difference of averages 95% CI: -1.20(-1.97–0.44)].

Conclusion: In this Spanish cohort, compliance with quality indicators was high, and satisfaction with healthcare scored, favorably.Adherence to quality indicators showed little relation to patient satisfaction.

Quality health care requires the achievement of the health objectives proposed by scientific societies but also in meeting patient expectations.

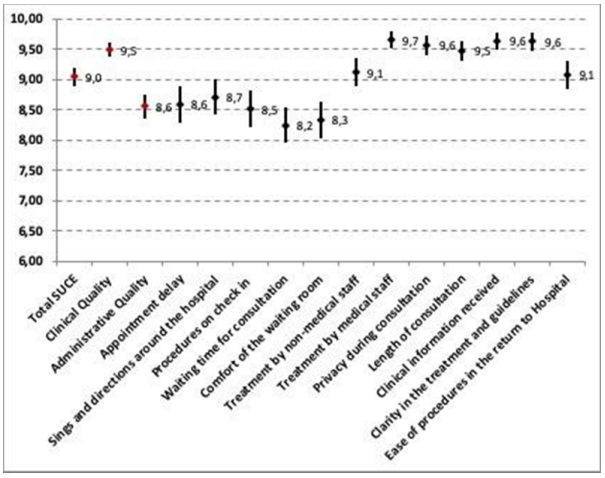


Figure 2. Result of the satisfaction questionnaire (SUCE) in the patients interviewed

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Table 1. Univariate analysis of quality indicators and satisfaction (SUCE)

		SUCE
N	Indicadores de calidad asistencial	Difference of means CI 95%
6	Delay in referral to specialty care	-0.26 (-1.33; 0.81)
7	Late diagnosis of HIV in specialized care	-0.23 (-0.81; 0.35)
8	HIV diagnosis with previous negative serology	-0.10 (-0.65; 0.44)
10	Complementary tests in the initial assessment	0.01 (-1.07; 1.10)
11	HIV Plasma Viral Load	-
12	Determination of lymphocyte subpopulations (CD4)	-
13	Health education in the initial assessment	0.24 (-0.06; 0.54)
15	Indication of treatment with <350 CD4 and without previous ART	-
16	Periodicity of visits (regular follow-up)	0.62 (0.13; 1.11)*
17	Basic renal study in HIV patients	-0.57 (-2.49; 1.35)
20	LTI Detection	0.09 (-0.27; 0.44)
21	Vaccination against Hepatitis A	1.14 (0.16; 2.12)*
22	Vaccination against Hepatitis B	0.49 (-0.41; 1.40)
23	Vaccination against pneumococcal infection	0.74 (0.10; 1.38)*
24	Prophylaxis against Pneumocystis jiroveci and Toxoplasma	-0.14 (-3.03; 2.76)
25	Treatment and prevention of smoking	0.11 (-0.52; 0.75)
26	Assessment of alcoholic intake	-1.20 (-1.97; -0.44)*
29	Screening for syphilis	0.03 (-0.35; 0.41)
30	LTI Treatment	-0.60 (-2.18; 0.98)
35	Adaptation of the initial ART guidelines to the guidelines	-
36	Initiation of ART in patients with symptomatic B/C events	-
37	First visit after the introduction of an ART	-0.69 (-1.61; 0.23)
38	Undetectable viral load (< 50 cop/ml) in week 48	-0.62 (-2.76; 1.52)
39	Treatment with Abacavir (ABC) without previous HLA-B 5701	-
40	Changes in treatment during the first year	-0.08 (-0.87; 0.71)
41	Registration of adherence to treatment	0.33 (-0.14; 0.79)
42	Study of resistance in virological failure	-0.48 (-1.85; 0.90)
45	ART in HIV-positive pregnant women	-
47	Incidence of vertical transmission	-
49	CHILD or MELD evaluation of chronic liver disease	1.67 (-1.34; 4.67)
50	Evaluation of HCV co-infected patient	-
54	HBsAg patients receiving effective treatment	
55	Echographic monitoring in cirrhotic patients	1.25 (-3.23; 5.73)
56	Cardiovascular risk assessment	-0.01 (-0.34; 0.31)

Toxicities

PE32/1

Sleep and functional characteristics of Central London Outpatient HIV Cohort

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Background: Studies conducted in people living with HIV (PLWH) report high rates of sleep disturbance, without clear explanation as to cause or effect. We designed a study to assess overall quality of sleep, daytime functioning and wellbeing in a central London outpatient cohort of PLWH.
Methods: Outpatients attending 56 Dean Street were administered 8 validated sleep and wellbeing questionnaires: PSQI, FOSQ, ESS, ISI, FSS, GAD, PHQ and Wellness Thermometer. Associations were analyzed by univariable/multivariable analyses.
Results: Of 254 patients, >99% were men (96% MSM), 60% British, mean age 41 (SD±9.9) years, mean HIV duration 8 years (SD±6.3). 94% were on ART (24% EFV and 33% INSTI). Viral load was <40 copies/mL in 81% and mean CD4 count 724 cells/mm^3. 86% were employed, 72% university educated, 25% smokers, 42% used alcohol >once a week, 61% recreational drug use.
Daytime functioning was good (FOSQ 17, SD±2.9). 45% reported poor quality sleep (PSQI>5), 22% insomnia (ISI≥15), 21% daytime sleepiness (ESS≥10), 33% fatigue (FSS≥36), 14% moderate/severe anxiety (GAD≥10), 19% moderate/severe depression (PHQ≥10). Mean self-reported wellbeing score was 7 (score 0-10) SD±2.2.
HIV duration ≥10 years, anxiety and depression were associated with poor quality sleep (OR 3.7; 95% CI 1.1-12.4; p=0.04), fatigue (OR 6.7; 95% CI 1.8-24.8; p=0.01), and poorer functional outcomes (β=–1.0; 95% CI -2.0–0.0; p=0.05). There was a trend for association with poorer sleep quality for EFV or PI but not INSTI (p>0.05). Use of crystal methamphetamine and cocaine were associated with fatigue.
Conclusions: Poor quality sleep in our patients was associated with depression, anxiety and HIV duration but not ART class. Recreational drug use as a whole was not associated with poor sleep outcomes, although crystal methamphetamine and cocaine use were associated with fatigue. Despite high rates of poor sleep quality, daytime functioning was good.

PE32/2

Osteopenia and osteoporosis in young HIV-infected patients less than age of 40 years: incidence and risk factors

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Purpose: Reduced bone mineral density (BMD) is a common problem to the successful long-term management of human immunodeficiency virus (HIV) infection among patients with access to combination antiretroviral therapy (cART). Data on the prevalence and associated factors of reduced BMD in Asian populations remain scarce. Therefore, the study was performed to evaluate the incidence and risk factors of osteopenia and osteoporosis.
Method: From December 2015 to December 2018, a cross-sectional survey was conducted among HIV- infected patients aged ≥ 20 years. We analyzed the medical history of the infected person, lifestyle and regimen of cART. Osteopenia was defined as a BMD T-score between -1.0 and -2.5, and osteoporosis was defined as a BMD T-score -2.5. Linear and ordinal logistic regression analyses were performed to evaluate factors of FRAX tool and other possible risk factors.
Results: Totally, 802 HIV-infected patients were included, and 541 patients had normal BMD result, and 238 (29.7%) and 23 (2.9%) patients were reported as osteoporosis and osteoporosis, respectively. There were 656 cases with an age of <40 years (81.8%). In multivariable conditional logistic regression analysis, ever exposed to TDF (aOR=1.49, 95% CI 1.09-2.04), BMI <18.5 (aOR=4.36, 95% CI 2.62-7.26), smoking (aOR=1.69, 95% CI 1.21-2.38), non-exercise (aOR=1.42, 95% CI 1.02-1.98) and history of fracture (aOR=1.46, 95% CI 1.02-2.09) were independently associated with reduced bone mineral density.
Conclusion: Among young HIV-infected MSM, low BMI is common and also the leading factor of osteopenia or osteoporosis. Besides, smoking, non-exercise, history of fracture and ever exposure of TDF have been implicated significantly; hence, TDF sparing regimen is more suitable for patients with risk factor of osteopenia and osteoporosis, and increasing body weight and exercise were encouraged to improve reduced bone mineral density.

PE32/3

Predictors of weight gain in patients treated with dolutegravir

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Purpose: Recent studies have highlighted a significant weight increase in HIV infected patients who began antiretroviral drugs (ART), particularly doultegravir (DTG). Aim of the present study was to evaluate predictors of weight gain in DTG treated patients in SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals) cohort.
Method: We analyzed data from SCOLTA prospective database. All patients initiating DTG and for whom weight was registered were considered. We defined as gainers those patients whose weight increased by at least 7% from baseline. Ninety-one patients with weight gain ranging from 1% to <7% were excluded. Non gainers were those whose weight increased <1% or decreased. The multivariable analysis was performed by logistic regression, with gainer y/n as the dependent variable, including baseline weight, age, sex, CDC stage, ART, years of previous ART, naïve/experienced, HCV treatment and statin use.
Results: A total of 503 patients were analyzed: DTG was associated to abacavir/lamivudine (ABC/3TC) in 276 patients (54.9%), tenofovir/emtricitabine (TDF/FTC) in 128 (25.4%), darunavir/ritonavir or cobicistat in 29 (5.8%), rilpivirine in 24 (4.8%), 3TC in 34 (6.8%) and tenofovir alafenamide (TAF)/FTC in 12 (2.4%). Among them, 503 and 393 patients reached 6 and 12 months follow-up. Eighty-one subjects (16.1%) were gainers (Table 1).In the multivariate analysis, the determinants for being gainers were lower baseline weight (OR by 5 Kg more 0.82, 95% CI 0.73–0.93), male sex (OR 2.04, 95% CI 1.01–4.13), TDF/FTC as compared to 3TC/ABC (OR 2.57, 95% CI 1.42–4.65), CD4 count (OR for cell/mL >500 vs <200 0.50, 95% CI 0.25–0.99), statin use (OR 2.43, 95% CI 1.06–5.05) and successful HCV treatment (OR 6.63, 95% CI 2.08–21.13).
Conclusion: In SCOLTA the use of TDF/FTC resulted as independent factor associated with weight gain in PLWHIV treated with DTG. Male patients with lower baseline weight and lower CD4 were those more prone to gain weight.

Table 1. Characteristics of patients in SCOLTA DTG cohort, according to weight gain status.

	Non Gainers		Gainers		All		p
	N=422	83.9%	N=81	16.1%	N=503	100%	
Male Sex	N=310	73.5%	N=64	79.0%	N=374	74.0%	0.29
Age, years (mean±SD)	47.43±11.7		46.0±12.0		47.1±11.7		0.36
Weight, Kg (mean±SD)	71.2±13.3		67.4±15.4		70.6±13.7		0.02
CD4, cells/mmc (mean±SD)	594±360		440±370		570±365		0.0006
Naive Status	N=96	22.7%	N=29	35.8%	N=125	24.9%	0.013
HCV active infection (baseline)	N=32	7.6%	N=13	16.0%	N=45	9.0%	0.014
HCV eradication during follow-up (N=45)	N=8	25%	N=7	53.8%	N=15	33.3%	0.06
Statin use at baselin	N=34	8.1%	N=8	9.9%	N=42	8.3%	0.58

PE32/4

Effects of lamivudine plus dolutegravir 2-drug-regimen on bone mineral density in a multicenter Italian cohort

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Purpose: We aimed to assess the effects on bone mineral density (BMD) of a dual therapy with lamivudine (3TC) plus dolutegravir (DTG).
Method: We analyzed a multicenter cohort of HIV-1 infected, virologically suppressed patients switching to 3TC+DTG. DEXA scans were performed at baseline and at weeks 48 and 96 of follow-up; areal BMD (g/cm^2) was measured at the lumbar spine and at the femoral neck. Changes were compared using non-parametric tests; we assessed predictors of changes by linear regression.
Results: Eighty-one patients were analyzed. Full patients' characteristics are shown in tables 1 and 2. Overall, after 48 weeks, we observed a significant improvement in both spine BMD (+0.06 g/cm^2, p=0.048) and femoral neck BMD (+0.03 g/cm^3, p<0.001). At a multivariate analysis, improvement in femoral neck BMD was negatively associated with baseline femur BMD (per 1 g/cm^2 more, −0.29, p=0.002); meanwhile, the improvement in spine BMD was negatively predicted by peak HIV-RNA value (per 10 log10 copies/mL more, −0.11, p=0.021) and baseline spine BMD (per 1 g/cm^2 more, −0.08, p=0.036), after adjusting for age, sex, HCV-coinfection, BMI and cumulative time on TDF or PIs.
After 96 weeks, we registered a significant improvement in femoral neck BMD (+0.04 g/cm^2, p=0.014); we also registered an improvement, although not significant, in spine BMD (+0.005 gr/cm^2, p=0.065).
Changes in spine BMD at 48 weeks were significantly different between patients coming from a TDF-based regimen and those who didn't (+0.015 and +0.001 respectively, p=0.029); changes in spine BMD also differed in patients with osteoporosis at baseline compared to those without at both 48 weeks (+0.038 and +0.002, p=0.036) and at 96 weeks (+0.038 and +0.004, p=0.020).
Conclusion: 3TC+DTG showed a favorable effect on BMD in our cohort. A greater improvement was observed in patients coming from a non INI-based strategy and those with osteoporosis.

Table 1. Patients' characteristics at baseline (n=81).

Males, n (%)	59 (72.8)
Age (years), median (IQR)	52 (49; 58)
Anti-HCV positive, n (%)	22 (27.8)
CDC Stage C, n (%)	24 (29.6)
Years from HIV diagnosis, median (IQR)	24.0 (17.6;34.7)
Years on cART, median (IQR)	14.0 (10.0; 21.5)
Months on PI, median (IQR)	93.0 (31.0; 204.0)
Months on TDF, median (IQR)	73.0 (30.2; 109.0)
Osteoporosis at any site, n (%)	21 (25.9)
Osteopenia at any site, n (%)	39 (48.1)

Table 2. Patients' characteristics at baseline (n=81).

Nadir CD4+ cell count (cells/mm^3), median (IQR)	252 (148; 349)
Zenith viral load (log10 copies/mL), median (IQR)	4.64 (3.72; 5.31)
Lumbar spine BMD, median (IQR)	0.918 (0.810; 1.019)
Lumbar spine T-score, median (IQR)	−1.60 (−2.40; 0.43)
Lumbar spine Z-score, median (IQR)	−1.00 (−1.70; 0.10)
Femur neck BMD, median (IQR)	0.728 (0.644; 0.818)
Femur neck T-score, median (IQR)	−1.40 (−2.00; −0.70)
Femur neck Z-score, median (IQR)	−0.60 (−1.10; 0.10)

PE32/5

Switching from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) lowers alanine transaminase (ALT) and aspartate transaminase (AST) in patients with HIV infection with or without viral hepatitis co-infection

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Purpose: Our aim was to investigate the effect of switching TDF to TAF on liver enzymes and renal and lipid profile.
Method: Consecutive HIV patients enrolled in Surveillance Cohort Long-term Toxicity Antiretrovirals/Antivirals (SCOLTA) project switching from TDF to TAF for any reasons were included. Changes from baseline (T0) to 6-month follow-up (T1) were evaluated using paired t-test if differences were normally distributed and using signed rank test if not.
Results: 291 patients switched from TDF to TAF, 163 had at least one follow up visit. They were mostly males (131, 80.4%) and Caucasian (151, 92.6%). Forty-three (26.4%) were in CDC stage C, 48 (29.4%) on second-line antiretroviral therapy (ART), 154 (94.5%) had HIV-RNA <50 copies/mL, 35 (21.5%) were HCV-Ab positive (8 with detectable HCVRNA), and 14 (8.6%) HBsAg positive. Median time on TDF was 669 days (IQR 417–911). Median aspartate aminotransferase (AST) 23 IU/L (IQR 18–30), alanine aminotransferase (ALT) 24 IU/L (IQR 17–34). See table 1 for other patients'characteristics.Changes from switch (T0) to 6-month follow up (T1) are shown in the Table 2. At T1, both ALT (median -2, IQR -7 to 3 IU/L, p=0.0008) and AST (median -1, IQR -5 to 2 IU/L, p=0.003) were significantly reduced. AST and ALT reduction remained significant in patients negative for HCV-Ab and HBsAg (p<0.05 for both). Among 24 pts with ALT >40 IU/L, a significant proportion reduced this parameter (median change -20, -34 to -4, p<0.0001). Total cholesterol (TC) and HDL Cholesterol increased significantly [mean change 14.8±4.3 mg/dL (p<<0.0001) and 3.0±1.3 mg/dL (p<0.05), respectively] and eGFR decreased significantly (3.3±1.0 mL/min, p=0.002).
Conclusion: Switching from TDF to TAF demonstrated a significant reduction of ALT and AST and was associated with an improvement in eGFR and increased TC and HDL.

Table 1. Patients switching from TDF to TAF.

Variables	N=163 N (%) or mean±SD or median (IQR)
Age (years)	46.3±10.7
BMI (Kg/m^2)	24.9±3.7
Risk factor IVDU	27 (16.6)
CD4+ (cells/mL)	637 (440–898)
ART duration (years)	5.5 (2.2–13.4)
Second-line ART	48 (29.4)
Total cholesterol (mg/dL)	196±40
HDL cholesterol (mg/dL)	49±16
eGFR (mL/min)	86±19

Table 2. Liver enzymes changes from switch to 6-month follow-up in 163 patients enrolled in SCOLTA cohort

Number of patients according to HCV or HBV co-infection	HCV-Ab Neg (n=128)		HCV-Ab Pos (n=35)		HBsAg Neg (n=149)		HBsAg Pos (n=14)	
Liver enzymes	Median change (IQR)	p	Median change (IQR)	p	Median change (IQR)	p	Median change (IQR)	p
AST (IU/L)	−1 (−5 to 3)	0.049	−2 (−9 to 1)	0.01	−2 (−5 to 2)	0.01	1 (−5 to 14)	0.56
ALT (IU/L)	−1 (−7 to 3)	0.024	−3 (−14 to 2)	0.006	−2 (−7 to 2)	0.009	4 (1 to 11)	0.28

PE32/6

Weight gain in people living with HIV switched to dual therapy with dolutegravir plus rilpivirine: changes in body fat mass

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Purpose: We investigated changes in weight and body composition, and associated factors, in virologically suppressed HIV-infected adults switching to a dolutegravir-based dual therapy.
Method: Weight, fat mass and lean mass were measured in a prospective cohort of HIV-infected individuals switching to dolutegravir-based dual therapy using whole-body dual-energy X-ray absorptiometry (DXA) (NCT02491242). Data were compared with a control group of HIV-infected adults switched to boosted darunavir-based dual therapy. Individuals with lipodystrophy, or prior exposure to integrase inhibitors were excluded.
Results: Overall, 54 individuals met the inclusion criteria (mean age 53 years, male 61%), 37 (69%) switched to dolutegravir plus rilpivirine and 17 (31%) switched to darunavir plus lamivudine. At baseline, median weight was 73 Kg (standard deviation, SD 14.7) and 70 Kg (SD 13.1) in the dolutegravir and darunavir group, respectively (P=0.14). After 48 weeks, weight increased by 1.80 Kg (SD 3.8, +2.5%, P=0.03) in the dolutegravir group and 0.70 Kg (SD 3.9; +1%, P=0.28) in the darunavir group, without significant differences between groups (P=0.45).
After a median of 16 months (IQR 11.1–22.6) of switching, DXA scan exhibited similar increases in median fat mass in trunk, arms and legs in both groups (Table 1). Fat mass ratio was unaltered, and there were no significant changes in lean mass or muscle-related index in any group. In adjusted multivariable linear regression analysis, total fat mass increase was associated with baseline fat mass (Beta, −0.19, 95% confidence interval, CI: −0.08, −0.30) and nadir CD4+ count (Beta, −0.006, 95% CI: −0.0001, −0.012).
Conclusion: Weight gain observed with dolutegravir plus rilpivirine dual therapy was significant and related with fat mass gain in the different body compartments, with no modifications of lean mass. Nevertheless, comparable changes were observed in individuals switching to darunavir plus lamivudine. Fat mass increase was associated with baseline fat mass and immunological status.

Table 1. Changes in body fat mass. *p<0.05, Wilcoxon rank test

	Dolutegravir plus rilpivirine (n=37)	Boosted darunavir plus lamivudine (n=17)	p-value
Total fat mass [%], median (SD)	31.7 (8.2)	25.6 (8.4)	0.13
– Median change in percentage (IQR)	+1.1 (0–2.75)	+ 1.7* (−0.5, 3.8)	0.69
Trunk fat mass [%], median (SD)	32.8 (9.1)	25.6 (8.4)	0.07
– Median change in percentage (IQR)	+1.4* (−0.3, +3.8)	+1.85* (−0.1, 4.1)	0.57
Arms fat mass [%], median (SD)	35.3 (12.2)	26.1 (12.2)	0.05
– Median change in percentage (IQR)	+1.45* (−0.9, 3.87)	+2.45* (0.2–5.1)	0.22
Legs fat mass [%], median (SD)	28.2 (9.2)	26.5 (10)	0.67
– Median change in percentage (IQR)	+1.2* (−0.55, 2.6)	+0.7 (−0.4, 4.9)	0.72

PE32/7

Does switching to tenofovir alafenamide fumarate impair recovery of renal function in individuals newly diagnosed with tenofovir disoproxil fumarate induced renal tubular toxicity?

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Purpose: Tenofovir disoproxil fumarate (TDF) causes renal proximal tubulopathy in a minority of people living with HIV (PLHIV). Tenofovir alafenamide fumarate (TAF), a second generation tenofovir prodrug associated with much lower plasma tenofovir levels, appears to lack renal toxicity, but its safety when used in PLHIV with a new diagnosis of TDF-tubulopathy has not been confirmed. We sought to assess the outcomes of PLHIV switching from TDF to TAF for the indication of TDF-tubulopathy, compared to those switching to non-TAF regimes.
Method: In this retrospective, single-centre observational study, we identified all PLHIV switching combined antiretroviral therapy (cART) regimens for the indication of newly diagnosed TDF-tubulopathy between

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2014 and 2018. Demographic data, renal (serum creatinine, urine protein: creatinine ratio [uPCR], serum phosphate, fractional excretion of phosphate [FEPO4]), and HIV (viral load and CD4) parameters were extracted from clinical databases for each individual at diagnosis of tubulopathy and last recorded clinic visit post-switch.

Results: 16 PLHIV with TDF-tubulopathy were identified; 7 converted to TAF, and 9 to non-TAF cART, with mean exposure to TDF of 8.4±3.9 years and 9.2±3.9 years respectively. Significant reductions in uPCR (67±57 to 15±8 mg/mmol; p=0.04) and serum creatinine (119±12 to 115±14 µmol/l; p=0.03) and increase in serum phosphate (0.68±0.12 to 0.89±0.08 mmol/l; p=0.02), were observed in PLHIV switching to TAF, after 352±215 days follow-up. No significant difference in the magnitude of change in any renal or HIV variable was observed when comparing TAF and non-TAF switch groups (Table 1). All patients had HIV PCR RNA <200 copies/mL at last follow-up.

Conclusion: Switching to TAF-based cART in PLHIV with newly diagnosed TDF-tubulopathy appears safe and effective and does not impede renal recovery.

Comparison of renal variables at last follow-up, and the proportional change observed from baseline (mean±SD). *Data available in n=12/16

	TAF cART	Non-TAF cART	p value
uPCR (mg/mmol)	15±8	22±25	0.45
Serum creatinine (µmol/l)	115±14	126±47	0.55
Serum phosphate (mmol/l)	0.89±0.08	0.97±0.22	0.42
Urine FEPO4 (%)*	23±8	26±6	0.62
	% change from baseline	% change from baseline	
uPCR	- 66±21	- 75±28	0.48
Serum creatinine	- 4±3	- 18±35	0.31
Serum phosphate	+ 36±36	+ 88±132	0.33
Urine FEPO4*	- 20±55	- 12±50	0.80

Figure 1: Relative increase of weight over time for the patients treated with EVG

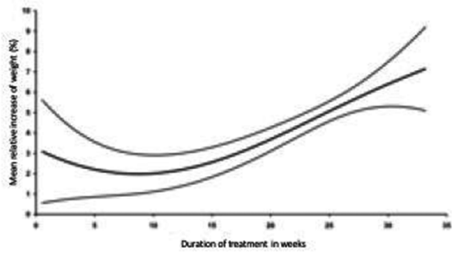
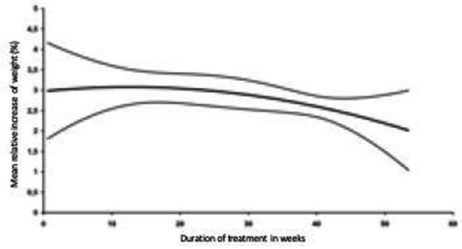


Figure 2: Relative increase of weight over time for the patients treated with DTG



PE32/8

Weight gain among HIV-positive persons treated with dolutegravir or elvitegravir

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Objectives: Integrase inhibitors-based regimens are recommended as first line antiretroviral therapy but they could lead to weight gain. The aim of our study was to evaluate the weight gain in HIV-1 infected persons treated either by dolutegravir (DTG) or Elvitegravir (EVG).

Methods: We retrospectively compared weight changes after initiating DTG or EVG among persons living with HIV (PLHIV) followed in the AIDS reference center of Cliniques universitaires Saint-Luc, Brussels. Of the 619 PLHIV included in the study, 508 were treated with DTG and 111 with EVG. The weight gain over time for patients on DTG and EVG was estimated by performing univariate and multivariate linear regressions adjusted for age, sex and race.

Results: In the total cohort, we observed a significant relative increase in weight of 2.80% (SEM of±0.23) (p<0.001) during a median time of 31 weeks (0.9–64.9). This increase was more pronounced in black people than white people (3.41%±0.39 vs 2.12%±0.31, respectively, p=0.0043) but less pronounced in elderly patients: the relative weight gain decreased by an average of 0.108%±0.019 per year of age. Sex bared no significant influence. In multivariate analyses adjusting for age, sex, race, only age remains significant (p<0.001). The average relative increase in weight for the 508 patients treated with DTG and the 111 treated with EVG was 3.80%±0.35 and 4.11%±0.63, respectively (p<0.001). The relationship between weight gain and duration of treatment was significant for EVG (r=+0.209; p=0.029) but not for DTG (r=−0.035; p=0.43) (Figure 1 and 2).

Conclusion: Significant weight gain was associated with DTG and EVG treatment. This effect was less pronounced in elderly patients. On EVG, weight gain was continuous over time, whereas on DVG, weight initially increased and then stabilized. Further studies with larger cohorts are warranted to confirm these observations.

PE32/9

NRTI backbone modification impact on weight, lipids and cardiovascular risk

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Purpose: Switch from tenofovir disoproxil fumarate (TDF) to tenofovir alafenamide (TAF) may be associated with weight gain and worsening of lipid profile. It is unclear if this is related to loss of protective effect of TDF or an effect of TAF. The impact of these findings on cardiovascular risk (CVR) has not been specifically investigated.

Method: This is a retrospective data collection from clinical notes of people living with HIV, switched to TAF-based antiretroviral treatment at Chelsea and Westminster Hospital, London, without changing other regimen components. Body weight, lipid profile, blood pressure were measured and CVR scores (QRISK2-2017 and Framingham) calculated before and every 12–24 weeks after the switch.

Results: 274 patients were included in the analysis: 216 switched from TDF (group 1), and 58 switched from non-TDF-containing regimens to TAF (group 2). Mean (SD) age was 59±9.9 years, 88.7% were male, 75.2% Caucasian, with a BMI of 23.95±4.6 m^2/Kg and CD4 count of 682±300 cells/µL at switch. Overall, weight increase one year post-switch to TAF was 1.7±6.8 Kg. Statistically significant weight and cholesterol increases from baseline were observed in group 1 (1.4±5.6 Kg p=0.02 and 0.3 mmol/l±1.0; p<0.05). One year after the switch to TAF the proportion of subjects with BMI >25 Kg/m^2 had risen by 10%. In a logistic regression analysis the odds of having a BMI increase >10% was associated with older age (odds ratio: 0.9; 95% CI (0.9, 1.0) p=0.02); CD4<200 cells/µL (p=0.04) and smoking (p=0.04).

QRISK2-2017 and Framingham scores remained stable (p=0.0997 and p=0.17) with no changes observed from baseline to one year post-switch.

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Conclusion: Our real world analysis suggests that weight and lipid increases may relate to switching away from TDF rather than the independent effect of TAF, however, long term data in larger populations are warranted.

PE32/10

Comparative neuropsychiatric toxicity profile of dolutegravir (DTG) versus efavirenz (EFV) versus other antiretroviral third drugs used either in first-line or switch antiretroviral therapies (ART): data from Icona Foundation Study Cohort

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Purpose: The aim of this study was to compare the risk of neuropsychiatric toxicity among DTG-based, EFV-based and other different antiretroviral regimens used as either first-line or switch ART.

Method: We included all ART-naive or virologically-suppressed treatment-experienced HIV+ patients, enrolled in the Icona cohort, who started or switched to an antiretroviral regimen including DTG or EFV or other currently used third drugs (boosted darunavir, atazanavir, rilpivirine or other integrase strand transfer inhibitors [INSTIs]). Probabilities of discontinuing third drug due to neuropsychiatric adverse events (NPAEs) were estimated by Kaplan Meier analysis. Predictors of treatment discontinuation due to NPAEs were identified by Cox regression analysis. A sensitivity analysis was performed in ART-naive patients starting ART from 2011 (first year in which DTG was available in Icona database).

Results: Overall, 7,854 ART-naïve patients (starting regimens based on DTG in 17%, EFV in 20% and non-EFV non-DTG in 63%) and 3,300 treatment-experienced patients (switching to regimens based on DTG in 31%, EFV in 15% and non-EFV non-DTG in 54%) were included. Main baseline characteristics are shown in Table 1. At survival analysis, patients on EFV-based ART were more likely to stop third drug due to NPAEs compared to patients on DTG-based or other ART both in ART-naïve ($p<.001$) and in treatment-experienced ($p<.001$) population [Fig. 1a,1b]. In both populations, at multivariable analysis, DTG as third drug was associated with a risk of discontinuing treatment due to NPAEs significantly lower than EFV but higher compared to other non-DTG non-EFV drugs [Table 2]. In ART-naïve patients, this result was also confirmed restricting the analysis to patients starting ART after 2011 [Table 2].

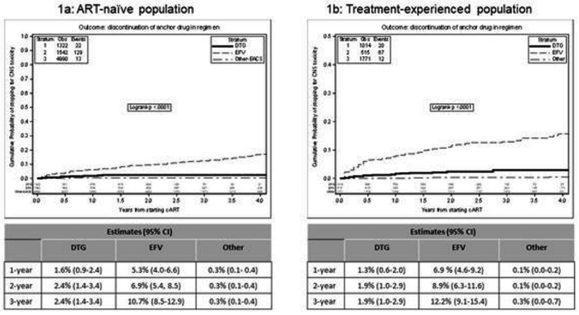
Conclusion: In this large cohort, both ART-naïve and treatment-experienced patients on DTG-based regimens showed a risk of experiencing treatment-limiting NPAES significantly lower than patients on EFV-based regimens but higher than people on non-EFV non-DTG ART.

Table 1: Baseline characteristics of patients enrolled according to the third drug in the regimen

	ART-naive population (n=7,854)				Treatment-experienced population (n=3,300)			
Characteristic	**DTG group (n=1,322, 16.8%)**	**EFV group (n=1,542, 19.6%)**	**OTHER group (n=4,990, 63.5%)**	**p-value**	**DTG group (n=1,014, 30.7%)**	**EFV group (n=515, 15.5%)**	**OTHER group (n=1,771, 53.7%)**	**p-value**
Female gender*	223 (16.9)	230 (14.9)	1016 (20.4)	**<0.001**	228 (22.5)	126 (24.5)	437 (24.7)	**0.411**
Age, years**	40 (31-49)	39 (32-46)	39 (31-47)	**0.051**	48 (39-56)	41 (35-47)	45 (38-52)	**<0.001**
Non-Italian born*	556 (42.1)	289 (18.7)	1351 (27.1)	**<0.001**	124 (12.2)	46 (8.9)	225 (12.7)	**0.065**
Risk Factor for HIV*				**<0.001**				**<0.001**
- Homosexual contacts	703 (53.7)	701 (45.9)	2293 (46.4)		421 (41.6)	165 (32.1)	610 (34.6)	
- Heterosexual contacts	442 (33.4)	599 (38.8)	1948 (39.0)		412 (40.6)	212 (41.2)	746 (42.1)	
- IDU	62 (4.7)	121 (7.9)	381 (7.7)		122 (12.1)	114 (22.2)	307 (17.4)	
- Other/Unknown	102 (7.8)	107 (7.0)	322 (6.5)		56 (5.5)	23 (4.5)	102 (5.8)	
AIDS diagnosis*	163 (12.3)	136 (8.8)	486 (9.7)	**0.005**	164 (16.2)	105 (20.4)	276 (15.6)	**0.033**
HCV-Antibodies Positive*	69 (5.2)	151 (9.8)	416 (8.3)	**<0.001**	151 (14.9)	139 (27.0)	366 (20.7)	**<0.001**
CD4 count nadir, cells/mm³**	333 (129-526)	307 (213-399)	337 (191-480)	**<0.001**	271 (141-384)	236 (109-334)	258 (132-361)	**<0.001**
BL calendar year**	2016 (2016-2017)	2011 (2009-2012)	2014 (2012-2016)	**<0.001**	2016 (2016-2017)	2007 (2003-2011)	2014 (2010-2016)	**<0.001**
Months from HIV diagnosis to ART**	1 (1-3)	11 (2-39)	3 (1-24)	**<0.001**	71 (32, 171)	61 (28, 124)	92 (42, 172)	**<0.001**
BL CD4 count, cell/mm³**	349 (139-562)	324 (226-420)	351 (199-503)	**<0.001**	658 (463-882)	500 (355-720)	616 (442-821)	**<0.001**
BL HIV-RNA, log_{10} copies/mL**	4.62 (4.10-5.24)	4.75 (4.23-5.14)	4.57 (4.00-5.04)	**<0.001**	-	-	-	-

* n (%), ** median (IQR)

Figure 1: Probability of discontinuing third drug due to NPAEs according to treatment group (1a ART-naïve population, 1b Treatment-experienced population).



Estimates (95% CI)			
	DTG	EFV	Other
1-year	1.6% (0.9-2.4)	5.3% (4.0-6.6)	0.3% (0.1- 0.4)
2-year	2.4% (1.4-3.4)	6.9% (5.4, 8.5)	0.3% (0.1-0.4)
3-year	2.4% (1.4-3.4)	10.7% (8.5-12.9)	0.3% (0.1-0.4)

Estimates (95% CI)			
	DTG	EFV	Other
1-year	1.3% (0.6-2.0)	6.9 % (4.6-9.2)	0.1% (0.0-0.2)
2-year	1.9% (1.0-2.9)	8.9% (6.3-11.6)	0.1% (0.0-0.2)
3-year	1.9% (1.0-2.9)	12.2% (9.1-15.4)	0.3% (0.0-0.7)

Table 2. Relative hazards (RH) of discontinuing third drug for neuropsychiatric toxicity from fitting Cox regression models according to treatment hist

	Adjusted* RH (95% CI) of treatment discontinuation due to NPAES in ART-naïve population	p-value	Adjusted* RH (95% CI) of treatment discontinuation due to NPAES in ART-naïve population#	p-value	Adjusted** RH (95% CI) of treatment discontinuation due to NPAES in treatment-experienced population	p-value
DTG-based regimens	1.00		1.00		1.00	
EFV-based regimens	7.02 (2.98–16.58)	<0.001	6.29 (2.28–17.34)	<0.001	5.09 (1.6–15.98)	0.005
Other regimens	0.10 (0.03–0.30)	<0.001	0.08 (0.02–0.27)	<0.001	0.24 (0.09–0.66)	0.006

*Adjusted for: gender, age, mode of HIV transmission, nationality, calendar year of starting ART, AIDS diagnosis, BMI, STR (yes vs no), backbone, CD4 count nadir, highest level of education, employment and NPS symptoms at baseline.

#Sensitivity analysis on pts starting ART from 2011.

**Adjusted for gender, mode of HIV transmission, nationality,STR, CD4 count, age, NRTI pair, calendar year, employment, max level of educationand NPS symptoms at baseline.

PE32/11

SWORD 1&2: maintenance or improvement in renal function in PLWH through 148 weeks after switch to the dolutegravir + rilpivirine 2-drug regimen

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Purpose: The SWORD studies demonstrated noninferiority post-switch to dolutegravir (DTG) + rilpivirine (RPV) vs. 3- or 4- drug current antiretroviral

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therapy (CAR) at Week 48 and maintained viral suppression to Week 148. The NRTI tenofovir (TDF) and certain protease inhibitors (lopinavir, atazanavir) are associated with renal toxicity. DTG+RPV may be a suitable therapy for renally impaired patients. We report pooled SWORD study data of renal parameters through Week 148.

Method: Adults with suppressed HIV-1 RNA were randomized to DTG+RPV (Early-Switch group, ES) or continue CAR. CAR participants suppressed at Week 48 switched to DTG+RPV at Week 52 (Late-Switch group, LS). Renal function post switch to DTG + RPV was evaluated using eGFR estimated by serum cystatin C (CKD-EPI Equation), retinol binding protein (RBP): creatinine ratio and beta2-microglobulin (β2M): creatinine ratio by receipt of TDF pre-switch. Changes in eGFR for subjects with moderate renal impairment (i.e. eGFR=60–90 ml/min/1.73 m^2) were assessed.

Results: Following switch to DTG+RPV, minimal change was observed in eGFR, irrespective of pre-switch TDF exposure (Table 1). For participants with moderate renal impairment pre-switch (53 subjects in ES group, 31 in LS group), eGFR remained stable or slightly increased post-switch to DTG+RPV (median change from Baseline and LS Baseline was +13.1 and 0.0 for the ES and LS groups, respectively, at Week 148), with few participants decreasing below 60 ml/min/1.73 m^2 at any time. RBP and β2M: creatinine ratios had numerically greater improvements in the participants taking TDF prior to switch (Table 2).

Conclusions: Irrespective of pre-switch status, renal function was maintained for SWORD participants through 148 weeks post-switch to DTG+RPV with greater improvement in renal tubular function for those switching off TDF. The switch to DTG+RPV in suppressed patients, including those with moderate impairment, did not adversely affect renal function while maintaining suppressive HIV treatment.

Change in eGFR following switch to DTG + RPV for the Pooled SWORD-1/-2 Population Estimated by Serum Cystatin C Using CKD-EPI Equation by Pre-switch TDF exposure

Visit	Early Switch DTG + RPV group n	Early Switch DTG + RPV group Median (IQR) mL/min/1.73m²	Late Switch DTG + RPV group n	Late Switch DTG + RPV group Median (IQR) mL/min/1.73m²
TDF exposure pre-switch				
Baseline[1]	369	115·4 (101·3 to 124·6)	-	NA
Week 48	348	0 (-6.93 to 9.42)	-	NA
LS Baseline[2]	-	NA	335	116·8 (108·0 to 124·6)
Week 100	330	0 (−10·2 to 0)	316	−6·8 (−12·1 to 0)
Week 148	307	0 (-8.92 to 8.22)	304	0 (-8.45 to 0)
No TDF exposure pre-switch				
Baseline[1]	142	119·7 (109·5 to 127·7)	-	NA
Week 48	135	0 (-9.15 to 0)	-	NA
LS Baseline[2]	-	NA	142	118·0 (107·6 to 125·2)
Week 100	130	−7·2 (−15·5 to 0)	132	−7·3 (−12·8 to 0)
Week 148	125	0 (-9.92 to 0)	129	0 (-12.40 to 0)

CKD-EPI, chronic kidney disease–epidemiology collaboration; eGFR, estimated glomerular filtration rate; IQR, interquartile range; NA, not applicable

Footnotes

1 – Baseline for the Early Switch DTG+RPV group is the value at Day 1

2 - Late Switch Baseline (LS Baseline) for the Late Switch DTG +RPV group is the latest pre-switch value (usually from the Week 48 visit)

Table 1

Percent Change in Retinol Binding Protein: Creatinine Ratio and Beta2-microglobulin: Creatinine Ratio Post switch to DTG + RPV Through Week 148 by Pre-switch TDF exposure

Renal biomarker Visit	Early Switch DTG + RPV group n	Early Switch DTG + RPV group Median (IQR)	Late Switch DTG + RPV group n	Late Switch DTG + RPV group Median (IQR)
Retinol binding protein/creatinine ratio (urine), µg/mmol				
TDF exposure pre-switch				
Baseline[1]	352	9.02 (6.11, 14.96)	-	NA
Week 48	326	-43.4% (-65.1%, -12.6%)	-	NA
LS Baseline[2]	-	NA	335	7.33 (4.37, 13.29)
Week 100	312	-59.5% (-83.0%, -34.3%)	313	-50.2% (-78.8%, -8.6%)
Week 148	285	-28.8% (-56.3%, 8.76%)	294	-22.3% (-52.8%, 25.8%)
No TDF exposure pre-switch				
Baseline[1]	134	6.27 (4.41, 8.74)	-	NA
Week 48	125	-23.7% (-50.4%, 15.7%)	-	NA
LS Baseline[2]	-	NA	138	6.11 (3.94, 9.32)
Week 100	123	-37.4% (-70.8%, -2.1%)	127	-34.5% (-61.6%, 28.9%)
Week 148	114	-2.27% (-33.8%, 32.4%)	125	0.4% (-31.0%, 53.3%)
Beta-2 microglobulin/creatine ratio (urine), mg/mmol				
TDF exposure pre-switch				
Baseline[1]	222	0.02 (0.01, 0.04)	-	NA
Week 48	112	-30.7% (-55.5%, 6.0%)	-	NA
LS Baseline[2]	-	NA	255	0.02 (0.01, 0.05)
Week 100	108	-38.4% (-62.4%, -3.4%)	139	-38.5% (-69.9%, 1.45%)
Week 148	102	-34.8% (-68.9%, 14.2%)	118	-41.5% (-68.9%, 11.9%)
No TDF exposure pre-switch				
Baseline[1]	94	0.01 (0.01, 0.02)	-	NA
Week 48	48	7.11% (-15.9%, 60.9%)	-	NA
LS Baseline[2]	-	NA	111	0.01 (0.01, 0.02)
Week 100	40	3.6% (-29.0%, 44.3%)	60	12.3% (-27.3%, 56.4%)
Week 148	38	28.9% (-23.2%, 68.9%)	58	1.6% (-19.6%, 51.4%)

IQR, interquartile range; NA, not applicable

Footnotes

1 – Baseline for the Early Switch DTG+RPV group is the value at Day 1

2 - Late Switch Baseline (LS Baseline) for the Late Switch DTG +RPV group is the latest pre-switch value (usually from the Week 48 visit)

Table 2

PE32/12

Neurotoxicity related to efavirenz does not predict neurotoxicity related to dolutegravir

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Purpose: Central nervous system (CNS) disturbances, especially sleep disorders, are the main cause of interruption of dolutegravir (DTG)-based therapies. Predisposing factors are not well-known. In pretreated patients, previous efavirenz (EFV)-related neurotoxicity, also frequently consisting of sleep disorders, could be predictive of neuropsychiatric intolerance to DTG and question its use in these patients.

Method: The medical records of all HIV-infected patients who ever received DTG were retrospectively reviewed, and selected those who previously had received EFV. Any neuropsychiatric symptom temporally related to these drugs was recorded.

Results: In our hospital, a total of 481 patients have received or are currently taking DTG-based therapies since 2014. Of them 184 (38.3%) had received EFV previously.

Of the 184 patients exposed to both drugs, 79 (43%) presented adverse CNS reactions in clear temporal association with EFV, considered clinically relevant (classified 3–4 by the patients or resulting in EFV interruption) and 19 (10.3%) developed CNS toxicity under DTG, as defined above. From 79 patients who presented previous CNS toxicity under EFV, only 12 (15.1%) also presented clinically relevant neuropsychiatric disorders, after their exposure to DTG.

No association was found between prior EFV neurotoxicity and DTG neurotoxicity ($\chi 2$=6.5, p=0.16).

The relationship between sociodemographic and HIV-related variables and the development of neuropsychiatric toxicity related to EFV and DTG was analyzed. A lower age and shorter time of HIV infection showed a statistical trend to relate to EFV toxicity (p=0.052 and p=0.051 respectively). The younger age and the female gender seem to relate to DTG toxicity (p=0.01 and p=0.004 respectively).

Conclusion: The history of neuropsychiatric adverse effects related to EFV does not predict the development neuropsychiatric toxicity by DTG.

PE32/13

Human embryonic stem cells exposed to dolutegravir show decreased cellular proliferation, reduced pluripotency, and increased mitochondrial toxicity, in a dose-dependent manner: preliminary data

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Purpose: Approximately 80% of women living with HIV worldwide now receive cART during pregnancy, reducing their vertical transmission rates to <2%. Most ARVs can cross the placenta, but their safety has not been fully characterized in the context of pregnancy, especially for InSTIs. A recent study suggested an early signal for increased neural tube defects with dolutegravir (DTG) exposure from conception. As neural tube develops during the first four weeks of gestation, early exposure to certain ARVs may be detrimental. Previous work in our lab showed that DTG (but not raltegravir [RAL]) affect mitochondria, something that could adversely affect early embryonic development. Our objective was to characterize and compare the dose-dependent effects of InSTIs DTG, RAL, elvitegravir (EVG), and bictegravir (BIC) on cultured human embryonic stem cells (hESCs), with respect to cellular and mitochondrial health, as well as pluripotency.

Method: CA1S hESCs were cultured in the presence of DTG, RAL, EVG, or BIC at 10 doses ranging from 0.001 to 3 C_{max} for 3 days, then harvested and assessed for pluripotency with stage-specific embryonic antigen (SSEA-3), and mitochondrial characteristics (mass, intermembrane potential and reactive oxygen species (ROS) via flow cytometry.

Results: DTG exposure at levels ≥0.1 Cmax decreased cellular proliferation, increased mitochondrial reactive oxygen species, and induced differentiation as indicated by the loss of the SSEA-3 pluripotency marker, in a dose-dependent manner. This was not seen with other InSTIs. However >0.5 C_{max} BIC and >2 C_{max} DTG induced hESC death that precluded flow cytometry.

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Conclusion: These preliminary data suggest that even low dose exposure to DTG may induce mitochondrial toxicity and differentiation in hESCs. Given the widespread use of DTG and other InSTIs prior, during, and after conception, it is imperative to further elucidate their short and long-term safety in the context of pregnancy.

PE32/14

Dolutegravir but not raltegravir reduces cell proliferation and increases mitochondrial toxicities in cultured fibroblasts; effects that are not mitigated by telomerase reverse transcriptase

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Purpose: Dolutegravir (DTG) and raltegravir (RAL) have excellent clinical tolerance and increasing usage but little is known regarding their long-term toxicities. Older NRTIs inhibit mitochondrial pol γ and affect mitochondrial DNA (mtDNA), while some PIs induce reactive oxygen species (ROS). Under oxidative stress, human telomerase reverse transcriptase (hTERT) translocates to mitochondria, where it protects mtDNA. Our objective was to evaluate cellular and mitochondrial effects of exposure to InSTI-containing cART, and their modulation by hTERT.
Method: Transformed human fibroblast cells that utilize the alternate lengthening of telomeres (ALT) mechanism to maintain telomeres were transduced with either control vector, vector encoding mutant hTERT that cannot translocate to mitochondria, or WT hTERT. The three cell lines were exposed to various cART (1X C_{max}) for nine days, then allowed to recover in media for six days. Cell viability and proliferation were determined every three days, while mitochondrial mass, inter-membrane potential, ROS and cellular apoptosis were quantified via flow cytometry on days 9 and 15.
Results: At day 9, cell proliferation was significantly reduced, while apoptosis, mitochondrial ROS, mass and membrane potential were increased in DTG-containing cART exposed cells compared to control cells (0.1% DMSO). Cells exposed to RAL-cART were similar to controls. Lopinavir-containing cART also induced apoptosis and ROS. A positive correlation between mitochondrial ROS and apoptosis was observed. ROS levels were highest in DTG-, and lowest in RAL- and efavirenz (EFV)-cART-exposed cells. WT hTERT (but not mutant hTERT) mitigated PI-induced effects but did not protect against DTG effects. All effects were reversed following drug removal.
Conclusion: In this cell model, DTG but not RAL induced mitochondrial and cellular toxicities. Furthermore, the mechanism behind DTG toxicity appears different from that of boosted-PIs. Additional investigations are required to determine whether these effects may be relevant to human health.

Treatment as prevention

PE33/1

HIV-1 viral load quantification using Aptima HIV-1 Quant Dx assay in Kenya: a diagnostic accuracy study

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Purpose: Accurate quantitation of HIV-RNA (viral load) is critically significant for diagnosis, treatment, monitoring and assessment of HIV-1 infection. The choice of assay platform is very important in influencing treatment decisions of HIV patients. This study is important to determine the diagnostic accuracy of the new assay to be used in Kenya and other low- and middle-income countries.The objective of this study is to evaluate viral load diagnostic accuracy of Aptima HIV-1 Quant Dx assay in HIV-positive people on antiretroviral therapy.
Method: The performance of the Aptima assay was compared against the Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Version 2.0 (CAP/CTM) assay. The analytical sensitivity, specificity, diagnostic agreement with CAP/CTM, carryover contamination and precision of Aptima HIV-1 assay was analyzed using 219 HIV positive viral load remnant samples. Sensitivity of Aptima and CAP/CTM was assessed using clinical specimens from HIV-1 patients on antiretroviral therapy (ART) with quantifiable results. Aptima assay specificity was determined using individual donor 40 HIV-1 seronegative plasma specimens. Linearity and accuracy of quantitation was assessed using clinical specimens ranging in concentration from 1.0–7.0 $\log_{10}$ copies/mL. A method comparison was performed and Bland Altman analysis was used to analyze the level of agreement between the two assays.
Results: Analytical sensitivity of Aptima HIV-1 assay using clinical samples was 99.1% (95% CI: 95.3%–100.0%). Using the 40 HIV-1 negative plasma specimens, all results were negative (specificity of 100%: 95% CI: 99.4–100%). High pearson correlation ($r>0.92$) and excellent agreement was observed between Aptima HIV-1 assay and CAP/CTM. Aptima's precision as per the coefficient of variation was less than 3%.
Conclusion: The Aptima® HIV-1 Quant assay on the Panther system is a suitable platform for detecting and monitoring HIV-1 viral load in HIV-1 infected patients in Kenya. This will increase access of HIV viral load tests thus contributing to effective HIV treatment management.

PE33/2

Contact tracing of HIV by Assessing sexual partners, spouses and children of newly diagnosed patients through referral method in Nigeria

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Purpose: Ekiti state, located in the South-West Nigeria, has one of the lowest HIV/AIDS prevalence in the country. (1% in 2008) However, there was an increase from 1% to 2.9% between 2008 and 2014 according to the HIV Sentinel Survey. This increase was attributed to continual spread to healthy individuals from positive patients who are ignorant of their status. Hence, this study focused on using contact tracing to improve access to testing, counseling and access to treatment for HIV-infected individuals.
Method: The study data was extracted from "Improving Comprehensive AIDS Response Enhanced for Sustainability (iCARES)" project with the objective of achieving first 90 of the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 by providing HIV Testing Services (HTS) to patients attending State Specialist Hospital (SSH), Ikere-Ekiti. The study assessed sixty-two subjects (43 females and 19 males) between the ages of 2 and 45 years who were sexual partners, spouses and children of fifteen (15) subjects diagnosed with HIV, as index patients. These 15 index patients were randomly selected from reactive patients who consented to refer their children and sexual partner(s) for HTS. For quality assurance, 'Determine test kit' was used for rapid test, while 'Uni-Gold' and 'Stat-Pak' kits were used for confirmation. Positive patients were counseled by mentor mothers and referred for treatment.
Results: Of the total examined subjects, 5 (8.1%) were positive for HIV; 3 were children while 2 were spouses of 2 index patients. The 3 children were delivered by Traditional Births Attendants (TBAs), hence no proper measure was taken to prevent mother to child transmission.
Conclusion: The tracing of children and spouses of HIV patients yielded additional diagnosis of HIV. This strategy is effective and could be a cost-effective method in diagnosing HIV in Nigeria.

PE33/3

Rapid ART start in primary HIV infection: time to viral suppression in a London cohort

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Purpose: Rapid antiretroviral therapy initiation is now recommended in primary HIV infections (PHI) as it limits HIV transmission and reduces the viral

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Baseline characteristics and outcomes

	Total rapid starters (n=153)*	INSTI starters (n=29)	PI starters (n=77)	PI/INSTI^ switch (n=42)	INSTI vs. switch p	PI vs. switch p
Median age, years (IQR)	27 (33–40.5)	26 (33–43)	31 (26–38)	31 (26–41)	0.92	0.58
Median time from HIV diagnosis to ART start, days (IQR)	6 (3–10)	11 (10–14)	4 (2–8)	5 (3–7)	**<0.01**	0.83
Baseline HIV viral load, log10 (IQR)	4.90 (4.21–5.83)	5.22 (4.53–6.45)	4.84 (4.08–5.75)	5.14 (4.28–5.83)	0.65	0.20
Baseline HIV viral load >1 million cp/mL, n (%)	32 (20.9)	10 (34.5)	12 (15.6)	9 (21.4)	**0.03**	0.22
Baseline CD4 cell count, mmc (IQR)	551 (431–700)	610 (430–750)	541 (418–714)	515 (435–666)	0.23	0.64
Time from ART start to first HIV-VL <200 cp/mL, days (IQR)	56 (31–108)	31 (28–56)	80 (39–121)	49 (42–63)	**0.03**	**0.01**

Legend * = Of 153 starters, 5 started with a non-nucleoside reverse transcriptase inhibitors regimen and were not reported in the sub-analyses ^ = patients who switched from an initial PI-based regimen to either raltegravir, n=32 or dolutegravir, n=10 within 28 days from ART start IQR = interquartile range

reservoir. In the absence of baseline viral resistance test results (VRT), immediate ART is historically given as protease inhibitor-based (PI) combinations and integrase inhibitor-based (INSTI) regimens are delayed until VRT is reported, usually in 7 days. We analysed outcomes in PHI according to ART regimen at 56 Dean Street, a sexual health clinic in London (UK).
Methods: Clinical records of all individuals consecutively diagnosed with PHI between July 2016 and June 2018 were reviewed. PHI was defined as documented plasma HIV-RNA positivity with a negative HIV enzyme immunoassay (EIA) test, or HIV-EIA test switching from negative to positive within six months. Rapid start was defined as ART initiated within 14 days of HIV diagnosis. The Mann-Whitney U test was used to measure differences between groups.
Results: 262 individuals (97% MSM) were diagnosed with PHI: 153 (58%) agreed to rapid ART start (full details in Table 1). Median time from HIV diagnosis to first doctor appointment was 8 days (IQR 4–14). PI-based (all Darunavir-based) regimens were the main option chosen when VRT was not available at time of rapid start and switch was encouraged once VRT was available. Raltegravir was preferred in 97% of those starting INSTI. Median time from PI start to INSTI switch was 16 days (IQR 14–23.5).
Conclusion: Rapid start with INSTI regimens results in quicker viral suppression than with PI-based regimens in PHI, even when PIs are subsequently switched to INSTIs. Concerns about lack of a baseline VRT result prior to rapid ART start may potentially be overcome by the use of the newer INSTIs with a high genetic barrier such as dolutegravir and bictegravir.

PE33/4

Reality check: HIV post-exposure prophylaxis (PEP) in real-life at a tertiary care centre prior to the PrEP era

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Purpose: Published data on the use of PEP in German-speaking countries are rare potentially impeding identification of candidates for HIV pre-exposure prophylaxis (PrEP). Here we report data of PEP-patients at the University Hospital Bonn.
Method: Data of 101 patients referred for advice regarding PEP after occupational (OE) or non-occupational HIV-exposure (NOE) between January 2014 and December 2017 to the University Hospital Bonn were analysed retrospectively. The German-Austrian guidelines for HIV-PEP were used as reference.
Results: Median age was 30 years (95% IQR: 29–33). 43% presented after OE, 49% after NOE (8% not documented). 66.3% were male, 33.7% were female. 64% of male patients and 21% of female patients came after NOE. 64.4% of NOE were MSM. 61.0% of OE were nurses, 24.3% were doctors. 87.9% presented within 24 hours. 65.1% of OE and 89.8% of NOE received PEP. PEP was prescribed in accordance to guidelines in 89.9% in OE, 93.2% in NOE. 82.1% of OE and 33.3% of NOE were vaccinated against hepatitis B. 66.7% completed the 28-day PEP regime, 33.3% reported inconsistent drug intake: 25% because of adverse drug reactions, 75% stopped due to HIV negative testing of index person. 40 patients returned for HIV testing 3 months after PEP, all were tested negative for HIV.
In univariate analysis PEP patients presenting after NOE were significantly more often of male gender (64% vs. 21%; p≤0.000), were less often vaccinated against hepatitis B (33.3% vs. 82.1%; p=0.003) and received PEP more often (89.8% vs. 65.1%; p=0.001) than patients presenting after OE.
Conclusion: The majority of PEP patients at the University Hospital Bonn were MSM. This underlines the importance of a generous roll-out of PrEP in this population at high risk for HIV infection. The subsequent engagement in regular medical check-ups should be used to improve hepatitis B vaccination rates.

Treatment in resource-constrained settings

PE34/1

Peer navigation improves linkage to HIV treatment and retention in Malawi

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Purpose: In Malawi, LINKAGES project reaches men who have sex with men (MSM) with HIV prevention, care, and treatment through Centre for the Development of People (CEDEP). Despite the success registered in identifying HIV infected clients using the peer educators, there has been low linkage to antiretroviral treatment. We present a successful story of linkage to treatment after training and using peer navigators (PNs) to support their peers.
Method: We trained 18 PNs from districts of Lilongwe, Mzuzu, Blantyre and Mangochi to identify and support their hard-to-reach KPLHIV peers and assist in provision of community care services to support them with treatment uptake. These PNs are HIV-positive persons trained and willing to support their MSM and Transgender (TG) peers on the community care for HIV/AIDS and its treatment, Sexually transmitted infections (STIs), self care, gender based violence (GBV), disease progression, safer sex for and income generating activities.
Results: In the period before the training of PNs the linkage to treatment was 97 key population (KP) members between the month February 2016 to September 2017). Following the training, the one year period (between October 2017 to September 2018linkage to treatment moved to 493 KPs. Peer navigators also supported 57 KPs who defaulted on ART to be re-initiated on ART. Three hundred and Eighty four KPs were eligible for viral load testing against none ascertained for viral load testing the previous year. From this number, Three Hundred and Seventy-Nine viral loads came out of which, 365 were virally suppressed representing (96% suppression rate)
Conclusion: Peer navigators are playing a significant role in increasing and improving the linkage to treatment and viral load testing. Another unique success is the identification of new HIV positive MSM and TG networks to access HIV care and treatment services including support services on gender-based violence.

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PE34/2

Optimizing clients linkage into ART using family-centered differentiated approach (FCDA) in Kebbi state, northwestern Nigeria: successes and challenges

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Purpose: Linking newly diagnosed HIV positive clients into ART is an important task in the pursuit of the ambitious UNAIDS 95-95-95 targets. Although there is a sustained improvement in access to HIV testing services globally, connecting newly diagnosed clients into sustainable anti-retroviral therapy has remained a challenge in HIV treatment programs. Renewed efforts and strategies are required to surmount this challenge. This evaluation shares the successes and challenges of using family-centered differentiated approach (FCDA) as a strategy to improve new clients' linkage into ART.
Method: In Oct 2018, the CaTSS project funded by USAID and implemented by Management Sciences for Health initiated the FCDA strategy in 2 partner PMTCT-only facilities - GH Warrah and GH Kaoje- to improve ART linkage of clients identified through partner notification services (PNS). Prior to the commencement of the FCDA, new HIV positive clients identified through this process in the PMTCT-only facilities were referred to the comprehensive facilities for ART services. Using the FCD approach, newly diagnosed HIV positive children and spouses of pregnant and breastfeeding women were provided access to ART services in the same PMTCT-only facilities as the index women. Appropriate training was provided to relevant health care workers at the inception of the program.
Results: From pre-intervention rate of 67% (10/15) and 40% (4/7) in Oct 2018, ART linkage improved to 100% (12/12 and 5/5) respectively in GH Warrah and GH Kaoje. About $10 required to complete a 2-way referral per client for ART initiation in the distant comprehensive facilities was eliminated. However, a reliable commodity supply chain was required to operationalize the system.
Conclusion: FCDA is a reliable way of improving client linkage into ART and reducing incidental cost of initiating ART services. This strategy could be scaled up and prioritized in facilities where PNS is adopted as targeted HTS.

PE34/3

A multi-stakeholder evaluation of the early implementation experiences of differentiated anti-retroviral therapy (ART) delivery roll-out across Uganda: a qualitative analysis

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Purpose: World Health Organization recommends Differentiated ART delivery in resource-constrained settings. There is a paucity of evidence on national roll-out of Differentiated ART models in Uganda since initial implementation in 2017. We sought to explore national stakeholders' perceptions of the early implementation outcomes of differentiated ART delivery roll-out across Uganda.
Methods: Between April and June 2019 we conducted 76 in-depth interviews with national-level HIV program managers (n=18), district health leaders (n=24), representatives of PEPFAR implementing organizations (11), ART clinic in-charges (23) in six purposively selected Uganda districts (Kampala, Luwero, Wakiso, Mbale, Budadiri, Bulambuli) with relatively high HIV burden. Six focus group discussions (48 participants) were held with patients enrolled in DSD (Differentiated Service Delivery) models in case-study districts. Data were analyzed by inductive content analysis.
Results: HIV program managers identified low patient literacy of DSD models, limited DSD competence among health workers, supply chain barriers to multi-month ART dispensing as barriers to DSD implementation. PEPFAR implementing organizations identified a lack of funding and guiding protocols for operationalising community-based DSD models as barriers to uptake at the sub-national level. Existing community health systems such as Village Health Teams (VHTs) were identified as an under-utilized resource. Patients identified stigma as a major barrier to the uptake of community-based DSD models particularly Community Drug Delivery Points (CDDP). Private pharmacy networks were proposed as an alternative to CDDP. Overall, clients expressed preference for facility-based individualized DSD models. Patients perceived current choices of DSD models to be provider-directed and not sufficiently patient-centred.
Conclusion: This is one of the first national-level stakeholder evaluations of DSD implementation in Uganda since 2017. Our study suggests that DSD models will require continuous refinement to ensure that they are truly patient-centered. Increasing patient literacy of DSD models and sustained stakeholder engagement are critical to further DSD roll-out in Uganda.

PE34/4

Why treatment does not work: findings of one year project survey about IDUs treatment in Quetta, Pakistan

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Purpose: There are around 11 Drug treatment centers including govt; sector providing treatment to IDUs, DUs but the relapse ratio still sustaining at 87%. It is reported that there are more than 47,000/- addicts, IDUs living across Quetta city areas including women.
Method: Community Development & Entrepreneurship Foundation a NGO in collaboration with local drug treatment center carried out a one year project based survey in 2016 to see the factors involved in relapse ratio. Total 700 drug users were interviewed mostly from indigenous tribes including Dari Hazaras 20%, Pasthons 46%, Panjabi 8% and Afghan migrants 26 %. The survey allowed for a clear comparison and defines groups at risk.
Results: During the survey intervention, 700 drug users were recruited/ interviewed mostly received treatment more than once. Relapse ratio of 87% shows that it is nourishing despite treatment and detoxification services. The factors identified involved including personal frustration, domestic violence, joblessness; family disrespect, lack of sustainable economic support and social status/ownership.
Conclusion: Harm reduction services needs to be sensitized by local CBOs. More community based interventions such as sports, social, cultural, and recreational activities to be initiated and a regular awareness campaign to IDUs and general public. Drug users need sustainable health care series for knowledge building and better understanding. Government is has a central role to play.
Keywords: Care & harm reduction, IDUs, community mobilization, social protection

PE34/5

Evaluation of the financial cost of treating people living with human immunodeficiency virus in the United Kingdom versus matched HIV-negative controls in 2004, 2010 and 2017

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The purpose of this study was to evaluate the quantum of NHS financial costs attributed to the care of people living with HIV (PLHIV), in comparison to matched HIV-negative controls. Survival rates of PLHIV have dramatically improved over the last two decades, and the changing pattern of illness in the ageing cohort of PLHIV has resulted in differing costs of care. The purpose of this study is to characterise these changes and associated costs in the UK population.
The Clinical Practice Research Datalink (CPRD) was used for this analysis as it captures approximately 10% of GP records and is representative of the UK as a whole. PLHIV were matched to HIV-negative controls and costs were calculated for hospital admissions, outpatient visits, GP attendances and primary care prescriptions in 2004, 2010 and 2017 (in GBP at 2016/2017 pay and prices). Costs of anti-retroviral (ARV) drugs were excluded from analysis due to the majority of ARVs being prescribed in secondary care.

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It was possible to identify and match 2,945 PLHIV to 5,890 HIV-negative controls. The mean costs of care per person year (PPY) for PLHIV were £5,013, £1,378 and £867 in 2004, 2010 and 2017, respectively. For HIV-negative controls, these values were £531, £692 and £648, respectively. Therefore, the ratio of mean total cost for PLHIV compared to HIV-negative controls was 9.4:1, 2:1 and 1.3:1 for the three annual periods, respectively.

Table 1. Comparison of mean cost of care PPY for PLHIV to HIV-negative controls (£)

Year	Cohort	Primary care costs	Prescription costs	Inpatient costs	Outpatient costs	Total costs
2004	HIV-negative	108	86	253	84	531
	PLHIV	267	130	3,986	630	5,013
2010	HIV-negative	143	106	266	176	692
	PLHIV	225	149	301	703	1,378
2017	HIV-negative	149	115	220	165	648
	PLHIV	164	139	72	493	867

Excluding ARVs, the marginal cost of treating PLHIV has converged markedly towards that of the general population over the previous 15 years. This convergence may be positively attributed to improvements in HIV specialist care and treatment options. With decreasing cost of management, this alleviates funds for investment in innovation. Future care should focus on providing care that ensures good quality of life for people living with HIV, in addition to longevity.

PE34/6

Continuous quality improvement across the viral load testing spectrum at the Infectious Diseases Institute, Uganda

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Purpose: Viral load (VL) testing is the gold standard for monitoring patients on antiretroviral therapy. However, efficient implementation of VL monitoring (low rejection or failed samples rates and short turnaround time) for all patients poses complex technical and logistical challenges. We introduced a quality improvement (QI) initiative, to improve efficiency and coverage of routine VL testing at the Infectious Diseases Institute (IDI). We present annual VL coverage in the subsequent two years and the proportions for rejected/failed samples.
Method: We used retrospective clinic data from electronic records to populate a VL cascade at the clinic. It comprised patient identification, sample collection/transfer for testing at national level, management of results returned, and patient management actions based on the result. At baseline (Jan 2015), point prevalence of VL coverage was 14%. The QI team brain stormed root causes, analyzed using fishbone tool, and formulated three key areas for improvement; 1) Increase VL coverage and reduce proportion of failed/rejected samples 2) Reduce turn-around time by providing a dedicated QI VL focal person to manage VL results 3) Introduce a special clinic to ensure appropriate action for those with detectable VL.
Results: Viral load coverage at IDI increased substantially from 14% (2015) to 82% tests (2016) and 89% (2018). Failed samples reduced from 70 (2015) to 21 (2017). However, the rejection proportion increased to 1.054% (2016) from 0.168% (2015), this was addressed by meeting with the laboratory team and reduced to 0.78% (2017). Failed and rejected samples resulted from: insufficient/clotted samples, improper handling/transportation and poor sample labeling. Overall 10% results (VL>75 copies/mL) were appropriately referred to the clinic. The QI team addressed VL challenges in the monthly clinic meeting.
Conclusion: Implementing a quality improvement system increased VL coverage. A VL monitoring cascade is key in identifying gaps for better treatment outcomes.

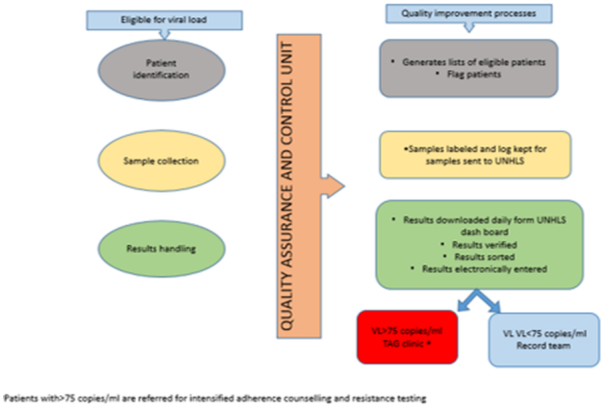


Figure 1. Routine viral load cascade at the Infectious Diseases Institute

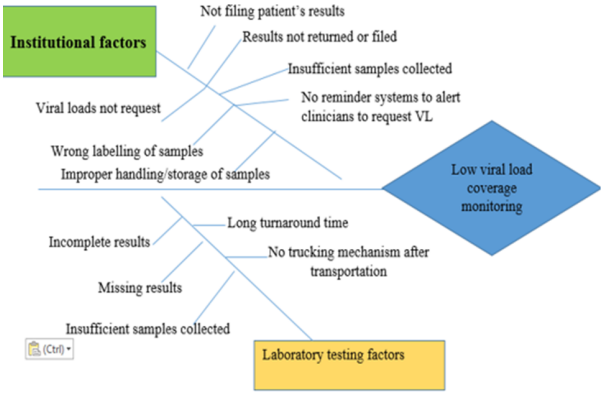


Figure 2. Fish bone analysis of the root cause of low viral load coverage

PE34/7

Pediatric HIV viral load suppression: qualitative insights of barriers and facilitators among caregivers of children on ART in high volume sites in Kisumu County, Kenya

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Purpose: The number of virally suppressed HIV+ children remains unacceptably low; the experiences of caregivers of children on antiretroviral treatment (ART) are critical to developing interventions to achieve maximum viral load (VL) suppression in this population.
Method: Eight focus group discussions (FGDs) were conducted among a purposively sampled cohort of 76 caregivers of children (<18 yrs.) on ART (≥ 6 months) at eightfacilities in Kisumu County. A trained qualitative researcher used semi-structured guides to explore VL testing and suppression; translated audio transcriptions were coded using a collaboratively developed framework andDedoose.

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Results: Most caregiverswere female (63%), aged 19- 85 (median age 40), and biological parents (71%). Caregiversexpressed a general understanding of VL; weight-based dosing and medication and appointments adherence were facilitators. VL testing schedules were challenging and ambiguous. HIV-disclosure to children was a facilitator; determining the appropriate age for disclosure, managing anticipated stigma, and disclosure beyond the immediate family were challenges. Medication-specific barriers included timing of pills, management of side effects, medication refusal, and daily pill burden. Health system barriers included long wait times, high frequency of appointments for high VLs, insufficient medications dispersion, and negative provider reactions to missed ART doses. Assisted disclosure and ART management were facilitators; caregivers requested additional disclosure support for school-age children.
Conclusion: Facilitated disclosure and support for caregivers and their children is critical. Facility-level interventions and differentiated care models are needed to improve caregiver-provider interaction. FGDs were conducted with providers and young adults on ART to triangulate findings in this study.

PE34/8

Boosting economic affordability of HIV medicines while considering safety and effectiveness within transition from donor funding. Enabling access to TAF regime with better safety profile in Ukraine through advocacy campaign of community organization

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Purpose: Drop of HIV-treatment because of side effects precludes achievement of 90-90-90 global target in Ukraine. Transition from donor to national funding requires constant review of the HIV-medicines national procurement list using economic approach. Including tenofovir alafenamide (TAF) treatment regime with lower procurement price ensures increase in HIV-treatment coverage while securing treatment with better safety profile comparing to tenofovir disoproxil fumarate (TDF) regime.
Method: In 2018, procurement price for tenofovir disoproxil fumarate/emtricitabine and dolutegravir (TDF/FTC+DTG) for Ukraine constituted 10,15 USD per monthly course. According to the WHO, price for fixed-dose combination of TAF/FTC/DTG is lower. At the same time, equally effective TAF-based regime has reduced potential for kidney injury and loss of bone mineral density. In 2019, All-Ukrainian Network of PLWH (Network) facilitated inclusion of TAF/FTC/DTG into the medicines procurement list for 2020. Simultaneously, Network sent several requests to the generic producer to discuss entering Ukrainian market and possible price for Ukraine. As a result of advocacy efforts, the meeting between the generic manufacturer and state health officials was organized in Ukraine to consolidate previous agreements.
Results: In 2019, Ministry of Health of Ukraine received confirmation from the generic producer on 6,25 USD price per monthly course. Based on the Network's expert official report, TAF/FTC/DTG was included into the procurement list of HIV-medicines for 2020. Considering 23988 patients receiving TDF/FTC + DTG in 2019, the state budget savings for annual course constitutes 978798 USD.
Conclusion: Network interventions demonstrated effectiveness of integrated approach to achieve the global target, which includes decreased price and increased safety of medicines. Saved budget funds enable procurement of additional social HIV-services for key groups essential while shifting to the national funding. Procurement of medicines with better safety profile secures sustainability of treatment that is vital for achieving the second and third 90s of the global targets.

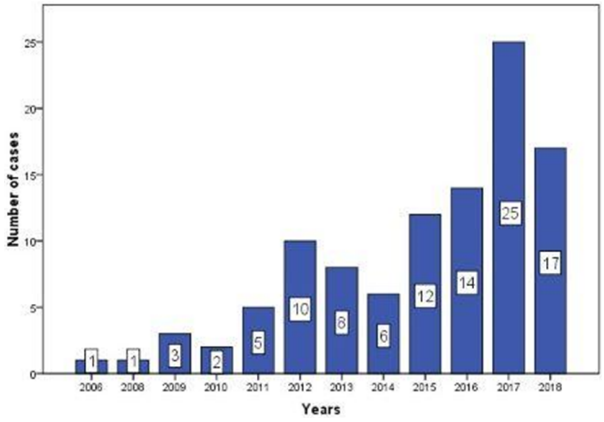
Tuberculosis and opportunistic infections

PE35/1

Nontuberculous mycobacteria infections in Russian HIV patients: clinical features and outcomes

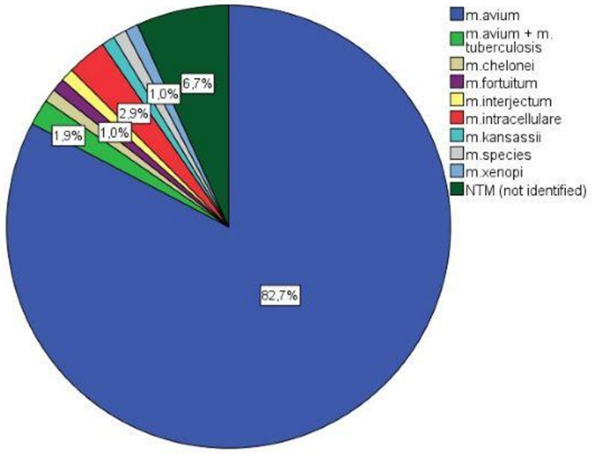
M Savchenko[1] and A Panteleev[2]
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Purpose: This study was conducted to investigate nontuberculosis mycobacterial rates in HIV patients in Russian infectious diseases hospital for a last decade, describe clinical features and analyze outcomes on different treatment regimens.
Method: Data was collected at the Saint-Petersburg Botkin Clinical infectious diseases hospital from January 2006 to January 2019. Cases were divided by etiology, forms of process. Student's t-test was used, survival time on different treatment regimens was evaluated with Kaplan-Meier estimator.
Results: We enrolled 104 HIV patients with different forms of NTM infections. We received a prominent increase of NTM incidence.



Incidence of nontuberculous mycobacteria at Botkin Clinical infectious diseases hospital (from January 2006 to January 2019).

In the absolute majority of cases m. avium (86; 82.7 %) acted as an etiological agent.



Distribution of etiological agents.

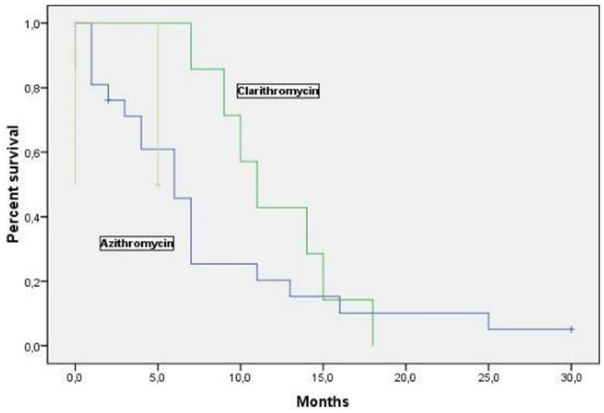
Disseminated infection developed in 75 (72.1 %) of cases, pulmonary NTM infection - in 29 (27.9 %). CD4 was significantly higher in patients with pulmonary than disseminated forms: 47.7±9.9 and 19.8±3.9 cells/mm^3 ($p<0.05$). Significant difference as well was obtained in the hemoglobin level: 108.1±4.5 and 88.7±2.3 g/l ($p<0.05$).

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Laboratory data for patients with pulmonary and disseminated forms.

	Form	Mean	Standard deviation	Standard error
CD4 account (cells/mm^3)	pulmonary/ disseminated	47.7/19.8	50.9/33.6	9.9/3.9
CD 3 account (cells/mm^3)	pulmonary/ disseminated	470.9/331.4	454.2/413.8	94.7/53.8
Hemoglobin (g/l)	pulmonary/ disseminated	108.1/88.7	23.8/19.6	4.5/2.3
CD4 account on treatment (cells/mm^3)	pulmonary/ disseminated	125.7/55.7	78.8/70.8	20.3/10.0
Alkaline phosphatase (U/l)	pulmonary/ disseminated	128.1/156.1	140.2/217.6	38.9/33.1
LDH (U/l)	pulmonary/ disseminated	333.5/291.0	177.1/138.8	41.7/21.6

A high death rate of 34.6 % (36 patients) was recorded regardless of prolonged antibacterial therapy (5.0±0.9 months of treatment). Clarithromycin showed some advantage over azithromycin when analyzing survival by the method of Kaplan-Meier (p<0.05 Breslow).



Kaplan-Meier survival analysis comparing clarithromycin and azithromycin based treatment regimens.

Conclusion: Despite the widespread introduction of antiretroviral therapy, unlike other countries in Russia there is a significant increase in the number of cases of infections caused by NTM in HIV patients.
Pulmonary forms are characterized by higher levels of CD4 and good immunological response. Clarithromycin is preferable when choosing a macrolide base in the treatment regimen.

PE35/2

Human immunodeficiency virus and the outcome of treatment for pulmonary tuberculosis: a retrospective study in Tehran, Iran

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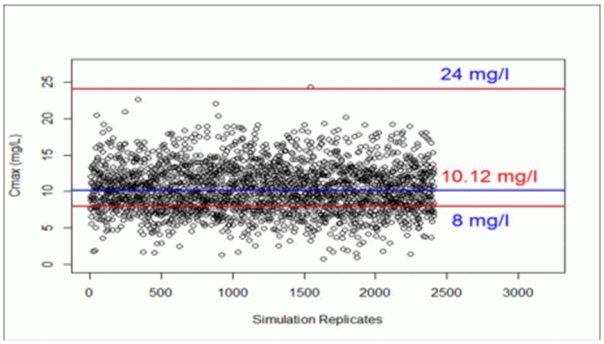
Purpose: Tuberculosis (TB) is among the major clinical challenge in Iran. The risk of treatment failure and mortality among TB patients is significantly increased in patients with human immunodeficiency virus (HIV). We aimed to assess the treatment outcomes and mortality among TB patients co-infected with HIV.
Method: We analyzed the records of 224 TB patients referred to health centers of Tehran, in year 2018. Multivariate analysis using logistic regression model was used to analyze the association between treatment outcome and potential predictor variables.
Results: Among included patients with TB, the overall treatment success was significantly higher in HIV-negative than HIV-positive persons (60.6% vs 39.4%; P value<0.05) and the treatment failure was higher in TB patients with HIV. Mortality rate was significantly higher in HIV-positive than HIV-negative patients (66.7% vs 33.3%; P value<0.05). In the final multivariate logistic model, the odd of death was higher among patients older than 40 years of age, patients with extrapulmonary TB and intravenous drug users.
Conclusion: The treatment success rate of TB patients with HIV was unsatisfactorily low and a high proportion of patients died of defaulted, which is a serious public health concern. Efforts to improve treatment for these patients, additional follow-up and social support are urgently needed.

PE35/3

Rifampicin pharmacokinetics and pharmacogenetics in Ugandan patients with multi-drug resistant tuberculosis

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Purpose: Suboptimal antituberculosis drugs exposure may cause multi-drug resistant tuberculosis. The role of African predominant *SLCO1B1* variant alleles on rifampicin pharmacokinetics and subsequent effect on *M. tuberculosis* - rifampicin sensitivity requires to be defined. We described rifampicin population pharmacokinetics profile and investigated the relevance of *SLCO1B1 genotypes* on rifampicin pharmacokinetics and rifampicin-TB sensitivity status.
Method: Fifty patients with tuberculosis (n=25 with Rifampicin resistant TB and n=25 with rifampicin susceptible TB) were genotyped for *SLOC1B1* rs4149032 (g.38664C>T), *SLOC1B1*1B (c.388A>G)*, and *SLOC1B1**5 (*c.521T>C)*. Steady state plasma rifampicin levels were determined among patients infected with rifampicin sensitive TB. Data were analysed using NONMEM to estimate population rifampicin pharmacokinetics as well as the effect of *SLOC1B1* genotype on rifampicin-TB sensitivity status.
Results: Overall allele frequencies of *SLOC1B1* rs4149032, **1B* and *5 were, 0.66, 0.90 and 0.01 respectively. Median (IQR) C_{max} and T_{max} were 10.2 (8.12–12.47) mg/L and 1.7 (1.125–2.218) hours respectively. Twenty four percent of patients exhibited C_{max} below the recommended 8–24 mg/l range. *SLOC1B1* genotypes, sex and age did not influence rifampicin pharmacokinetics or TB-rifampicin sensitivity.
Conclusion: Although *SLOC1B1* genotype, age and sex influence neither rifampicin pharmacokinetics nor rifampicin-TB sensitivity status, one of every four Ugandan TB patients achieve sub-therapeutic plasma rifampicin concentrations.



A scatter plot of Cmax for the 2400 simulated individuals. The figure also shows the documented ther

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PE35/4

Mycobacteria-induced immune responses by mucosal-associated invariant T (MAIT) cells are impaired in patients with tuberculosis (TB) and HIV-associated TB

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Purpose: MAIT cells are non-classical T lymphocytes that recognize and rapidly respond to microbial vitamin B metabolites and have the capacity to kill bacteria-infected cells. Circulating MAIT cell numbers decrease in patients with active TB and HIV, but previous findings regarding functional changes have been conflicting. We conducted a cross sectional study to assess the effect of HIV, TB and HIV-associated TB (HIV-TB) on MAIT cell numbers, activation, inhibitory and functional profile in a TB endemic setting in South Africa.
Methods: Blood was collected from healthy controls (HC, n=26), individuals with HIV infection only (HIV, n=30), with active TB only (aTB, n=30), and with HIV-TB (n=26). All TB participants were newly diagnosed with TB and sampled prior to treatment. Peripheral blood mononuclear cells (PBMC) were isolated and stimulated with BCG expressing GFP (BCG-GFP) or heat-killed (HK) *Mycobacterium tuberculosis* (Mtb) and analyzed using flow cytometry.
Results: There were lower frequencies of MAIT cells in HIV (median: 0.3%; p=0.04), and aTB (0.4%, p=0.02) compared to HC (0.7%). BCG-specific MAIT cell activation (measured by HLA-DR expression (median fluorescent intensity)) was higher in aTB (230, p=0.006) and HIV-TB (280, p=0.0008) compared to HC (114). BCG-induced MAIT cell degranulation (measured by CD107a expression) was lower in aTB (4.5%; p=0.003) and HIV-TB (4.6%; p=0.04) compared to HC (9.8%). Similarly, IFN-g expression was lower in aTB and HIV-TB (3.2% and 1.0%; p=0.0005 and p=0.0006, respectively) compared to HC (17.6%). Similar results to BCG were obtained with HK-Mtb stimulation. Compared to HC, MAIT cells from individuals with aTB had higher basal PD-1 expression (2.1% vs 5.2%; p<0.0001).
Conclusions: Our data show that compared to HC, HIV and aTB result in a decrease in circulating MAIT cells, while aTB and HIV-TB resulted in a significant increase in activation and inhibitory status, and an impaired mycobacteria-induced functional profile.

PE35/5

Acute onset of cerebral toxoplasmosis in patients with HIV infection

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Purpose: The analysis of clinical picture of Cerebral toxoplasmosis (CT) in patients with AIDS in Moscow.
Methods: The diagnosis of toxoplasmosis was confirmed in 207 patients (IgG to *T. gondii* in high concentration in 70%; *T. gondii* DNA in the cerebrospinal fluid in 42.5%, and the presence of lesions of the CNS in MRI in 100%).
Results: 44 (21.3%) seemingly "healthy" patients had an acute onset of illness. The majority of patients did not know about their HIV status. CT was the first AIDS-indicator disease. 55% of patients had body temperature above 38^0 C, 46% of patients had headache. 32% patients were admitted to hospital in a coma and only 17% with a gradual onset of the disease.
We have identified several options for the development of acute onset of the disease. The most frequent (50%) begins as an acute cerebrovascular accident (stroke): the sudden development of hemiparesis, dysarthria or aphasia, followed by rapidly increasing brain edema. These patients often arrive to the neurological Departments. 25% of patients develop acute tonic-clonic convulsions in the absence of other focal neurological symptoms. They often arrive to the Department of neurosurgery, and after detection of lesions on MRI some patients even underwent surgery for "brain tumor". Another 25% of patients who arrived to the intensive care unit with a diagnosis of «brain coma» and rapidly increasing depression of consciousness and swelling of the brain. Lethal outcome was in 48% of patients with acute onset of CT in contrast to 30% with the gradual development of the disease.
Conclusion: Thus it should be remembered that AIDS patients with CNS lesion often - one in 5 patients - may have acute onset of CT and it may have different developments with rapid fatal outcome.

PE35/6

Association between immunological status and TB disease development in HIV-infected individuals with LTBI

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Purpose: Limited research has addressed factors associated with TB disease development in HIV-infected patients with latent tuberculosis infection (LTBI). This study aims to examine the association between immunological status and TB disease development in HIV-infected individuals who have ever tested tuberculin skin test (TST) positive during HIV care.
Method: Retrospective anonymous baseline, clinical and LTBI testing records of HIV-infected individuals were collected from a major HIV specialist clinic in Hong Kong. Patients who were diagnosed with HIV between 2002 and 2013 and had tested TST positive, but without any history of active TB at or before HIV diagnosis, were included in the analysis. The main outcome variable was TB disease development, after exclusion of TB cases whose interval between positive TST and TB diagnosis was <1 year. Univariable and multivariable cox regression models adjusted by history of LTBI treatment were performed.
Results: A total of 508 subjects met the inclusion criteria, of whom 87% were male, 93% had initiated ART, 40% were positive at the first LTBI test, and 86% had received LTBI treatment. TB incidence from the last negative TST time point was 4.68 per 1000 person-years (95% C.I.=2.72–7.55). Adjusted by history of LTBI treatment, local residency (aHR=0.18, 95% C.I.=0.06–0.60), ART (aHR=0.18, 95% C.I.=0.05–0.65), and number of negative TSTs before positive results (aHR=0.36, 95% C.I.=0.15–0.85) were negative predictors of TB disease development, while positive result at the first TST was a positive predictor (aHR=5.73, 95% C.I.=1.61–20.43). Immunologically, CD4 count (aHR=0.997, 95% C.I.=0.99–0.9999) and CD4/CD8 ratio (aHR=0.08, 95% C.I.=0.01–0.93) at the time of positive TST result, CD4 ≤200/μL (aHR=2.84, 95% C.I.=1.003–8.02), concurrent CD4 ≤200/μL and CD4/CD8 ratio≤0.5 (aHR=3.11, 95% C.I.=1.10–8.73) after the last negative TST were significantly associated with TB disease development.
Conclusion: Poorer immunological status markers from positive TST results could be used as a surrogate for predicting TB disease in HIV-infected patients.

PE35/7

Amoeba- a swiss army knife for diagnosis and mechanistic understanding of Legionella infection

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Purpose: Considering the high burden of disease and low yield of current diagnostic strategies, we aimed to develop an amoeba model for improving HIV and pneumonia diagnostics and to investigate host-pathogen interactions.
Methods: An *in vitro* model of *Acanthamoeba castellanii* was used to detect and visualize intracellular bacteria from HIV-infected respiratory samples. Model optimization and validation was carried out using *Legionella (*pneumophila and non-pneumophila control strains) as a type organism. Following optimization, *A. castellanii* was grown in 24-well plates and infected with *Legionella* qPCR positive HIV induced sputum samples and incubated for 4 days at 37°C, 5% CO_2 at which time, amoeba were lysed and *Legionella* was quantified using culture. Next, confocal microscopy was used to study the *Legionella*-host interaction. Amoeba were grown on chamber slides and infected at an MOI of 1. After incubation, infected amoeba were prepared for imaging using antibodies against the endoplasmic reticulum and *Legionella,* and a stain for the nucleus.
Results: All 5 of the *Legionella* control strains grew well in *A. castellanii*, increasing up to 6 logs with a limit of detection of 10 colony forming units/mL. Although experiments with clinical samples are ongoing, of the 5 qPCR positive patient samples tested to date, this model was able to recover *Legionella* from 4 of them. Lastly, preliminary microscopy work indicates that *Legionella* spp. may parasitize the host cell through different mechanisms.
Conclusion: Diagnosing and studying intracellular pathogens, organisms often responsible for causing pneumonias among the HIV-infected

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population, can be challenging. However, this model provides a way to enrich for *Legionella* spp. and can serve as an outline for developing similar protocols for other difficult-to-study intracellular bacteria while providing a cheaper alternative to standard cell culture. Improving diagnostic tests and better understanding bacterial pathogenesis can translate to improved outcomes for HIV-infected individuals with pneumonia.

PE35/8

Causes and outcomes of hospitalizations among HIV positive persons in Georgia's referral institution, 2012–2017

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Purpose: We assessed trends in causes and outcomes of hospitalization among HIV patients receiving care at the Infectious Diseases, AIDS and Clinical Immunology Research Center (IDACIRC).
Method: Retrospective analysis included adult HIV patients admitted to IDACIRC for at least 24 hours. Data were abstracted through chart review. Trends in causes of hospitalizations and mortality were tested using adjusted test for trend. Factors associated with mortality were evaluated in multivariate logistic regression analysis. AIDS admissions were split in 3 groups based on mortality rates for the individual AIDS diseases: severe (>15%), moderate (5–15%) and mild (<5%).
Results: A total of 2085 hospitalizations among 1123 HIV patients were registered over 2012–2017. 72.3% (814/1123) of patients had CD4 count<350 at time of HIV diagnosis and 51.9% (583/1123) of patients were hospitalized within 3 months of HIV diagnosis. 931 (44.7%) hospitalizations were due to AIDS-defining conditions and 1154 (55.3%) were due to non-AIDS conditions. AIDS conditions accounted for 50.3% of admissions in 2012 and 41.6% in 2017 (p=0.16). Overall, 167 hospitalizations (8.0%) resulted in lethal outcome, AIDS admissions had higher mortality (11.5% vs. 5.2%, p<0.0001). Between 2012 and 2017 overall mortality decreased from 9.0% to 4.5% (p=0.18), deaths following AIDS admissions decreased from 13.9% to 5.1% (p=0.09). Among 167 deceased patients 137 (82.0%) had CD4 count <200 at the time of hospitalization, including 88.8% (95/107) among AIDS admissions. In multivariate analysis, severe AIDS admission was associated with significantly higher odds of mortality compared to non-AIDS admission (OR 3.55, 95%-CI:1.70–7.40). CD4 cell counts of <50 and 50–100 at hospitalization were also significantly associated with mortality compared to >200 (OR 3.34, 95%- CI: 1.83–6.09 and OR 2.06, 95% CI: 1.08–3.95).
Conclusion: AIDS remains a significant cause of hospitalization and fatal outcome in Georgia. Earlier diagnosis of HIV is critical for decreasing AIDS hospitalizations and mortality.

PE35/9

Population pharmacokinetic analysis of dolutegravir in HIV/TB co-infected people with and without rifampicin

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Purpose: Treatment of HIV/TB co-infection is complicated by drug-drug interactions, toxicities, and immune reconstitution inflammatory syndrome. The antiretroviral integrase inhibitor dolutegravir is a substrate of UGT1A1 and CYP3A4, both of which are induced by rifampicin. Our objective was to characterize the population pharmacokinetics of dolutegravir in HIV/TB co-infected participants receiving rifampicin-based treatment.
Method: Data from INSPIRING (NCT02178592), a Phase III randomized open label study in HIV-1 infected ART naïve adults on rifampicin-based TB treatment (isoniazid, rifampin, pyrazinamide, ethambutol; ≤8 weeks prior to initiating HIV treatment) were used in this analysis (n=65). Participants were randomized to dolutegravir (50 mg twice-daily during and 2 weeks post-tuberculosis therapy, then 50 mg once-daily) or efavirenz (600 mg) and two nucleoside reverse transcriptase inhibitors for 52 weeks. In dolutegravir treated participants, pre-dose plasma samples were collected at Weeks 8, 24, 36, 48 and post-dose samples at Weeks 8 and 36. A nonlinear mixed-effects modeling approach was used for the population pharmacokinetic analysis, using NONMEM program version 7.3 (ICON, Ellicott City, MD).
Results: A one-compartment PK model with linear elimination and lag time in absorption was used to describe dolutegravir pharmacokinetics. The population clearance with and without rifampicin were 2.36 L/hr and 1.09 L/hr, respectively, resulting in ~half exposure in subjects with rifampicin following dolutegravir 50 mg dose. The apparent volume of distribution and absorption rate were 28.9 L and 2.02 hr^{-1}, respectively and Lag time was fixed to 0.263 h. Weight, albumin and age were statistically significant predictors of dolutegravir clearance and albumin and age were predictors of volume of distribution.
Conclusion: A 50 mg BID dose in presence of rifampicin (~2-fold induction) was adequate to achieve comparable exposure (AUC and Ctrough) to 50 mg QD administration without rifampicin. The effect of covariates was not considered clinically significant, therefore, no DTG dose adjustment by these covariates is necessary.

PE35/10

Lung function and health-related quality of life among patients following pulmonary tuberculosis treatment in urban Uganda: a cross-sectional study

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Purpose: We sought to determine the prevalence and predictors of abnormal lung function and health-related quality of life (HRQoL) in patients completing treatment for pulmonary tuberculosis (PTB) and to determine whether these outcomes differed by HIV status.
Method: In this cross-sectional study, we included participants from an ongoing lung disease cohort in Uganda. Eligible patients were aged 18–60 years. Lung function was assessed using spirometry and the tests graded according to GOLD criteria for obstructive lung disease. Poisson regression was used to assess for factors associated with abnormal lung function. St. George's Respiratory Questionnaire (SGRQ) was used to measure HRQoL, while the Mann-Whitney test was used to assess for differences in SGRQ scores.
Results: 162 patients were included in the analysis. Eighty-nine (54.9%) were male and 65 (40.1%) were coinfected with HIV; median (IQR) CD4 count of 145 (53–296) cells/uL. The median (IQR) age was 32 (26–39) years, and the mean (SD) FEV1 and FVC were 2.57L (0.77) and 3.1L (0.85), respectively. Overall, 65 (40.1%) of the participants had abnormal lung function, 57 (87.7%) of whom had restrictive pattern. Smoking was associated abnormal lung function (PR_{adj} 1.88, 95% CI 1.11–3.16, **p=0.018**), while males were less likely to have abnormal lung function (PR_{adj} 0.55, 95% CI 0.35–0.8, **p=0.01**). There was a non-statistically significant trend towards reduced risk of abnormal lung function in patients living with HIV (PR_{adj} 0.76, 95% CI 0.51–1.15, **p=0.19**). The SGRQ total and domain scores were higher in participants with cavitation or consolidation on initial chest x-ray, **p<0.001**).
Conclusion: Abnormal lung function is common in patients completing PTB treatment. The HRQoL is lower in patients with features of severe PTB disease.

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Emphasis should be placed on screening PTB patients with severe disease in the presence of other risks factors for abnormal lung function at end of PTB treatment.

PE35/11

Clinical and laboratory characterization of progressive multifocal leukoencephalopathy in HIV-infected patients in the intensive care unit

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Progressive Multifocal Leukoencephalopathy (PML) is an opportunistic infection of the CNS, which has a high mortality rate. There is no specific treatment for PML. Routine algorithms for diagnosis of PML in HIV-positive patients have not yet been developed in Russia.

Purpose: To identify the clinical and diagnostic aspects of PML in HIV patients.

Method: Retrospective medical records study of HIV patients admitted to the intensive care unit (ICU) at Infectious Clinical Hospital in Moscow, from 2015–2017.

Results: Data from 60 patients were analyzed (40% female; median age - 39.8 (27–61) years). HIV infection had been diagnosed for the 1st time during hospitalization in 13.3% cases, while 36.6% had been HIV diagnosed >5 years. 91.6% were admitted >14 days after the initial symptoms. Focal neurological signs were present in 100% cases: limb paresis (73.3%), speech disorders (63.3%), gait abnormalities (38.3%), cognitive impairment (33.3%), visual impairment (23.3%), dysphagia (3.3%). 96.7% had disturbance of cerebral function, meningeal signs and fever were present in 10% and 70% respectively. 70% patients were ART-naïve before hospitalization. Patients had substantial immunodeficiency (CD4+ <50 cells/μL - 61.6%, 51–200 cells/μL - 26.6%) and high HIV RNA level (>100 000 copies/mL - 46.6%). The JC polyomavirus DNA was detected in CSF in 93.3% cases. MRI was performed in 58.3% patients, 91.4% of whom had positive PML scans. Patients with PML were mainly treated with ART. ICU stay was longer than 2 weeks in 70% of cases while in total 91.6% had died.

Conclusion: PML manifests in severe immunocompromised HIV patients without ART and characterized by high mortality, triggered by a delay to seek medical aid, despite substantial manifestations. Basic neurological manifestations include focal symptoms and disturbance of cerebral function. MRI identify typical changes in the brain. Detection of JC polyomavirus DNA in the CSF is an important diagnostic tool.

PE35/13

Cryptococcal and tuberculosis coinfection: case series identified through the implementation of an advanced HIV disease package of care linked to a TB active case finding strategy in rural Mozambique

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Background: One third of people living with HIV (PLHIV) are diagnosed with advanced HIV disease (AHD) globally. Tuberculosis (TB) and cryptococcal disease (CD) are responsible for ~50% AIDS-mortality in sub-Saharan Africa. Innovative strategies to increase detection and improving AHD-outcomes are needed.

Methods: An active TB-case finding study was implemented in the Manhiça district, Mozambique. Community workers reached all household and community contacts of new TB-cases reported during the study period. Participants were tested for HIV and TB (Xpert® Ultra in induced sputum). ART-naïve or poorly ART-adherent PLHIV were screened for AHD. Those with AHD (CD4 counts <200 cells/mm^3 or WHO stage 3/4) received a WHO-recommended package of interventions, including: OI-screening (Xpert® MTB/RIF; TB-lipoarabinomannan (TB-LAM), plasma cryptococcal antigen (CrAg); OI treatment and/or prophylaxis; rapid ART initiation; and adherence support. Patients were followed-up for 6 months.

Results: Between June-December 2018, 589 adult TB-index cases and 2347 of their contacts were identified (Figure 1). HIV was confirmed in 688 participants, including 155 ART-naive/poorly ART-adherent who accepted AHD screening. 59.4% (92/155) had AHD, including 5.4% (5/92) with TB/CrAg+. Of those, 3/5 had cryptococcal meningitis (TB/CM) and 2/5 were serum CrAg-positive (TB/CrAg+) without CM (Table 1). Patients with TB/CM received short-course amphotericin-B, high-dose fluconazole and management of intracranial pressure with repeated lumbar punctures (LP). TB/CrAg+ patients were treated with high-dose fluconazole. ART was started 2 and 6 weeks after diagnosis among TB/CrAg+ and TB/CM respectively. Mortality was 0 among TB/CrAg+ and 2/3 in CM patients.

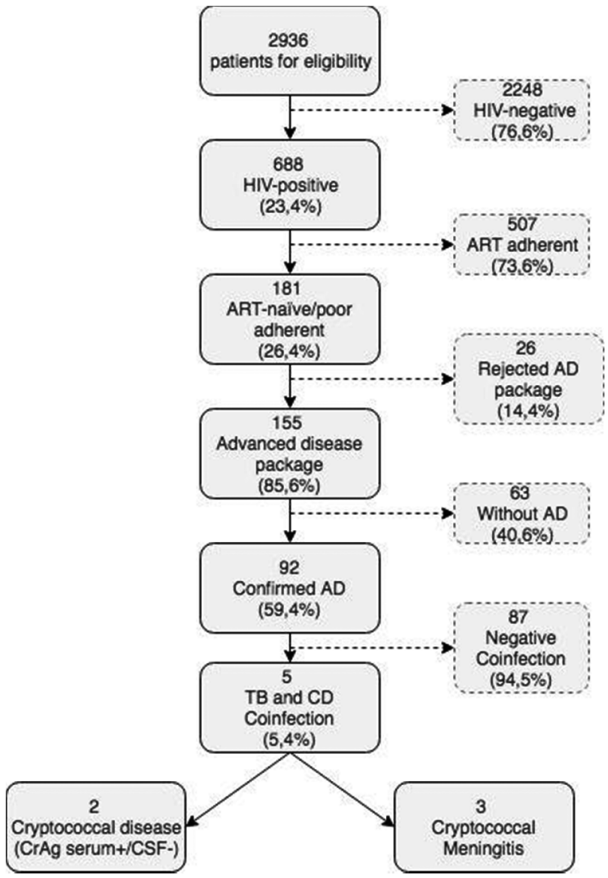


Figure 1. Flowchart: identification of TB/CD coinfected patients

Conclusion: CD and TB coinfection remains underdiagnosed in sub-Saharan Africa. Most cryptococcemic cases go unnoticed in the absence of CrAg-screening. Several challenges exist regarding the management of TB/CD patients, including the lack of first-line antifungals and the low implementation of secondary prophylaxis, and the resulting in high mortality. The WHO package of interventions offers an opportunity to address these gaps.

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Table 1. Baseline characteristics of CD/TB coinfected patients

Case	Age/Sex	ART history	CD4	LAM	Xpert Ultra Sp/ CSF	CrAg Serum/ LCR	Crypto. CSF culture	ART timing	6-month Outcome
1	43 (M)	Naive	92	+	+/+	+/-	-	2 weeks	Alive
2	29 (F)	Non adherent	111	-	-/NP	+/-	-	2 weeks	Alive
3	28 (F)	Naive	1	+	-/-	+/+	+	6 weeks	Alive
4	40 (F)	Naive	45	+	NP/-	+/+	+	6 weeks	Death, 9 weeks after discharge
5	32 (M)	Non adherent	18	+	NP/-	-/NP	+	-	Death, 48 days after discharge

PE35/14

Trends in latent tuberculosis screening in a cohort of HIV-infected patients from a low tuberculosis incidence country

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Purpose: Latent tuberculosis (LTB) screening is recommended in HIV-infected patients by international guidelines. Portugal is a low tuberculosis incidence country, where national guidelines for LTB screening were implemented in 2015. Our aim was to evaluate the trends in LTB screening in a cohort of HIV-infected patients over a 9 year period.

Methods: Cross-sectional, retrospective study of HIV-infected patients with a diagnosis of HIV infection in 2008–2017. LTB was defined as having a positive tuberculin skin test, interferon-gamma release assay and/or recent contact history. Active TB (ATB) was defined as having microbiological or clinical diagnosis. ATB cases before HIV diagnosis were excluded. Logistic regression was performed to identify independent factors associated with likelihood of screening.

Results: Of 967 included patients, LTB screening was performed in 596 (68.2%): screening was negative in 435 (44.9%) and LTB diagnosed in 161 (16.6%). ATB was diagnosed in 91 (9.38%) patients. We found an increase in likelihood of LTB screening over 2008–2017 (from 61.5% to 77.8%, p=0.01). Factors correlated with likelihood of LTB screening were diagnosis in the outpatient setting (OR 4.34 95% CI: 3.05–6.18) and sexual acquisition of HIV infection (OR 2.40 95% CI: 1.59–3.61). Patients aged >51 years (OR 0.54 95% CI: 0.39–0.75), migrants (OR 0.58 95% CI: 0.37–0.91), those with CD4 count <50 cells/mm^3(OR 0.35 95% CI: 0.22–0.52) and hepatitis C and/or B (OR 0.42 95% CI: 0.27–0.65) were less likely to be screened. LTB screening increased from 2015 onwards after implementation of national guidelines (OR 2.00 95% CI: 1.43–2.82). LTB diagnosis was also more likely after this period (6.06–46.51% vs. 0.95–36.56%) and cases of ATB decreased (4.65–5.38% vs. 7.53–17.27%; p<0.001).

Conclusion: Despite some improvement in LTB screening, adherence to recommendations remains low. Measures should be implemented to strengthen screening in identified at-risk groups, such as migrants and older-aged patients.

PE35/15

Drug-induced hepatic injury developed in tuberculosis/HIV co-infection treatment

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Objective: The objective of the study was to evaluate the Drug-Induced Hepatic Injury (LHIM) in the treatment of tuberculosis (TB) in people living with HIV through the instruments of Naranjo and RUCAM, in a reference center in the Southeast of Brazil for infectious-contagious diseases.

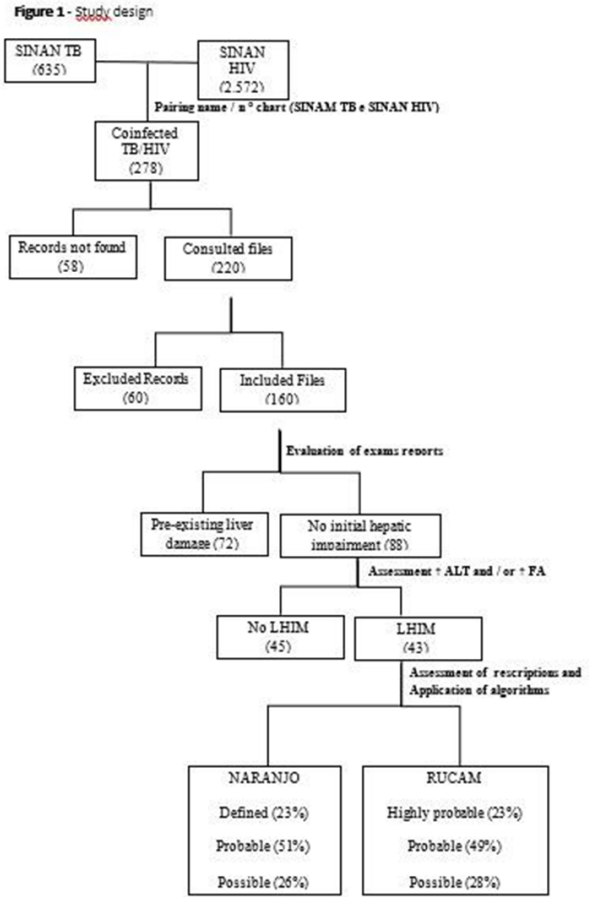


Figure 1. Study design

Method: A retrospective cohort study was performed . Data were collected from medical records and laboratory reports of patients notified for TB and HIV in the period from April 2015 to December 2018. Laboratory records and laboratory reports with potential for the evaluation of LHIM were considered, those that presented dosages ofalanine aminotransferase and phosphatase alkaline levels above the limit after the introduction of TB treatment, and the Naranjo and RUCAM algorithms were used to determine causality. A statistical analysis was performed using the Software for Statistics and Data Science STATA® 12.

Results: A total of 160 patients were included in the study, of which 76% were male. Age ranged from 19 to 69 years, with a median of 41 years. Most of the lesions were cholestatic and classified as probable by the algorithm of Naranjo and RUCAM. The incidence of LHIM was 49% estimated from the determination of the cases where the lesion was causally associated with measurement . The T-CD4 + lymphocyte count had a statistically significant association (OR=4, p=0.010).

Conclusion: The high incidence of LHIM in this study is an alert for health professionals in the therapeutic orientation of these patients. The use of the Naranjo and RUCAM algorithms contributes to the treatment, safety and detection of coinfection collaborating in the sanitary notification process.

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Table 1 - Characterization of liver injury (n = 160)

	N	%
Hepatic injury		
Yes	115	72
Not	45	28
Liver injury (pre-existing)	72	45
Hepatocellular	1	1
Chastising	63	88
Mixed	8	1 1
Medicated liver damage	43	38
Hepatocellular	2	5
Chastising	36	84
Mixed	5	12
Algorithm of Naranjo		
Defined	13	23
Likely	29	51
Possible	15	26
RUCAM Algorithm		
Highly probable	13	23
Likely	28	49
Possible	16	28

RUCAM: Roussel Uclaf Causality Assessment Method

Table 1. Characterization of liver injury (n=160)

Vaccines and immune based therapies

PE36/2

Development of engineered nanocarrier for controlled delivery of a protease inhibitor

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Purpose: AIDS is a chronic, progressive syndrome, characterized by intense viral replication and profound immunosuppression, resulting in the development of life threatening opportunistic infections. HIV infection leads to deterioration of immune functions.The objective of the present study was to develop, optimize and characterize engineered nanocarriers for controlled delivery of a protease inhibitor. Lopinavir was the drug of choice as it is an effective antiretroviral drug having specific and prominent anti-HIV action. In the present study, it is envisaged to develop and characterize a controlled delivery system wherein the drug lopinavir (LPV) will be entrapped in engineered nanocarrier.
Engineered nanocarriers targeted towards the prespecified target tissues by coupling with mannose delivers the drug in a controlled manner to the site of action. Thus it results in increased bioavailability and avoids the adverse effects associated with the drug. Overall the approach leads to a safe, economical and effective Anti-HIV formulation.
Method: The uncoupled Solid Lipid Nanoparticles (SLN) were prepared by Solvent diffusion method and then coupled with mannose. Characterization studies were done by Scanning & Transmission Electron Microscopy (SEM & TEM). X-ray diffraction (XRD) and Differential scanning calorimetry (DSC) studies were performed along with the in-vitro studies followed by in-vivo studies on albino rats.
Results: In-vitro & *in-vivo* studies results shows Mannose coated SLNs (MSLN) deliver their contents to macrophage rich organs and tissues, which are the reservoir of HIV. Low elimination and better distribution profile can be achieved by MSLNs. The dose of the antiviral agent can be reduced due to the site-specific delivery from this carrier.
Conclusion: Conclusively, ligand-mediated bio-disposition and cellular interaction of MSLNs, especially at target sites, would be a focal paradigm for upcoming research in the field of anti-HIV drug delivery. MSLNs have paved the way for the bio-stable, site-specific and ligand-mediated delivery systems with desired therapeutics.

Viral hepatitis

PE37/1

Acute hepatitis C infection in HIV-infected patients who achieved viral suppression: incidence and risk factors

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Background: The cases of sexually transmitted diseases (STDs) are commonly reported among HIV-infected men who have sex with men (MSM), especially syphilis, gonorrhea, acute hepatitis A and genital wart, but acute hepatitis C (AHC) became one of rampant STDs recently, even those living with fully suppressed HIV. The study was performed to evaluate the incidence and risk factors of AHC.
Materials and methods: We used Taiwan Centers for Disease Control (TCDC)-operated National Disease Surveillance Systems (NDSS) to identify incidence of AHC in Taoyuan General Hospital during October 2016 to October 2018. Overall, a total of 43 AHC with HIV co-infection cases were documented, and each AHC case was matched to four HIV-infected controls without AHC reported in the NDSS on age (±5 years), risk factor of HIV infection, CD4 lymphocyte counts (±50 cells/mL).
Results: Forty-three HIV/AHA cases were matched to 182 controls, and all cases and controls were males and MSM. The mean age (SD) was 31.0 (±5.6) years in AHC cases, and 30.6 (±6.7) years in controls, respectively (p=0.695). Forty-two cases (97.7%) and 182 controls (100%) took ART (anti-retroviral therapy) (p=0.191), and 39 cases (90.7%) and 182 controls (100%) had recent HIV RNA <200 copies/mL (p<0.001) and CD4 lymphocyte count were 700 (±262) versus 695 (±282) (p=0.972). In multivariable conditional logistic

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regression analysis, a history of chemsex with amphetamine abuse (adjusted OR=3.11, 95% CI 1.39-6.96) and syphilis infection (aOR=3.55, 95% CI 1.25-10.13) were independently associated with acute hepatitis C infection.
Conclusions: Acute HCV cases continued to increase particularly among sexually active HIV-infected MSM with a syphilis diagnosis and a history of chemsex. We recommend surveillance of associated behavioral and virologic characteristics and HCV counseling and testing for HIV-infected men in Taiwan.

PE37/2

HBV infections among HIV infected HAART receiving mothers and their exposed infants in a tertiary hospital in Kenya

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Purpose: Mother-to-child transmission (MTCT) of Hepatitis B virus (HBV) is responsible for more than one third of chronic HBV infections worldwide. Antiretroviral therapy (ART) naïve HBV/HIV co-infected mothers have a high tendency of transmitting the two viruses. This study aimed to determine prevalence & predisposing factors of HBV infections among HAART-receiving HIV-infected mothers and their exposed infants.
Method: A structured questionnaire was used to capture socio-demographic data and factors associated with HBV infections. aA 4_ml sample of paired whole blood obtained from HIV positive mothers & their exposed infants was analyzed for Hepatitis B surface antigen (HBsAg) using both rapid and Enzyme-linked immunosorbent assay (ELISA) tests. HBsAg positive samples were further screened for HBV envelope antigen (HBeAg) using ELISA. HBsAg positive samples with both ELISA and rapid tests were subjected to a nested Polymerase chain reaction (PCR) targeting the preS1 region.
Results: A total of 534 HIV-infected mothers – infant pairs were recruited. Mean age of mothers was 31.2 years (SD 5.4 years) and infants' median age of 6 months (IQR 3-10 months). 502 (94%) of the mothers were taking TDF/3TC/NVP and 32(6%) were on AZT/3TC/NVP or EFV. 19 of 534 (3.6%) mothers were HBV positive by both HBsAg rapid and ELISA tests. All 19 HBsAg positive samples tested HBeAg negative. 12 of the 19 HBsAg positive samples also tested positive on PCR targeting the preS1 gene. All infants' samples tested HBV negative with all tests. History of dental surgery was associated with increased rate of HBV infection (OR 3.3 (95% CI 1.1-9.6).
Conclusion: In this population of HIV-infected pregnant mothers, our observations suggest that the HAART regimen received by them may have prevented vertical transmission of HBV infections to exposed infants.

PE37/3

Direct-acting antivirals (DAAs) improve liver stiffness measurements but do not improve the Veterans Aging Cohort Study (VACS) Index in HIV/HCV co-infected Egyptian patients: is improved discrimination needed?

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Purpose: We aimed to investigate whether VACS index might reflect the post sustained virological response (SVR) clinical amelioration in a cohort of HCV/HIV coinfected Egyptian patients, given the recent evidence of reduced mortality risk with the achievement of SVR in HCV patients received DAAs coupled with hepatic fibrosis regression and inflammatory mediators' improvement, factors known to correlate with VACS index.
Method: Prospective cohort study conducted in Cairo University Hospitals between March 2017 and March 2019. We enrolled 50 HCV/HIV coinfected patients achieved SVR 24 weeks following 12 weeks of sofosbuvir-based therapy (T24). Before DAAs introduction (T0), all patients received emtricitabine/tenofovir plus efavirenz ≥ 6 months with CD4 count ≥ 100 cells/mm^3 and suppressed HIV viral load.
At T0 and T24 we measured: VACS index, liver stiffness (LS) by transient elastography (TE) and the fibrosis-4 (FIB-4) score. Changes in VACS index components were assessed as both continuous and categorical variables.
Results: Mean age was 34.6±10 years, 41 were males (82%). While VACS index was stable over time (T0, 23.2±13.8 vs T24, 22.85±8.17, p=0.68), we observed a significant improvement in LS (T0, 7.05±4.84 kPa vs T24, 5.66±2.63 kPa, p<0.001), in FIB-4 (T0, 1.24±1.08 vs T24, 0.93±0.64, p=0.001) and in hemoglobin (T0, 13.41±1.72 vs T24, 13.92±1.71, p=0.04). Other individual components were comparable between both checkpoints (All p >0.1). The significant improvement in the parameters as continuous variables was not confirmed in the categorical model used in VACS index calculation (All p >0.1).
Conclusion: This reported discrepancy might be explained by considering
(i) categorical but not continuous variables and
(ii) HCV serostatus but not viral load in VACS index calculation.
So, it needs to be modified to enhance its discrimination for post HCV cure changes.

PE37/4

HCV/HIV coinfection in the DAA era: which patients have not been treated for HCV?

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Purpose: Directly acting antiviral agents (DAAs) have revolutionized the treatment of hepatitis C (HCV) infection. However, not all HCV/HIV patients have been treated for HCV, yet. Here we identify patient characteristics that were associated with not receiving DAA therapy within the Bonn University Hospital HIV cohort.
Method: 397 HCV/HIV co-infected patients from the HIV outpatient clinic at the university hospital in Bonn were analyzed retrospectively regarding sociodemographic, laboratory, HIV and DAA therapy data. Fisher's Exact Test, T-test and Chi-Squared Test were used for statistical analysis.
Results: The median age of the 397 patients was 49.9 years (IQR 40.5-59.3), 83.6% were male. Main HIV transmission routes were: 27.2% men who have sex with men (MSM), 28.7% hemophilia, 25.4% intravenous drug use (IVDU). 95.5% received antiretroviral therapy, 84.2% were undetectable for HIV. 14.1% had cleared HCV spontaneously, 49.1% had achieved SVR in the past, 24.7% were lost to follow-up (LTFU), and 8.9% (n=35) had a replicating HCV infection: 8.6% were currently receiving DAA therapy, 5.6% had an acute HCV infection and were monitored for spontaneous clearance, 20% were LTFU, 11.4% had competing medical interventions, 8.6% had failed DAA treatment, and in 45.7% (n=16) DAA therapy was not initiated due to compliance issues: 88% of these patients were active IVDU. In univariate analysis patients with cured HCV infection were older (p=0.022), less often IVDU (p=0.001) and had higher rates of therapy compliance (p<0.001) than patients with replicating HCV infection.
Conclusion: In our cohort the majority of HCV/HIV patients not having received DAA therapy yet were active IVDU potentially reflecting practical issues around regular attendance for (HIV) clinical visits. This underlines the importance of involving substitution clinics to promote HCV elimination in this hard-to-reach patient population.

PE37/5

Hepatitis E seroprevalence in HIV-positive patients

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Purpose: Hepatitis E virus (HEV) infection is usually an acute self-limiting disease, leading rapidly progressive cirrhosis and a chronic infection in patients

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with hematological malignancies, patients with chemotherapy requirement and patients with HIV-infected. The aim of this study was to investigate the seroprevalence of HEV in HIV-positive patients.
Method: In this study, serum samples of patients who applied to the Clinical Microbiology Laboratory of Sakarya University Education and Research Hospital between October 2017 and December 2018 were evaluated for anti-HEV IgG and IgM. The study group consisted of 126 patients with HIV infection. Sixty healthy volunteers were used as the control group. Anti-HEV IgG and IgM antibodies were investigated by ELFA (Enzyme-linked Fluorescent Assay) method and commercial kits (Biomerieux diagnostic, France) from the plasma samples of the patients. In addition, ALT, AST, CD4, CD8, HIV-1 RNA viral load, anti-HCV, HBsAg, and VDRL results of patients were evaluated.
Results: The study group consisted of 114 (90.5%) males and 12 (9.5%) females with a mean age of 38.11±13.32 (min: 18, max: 80) years. Anti-HEV IgG was positive in 5 (4.0%) HIV-positive patients. Anti-HEV IgM was not positive in any patient. In the control group, anti-HEV IgG positivity was detected in only 1 of 60 patients. None of the patients with anti-HEV IgG positivity had anti-HCV and HBsAg positivity. There was no statistically significant difference between anti-HEV IgG positive and negative patients in terms of ALT, AST, CD4 and CD8, HIV-1 RNA viral load values ($p > 0.05$).
Conclusion: Anti-HEV IgG positivity was found to be 4% in HIV-positive individuals and HCV and HBV co-infection was not detected in any patients with HIV-HEV co-infection. HEV infections do not emerge as a priority in HIV-infected people, but HEV should also be investigated in HIV-infected individuals with uncertain etiology of liver abnormalities.

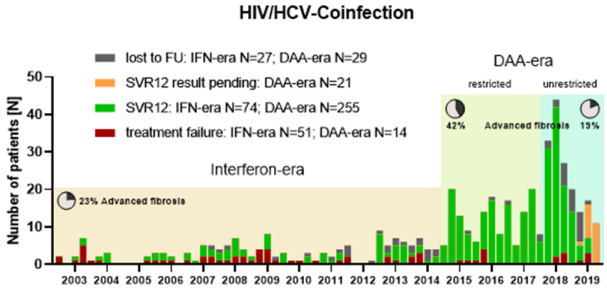
PE37/6

Success of unrestricted DAA therapy is limited by HCV reinfections and loss to follow-up in HIV-positive patients

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Purpose: In contrast to interferon (IFN)-based therapy, direct-acting antivirals (DAAs) achieve hepatitis C virus (HCV) elimination in most individuals living with HIV. We assessed temporal trends in patient characteristics, transmission risks, treatment uptake and outcome (SVR) in eras of (i) IFN, (ii) restricted DAA-access (R-DAA), and (iii) unrestricted DAA-access (UNR-DAA) in HIV/HCV.
Method: Consecutive HIV/HCV starting HCV treatment at the Medical University of Vienna between Q3/2002-Q2/2019 were enrolled.
Results: Overall, 471 HIV/HCV initiated HCV treatment: n=152(32%) in IFN, n=129(27%) in R-DAA and n=190(41%) in UNR-DAA eras (Figure). Comparing IFN vs. R-DAA vs. UNR-DAA eras, distribution of age (38.4 vs. 45.9 vs. 41.5 years), gender (76% vs. 76% vs. 80%male) and transmission routes (intravenous drug-use: 66% vs. 60% vs. 58%) were similar, whereas more patients with advanced fibrosis were treated during R-DAA (42% vs. 20%; $p<0.001$). Time from HCV diagnosis to therapy was significantly shorter in the UNR-DAA and IFN eras (median years UNR-DAA: 3.23 vs. IFN: 2.83 vs. R-DAA: 8.82; $p<0.001$). The number of therapies for HCV reinfections increased to n=40(21%) in the UNR-DAA (vs. n=0 0% in the IFN and n=4 3%) in the R-DAA eras ($p<0.001$).
SVR was achieved in 49%, 95% and 79% in the IFN, R-DAA and UNR-DAA eras, respectively. While virologic failure was mostly limited to the IFN era (34% vs. UNR-DAA:5% vs. R-DAA:4%, $p<0.001$), lost-to-follow-up re-occurred as major reason for non-SVR in the UNR-DAA era (16%; vs. IFN:18% vs. R-DAA:2%, $p<0.001$). Without considering lost-to-follow-up patients, SVR was 95% in the UNR-DAA era.
Conclusions: With unrestricted DAA access, SVR is now achieved in 79% of HIV/HCV since loss-to-follow-up emerged as main reason for non-SVR, while virological failure occured only in 5%. Most HIV/HCV patients with advanced fibrosis were treated in the R-DAA era. A rising number of HCV re-treatments for reinfections are observed in the UNR-DAA-era.



Timeline of treatment initiations

PE37/7

Efficacy and safety of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide as maintenance treatment of patients with HIV and Hepatitis B Virus (HBV) coinfection

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Purpose: Tenofovir alafenamide (TAF) can suppress both HIV and HBV. The efficacy and safety of switching from TDF-based antiretroviral therapy to coformulated elvitegravir/cobicistat/emtricitabine/TAF (E/C/F/TAF) has not been widely investigated in HIV/HBV-coinfected Asian populations.
Methods: Between January 2018 and October 2018, HIV/HBV-coinfected patients who had achieved HIV viral suppression with TDF-containing regimens were switched to E/C/F/TAF in this multicenter study. Assessment of plasma HBV and HIV viral load, HBV serology, renal function, metabolic profiles, and bone mineral density (BMD) were performed at Weeks 24 and 48 after initiation of E/C/F/TAF.
Results: A total of 275 HIV/HBV-coinfected participants were enrolled, of whom 13.5% were HBeAg-positive at baseline and 94.2% had plasma HBV DNA <20 IU/mL. 275 and 200 have completed 24 and 48 weeks of follow-up, respectively. In snapshot analysis, 92.7% and 90.0% of the participants achieved plasma HBV DNA <20 IU/mL; 4.7% and 4.5% had HBV DNA ≥20 IU/mL and 2.5% and 5.5% had no virological data, respectively. At Weeks 24 and 48, 89.1% and 63.0% maintained HIV viral suppression, and 9.1% and 36.5% had no virological data due to discontinuations or missing virological testing, respectively. Compared with baseline, the median urine protein-creatinine ratio (79 vs 73 mg/g, $p=0.002$), and urine β2-microglobulin-creatinine ratio (257 vs 142 μg/g, $p<0.001$) at Week 48 decreased significantly. BMD of the lumbar spine and hip improved at Week 48 (median T-score change, lumbar spine, −0.3 vs −0.1, $p<0.001$; hip, −0.3 vs −0.1, $p<0.001$). Significantly higher lipid profiles were observed after switch to E/C/F/TAF (Table 1). Eleven (4.0%) participants withdrew from the study before Week 48, with 7 (2.5%) due to adverse effects.

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Conclusions: E/C/F/TAF achieved both HBV and HIV viral suppression in HIV/HBV-coinfected participants. Switch to E/C/F/TAF resulted in less proteinuria, improved BMD of the lumbar spine and hip, but increased lipids at Week 48.

Table 1. Lipid profiles of the patients at baseline and 48 weeks

	Baseline N=275	24 weeks N=275	48 weeks N=200	Baseline vs 48 week, p
Triglyceride (mg/dL), median (IQR)	118 (87-174)	132 (100-204)	139 (99-189)	<0.001
Triglyceride, median change from baseline		18 (-19-57)	30 (-21-74)	
Total cholesterol (mg/dL), median (IQR)	166 (151-192)	198 (174-224)	192 (167-222)	<0.001
Total cholesterol, median change from baseline		31 (9-52)	25 (6-45)	
LDL (mg/dL), median (IQR)	100 (84-117)	121 (100-144)	121 (97-138)	<0.001
LDL, median change from baseline		22 (4-37)	22 (5-35)	
HDL (mg/dL), median (IQR)	42 (36-49)	47 (39-56)	46 (39-53)	<0.001
HDL, median change from baseline		5 (-1-11)	3 (-2-8)	
Total cholesterol: HDL ratio, median (IQR)	4.0 (3.4-4.7)	4.3 (3.4-5.1)	4.2 (3.5-4.9)	<0.001

PE37/8

Effectiveness of hepatitis a vaccination among people living with HIV in Taiwan: is one dose enough?

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Purpose: Single dose of hepatitis A virus (HAV) vaccine had been proven its efficacy in short-term and over 5 years effectiveness in immunocompetent hosts, but not in immunocompromised hosts. We aim to compare the effectiveness of one dose versus 2 doses HAV vaccine among people living with HIV (PLHIV) during the outbreak of acute hepatitis A in Taiwan between June 2015 and December 2017.
Method: We conducted a 1:1 retrospective case-control study for PLHIV in a single center designed for HIV care in Northern Taiwan. Nationwide campaign of single dose HAV vaccine had been practiced for high risk population including PLHIV and those who newly diagnosed sexually transmitted diseases. More than 70% of the subjects completed the second dose of HAV vaccine 6 months later based on the suggestion from current guideline.
Results: Among 423 PLHIV during February 2016 and December 2017, 90 cases received single dose of HAV vaccine provided by the campaign while the other 90 age-matched cases completed second dose 6 months later which was not provided by the campaign. Between the 2 groups, more injection drug users in single dose group than 2 doses group (22.2% vs. 1.1%, p<0.001) and co-infection with viral hepatitis C (HCV) was also higher (28.9% vs. 5.6%, p<0.001). Other factors such as mean CD4 cell count, antiretroviral status when initiating vaccination, or viral suppression showed no significant difference. Seroconversion rate at one year was higher in 2 doses group than single dose group (97.8% vs 56.7%, p<0.001, aOR: 33.6, 95% CI: 7.80-145.21). Moreover, HCV coinfection was associated with less seroresponse among single dose group at one year (aOR: 0.22, 95% CI: 0.08-0.58, p=0.002).
Conclusion: 2 doses of hepatitis A vaccine are necessary among PLHIV to achieve adequate seroresponse at one year in the setting of HAV outbreak, especially for patients with HIV/HCV coinfection.

PE37/9

HIV patients remain at high risk for advanced liver fibrosis after curing HCV infection

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Purpose: The aim of this study was to evaluate changes in liver fibrosis among HIV/HCV co-infected persons after curing HCV infection.
Method: Study included adult HIV/HCV co-infected patients, who cured HCV infection during 2015-2017 and were followed at least for 6 months after achieving sustained virologic response (SVR). Primary outcome of interest was change in the advanced liver fibrosis status defined as FIB-4 score of >3.25 or LS ≥9.5 kPa on transient elastography, with preference given to LS when available. FIB-4 and LS measurements closest to HCV treatment initiation were considered as baseline, while measurements closest to 31 December 2018 were defined as follow-up.
Results: Among 343 patients included the median age was 44 (IQR: 39-49) years, 301 (87.8%) were men and 237 (69.1) were infected through injection drug use (IDU). Patients were known to be HIV positive for the median 6.2 (IQR: 3.6-9.2) years. Overall 227 (66.2%) had advanced fibrosis at baseline. Patients were followed after SVR for the median 1.9 (IQR: 1.4-2.2) years. FIB-4 was available for all patients at baseline and follow-up, LS was available for 243 (70.8%) patients at baseline and 92 (26.8%) patients at follow-up. At the end of follow-up 212 (61.8%) patients had advanced liver fibrosis. Advanced fibrosis persisted in 148 (43.1%) patients, advanced fibrosis regressed in 79 (23.0%) patients, liver fibrosis progressed to advanced stage in 64 (18.7%) patients based on combined FIB-4 and LS data. Among 92 patients with follow-up LS data, 39 (42.4%) had persisted advanced liver fibrosis, 35 (38.0%) had regression in advanced liver fibrosis and 5 (5.4%) had progression to advanced liver fibrosis based on LS data only.
Conclusion: Despite curing HCV infection, HIV patients remain at high risk for persisted liver damage and progression to advanced liver fibrosis as measured predominantly by FIB-4.

PE37/10

HIV/HCV coinfection in Spain: trouble will soon be over

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Purpose: We assessed the prevalence of anti-HCV antibodies (HCV-Ab) and active HCV infection (HCV-RNA-positive) in people living with HIV (PLWH) in Spain in 2018 and compared the results with similar studies performed in 2015, 2016, and 2017.
Method: The study was performed in 43 centers (October-November 2018). The sample size was estimated for accuracy of 1.25%, the number of patients from each hospital was determined by proportional allocation, and patients were selected using simple random sampling. All oral DAA-based therapy has been available in Spain since the third trimester of 2014. Since June 2017, free access to treatment has been available to all HCV-infected individuals.
Results: The reference population comprised 40,650 PLWH (approximately 1/3rd of PLWH in Spain), and the sample size was 1,733. HCV serostatus was known in 1,721 (99.3%), and 578 (33.6%) were HCV Ab-positive (78.1% PWID

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and 10.9% MSM). Of these 578, 409 cleared HCV after anti-HCV therapy, 104 cleared HCV spontaneously, 64 were HCV-RNA-positive, and 1 had unknown HCV-RNA. The prevalence of HCV-RNA-positive was, therefore, 3.7%. As 21 of 64 patients were receiving DAAs, and assuming treatment effectiveness of 95%, the prevalence of HCV-RNA-positive could be considered to be 2.5%. A summary of the main findings in the four national cross-sectional studies is shown in the table. Overall, HCV-related liver cirrhosis was present in 6.6% of the PLWH, 10.9% of HCV-RNA-positives, and 26.4% of those who cleared HCV after anti-HCV therapy (P=0.007).

Conclusion: Active HCV infection among PLWH in Spain at the end of 2018 was 3.7%, that is, 83.3% lower than in 2015. Increased exposure to DAAs was the reason for this sharp decrease. The elimination of HCV infection among PLWH in Spain is an achievable goal shortly, but the burden of HCV-related cirrhosis will continue to be significant among these individuals.

Trends in HIV/HCV coinfection in Spain

	2015	2016	2017	2018	p trend
Centers	41	43	43	43	
Reference population	35,791	38,904	40,322	40,650	
Sample size	1,867	1,588	1,690	1,733	
Tested for HCV Ab	98.7%	99.8%	99.1%	99.3%	
HCV Ab-positive	37.7%	34.6%	34.0%	33.6%	
HCV-RNA-positive	22.1%	11.8%	8.0%	3.7%	<0.001
Anti-HCV treatment uptake	59.3%	74.7%	82.4%	92.2%	<0.001

PE37/11

Care cascade of incident HCV infection among HIV-positive patients in Taiwan

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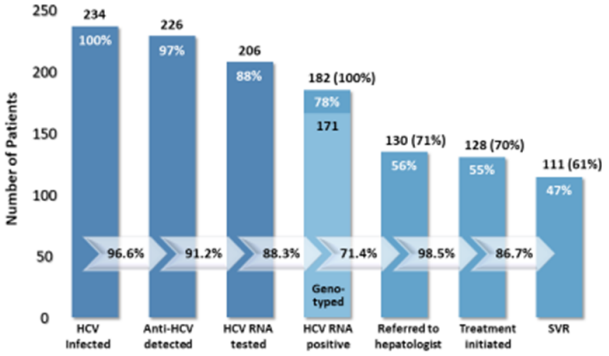
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Purpose: Direct acting antivirals (DAA) have replaced pegylated interferon plus ribavirin (Peg/RBV) and have been reimbursed for the treatment of chronic HCV infection in Taiwan in 2017-2018. Despite the government's commitment to elimination of HCV by 2025, little is known about the engagement and completion of HCV treatment in HIV/HCV-coinfected patients, in whom the incidence rate of HCV infection has steadily increased to 28.5 per 1000 PYFU in 2018.

Method: From January 2011 to December 2018, HIV-positive patients testing negative for anti-HCV antibody at baseline followed by subsequent HCV seroconversion were identified as having incident infections. Care cascade of HCV infection included the total case number of incident HCV infection identified by retrospectively testing all archived blood samples, HCV seroconversion detected by treating physicians, HCV RNA load determined, HCV RNA positivity, HCV treatment initiated, and sustained virologic response (SVR) achieved. We calculated the duration of HCV viremia, from the diagnosis of incident HCV infection until viral clearance by treatment or end-of observation on 30 June 2019. The number of sexually transmitted infections during the HCV viremia period was recorded.

Results: Among 3671 HCV-seronegative, HIV-positive patients, 234 (91.5% being MSM) developed HCV seroconversion between 2011 and 2018. Of those patients, 226 (96.6%) were found to have HCV seroconversion by HIV-treating physicians, 206 (88.0%) had an HCV RNA load determined and 182 (77.8%) were viremic. Of those known to have HCV viremia, 128 (70.3%) initiated treatment and 111 (61.0%) achieved SVR. The median interval of HCV viremia was 535 days (IQR, 331-1036), during which time a total of 226 episodes of sexual transmitted infections were recorded.

Conclusion: Despite improved access to treatment for HCV infection in Taiwan, HCV RNA load testing and early initiation of anti-HCV treatment need to be improved in order to prevent onward transmission among HIV-positive patients in Taiwan.



Care cascade of incident HCV infections, 2011-2018

PE37/12

Current characteristics of HIV/HBV coinfected patients in a single HIV reference centre of Madrid

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Purpose: HIV epidemiology and prognosis has changed in Spain since the beginning of the epidemic. The objectives of our study were to assess if changes in epidemiologic characteristics have changed also in HIV patients with chronic hepatitis B (CHB) and to study clinical evolution of HIV/HBV+ patients over the years.

Methods: Retrospective review of CHB coinfected patients in a single reference HIV clinic in Madrid, Spain. We compared incidence and baseline characteristics in different time periods (before 2000, 2000-2004, 2005-2009, 2010-2014, 2015-2018). Univariate and multivariate logistic regression analysis (including age, gender, diagnosis before 2000, intravenous drug use [PWID], CD4 cell count, HCV and HDV coinfection and fibrosis) was done to study factors associated with mortality and advance fibrosis (AF). AF was considered when the last fibroscan was >12 Kp/mL or clinical cirrhosis was diagnosed.

Results: Out of 5453 HIV+ patients included, 163 had CHB (prevalence 3%; 95% CI 2.6-3.5). Incidence rate has not change since year 2000 (2.4/100 patients*year). Most CHB are men (85.5%) without difference among study periods. In the last periods we have seen differences in origin (fewer Spanish native patients and more latin americans), fewer former PWID, coinfeccion with HDV and HCV.

After a median follow-up of 18.9 (IQR 8.8-25.4) years since diagnosis, twenty patients had died (0.69*100 patients-year): 9 liver related, 5 cancer, 3 HIV related, 3 other.

Having a first fibroscan >12 Kp/mL was independently associated with death [Table 2].

At the end of follow up 31/122 (25.4%) had AF. AF was independently associated with diagnosis before year 2000 and coinfection with hepatitis delta.

TABLE 1: PATIENT CHARACTERISTICS REGARDING YEAR OF DIAGNOSIS

Years	<2000	2000-4	2005-9	2010-14	2015-18	p
Number of patients	86	16	28	18	11	
Male	72 (83.7)	14 (87.5)	27(96.4)	15(83.3)	8 (72.7)	0,3
Age*	29.1 (25.3-33.7)	35.5 (30.1-42.5)	36.4 (32.8-40.5)	32.7 (30.7-38,8)	33.5 (31.9-53)	**<0,01**
Origin						**<0.01**
-Spain	74 (90,2)	10 (66,7)	15 (60)	5 (27,8)	1 (9,1)	
-Rest of Europe	3 (3,7)	0	1 (4)	2 (11,1)	1 (9,1)	
-Latin America	3 (3.7)	2 (13.3)	4 (16)	8 (44.4)	6 (54.5)	
-África	1(1.2)	2 (13,3)	5 (20)	3 (16.7)	3 (27.3)	
-Asia	1 (1,2)	1 (6,7)	0	0	0	
Risk						**<0.01**
-IDU	42 (52.5)	3 (20)	2 (8)	1 (5.9)	0	
-MSM	30 (37.5)	7 (46.7)	18 (72)	14 (82.4)	8 (72.7)	
-Other	8 (10)	5 (33.3)	5 (20)	2 (11.8)	3 (27.3)	
Chronic hepatitis C						
-Former or current	25 (29.4)	6 (37.5)	6 (22.2)	2 (12.5)	0	
-Never	41 (48.2)	10 (62.5)	19 (70.4)	14 (87.5)	10 (100)	**<0.01**
-Spontaneus clearance	19 (22.4)	0	2 (7.4)	0	0	
Hepatitis Delta	24 (34.3)	1 (10)	1 (5)	1 (7.7)	0	**<0.01**
Baseline HBeAg +	37 (44.6)	6 (37.5)	16 (57.1)	10 (55.6)	8 (72.7)	0,3
Baseline liver stiffnes (fibroscan)*	7.6 (5.9-11.6)	5.2 (4,2-12.6)	5.6 (4,7-8.4)	6 (4,5-8.9)	5.5 (4,7-9.4)	**0.03**
Cirrhosis at first FS	18 (24)	3 (23)	1 (3.8)	1 (7.1)	0	**0.02**
Median time of follow-up (years)*	25 (20.9-27.7)	15.5 (11.6-16.9)	9.8 (8.3-11.9)	4.9 (3.8-7.2)	1.4 (0.9-2.05)	
Cirrhosis at last FS	22 (31.4)	6 (40)	2 (8.3)	1 (11)	0	0.06
Mortality	15 (17.6)	4 (25.4)	1 (3.7)	0	0	**0.03**

* Median (IQR), IDU: former intravenous drug addict; MSM: Men sex with men.

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Conclusions: The epidemiology of CHB in our cohort is changing, with less native Spanish and less coinfection with other hepatotropic virus. Liver fibrosis predicts mortality while coinfection with hepatitis delta and diagnosis before year 2000 predicts advanced fibrosis.

TABLE 2: FACTORS ASSOCIATED WITH MORTALITY

	UNIVARIATE ANALYSIS OR 95% CI	p	MULTIVARIATE ANALYSIS OR 95% CI	p
Gender	1.03 (0.2-3.8)	0.9		
Age at the end of follow-up	1.01 (0.9-1.07)	0.5		
Diagnosis before year 2000	**2.9 (0.9-8.3)**	**0.09**	2.2(0.4-11.8)	0.2
PWID*	**4.9 (1.8-13.2)**	**<0.01**	0.3(0.03-2.7)	0.2
Nadir CD4 cell count++	0.9 (0.3-2.3)	0.8		
Chronic heptitis C	**2.9 (1.09-7.7)**	**0.03**	1.9 (0.5-6.9)	0.3
Hepatitis Delta	**4.3 (1,3-13,6)**	**0.01**	2.9 (0.8-10.5)	0.09
Baseline Fibroscan >12	**4.9 (1.6-15.2)**	**<0,05**	**3.9 (1.05-14.4)**	**0.04**

* PWID: patients infected by injection of intravenous drugs. ++Per 100 CD4 cell count/ml increment.

PE37/13

High HCV reinfection rate in MSM living with HIV in Barcelona: the need to focus on high risk population to achieve HCV elimination

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Purpose: The aim of this study is to describe the characteristics and the incidence of HCV reinfection among men who have sex with men (MSM) living with HIV (LWHIV) from the Hospital Clínc HIV cohort in Barcelona, Spain.
Methods: The MSM HIV-HCV co infected patients who have had one or more HCV reinfections in this cohort have been analysed retrospectively from January 2010 until the December 2017. Demographic, epidemiological and HIV-HCV variables have been collected at the time of the first HCV reinfection and in the following episodes. Data were analysed using Stata (StataCorp. 2017)
Results: 194 patients were diagnosed with an AHC during the period time. 174 were treated for the first episode infection and 95 achieved a SVR. During the follow-up, 35 HCV reinfection episodes were identified in 30 MSM HIV patients. Baseline characteristics are shown in Table 1. Twenty-six (87%) patients with one reinfection, three (10%) with two and one (3%) with three reinfections. Fourteen (40%) subjects had a concomitant STI at the first episode, being 75% in the second episode. Twenty-seven (77%) patients were asymptomatic. 21 patients, agreed to answer about risk factors and sexual behaviours: 9 (42%) disclosed multiple sexual partners in the last month before the reinfection; 14 (66%) had unprotected anal sex, and 13 (61%) used no intravenous drugs in sexual context. The global incidence rate for reinfection is 22/100 person-year follow-up (py), 24/100 py in the first reinfection episode and 19/100 py in the second reinfection.
Conclusions: High rate of HCV reinfection has been observed in MSM LWHIV in our cohort, most of them being asymptomatic and mainly associated to other concomitant STI. HCV-RNA should be tested regularly in HIV-positive MSM already cured from an AHC and routine screening of HCV should be done when an STI is diagnosed.

Table 1. Baseline characteristics of the patients included in the study (n=35).

Number of reinfections, n - %	35 (17.7)
Median age in years, median (IQR)	46 (40-50)
IL-28 polymorphism (n=29), n - %	
C/C	12 (41)
C/T	16 (55)
T/T	1 (3)
Genotypes (n=30), n - %	
1	15 (50)
4	15 (50)
Median CD4 cell count, median (IQR)	554.5 (428-728)
Viral HIV copies	
Undetectable, n - %	32 (91)
Detectable, n - %	3 (9)
HIV therapy, n - %	33 (94,3)
AST, UI/mL - median (IQR)	51 (34-88)
ALT, UI/mL - median (IQR)	87 (43-173)

PE37/14

Liver disease in HIV-infected subjects in the post-HCV DAA treatment era

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Purpose: Hepatopathy in HIV-infected patients has changed after the ART era, even more so after HCV treatment and cure. The objective of our study was to analyze liver function tests and the severity of hepatopathy and hepatic fibrosis in a HCV-HIV Spanish cohort in the post-HCV DAA treatment era.
Method: Cross-sectional study in a cohort of 4009 HIV-infected patients in February 2019 in a clinical unit in Madrid, Spain. We analysed the demographic, clinical and analytical records of all patients with HIV infection followed regularly in our cohort. We compared HCV-HIV coinfected and HIV monoinfected patients regarding liver function tests, metabolic parameters and liver fibrosis severity with transient elastography (FS). Advanced fibrosis was considered when the FS was >9.6 kPa.
Results: The main clinical and demographic characteristics are shown in table 1. Out of 4009 HIV patients, 1065 were HCV-coinfected (26.6%), 1028 HVC-patients had been treated (96.5%) with a sustained viral response of 96.7%. 123 (3%) have treated chronic hepatitis B. FS has been performed in 2153 patients (53.7%):1021 HVC-coinfected (95.9%) and 1129 (38.5%) HIV-monoinfected patients. Advanced fibrosis was identified in 272 patients (12.6%) being most prevalent in HCV coinfection (19.6% vs 6.4%; p<0.005). Liver function tests, lipid profiles and glycaemia were similar among HCV-HIV-coinfected and HIV-monoinfected subjects. The only differences found were in platelets, protrombine time, albumin, FS measurements and non-invasive markers of fibrosis between both populations (table 2).
Conclusion: Nowadays HCV infection is almost eradicated in HIV-infected subjects from our cohort. Most of the HCV-HIV infected subjects who have reached SVR present normal liver function tests as well as metabolic profile are similar to those of HIV-monoinfected subjects. Patients with advanced liver fibrosis maintain analytical alterations related to portal hypertension and would require close and specific follow-up.

Table 1. Clinical and demographic characteristics

Gender, woman, N (%)	819	20,5%
Race, causasian, N (%)	3370	88,6
Transmission route N(%)		
- MSM	1883	47,4
- Hetero	888	22,4
- IDU	892	22,5
CDC Stage C, N (%)	759	23
Chronic Hepatitis B, N (%)	123	3.1
Hepatitis C, N (%)		
- Negative	2742	68,5
- Chronic and SVR	1028	25,6
- Spontaneus resolution	194	4,8
Nadir CD4 cell count, (cel/ µL), Median (IQR)	220	103-336
HIV viral load<50 (cop/ml), N (%)	3715	93
CD4 cell count (cell/µL), Median (IQR)	697	505-914
BMI(kg/ m2), Median (IQR)	25	22-27
Age (years), Median (IQR)	50	42-56

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Table 2. Differences between HCV positive and negative HIV-subjects

	Negative HCV		Positive HCV		
	N	Median (IQR)	N	Median (IQR)	p
Platelets (mm3),	2897	234000 (197000-274000)	1045	209000 (166000-250000)	<0,05
Glucose (mg/dl)	2840	90 (84-98)	1050	91,5 (84-100)	<0,05
Cholesterol (mg/dl)	2828	178 (155-204)	1052	178 (153-201)	0,134
HDL(mg/dl)	2760	43 (37-52)	1029	44 (36-52)	0,852
LDL (mg/dl)	2752	108,0 (89-129)	1027	106 (86-126)	<0,05
Triglycerides (mg/dl)	2757	114 (82-164)	1029	115 (84-165)	0,481
GOT (UI/L)	2784	24 (20-29)	1014	24 (20-31)	>0,05
GPT(UI/L)	2893	23 (17-31)	1054	21 (15-29)	>0,05
GGT(UI/L)	2709	25 (17-39)	1009	27 (18-47)	<0,05
FA(UI/L)	2736	72 (60-87)	1015	73 (61-88)	0,269
Creatinine (mg/dl)	2845	1,0 (0,8-1,1)	1057	0,9 (0,8-1)	>0,05
Bilirubin (mg/dl)	2829	0,5 (0,4-0,7)	1052	0,5 (0,4-0,7)	0,462
Albumin (g/L)	1056	4,4 (4,0-4,5)	456	4,3 (0-4,6)	0,934
Fibrinogen (mg/dl)	727	301,0 (254-367)	321	314 (268-372)	<0,05
INR (%)	728	1,0 (1-1)	321	1,0 (1-1,1)	<0,05
APRI >1 (%)	25	0,9	24	2,3	
FIB4 >3,25 (%)	50	1,7	73	7	

Tables. Clinical and demographic characteristics. Differences between HCV positive and negative subjects

PE37/15

Seroprevalence of hepatitis E in a Portuguese cohort of human immunodeficiency virus infected patients

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Purpose: To study the seroprevalence of HEV and prevalence of chronic HEV in a population of HIV infected patients from Porto, Portugal.
Method: We randomly selected 299 patients from the cohort of HIV infected patient followed in Centro Hospitalar Universitário São João. We performed an ELISA to search for IgG for HEV (Wantai HEV-IgG ELISA). When the absorbance/cut-offwas inferior to 3.5 the test was repeated and a confirmatory test (recomLine HEV IgG/IgM) executed in the same sample. For reactive tests and for immunosuppressed patients (CD4 count less than 200/mm^3), an in-house Polymerase Chain Reaction (PCR) test is being performed. We used the most suitable descriptive and inference statistics, using a significance level of 0.05.
Results: Seventy-five patients (25.1%; 95% confidence interval: 20.1%–30.1%) had reactive IgG Hepatitis E serology. From the 299 patients included, 225 (75.3%) were men. The mean age was 48.18 (standard deviation 12.26). Patients with reactive test were older (statistically significant differences). We found no difference concerning place of birth, rural residence, cirrhosis or viral hepatitis coinfection. Regarding HIV infection, median follow-up time was 10 years, the acquisition was mainly through heterosexual relations and 94% were under antiretroviral therapy. Nadir and actual CD4 counts did not differ significantly from patients with HEV reactive and non-reactive. Regarding analytical alterations, gamma-glutamyl-transferase (GGT) was higher in patients with reactive IgG HEV. HEV PCR results will be presented.
Conclusion: Seroprevalence of HEV was 25.1% (95% confidence interval: 20.1%–30.1%) in HIV infected patients. Older age and higher GGT showed a relation to HEV reactive IgG test.

PE37/16

Loss of seroprotection against hepatitis B virus (HBV) was associated with lower CD4 counts among HIV-positive patients who were born in the era of nationwide neonatal HBV vaccination

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Purpose: HBV seroprevalence has declined among Taiwanese born in the era of the universal neonatal HBV vaccination implemented in 1986. However, 40% to 50% of these individuals lose seroprotection against HBV in their adulthood. Factors associated with loss of seroprotection against HBV among people living with HIV (PLWHIV) who were born in the HBV vaccination era remain unclear.
Method: PLWHIV who were born after 1 July, 1986 and tested negative for HBsAg and anti-HBc with anti-HBs titer <10 mIU/mL were defined as being "triple-negative". People testing negative for HBsAg and anti-HBc with anti-HBs titer ≥10 mIU/mL were considered being "seroprotective" against HBV. Clinical characteristics were analyzed, including age, sex, HIV risk group, CD4 count, plasma HIV RNA load, and presence of opportunistic infection, HCV infection, or syphilis.
Results: Between 2004 and 2015, 427 patients who were born in the neonatal HBV vaccination era were included: 8 (1.8%) were HBV carrier; 210 (49.2%) tested triple-negative; and 169 (39.6%) were seroprotective against HBV. Compared with patients testing triple-negative, those with persistent seroprotection had a higher CD4 count when HIV infection was diagnosed (372 [IQR 218-493] vs 411 [IQR 282-524] cells/mm^3, p=0.05), and were less likely to present with AIDS (29.8% vs 15.4%, p=0.03). Persistent seroprotection against HBV was correlated with CD4 count category (adjusted odds ratio, 1.79 [95% CI 1.01-3.19], p=0.05; and 2.06 [95% CI, 1.09-3.04], p=0.03 for patients with baseline CD4 count of 200-499 cells/mm^3 and ≥500 cell/mm^3, respectively, compared with those with CD4 count <200 cells/mm^3).
Conclusion: Among PLWHIV born in the nationwide neonatal HBV vaccination era, patients presenting with lower CD4 counts were more likely to lose their immunity against HBV. Strategies to improve HIV case finding and HBV revaccination for those who have lost seroprotection are needed in this country of higher endemicity of HBV infection.

PE37/17

Improvement of immunity and hepatic fibrosis after HCV treatment with DAA in people living with HIV and HCV

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Purpose: Treatment of HCV infection with direct-acting antivirals (DAA) has allowed achieving high rates of sustained virological response (SVR) in patients with HIV-HCV coinfection, but information on long-term impact is scarce. The aim of this study was to analyse the changes in hepatic fibrosis and immune response after HCV eradication with DAA in coinfected patients.
Methods: Retrospective, unicenter cohort study of HIV-HCV coinfected patients treated withDAA who achieved SVR between [A1] June 2013 and June 2018. Possible changes in hepatic fibrosis and immunity were compared between baseline and 24 months follow-up after HCV treatment. Hepatic fibrosis was assessed by Fibroscanâ and APRI and FIB-4 scores, and immunity was analysed with CD4, CD8 counts and CD4/CD8 ratio.
Results: Four hundred and seven patients were included in the study; 75% were men with a median age of 50 years (SD 8); most of the patients (78%) had a chronic HCV infection with 21 years of evolution and 27% had liver cirrhosis at baseline. Regression of liver fibrosis was seen in 45% of the patients, both in Fibroscan measures and biological scores, being more frequent in those with advanced baseline fibrosis (p<0.0001). Regarding the immunologic parameters, there was a significant decrease of CD8 counts

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(p=0.0005) and a progressive rise of the CD4/CD8 ratio was shown during the study follow up (p=0.0288).
Conclusions: Treatment with DAA is associated with a significant reduction of liver fibrosis in coinfected patients, which has a higher impact on those with more advanced baseline fibrosis. An improvement of the immune response is also observed with a progressive recovery of the CD4/CD8 ratio.

PE37/18

DAA treating Hepatitis C in HIV/HCV coinfected patients in two prisons of Rome: results and problems

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Purpose: The rate of hepatitis C infection in jail is estimated about 13%. Among HIV-positive prison inmates and the rate of hepatitis C co-infection is about 38%.
There are few data on real- world experience of Hepatitis C treatment with DAA in prison and, in particular, of HIV/HCV coinfected patients. Thus, we present the initial results of our project of DAA treatment in two prisons of Rome.
Method: HIV/HCV coinfected patients who started DAA treatment in "Rebibbia" and "Regina Coeli" prisons between 2016 and May 2019 were included. Primary outcome of the analysis was sustained virological response at 12 weeks after DAA completion (SVR12). Secondary outcome was assessing critical issues of treating prisoners and carrying out their follow-up to 12 weeks.
Results: overall, 48 coinfected patients were included, 45 of them started DAA therapy (3 patients did not start for personal motivation or getting out of prison. Main characteristics: males 9.2%; median age 47 years; non-Italian 20.8%; cirrhosis 12.5%; HCV genotype 1a 53.3%, 1b 4.4%, 3 20.0%, 4 22.3%, All patients but one were therapy naïve and all were in steady antiretroviral treatment.
Thirty-one patents can be evaluated at 12 weeks after end of treatment: 28 SVR, 1 virological failure and 2 interruption because out of prison. The per-protocol SVR12 proportion was 96.6% and intention-to-treat 90.3%.
Moreover, 5 patients got out of prison: were transferred to another prison or to home detention during DAA therapy. We know that 4 of them are continuing treatment.
Conclusion: our data suggest that DAA therapy in prison is feasible with acceptable SVR rates. However, the continuing changing imprisonment situation is the main obstacle to treatment success. Key points are: i) motivation of patients, ii) close collaboration with prison operators, iii) easy accessible follow-up clinic to manage patients out of prison.

PE37/19

Progress towards eliminating mother-to-child transmission of HIV in the Macha area in Zambia from 2010–2018

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Purpose: To assess progress made in prevention of mother-child transmission coverage in the Macha area.
Method: We analysed data of 1, 175 mother-infant pairs from the three studies conducted at Macha hospital, of HIV-infected mothers bringing their infants for early infant diagnosis from August 2010 to August 2018.
Results: The median age of the infants at their first HIV DNA test was 6 months. The majority of the mothers (85%) and infants (75%) received ARVs to prevent mother-to-child transmission of HIV. The proportion of mothers that received cART increased from 2010 (28%) to 2018 (91%). In 2010-2018, 101 (9%) infants tested positive for HIV. The proportion of infants testing positive decreased from 12% in 2010-2013 to 4% in 2016-2018 (P<0.0001). The proportion of infants who tested positive differed significantly by maternal receipt of PMTCT. Among infants whose mothers did not receive any PMTCT, 38% tested positive compared to 2% among infants whose mothers received cART for PMTCT (P<0.0001).
Conclusion: Comparing these data collected at different time periods in the Macha area indicates that significant progress has been made from 2010 to 2018. To continue with these gains, a concerted focus will be needed to target and improve on the integration of new guidelines into clinical practice at a facility level.

PE37/20

Evaluation of the hepatitis C care cascade in the country of Georgia: monitoring 4 years of progress towards elimination

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Background: With technical assistance of the U.S. CDC and support from Gilead Sciences, Georgia launched the world's first national hepatitis C elimination program in April 2015. The program aims at achieving 90-95-95 targets by 2020: a) diagnose 90% of HCV-infected persons, b) treat 95% of those diagnosed, and c) cure 95% of those treated. We report progress towards elimination targets 4 years into the elimination program.
Methods: The estimated number of persons living with HCV infection was based on 2015 population-based sero-prevalence survey, which showed that 5.4% of adult general population has chronic HCV infection (approximately 150,000 persons). We analyzed data among adults in the national HCV database during April 2015 to March 2019.
Results: As of March 31, 2019, 1,259,817 adults have been screened for HCV infection. Overall 110,322 (8.8%) persons tested positive for HCV antibodies and of those 84,669 (76.7%) underwent HCV confirmatory testing. 70,578 (83.4%) of persons tested had chronic HCV infection – 47.1% of estimated 150,000 adults living with HCV. A total of 55,356 persons initiated treatment – 43.2% of estimated target population to be treated (128,250). Of the 36,751 patients who were evaluated for sustained virologic response (SVR), 36,071 (98.1%) tested negative for HCV by PCR, representing 29.6% of estimated target population to be cured (121,837). High cure rates were achieved in patients with all prevalent HCV genotypes in the country: 98.4% in genotype 1, 98.4% in genotype 2, and 97.6% in difficult-to-treat genotype 3.
Conclusions: Georgia has made substantial progress towards eliminating hepatitis C. Over 45% of persons with HCV infection were diagnosed, most have initiated treatment and high cure rates are achieved. Challenges remain in identifying and linking to care persons living with HCV. Nationwide integrated, decentralized model of HCV treatment, which is already implemented, will be critical to improve linkage to care.

PE37/21

Epidemiology of HIV, HBV and HCV co-infection in Israel

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Purpose: Liver diseases have become common causes of death among people living with HIV. Our aim was to analyze the epidemiology of HIV-HBV-HCV coinfection in Israel.
Method: All adult patients followed at the Hadassah AIDS Center were included. Demographic, hepatitis serology and disease parameters were recorded at beginning and end of follow up (FU).
Results: 391 patients were included, 256 (63%) males, mean age 44 years, mean follow up period 9.3 years. HIV risk factors: 190 (49%) originated in countries with a generalized HIV epidemic (OGE); (mainly Ethiopia), 58 (15%) men who have sex with men (MSM), 30 (7.7%) intravenous drug users (IDU). **HBV carriage** (HBsAg+): 3.3% vs. 2.6% at start vs. end of FU (respectively, p=ns), significantly higher than the reported 1.75% in the general Israeli population (p=0.03). **HBV Exposure** (HBcAb+): 48.5% vs. 43.5% (p=ns);

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significantly higher in OGE (63%) & IDU (60%) as compared with MSM (20%) (p<0.001). **Acquired HBV immunity** (HBcAb+ & HBsAb+): 33% vs. 30% (p=ns); significantly higher in OGE (46%) as compared to MSM (20%) & IDU (33%) (p<0.001). Isolated HBcAb: 12.3% vs. 11%% (p=ns); similar to the reported Israeli rate. **Vaccine induced immunity** (HBsAb+): 17% vs. 29%; significantly higher at end of FU (P<0.001), the increase was significantly higher in MSM risk group (p<0.001). **HCV carriage** (HCVAb+): 7.5% vs. 9.5% (p=ns), significantly higher in IDU (68%) (p<0.001), and significantly higher than the Israeli prevalence of 2.3% (p<0.001).
Conclusion: We found higher HBV exposure & acquired immunity in the OGE risk group, probably due to higher prevalence in their country of origin. IDU patients had higher HBV and HCV carriage. MSM had higher vaccination rates, especially at end of FU, suggesting better vaccine compliance. This data is important to consider when planning prevention strategies in HIV infected patients.

PE37/22

Hepatitis C treatment outcomes of HIV infected people who inject drugs in a real-world cohort

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Purpose: Among the most marginalized populations is people living with HIV (PLWHIV) and inject drugs (PWIDs); access to HCV treatment remains problematic. The aim of this analysis was to assess efficacy and safety of direct acting antivirals (DAA) in a population of HIV-infected PWIDs in a real-world setting.
Method: Of 88 HIV-HCV co-infected PWIDs who initiated DAA treatment, 66 have already completed DAA treatment and sustained viral response data (SVR) data is available. Univariate logistic regression analysis was used to assess statistically significant predictors of achieving SVR.
Results: All patients were under highly active antiretroviral treatment (HAART) at the time of enrollment, although in 16/66 (24.2%) a change in HAART regimen was required due to drug interactions with DAAs. Demographic and clinical information is presented in the tables.
SVR was successful for 53/66 (80.3%). Two of our patients who failed SVR, had a different genotype when they were retested, implying a reinfection. A further one patient has been re-infected after achieving SVR. In univariate analysis, none of the listed parameters predicted SVR failure. However, lack of adherence was statistically significant in predicting failure (p=0.008, OR=7.7, 95% CI 1.7-34.7). Amongst those with good compliance, success was still only at 86% (49/57). Continuous IV drug use had a tendency for significance (p=0.081). A decrease (end – start of treatment) in APRI score (p=0.008, OR=15.3, 95% CI 2.0-116.6) but not FIB4 (p=0.393, OR=1.68, 95% CI 0.5-5.49) would predict SVR success. There were no serious adverse events during treatment.
Conclusion: Success rates for HCV infection in HIV infected PWID are lower than expected, partially due to lack of adherence. A significant proportion of patients require monitoring for drug interactions before or during HCV DAA administration. Larger studies are needed to identify modifiable risk factors in succeeding HCV elimination to those populations at high risk of ongoing transmission.

Demographic information

Variable	Mean (SD) or Median (IQR 25th, 75th) or n (%)
Age, mean (SD)	39.6 (7.2)
Male, n (%)	60 (90.9)
Greek nationality, n (%)	63 (95.5)
Steady occupation, n (%)	17 (25.8)
Alcohol abuse, n (%)	8 (12.1)
Benzodiazepine use, n (%)	31 (47)
Active IV drug use, n (%)	17 (25.8)
Polypharmacy (>2/d, excl. DAA), n (%)	20 (30.3)
Opioid Substitution program, n (%)	39 (59.1)

Clinical information pertaining to HIV and HCV infection

Variable	Mean (SD) or Median (IQR 25th, 75th) or n (%)	Variable	Mean (SD) or Median (IQR 25th, 75th) or n (%)
Undetectable HIV RNA, n (%)	62 (93.9)	Liver elastography (kPa), median (IQR)	6.25 (5.2, 7.72)
CD4/mm^3), mean (SD)	520 (296)	Previous HCV treatment, n (%)	10 (15.2)
Log HCV RNA, median (IQR)	6.19 (5.84, 6.72)	APRI score, median (IQR)	0.42 (0.29, 0.74)
HCV Genotype		FIB4 score, median (IQR)	1.09 (0.91, 1.56)
1a, n (%)	28 (42.4)	HCV treatment regimen	
1b, n (%)	1 (1.5)	SOF/LDV, n (%)	22 (33.3)
3, n (%)	23 (34.8)	SOF/VEL, n (%)	28 (42.4)
4, n (%)	13 (19.7)	ELB/GRZ, n (%)	12 (18.2)
Mixed genotype, n (%)	1 (1.5)	2D or 3D, n (%)	4 (6)

PE37/23

Treatment of acute HCV infection with direct acting antivirals (DAA) in HIV patients

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Purpose: The aim of this study is to describe cases of acute HCV infection treated with DAA in seven Andalusian (Spain) hospitals.
Method: Retrospective, multicentre study of HIV-infected patients treated with DAA during HCV acute infection (in the first six months after diagnosis), from Nov-15 to Dec-18. Epidemiological, clinical, analytical, therapeutic and evolutionary variables were analysed.
Results: 30 episodes of acute HCV infection in 27 patients (6 re-infection cases) were included; all were MSM, with a mean age of 40.9 (±8) years and a median HIV infection time of 33.6 months (IQR: 20.4-67.2). All were on ART with undetectable viral load except two cases (65 and 68 copies/mL) and median CD4 cell count was 669 cells/mm^3 (IQR: 553-896). Nineteen patients (63.3%) had previous or coincidental episodes of other sexually transmitted infections (STIs): syphilis 15, venereum lymphogranuloma 3, chlamydia 1 and gonococcus 4. Acute HCV infection was asymptomatic in 24 (80%) cases. Distribution of genotypes was 56.7% for G1a, 40% for G4 and 3.3% for G1b. The median time to HCV-treatment was 7.0 (4.3-18.3) weeks and the median baseline HCV-RNA was 6.1log (IQR: 5.6-6.5). Treatment with SOF-LDV was prescribed in 18 episodes (8 weeks in 11 patients and 12 weeks in 7), SOF/VEL for 12 weeks in 8, GRZ/ELB for 12 weeks was prescribed in 2 patients, GLE/PIB in 1 and 2D+RBV in another one. All patients presented SVR (94.4%) except the one treated with 2D+RBV. There was no discontinuation due to adverse effects.
Conclusions: All episodes of acute HCV infection were in MSM with good immuno-virological situation. More than half of the subjects presented a history of other STIs. HCV infection was asymptomatic in a high percentage of cases, forcing systematic screening in certain populations. Treatment of acute HCV infection with DAA was effective and safe.

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PE37/24

Hepatic fibrosis progression among HIV patients in Israel

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Purpose: Liver diseases have become common causes of death in people living with HIV. The aim of this study was to define the degree of fibrosis in HIV-HBV-HCV co-infected patients in Israel

Method: All adult patients followed at the Hadassah AIDS Center were included. Demographic data, hepatitis serology, HIV disease parameters and FIB-4 data were recorded at beginning and end of follow up (FU)

Results: A total of 391 patients were included in the study, 256 (63%) males, 191 (49%) born in Africa, all but one in Ethiopia, mean age at beginning of follow up (FU) 44 years, mean follow up period 9.3 years. The **HBV carriage** (HBsAg+) was identified in 3.3% of patients at start FU, with no significant differences among risk groups. This was significantly higher than the reported 1.75% prevalence in Israel (p=0.03). **HCV carriage** (anti-HCV+) was identified in 7.5% at start of FU, significantly higher (p<0.001) in IDU (68%), and significantly higher than the reported 2.3% Israeli prevalence (p<0.001). Low fibrosis (Fib-4<1.3) at start vs. end of FU was 63.3% vs. 67.9%, advanced fibrosis (Fib-4>2.67) 5.4% vs. 3.6%, respectively. Fibrosis severity was not affected by origin or hepatitis status, suggesting it was the result of fatty liver (metabolic, alcoholic or drug induced). However, HBV carriers had increased fibrosis at end of FU (p=0.049). Patients with CD4>200 had higher rates of low fibrosis than patients with CD4 <200 (73.1 vs. 54.5%, p<0.05).

Conclusion: Advanced fibrosis was found in 5.4% of the population. HBV carriers had increased fibrosis at end of FU, but origin and other hepatitis serologies were not associated with fibrosis. Lower fibrosis rates found in patients with elevated CD4 counts imply an important role for CD4 counts in the prevention of fibrosis in patients with HIV.

PE37/25

Acute hepatitis B in persons living with HIV in a low hepatitis B prevalence area during the last two decades

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Purpose: To review the incidence and characteristics of acute hepatitis B (AHB) in a large cohort of HIV infected patients followed in a low prevalence region during the last two decades.

Methods: Retrospective review of an HIV Cohort of patients in a single reference centre in Madrid, Spain. AHB was diagnosed in patients who developed a positive HBsAg after year 2000 (having a previous HBcAb negative). Previous serology, history of HBV vaccination, epidemiological and clinical characteristics, as well as HIV related factors were recorded. Incidence of AHB was calculated: number of cases/patients not previously infected by HBV (HBcAb negative).

Results: Out of 5443 HIV+ patients in our cohort (3098 HBcAb negative), 18 developed AHB from 2000 to 2018. Incidence was 0.58 (0.35 to 0.89) during 19 years. A linear regression shows an statitsticaly decrease of annual incidence (β=-0.006; p=0.047) (figure 1).

All 18 patients diagnosed with AHB were men, median age (range) 32 years (17-45), 16 were MSM and 2 had consume intravenous drugs, 9 native Spanish (50%), 8 (44.4%) Latin-Americans and 1 African (5.6%). 14 patients had never been vaccinated and 4 had been vaccinated without response. Regarding antiretroviral treatment (ART), 15 patients (83.3%), were not receiving ART. In 4 of them the diagnosis of HIV and AHB was simultaneous. Two patients were receiving ART that did not include lamivudine/emtricitabine or tenofovir and only one patient was treated with an anti-HBV drug (lamivudine). No cases of fulminant hepatitis were seen but in 2 patients (11%) AHB became chronic.

Conclusion: In our cohort, the incidence of AHB is low and shows a decrease. However, it still occurs in patients who had not been vaccinated or have been vaccinated without response and are not receiving ART with anti-HBV activity.

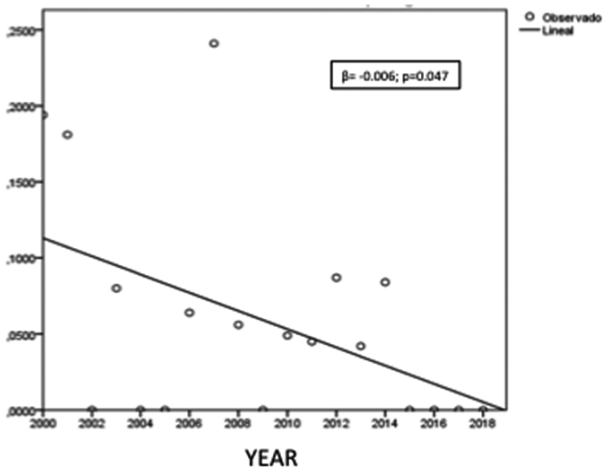


Figure 1. Linear regression of of annual acute hepatitis B incidence

PE37/26

Virological response to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide in HIV-positive patients with lamivudine-resistant hepatitis B virus coinfection

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Purpose: Tenofovir alafenamide (TAF) has potent antiviral effect on both HIV and hepatitis B virus (HBV). However, data are limited on the effect of TAF against lamivudine-resistant HBV. We aimed to assess the virological response of lamivudine-resistant HBV to TAF-containing regimens among HIV/HBV-coinfected patients.

Methods: Between January 2018 and June 2019, antiretroviral therapy-experienced HIV-positive patients coinfected with lamivudine-resistant or lamivudine-susceptible HBV who switched to coformulated elvitegravir/cobicistat/emtricitabine/TAF (E/C/F/TAF) were enrolled. Plasma HBV and HIV viral load, HBV serologic markers, and liver functions before and 48 weeks after the initiation of E/C/F/TAF were retrospectively collected and analyzed.

Results: A total of 107 HIV/HBV-coinfected patients with a median age of 44 years were enrolled. Thirty-four patients were coinfected with lamivudine-resistant (LAM-R) HBV, and 73 lamivudine-susceptible (LAM-S) HBV. At baseline, 37.5% of patients in the LAM-R group and 9.6% in the LAM-S group were tested positive for HBeAg (p=0.001). Prior to E/C/F/TAF, the percentage of patients who achieved plasma HBV DNA <20 IU/mL were 94.1% and 98.6% in LAM-R and LAM-S group, respectively. At 48 weeks of E/C/F/TAF, all patients in both groups achieved plasma HBV DNA <20 IU/mL. The rate of HBeAg loss at 48 weeks were 9.1% (1/11) of the LAM-R group and 28.6% (2/7) of the LAM-S group (p=0.528). Compared with baseline, the median HBsAg level at 48 weeks of LAM-R group increased significantly (157 vs 440 IU/mL, p=0.017) but that of the LAM-S group decreased significantly (615 vs 439 IU/mL, p=0.044).

Conclusions: Coformulated E/C/F/TAF achieved high rate of HBV viral suppression in HIV/HBV-coinfected patient with either lamivudine-resistant or lamivudine-susceptible HBV. A significant decrease in HBsAg level and a higher rate of HBeAg loss were observed in patients with lamivudine-susceptible HBV than those with lamivudine-resistant HBV.

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PE37/27

Impact of direct-acting antiviral (DAA) agents on T cell counts and liver stiffness in HIV/HCV-coinfected patients: a multicenter prospective observational cohort study

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Purpose: assess evolution of liver stiffness and peripheral CD4+ and CD8+ count in HIV/HCV patients treated with DAA.
Method: prospective observational multicenter open cohort study of HIV/HCV coinfected patients treated with DAA between June 2015 and June 2019 at Hospital Universitari Mutua Terrassa and Hospital Universitari Parc Tauli and followed-up until 96 weeks after the end of treatment (EOT). Sociodemographic, epidemiological, clinical, biochemical, immunological, virological, treatment-related variables and liver stiffness assessed by METAVIR score were collected at the beginning, at the EOT (W0) and 12 (W12), 24 (W24), 48 (W48) and 96 (W96) weeks after the EOT. X^2 test and Wilcoxon signed-rank test/Friedman test were used to determine differences between proportions or medians.
Results: 260 HIV/HCV coinfected patients enrolled, 80% male, mean age 50.4 years (±6.2). Most frequent transmission group was intravenous drug users (89%). Most frequent HCV genotype was 1A (39%). At baseline, medians and IQR:P25-P75 for Child-Pugh score were 6 (5-6); 48% of patients had F3-F4 METAVIR stage and medians and IQR:P25-P75 absolute and percentage for CD4+ and CD8+ were 583 cells/mm^3 (398-810), 31% (25-37) and 845 cells/mm^3 (567-1201) respectively. A 22 % of patients previously received interferon-based therapy. Sustained virological response 12 weeks after the EOT was demonstrated in 96% of patients. We observed a statistically significant increase from baseline in absolute CD4+ count at W12 ($p<0.005$) maintained over the follow-up period but not in CD4+/CD8+ ratio. About fibrosis evaluation, 46.7 % of patients with F3-F4 METAVIR stage dropped significantly ($p<0.005$) to a F1-F2, 12 weeks after the EOT.
Conclusion: Our data provide further evidence of the efficacy of DAA-based therapy in HIV/HCV coinfection and indicate that DAAs-based regimens improve liver stiffness 12 weeks after the EOT. Data from this study do not confirm the hypothesis that DAA enhance the host's immune response after treatment.

PE37/28

Trends of HCV infection among HCV-seronegative, HIV-positive patients in Taiwan between 2011-2018

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Purpose: The trends of HCV infection among HIV-positive MSM remain less investigated in Asia-pacific region. We aimed to examine the current status of HCV infection among HCV-seronegative, HIV-positive patients in Taiwan between 2011 and 2018.
Methods: Between 2011 and 2018, 3,495 consecutive HIV-positive patients were included. The HCV antibody screening was performed on sequentially collected archived blood samples with the use of IgG ELISA kit. For sample tested positive for HCV antibodies, HCV RNA load was further determined by Roche cobas system and HCV genotypes were determined by NS5B PCR and sequencing.
Results: During the study period, 294 cases of recent HCV infection were diagnosed, resulting in an overall incidence rate of 17.97 per 1000 PYFU, which increased from 12.96 in 2011 per 1000 PYFU to 25.38 per 1000 PYFU in 2018. The mean plasma HCV RNA load was 5.4 $\log_{10}$ IU/mL. In multivariate analysis, patients with HCV seroconversion were more likely to have elevated ALT levels (OR, 1.03; 95% CI, 0.02-0.04) and recent syphilis (OR 7.85; 95% CI, 1.49-2.63). The most prevalent genotype was 2a (39.7%), followed by 1b (29.1%), 6a (11.2%), 1a (9.9%), 3a (6.8%), and 6n (2.4%). Genotypes 3a and 6a increased from 0% and 5.2%, respectively, in 2011-2014 to 4.1% and 17.1% in 2015-2018. In phylogenetic analysis, three clusters of HCV infection were observed due to genotypes 2a and 6a, two clusters due to 3a and one cluster due to 1b. Almost all clusters occurred among MSM except one 2a cluster of two patients with unknown sexual orientation.
Conclusion: This study revealed a significantly increasing trend of recent HCV seroconversion among HIV-positive patients in Taiwan and HCV seroconversion was significantly associated with recent syphilis. The increasing trends of genotypes 3a and 6a and clusters suggest an expanding HCV epidemic among HIV-positive MSM in Taiwan.

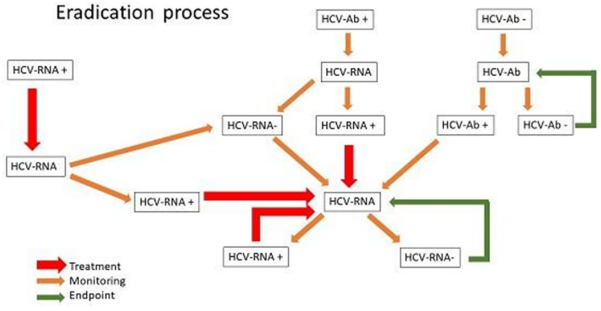
PE37/29

The micro-elimination approach to eliminating Hepatitis C: a Fast Track City project

F Maggiolo[1], A Callegaro[2], R Teocchi[3], D Valenti[4], E Di Filippo[1], L Comi[1] and M Rizzi[1]

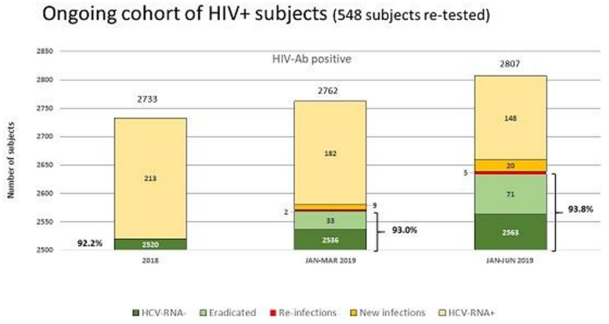
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Purpose: To eliminate HCV infection in a cohort of HIV-infected subjects within a FTCI project.
Method: Through intensive HCV re-testing and universal treatment with DAA, a single-center, large cohort of HIV-infected subjects in Northern Italy is closely monitored for HCV co-infection and all HCV-RNA positive subjects undergo antiviral treatment (figure 1). The project started at the end of 2018, the first 6 months results are reported. The project was approved by the local EC and all subjects gave their informed consent.
Results: At start 2733 PLWHIV were included in the cohort, 213 of them (7.8%) were still HCV-RNA positive. They were mostly males (74.1%), of Italian origin (87.8%) with a median age of 52 years (IQR 12). Almost half (48.1%) acquired HIV through heterosexual contacts, 26.9% were previous IVDUs and 24.3% MSM. During the 6 months of FU, 74 new HIV-infected subjects were enrolled, 7 of whom (9.52%) with an active HCV infection. During the same period of time 548 subjects were tested for HCV. Thirteen subjects (2.4%) already followed and previously HCV-Ab negative tested HCV-RNA positive (undiagnosed asymptomatic infections), 5 more subjects got re-infected after a DAA treatment. They are the 0.91% of the tested subjects, the 0.89% of patients at risk (HCV positive pre-treated and with HCV-RNA negative) and the 0.18% of the whole population. Finally, 1 patient (0.2 %) relapsed after DAA therapy. On the other hand, 71 subjects (13.0%) ended DAA treatment with SVR lowering the total proportion of HCV-RNA patients to 6.1% (173 subjects) (figure 2).
Conclusion: DAA universal treatment is a potent instrument to end HCV epidemic. Micro-elimination approaches limited to well-defined sub-populations may result an effective local answer. However, the risk of previously undiagnosed asymptomatic infections and the occurrence of re-infections may tamper the effect of DAA therapy. That makes intensive HCV monitoring mandatory



Project flow-chart

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First 6 months results

PE37/30

Road to HCV elimination in HV/HCV coinfected patients by screening and universal access to DAA: baseline data from the first screening of NoCo (No-Coinfection) study

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Purpose: The main objective of NoCo study is to evaluate the possibility of eliminating HCV in HIV/HCV population in Italy over 3-years. The aim of this analysis is to estimate the prevalence of active HCV infection in HIV-positive patients in care at present.

Method: Cross-sectional analysis using data from NoCo study. Subjects included are those screened for HCV from September-2017 to June-2019, independently of their HCV status. Prevalence of HCV infection (HCVAb-positive) and active HCV infection (HCV-RNA positive) was evaluated. Prevalence, incidence and predictors -using unadjusted and adjusted logistic regression- of HCV seroconversions were also assessed.

Results: 8,283 patients included. Prior to study entry 2,314 (27.9%) were HCVAb-positive, 4,800 (57.9%) HCVAb-negative and 1,169 (14.1%) had unknown HCV serology. At the 1st-NoCo screening 2,420 (29.2%) were HCVAb-positive and 5,863 (70.8%) HCVAb-negative. Demographic characteristics in Table1. 76/1,169 (6.5%) participants with unknown HCVAb status, were HCVAb-positive. 35/4,800 (0.7%) subjects previously HCVAb-negative reported an HCV seroconversion at 1st-screening. Injecting drug users had the higher probability of HCV seroconversion at 1st-screening (AOR vs heterosexual=9.44, 95% CI: 3.32-26.84) [Table 2]. 2,158/8,283 (26.0%) subjects had >=one subsequent HCV screening in a median follow-up of 0.7 years (IQR: 0.4-0.9). 7 participants/1446 PYFU had an HCV seroconversion after the 1st-screening (IR=4.8/1000PYFU, 95% CI: 2.3-10.1). Table 3 shows prevalence of HCV-RNA in HCVAb-positive at different timepoints. At 1st-screening 1,086/2,420 HCVAb-positive patients (44.9%) were HCV viremic, subject tested at least 2-times were viremic in 12.6% (157/1244) and overall 513/2427 (21.1%) where HCV-RNA positive.

Conclusion: At study entry, IDUs are the group at highest risk of new HCV infection in Italy. More than 75% of HCV patients have achieved viral eradication, suggesting that the target of HCV coinfection elimination within 3 years, could be achievable.

	HCVAb negative N=5,863	HCVAb positive N=2,420	p-value	Total N=8,283
Age, Median (IQR)	45 (37-54)	53 (49-57)	<.001	49 (40-55)
Age strata, n(%)				
<30	544 (9.3%)	40 (1.6%)	<.001	584 (7.0%)
30-39	1346 (22.9%)	129 (5.3%)		1475 (17.8%)
40-49	1791 (30.6%)	476 (19.7%)		2267 (27.4%)
50-59	1491 (25.4%)	1466 (60.6%)		2957 (35.7%)
≥60	691 (11.8%)	309 (12.8%)		1000 (12.1%)
Gender, n(%)			0.002	
F	1228 (20.9%)	581 (24%)		1809 (21.8%)
M	4635 (79.1%)	1839 (76%)		6474 (78.2%)
Nationality, n(%)			<.001	
Italian	4585 (78.2%)	2284 (94.4%)		6869 (82.9%)
Mode of HIV Transmission, n(%)			<.001	
Heterosexual	2214 (37.8%)	300 (12.4%)		2514 (30.3%)
IDU	173 (3%)	1655 (68.4%)		1828 (22.1%)
MSM	2653 (45.2%)	342 (14.1%)		2995 (36.2%)
Other/Unknown	823 (14%)	123 (5.1%)		946 (11.4%)
On ART, n(%)	4627 (78.9%)	2325 (96.1%)	<.001	6952 (83.9%)
Years from HIV diagnosis	6 (1.9-11.9)	22 (12.9-30.1)	<.001	8.8 (3.0-19.3)
Calendar Year of 1st NoCo screening, n(%)			<.001	
2017	159 (2.7%)	104 (4.3%)		263 (3.2%)
2018	4160 (70.9%)	2111 (87.3%)		6271 (75.7%)
2019	1544 (26.3%)	205 (8.4%)		1749 (21.1%)

Table1. Demographic Characteristics at first NoCo Screening according to HCVAb

	OR	(95%CI)		p	AOR*	(95%CI)		p
Gender M (vs.F)	1.28	0.53	3.10	0.634	1.24	0.45	3.38	0.677
Mode of HIV Transmission								
Heterosexual	1.00				1.00			
IDU	9.67	3.55	26.35	**<.001**	9.44	3.32	26.84	**<.001**
MSM	1.37	0.60	3.14	0.454	1.18	0.45	3.08	0.732
Other/Unknown	1.10	0.34	3.59	0.873	1.02	0.31	3.40	0.971
Age								
(per 10 years increase)	0.80	0.59	1.07	0.140	0.81	0.59	1.11	0.188
Italian	1.33	0.62	2.85	0.459	1.36	0.60	3.06	0.458
**Adjusted for all the variables shown in the table*								

Table 2. Predictors of HCV seroconversions using a logistic regression mode.

Table 3. HCV-RNA status in HCVAb positive subjects enrolled in NoCo: data at first screening, at second screening and overall.

	N HCVAb positive	HCV-RNA negative	HCV-RNA positive	HCV-RNA not tested
First screening (Subjs with at least 1 screening)	2420	1255 (51.9%)	1086 (44.9%)	79 (3.3%)
Last Screening (Subjs with at least 2 screenings)	1244	1072 (86.2%)	157 (12.6%)	15 (1.2%)
Overall (Subjs with 1 or more screening)	**2427**	**1832 (75.5%)**	**513 (21.1%)**	**82 (3.4%)**

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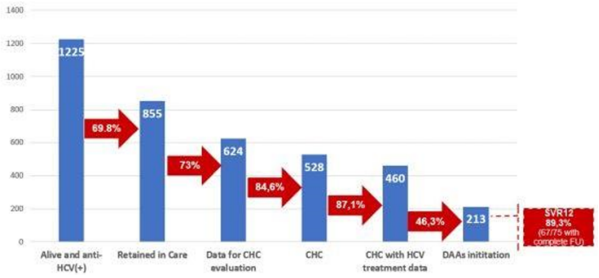
PE37/31

HCV cascade of care for HIV/HCV coinfected individuals in Greece and HCV treatment considerations in clinical practice

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Purpose: HCV cascade of care for HIV/HCV coinfected individuals in Greece and HCV treatment considerations in clinical practice.
Method: Analysis was performed for individuals alive in Athens Multicenter AIDS Cohort Study (AMACS) with available anti-HCV test by 31/10/2018. CoC stages were defined as: i) anti-HCV(+), ii) anti-HCV(+) retained in care, iii) chronic hepatitis C (CHC) retained in care, iv) CHC with HCV treatment data, v) DAA initiation, vi) SVR12. DDI potential between ART and DAAs was evaluated according to University of Liverpool Drug Interaction Checker.
Results: From a total of 9664 patients, 8202 (84.8%) had anti-HCV test available and 1225/8202 (14.9%) were anti-HCV(+): 4.4% in 4557 MSM, 93.8% in 841 IDU, 7.1% in 1970 heterosexuals and 11.6% in 834 patients with other/unknown route of infection. Loss-to-follow-up was 30.2%. Of 855 retained in care, 624 (73.0%) had available HCV status evaluation, 528 (84.6%) had confirmed CHC and 460 were eligible for DAAs. DAA treatment was initiated in 213 patients. SVR12 was achieved in 67 of 75 (89.3%) (figure). For 247/460 eligible for DAAs, 235 were on ART. Contraindications for DAA coadministration were more frequently predicted for NS3 protease inhibitors (EBR/GZR 54.5%, GLP/PIB 47.7%, OBV/PRV/r±DSV 38.7%, SOF/VEL/VOX 33.6% vs. SOF/VEL 11.9%, LED/SOF 0%), mostly due to the 3rd antiretroviral agent. Potentially clinically significant interactions were predicted for LED/SOF 70.6%, OBV/PTV/r±DSV 36.2%, SOF/VEL 11.2% and SOF/VEL/VOX 44.7%, mostly for TDF-containing regimens.
Conclusion: Linkage/retention in care is the main gap for HIV/HCV co-infected individuals in Greece, followed by HCV treatment uptake. Caution and careful selection of appropriate HCV DAAs regimen due to DDIs is warranted in clinical practice. HCV micro-elimination is a viable strategy, but requires optimization in linkage/retention in care, monitoring and treatment implementation.



Stages of CoC in HIV/HCV co-infected individuals

PE37/32

Hepatitis B core-related antigen and anti-hepatitis B core antibody are not associated with liver fibrosis evolution in HIV-HBV co-infected patients during treatment with tenofovir

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Purpose: To study the association between quantitative hepatitis B core-related antigen (qHBcrAg) and anti-hepatitis B core antibody (qAnti-HBc) on liver fibrosis evolution in HIV-positive patients with chronic hepatitis B virus (HBV) infection undergoing treatment with tenofovir (TDF).
Method: 154 HIV-HBV-infected patients initiating a TDF-containing antiretroviral regimen were prospectively followed. Data on qHBcrAg and qAnti-HBc obtained using immunoassays and liver fibrosis assessment using Fibrotest® were collected every 6-12 months during TDF treatment. Hazard ratios (HR) assessing the association between qHBcrAg/qAnti-HBc and liver fibrosis progression (F0-F1-F2 → F3-F4) or regression (F3-F4 → F0-F1-F2) were estimated using a time-homogeneous Markov model. HR were adjusted for age, gender, duration of antiretroviral therapy and protease inhibitor-containing antiretroviral therapy in multivariable analysis.
Results: At baseline, median age was 41 years (IQR=35-48) and patients were predominately male (84%). Advanced liver fibrosis or cirrhosis (F3-F4) was observed in 40 (26%) patients and was more frequently observed in males ($p<0.001$), at older ages ($p<0.001$), longer durations of HIV ($p=0.02$) and HBV ($p<0.001$) infection, with AIDS-defining illness ($p=0.01$), and past exposure to

Markers levels and their changes as determinants of transitioning between F0-F1-F2 and F3-F4 liver fibrosis stages

	Univariable		Multivariable	
Marker	F0-F1-F2→F3-F4	F3-F4→F0-F1-F2	F0-F1-F2→F3-F4	F3-F4→F0-F1-F2
qHBcrAg (log_{10} U/mL)				
At baseline	1.11 (0.99-1.25)	1.14 (0.98-1.33)	1.06 (0.92-1.23)	1.11 (0.92-1.35)
During follow-up	1.08 (0.95-1.23)	**1.23 (1.03-1.49)**	1.03 (0.87-1.23)	1.14 (0.91-1.43)
Change from previous visit	1.05 (0.58-1.88)	0.89 (0.53-1.51)	1.02 (0.50-2.07)	0.94 (0.46-1.93)
qAnti-HBc (log_{10} PEI U/mL)				
At baseline	**0.82 (0.69-0.97)**	0.86 (0.73-1.00)	0.87 (0.72-1.04)	1.02 (0.84-1.25)
During follow-up	**0.81 (0.68-0.98)**	0.93 (0.76-1.15)	0.92 (0.74-1.14)	1.12 (0.87-1.44)
Change from previous visit	1.48 (0.65-3.38)	**4.56 (1.91-10.91)**	2.04 (0.77-5.40)	**4.30 (1.41-13.05)**

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zidovudine (p=0.03) or zalcitabine (p=0.03). During a median follow-up of 48 months (IQR=31-90), 38 transitions of progression (IR=7/100 person-years) and 34 transitions of regression (IR=6/100 person-years) were observed. Baseline levels of either marker were not associated with liver fibrosis progression or regression (Table). Nevertheless, higher changes from the previous visit of qAnti-HBc levels were associated with liver fibrosis regression.
Conclusion: Baseline qHBcrAg and qAnti-HBc levels are not associated with liver fibrosis evolution in TDF-treated HIV-HBV co-infected patients. The link between strong changes in qAnti-HBc levels during follow-up and liver fibrosis regression merits further study.

PE37/33

Antiretroviral therapy: a possible role in lipid changes after HCV eradication by DAAs

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Purpose: HCV has complex interactions with lipid metabolism and a worse lipid profile has been observed after HCV eradication by DAAs. Among HIV+ patients, dyslipidemia is highly prevalent, partially due to cART. Aim of the analysis was to examine lipids changes in HIV/HCV+ patients at SVR24 and to investigate predictive factors of these changes according to cART exposure.
Method: This analysis included HIV/HCV+ patients treated with DAAs since 2016 who achieved SVR24 and on stable cART.Patients with laboratory data on baseline (DAA start) and SVR24,without cART modification during the observation period were selected. Mean changes of total cholesterol (TC),LDL-c, HDL-c and triglycerides were calculated as the mean difference between BL-SVR24, Wilcoxon test used to compare variations between BL-SVR24 and multivariable linear regression to investigate factors associated with the variations.

Total Cholesterol	Beta	95%CI		p-value
OBI				
No (reference group)				
Yes	8.56	-0.91	18.04	0.076
HCV Genotype				
Type 1 (reference group)				
Type 2	6.51	-18.67	31.68	16.22
Type 3	**24.12**	**11.54**	**36.70**	2.57
Type 4	**13.91**	**1.15**	**26.66**	**160.50**
Mixed	2.69	-28.71	34.08	16.22
TDF exposure				
-Not exposed before and after DAAs (reference group)				
-Exposed before and after DAAs	-2.35	-14.38	9.69	0.701
-Not exposed before, but exposed during DAAs	**-141.16**	**-221.32**	**-60.99**	**0.001**
-Exposed before DAAs. but not exposed during DAAs	-0.55	-21.23	20.13	0.958
DRV exposure				
-Not exposed before and after DAAs start (reference group)				
-Exposed before and after DAAs start	1.46	-9.97	12.88	0.802
-Not exposed before, but exposed during DAAs	**47.86**	**7.15**	**88.57**	**0.021**
-Exposed before DAAs, but not exposed during DAAs	73.81	-20.21	167.82	0.123
RPV exposure4				
-Not exposed before and after DAAs start (reference group)				
-Exposed before and after DAAs start	1.56	-13.10	16.22	0.834
-Not exposed before, but exposed during DAAs	-14.22	-31.01	2.57	0.096
-Exposed before DAAs, but not exposed during DAAs	**80.51**	**0.52**	**160.50**	**0.049**

Table 1. Factors associated with TC change by means of multivariable linear regression. Significant results in bold

Results: 382 patients were included, 27% on PI/b, 26.4% on NNRTIs and 24.3% on INSTI. Characteristics: 23% female, median (IQR) age 56 (53-59) years, 69.9% acquired HIV through IVDU, 97.4% Caucasian; TC 167(138–193) mg/dL, LDL-c93(71–123), HDL-c 43(35–52),triglycerides 110(81–163) mg/dL at baseline. HCV genotypes GT1 59%, GT3 21% and GT4 15%.TC and LDL-c significantly increased at SVR24 [(Δ +16.7 mg/dL (SD 38.1); +19.3 (SD 32.9), respectively].HDL-c and triglycerides remained unchanged.In patients who started DRV/b during DAAs,a significant increase of both TC and LDL-c was observed compared to patients who did not change DRV exposure (p=0.02 and p=0.001,respectively);being exposed to TDF-based backbone during DAAs was associated with a significant decrease of TC and LDL-c (p=0.001 and p=0.01, respectively) (Tables 1, 2).
Conclusion: An increase of TC and LDL-c was observed in HIV/HCV coinfected patients at SVR24.DRV/b seems to contribute to this increase;conversely,TDF appears to be associated with a better lipid profile. Longer follow up beyond SVR24 and a larger cohort are needed to better explore clinical implications of these findings.

LDL cholesterol	Beta	95%CI		p-value
HCV Genotype				
Type 1 (reference group)				
Type 2	-8.63	-31.17	13.91	0.451
Type 3	**13.91**	**2.72**	**25.10**	**0.015**
Type 4	**11.45**	**0.06**	**22.84**	**0.049**
Mixed	14.93	-13.26	43.11	0.298
TDF exposure				
-Not exposed before and after DAAs start (reference group)				
-Exposed before and after DAAs	3.64	-7.11	14.38	0.505
-Not exposed before. but exposed during DAAs	**-100.41**	**-176.31**	**-24.51**	**0.010**
-Exposed before DAAs. but not exposed during DAAs	14.49	-3.91	32.89	0.122
DRV exposure				
-Not exposed before and after DAAs, start (reference group)				
-Exposed before and after DAAs start	7.15	-2.89	17.18	0.162
-Not exposed before, but exposed during DAAs	**78.56**	**34.39**	**122.73**	**0.001**
-Exposed before DAA, but not exposed during DAAs	64.74	-23.21	152.70	0.148
RPV exposure				
-Not exposed before and after DAAs start (reference group)				
-Exposed before and after DAAs start	0.07	-13.04	13.19	0.991
-Not exposed before, but exposed during DAAs	-5.41	-20.49	9.68	0.481
-Exposed before DAAs, but not exposed during DAAs	21.01	-56.28	98.30	0.593

Table 2. Factors associated with LDL-c change by means of multivariable linear regression.

PE37/34

Treatment of cirrhotic monoinfected and HCV/HIV coinfected patients with direct acting antivirals (DAAs)

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Background: Several clinical trials have shown similar sustained virologic response (SVR) rates in HCV mono and HCV/HIV coinfected cirrhotic patients treated for chronic hepatitis C (HCV) with DAA.
Aim: To compare the baseline characteristics, the evolution of clinical parameters and the rate of sustained virologic response in mono and coinfected cirrhotic patients in a real-life setting.
Methods: Prospective study of cirrhotic patients treated for 12 to 24 weeks, between 2014 and 2018. We compared the baseline characteristics, the evolution of several parameters (AST, ALT, platelets, albumin, fibrosis) before and 12 week after the end of treatment and global SRV12 and response by genotype. Data was analysed with SPSS version 25.0.
Results: Of the 235 cirrhotic patients included, 146 (62.9%) were HCV/HIV coinfected. Mean age was 52 years in the monoinfected and 49 years in coinfected group. Men predominate in both groups (93.3% vs 88.4%); genotype 1 was the most frequent in both groups.

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At baseline we found statistical differences between IDU use, values of aminotransferases and in the prevalence of genotypes 1 and 3. Mean value of HCV-ARN was higher in coinfected patients (p=0.065).(table impact 1).The majority of patients were treated with SOF/LDV (66.8%).
The following tables show baseline biological, biochemical and fibrosis features (Table 1), the of treatment on laboratory values and fibrosis and the achieved rates of cure (Table 2) in the two groups.
Conclusion: HIV coinfection no longer appears to be a negative response factor for HCV treatment. Treatment of mono or coinfected cirrhotic patients induced a significant reduction of fibrosis and of the values of aminotransferases. The rates of SVR were very high and there were no differences between the two groups.

Table 1

	HCV (n=89)	HIV/HCV (n=146)	p
Mean age (years)	52	49	-
Males (%)	93.3%	88.9%	-
Intravenous Drug Use (IDU)	90.9%	96.5%	<0.05
Naive patients (%)	80.9%	70.5%	0.052
Baseline AST (UI/L)	89.9	67.5	<0.001
Baseline ALT (UI/L)	113	73.5	<0.001
Baseline platelets (cells/μL)	148,426	131,404	-
ARN HCV UI/mL	5.113.889	3.797.028	0.065
Mean Fibrosis (kPa)	24.5	25.8	-

Table 2

	HCV (n=89)	HIV/HCV (n=146)	p
Global SVR12	89.9%	93.8%	0.270
G1	(42/45) 93.3%	(104/109) 95.4%	0.69
G3	(28/32) 87.5%	(18/21) 85.7%	1.0
G4	9/10) 90%	(14/15) 93.3%	1.0
AST (pre and post TX)	87.4/29.3 (p<0.001)	68.6/27.9 (p<0.001)	
ALT (pre and post TX)	110/26.7 (p<0.001	74.8/24.6 (p<0.001)	
Albumin	4.44/4.65 (p<0.14)	4.73/4.59 (p<=0.31)	
INR	1.11/1.08 (p<0.24)	1.09/1.11 (p<0.52)	
Fibrosis (kPa)	25.0/18.7 (p<0.01)	26.1/19.1 (p<0.001)	

PE37/35

Predictors of vaccine efficacy after hepatitis B vaccination in people with HIV infection

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Purpose: Immunization against the hepatitis B virus (HBV) is indicated in people living with HIV/AIDS (PLHA). However, HBV vaccine efficacy (VE) is lower in PLHA, an optimal vaccination strategy has not been defined. The aim of this study is to identify predictors of HBV-VE in adult PLHA.
Method: All patients with HIV infection of our HIV outpatient clinic vaccinated between January 2011 and July 2018 were included in a case-control study. For the analysis of initially antiHBs-/antiHBc-negative patients after 3 doses of HBV vaccine, PLHA with "response" (antiHBs ≥100 IU/L) were compared to those with "low and non-response" (antiHBs <100 IU/L).
Results: 202 initially seronegative PLHA received ≥3 HBV vaccine doses. The majority were Caucasian (76%) and male (74%), mean age before vaccination was 43.8 years (IQR: 19-75). The median CD4+ T cell count was 566/μL, 88% received antiretroviral therapy (ART), the HIV plasma viral load (VL) was <50 cp/mL in 80%. At least 4 weeks after the third dose of HBV vaccine, 75 (37%) had an antiHBs titer of ≥100 IU/l. In univariate analysis the following were significantly associated with vaccine response (all p<0.025): female gender, non-Caucasian ethnicity, origin not from Germany, VL <50 cp/mL, and non-smoking status. Age, ART, and CD4 cell count, both nadir and at time of vaccination, were not significantly associated with vaccine response. Administration of further doses induced vaccine response in the majority of PLHA with primary non-/low-response (figure).
Conclusions: Female gender, ethnicity/country of origin, suppressed VL and non-smoking status were associated with HBV vaccine response. Following initial vaccine non-/low-response further doses are effective for eventually reaching antiHBs titers of ≥100 IU/L in the majority of PLHA. For the definition of an optimal vaccination strategy the identification of additional predictors, especially the co-administration of other vaccines, is still ongoing.

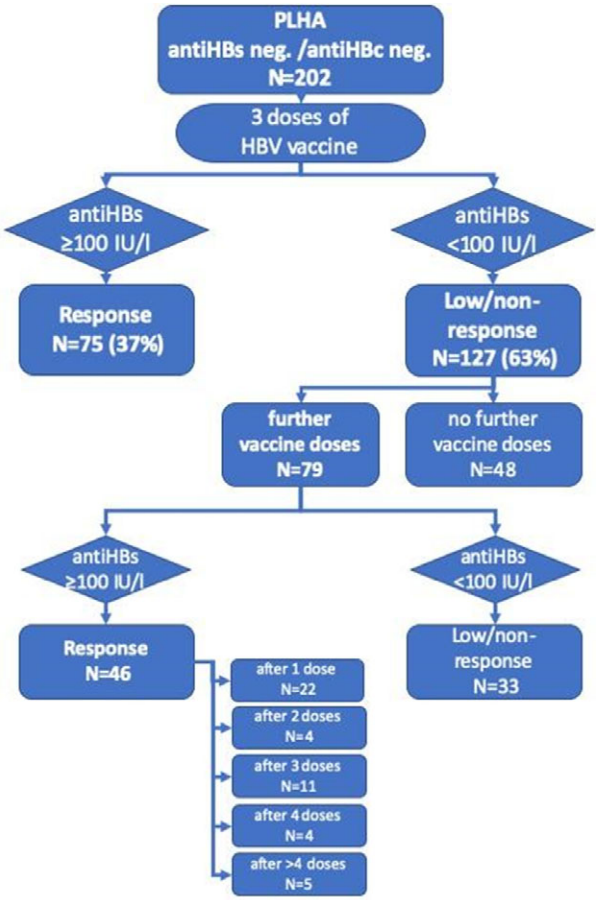


Figure: Disposition of PLHA undergoing HBV vaccination

PE37/36

Long term response to mandatory anti-HBV vaccination: risks for disease acquisition and opportunities for re-vaccination within the ICONA cohort

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In Italy, anti-HBV vaccination is mandatory from 1992, administered at the twelfth birthday for the cohort born in 1979-1991, and at the first year of age for the cohort born after 1992. According to the Italian Health Agency, HBV

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vaccination coverage is >90%. Efficacy after 20 years from administration is 60% in the general population.
Objectives: Assess long term vaccination response in horizontally infected HIV+ subjects who received anti-HBV vaccine in their childhood; evaluate proportion and risk factors for HBV acquisition despite vaccination.
Methods: Subjects born in Italy after 1979 with full serology for HBV available at ICONA enrollment (i.e. before antiretroviral treatment start) were included. Factors associated to maintaining protective anti-HBs levels (>10 IU/mL) were analyzed. Cumulative incidence of any new infection (HBsAg+, anti-HBs+/anti-HBc+, or anti-HBs-/anti-HBc+) and factors associated with HBV acquisition were calculated. Follow up was calculated as the interval between time of vaccination completion and date of serology performance.
Results: 1,628 individuals were included: 88.7% males with a median age of 29 years (IQR 25-32) mainly belonging to the 1979-1991 cohort (Table 1).
1,145 subjects (70.3%) showed a protective anti-HBs value: 393 (24.2%) resulted eligible for re-vaccination, 90 (5.5%) acquired HBV before ICONA enrollment. Cumulative incidence over the course of 29,343 years was 3 per 1000 patients/years of follow up (PYFU, 95% CI 2.5-3.7). Belonging to the >1992 cohort was the only factor associated with vaccine non-response (OR 0.47, 95% CI 0.34-0.66, p<0.0001), while no HIV-related feature played a role. Being HCV+, active smoker and alcohol daily user were factors associated with HBV acquisition before enrollment (Table 2).
Conclusion: In a large cohort of HIV+ individuals, anti-HBV vaccination response was high and similar to what observed in the general population. However, HIV+ population resulted at high risk for HBV acquisition: non-responders should undergo re-vaccination as harm reduction strategy.

Table 1. Demographic, clinical and behavioral features of study population.

		N=1628	%
Gender, Male		1444	88.7
Year of birth: 1979-1991 cohort		1465	89.9
Mode of HIV transmission	**Heterosexual**	348	21.4
	IVDU	76	4.7
	MSM	1128	69.3
	Other/unknown	76	4.7
BMI	**<18.5**	62	3.8
	18.5-25	891	54.7
	25-30	169	10.4
	>30	30	1.8
	Missing	476	29.2
Geographic area of residency	**North**	763	47.3
	Center	562	34.9
	South	287	17.8
Any STI in previous clinical history		235	14.4
Non-AIDS malignancies in previous clinical history		66	4.1
CD4 cell count at baseline	**<200**	216	13.3
	200-350	320	20.0
	>350	1037	63.7
	Missing	55	3.4
HIV RNA at baseline	**<100.000**	1022	62.8
	100.000-500.000	342	21.0
	>500.000	173	10.6
	Missing	91	5.6
CDC C stage		72	4.4
HCV-Ab positive		78	4.8
Active smokers		742	45.6
Alcohol use	**Abstainer**	536	32.9
	Occasional	573	35.2
	Daily	88	5.4
	Missing	431	26.5

IVDU: intra-venous drug users; MSM: men who have sex with men; STI: sexually transmitted infection.

Demographic, clinical and behavioral features of study population.

Table 2. Factors associated with being HBV infected (i.e. HBsAg+, anti-HBs+/anti-HBc+, or anti-HBs-/anti-HBc+) at enrollment by means of logistic regression.

	crude OR	95%CI		p-value	adjusted OR	95%CI		p-value
HCV-Ab								
negative	**1.00**				**1.00**			
positive	3.16	1.60	6.23	**0.001**	2.77	1.35	5.72	**0.006**
unknown	2.75	0.94	8.04	**0.065**	3.30	1.10	9.90	**0.034**
Nadir CD4 at BL								
<200	1.65	0.95	2.88	0.075	1.55	0.82	2.93	0.175
200-350	0.90	0.50	1.61	0.711	0.88	0.49	1.60	0.684
350+	**1.00**				**1.00**			
unknown	1.05	0.32	3.47	0.936	0.56	0.15	2.09	0.386
Smokers								
no	**1.00**				**1.00**			
yes	2.03	1.25	3.29	**0.004**	1.89	1.13	3.14	**0.015**
unknown	2.18	1.08	4.43	**0.030**	2.37	1.02	5.47	**0.044**
CDC stage C	2.25	1.04	4.84	**0.039**	2.08	0.86	5.01	0.104
Alchool use								
abstainers	**1.00**				**1.00**			
occasional use	1.13	0.66	1.95	0.662	0.99	0.56	1.74	0.974
daily use	3.23	1.56	6.69	**0.002**	2.55	1.19	5.44	**0.016**
unknown	1.15	0.64	2.06	0.633	0.84	0.43	1.61	0.590

Factors associated with being HBV infected (i.e. HBsAg+, anti-HBs+/anti-HBc+, or anti-HBs-/anti-HBc+

PE37/37

The assessment of HBsAg serum concentration during chronic hepatitis B phases' identification among HIV/HBV coinfected patients before antiviral therapy prescription

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Purpose: qHBsAg investigation in each CHB phase of HIV/CHB coinfected patients before antiviral therapy (it is supposed to differ); correlations estimation between qHBsAg and other parameters.
Method: Cross-sectional study of 80 HIV/HBV coinfected patients, observed in Vinnytsia regional AIDS Centre, Ukraine, conducted before antivirals prescribing. All HIV/HBV coinfection cases were confirmed and documented. Serum HBsAg quantification was carried out using " Abbott HBsAg Architect Kit (6C36)". Additionally HBV DNA, HBeAg, ALT, CD4, HIV VL have been done. Data were evaluated with "IBM SPSS Statistics".
Results: All coinfected people were divided into 3 subgroups accordingly with "EASL-2017": 7 (8.75%) patients were referred to "HBeAg positive Chronic hepatitis B (CHB)", 25 (31.25%) – to "HBeAg negative Chronic HBV infection (CHBVI)", 48 (60%) – "HBeAg negative Chronic hepatitis B (CHB)". "HBeAg positive Chronic HBV infection" excluded. See tables.
Significant differences by gender, coinfection duration (p<0.05) were observed in "HBeAg negative CHB" phase. QHBsAg levels among "HBeAg positive CHB" patients have qHBsAg 6.8 time bigger than "HBeAg negative CHB" patients and 177, 3 times bigger than "HBeAg negative CHBVI" (p<0.001). HBV DNA and CD4+ count were significantly higher among "HBeAg positive CHB" group (p<0.001). Simultaneously "HBeAg negative CHB" patients had highest ALT, HIV VL, APRI index (p<0.001) – see tables. Significant correlations of qHBsAg with HBV DNA (r=0.428, p<0.01) and ALT (r=0.347, p<0.05) were detected in "HBeAg negative CHB" group, whereas in "HBeAg negative CHBVI" group only correlation of qHBsAg with ALT (r=0.512, p<0.01) was found.
Conclusion: Significant differences of qHBsAg levels obtained through CHB phases in coinfected patients. Positive qHBsAg correlations were observed

Table 1. Demographical and HIV-related characteristics of HIV/CHB coinfected patients accordingly to chronic hepatitis B phases

Parameters	Total HIV/CHB co-infection, N=80	HBeAg positive Chronic hepatitis B, N=7	p value	HBeAg negative Chronic HBV infection, N=25	p value	HBeAg negative Chronic hepatitis B, N=48
Age, years	35.75±0.84	32±0.69	<0.001	35.68±0.91	0.1	35.29±0.79
Males, N (%)	52 (65%)	5 (71.4%)	0.17	11 (44%)	<0.05	36 (75%)
Females, N (%)	28 (35%)	2 (28.6%)	0.22	14 (56%)	<0.05	12 (25%)
HIV/CHB duration, years	4.38±0.35	4±0.37	0.36	4.12±0.28	<0.05	4.88±0.41
VL HIV, cop/mL	91183.84±35780.61	38291.43±4111.88	<0.001	2933.4±318.12	<0.001	144861.08±45342.36
CD4+ count, cells/μL	426.69±25.55	616.71±26.65	<0.001	491.04±20.09	<0.001	365.46±25.65

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Table 2. Clinical HBV characteristics of HIV/CHB coinfected patients accordingly to chronic hepatitis B phases

Parameters	Total HIV/CHB co-infection, N=80	HBeAg positive Chronic hepatitis B, N=7	p value	HBeAg negative Chronic HBV infection, N=25	p value	HBeAg negative Chronic hepatitis B, N=48
HBeAg, positive/negative	N/A	positive	N/A	negative	N/A	negative
qHBsAg, IU/mL	17357.17±4340.67	98007.94±9841.17	<0.001	552.89±46.58	<0.001	14347.83±2280.82
HBV DNA, IU/mL	3169095.31±1331469.13	12307612.57±1236315.77	<0.001	653.56±69.06	<0.001	3486624.96±1600372.96
ALT, IU/mL	49.15±6.58	55.91±1.11	<0.001	21.39±1.05	<0.001	62.43±7.98
Index APRI	0.76±0.08	0.57±0.02	<0.001	0.28±0.01	<0.001	1.03±0.09
Fibrosis F0-F1, N	25	-	N/A	25 (100%)	N/A	-
Fibrosis F2-F3, N	40	6 (85.7%)	N/A	-	N/A	34 (70.8%)
Fibrosis F4, N	15	1 (14.4%)	N/A	-	N/A	14 (29.2%)

with ALT and HBV DNA. Thus, qHBsAg will be helpful for estimation and demarcation of CHB phases in HIV/CHB coinfected people. Further qHBsAg levels estimation is needed after starting HIV/CHB antiviral treatment.

PE37/38

Predictors of liver fibrosis improvement after HCV eradication in HIV+ patients: data from an Italian cohort

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Purpose: The aim of the analysis was to evaluate liver stiffness and serum liver fibrosis scores in HIV/HCV patients at SVR24 after DAA and to investigate predictive factors of these changes according to cART exposure.
Method: This analysis included HIV/HCV+ patients consecutively treated with DAAs from 2016 who achieved SVR24. Patients with laboratory data at baseline (DAA start) and SVR24, without cART modification during the observation period, were selected. Mean changes of liver stiffness (kPa), Fibrosis-4 (FIB4) and AST to Platelet Ratio Index (APRI) were calculated as the mean difference between BL-SVR24. Wilcoxon test was used to compare values at BL-SVR24 and multivariable linear regression used to investigate associations with the variations.
Results: 533 patients were included, 23% female, median (IQR) age 56 (52-59) years, 70.1% IVDUs, 97% Caucasian. HCV GT1 57%, GT3 23% and GT4 16%. 27% were on PI/b, 26.4% on NNRTI and 24.3% on INSTI. At baseline, median (IQR) liver stiffness, FIB-4 and APRI were [10.2 (6.3–18.5), 2.12 (1.44–3.41) and 0.69 (0.42–1.28), respectively.
Liver stiffness, FIB4 and APRI significantly decreased at SVR24 (Δ-4.49 (SD 7.1);-0.89 (2.28); −0.62 (2.28); p<0.001).A pre-DAAs high fibrosis score (>9 kPa Metavir F4) significantly contributed to the decrease of FIB4, APRI and liver stiffness (p<0.001). Patients exposed to DRV/b who discontinued DRV at DAAs start had a significant increase in liver stiffness [B +6.46 kPa (p=0.007)] as compared to patients who did not change DRV/b (Table 1). An increase of liver stiffness was also observed in female vs male.
Conclusion: A reduction in liver stiffness and an improvement in fibrosis scores were observed in HIV/HCV coinfected patients at SVR24 post DAAs. A worse fibrosis evolution was found in female gender. The protective role of DRV/b versus fibrosis evolution is interesting although controversial, therefore further investigations are required.

Liver Stiffness	Beta	95%CI		p-value
Female gender	**2,31**	**0,51**	**4,12**	**0,012**
HCV Genotype				
Type 1 (reference group)				
Type 2	-3,08	-7,49	1,32	0,169
Type 3	-1,47	-3,43	0,50	0,142
Type 4	-1,30	-3,48	0,88	0,241
Mixed	0,92	-5,77	7,61	0,787
Fibrosis				
F1				
F2	-1,46	-4,15	1,02	0,267
F3	-1,98	-4,25	0,33	0,089
F4	**-8,30**	**10,27**	**-6,52**	**< 0,001**
DRV exposure				
-Not exposed before and after DAAs (reference group)				
-Exposed before and after DAAs	-1,38	-3,16	0,40	0,129
Not exposed before, but exposed during DAAs	-1,27	-7,86	5,32	0,705
-Exposed before DAAs, but not exposed during DAAs	**6,46**	**1,75**	**11,16**	**0,007**
DTG exposure				
-Not exposed before and after DAAs (reference group)				
-Exposed before and after DAAs	0,89	-2,32	4,10	0,586
-Not exposed before, but exposed during DAAs	-3,67	-8,05	0,72	0,101
-Exposed before DAAs, but not exposed during DAAs	10,80	-0,63	22,23	0,064

Table 1. Factors associated with Liver Stiffness change by means of multivariable linear regression. Significant results in bold.

PE37/39

Long-term follow-up of people who use drugs (PWUD) following HCV infection therapy: drug use patterns among HIV co-infected versus mono-infected patients

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Purpose: People who use drugs (PWUD) constitute the majority of Hepatitis C infection cases in developed countries. Co-infected patients with HIV may engage in high-risk drug use behavior even after successful HCV therapy. We sought to evaluate drug use behavior and to determine the health outcomes of HCV mono-infected and HIV co-infected individuals after HCV therapy.
Method: We undertook a prospective study of HCV-infected PWUD who received oral HCV treatment from 03/14-12/17 at our centre and who were followed up from the end of treatment to 06/19. The primary outcome of this analysis was the occurrence of an adverse event (recurrent viremia, death or loss to follow up).Drug use was evaluated by using urine drug screens. Statistical analyses were conducted using Chi square test, Cox proportional hazard models and Kaplan Meier survival analysis with SPSS IBM V24.
Results: There were 215 patients, 32 co-infected with HIV, (74 % male (n=160), 39 % active/recent drug users (n=83), 20% poly-drug users; 21% (46/215) consumed amphetamines, 17% cocaine (37/215) and 15% fentanyl (32/215). During the 267 patient-years of follow-up we observed three confirmed reinfection cases (1.12/100 person-years), 5 lost to follow-up and 8 deaths, all among mono-infected individuals. These outcomes occurred despite the fact that active drug users were more common among HIV co-infected individuals (56.3%; 18/32 vs. 30.6%; 56/183); p=0.005, including more frequent polysubstance use (p=0.007). Only mono-infected drug users had a higher prevalence of adverse events (HR: 2.85; CI: 95 % (1.20–6.75) p=0.017]
Conclusion: No significant difference between mono-infected and HIV co-infected individuals. In our analysis, co-infected patients used significantly more illicit drugs, but within the context of engagement in our care program, this did not affect long-term health outcomes. HIV co-infection should not be a factor to limit access to HCV treatment.

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PE37/40

Treatment outcome of HCV single vs multi tablet regimen in mono and HIV co-infected people who use drugs (PWUD): a long-term follow-up analysis

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People who use drugs (PWUD) have been identified as a priority population to receive HCV therapy. Adverse treatment outcomes such as treatment failure or reinfections remains a concern for this population. We sought out to determine the impact of the number of DAA tablets on HCV treatment outcomes among HCV mono-infected and HCV/HIV co-infected PWUD.
Method: We conducted a prospective study of HCV-infected PWUD who received oral HCV treatment from 03/14-12/17 at our centre and who were followed up from the end of treatment to 06/19. The primary outcome of this analysis was the occurrence of an adverse event (recurrent viremia, death or loss to follow up). Statistical analysis was conducted using Chi square test, Cox proportional hazard models and Kaplan Meier survival analysis with SPSS IBM V24.
Results: A total of 215 patients (mean age 55 years, 74% male, 20% cirrhotic, 32 co-infected with HIV, 39 % active/recent drug users (n=83)). HCV cure (SVR12) was achieved in 92.9% (170/183) mono-infected versus 84.4% (27/32) co-infected patients; (p=0.156). During the 267 patient-years of follow-up, 99 subjects received multiple tablets (46%) versus 116 subjects who had single tablet (54%). The number of adverse events rates noted were 13.1% (13/99) versus 17.2% (20/116) respectively (p=0.405). We noted 34 % (11/32) HIV/HCV infected patients who took multiple pills, among them, four had adverse outcomes vs (9/88) 10.2% HCV only infected patients (p=0.036). The number of tablets and HIV co-infection were not associated with adverse outcomes.
Conclusion: There were no significant differences with respect to treatment outcome between single and multiple DAA tablets. However HIV co-infected patients who took multiple tablets had significantly more adverse outcomes. single tablet regimens may be preferred among HIV co-infected individuals, given the fact they are often receiving multiple concomitant medications, including those taken as antiretroviral therapy.

Virology

PE38/1

Identification of an HIV-1 BC intersubtype recombinant form, which is circulating in Spain

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Introduction and Purpose: Human immunodeficiency virus (HIV-1) group M shows a great genetic diversity and rapid evolution, having led to the emergence of 9 subtypes, 94 circulating recombinant forms (CRFs) and numerous unique recombinant forms (URFs). 11 CRFs derived from subtypes B and C have been described in China, Brazil and Italy. Here we identify one additional CRF_BC, which circulates in Spain.
Method: Samples were collected from HIV-1-infected patients diagnosed in Spain from 2006 to 2018. Partial genome sequences (PR-RT) were analyzed and clustering was determined with phylogenetic trees constructed with FastTree and PhyML. Near full length genome (NFLG) sequences were obtained and recombination was determined by bootscanning. The time and location of the most recent common ancestor (MRCA) were estimated with a Bayesian coalescent method using BEAST v1.10.4, summarizing the set of trees of the posterior distribution in a maximum clade credibility (MCC) tree.
Results: By analyzing partial genome sequences (PR-RT) we observed a cluster of 15 viruses recombinant between subtypes B and C with coincident breakpoints. The cluster was associated with heterosexual transmission and 7 of the patients were diagnosed during the last 4 years. NFLG were obtained for 10 viruses collected in 3 cities, which showed identical mosaic structures, with a predominantly subtype C genome and 8 breakpoints delimiting 4 subtype B fragments, 2 in pol, 1 in vpr and 1 in nef. Phylogenetic analysis of NFLG revealed monophyletic clustering supported by a 100% bootstrap value. The subtype C fragments grouped with viruses from Brazil and the MRCA of the cluster was estimated around 2002 in the city of Vitoria (Basque Country) with a strongly supported ancestry in Brazil.
Conclusion: The analysis of NFLG from epidemiologically-unlinked viruses clustering in phylogenetic trees and with coincident mosaic structures allow to define a new HIV-1 CRF_BC.

PE38/2

Viral reservoir dynamics in very early primary HIV infection (PHI) patients receiving an intensified antiretroviral regimen (ART): a pilot clinical trial

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Purpose: ART during PHI has been associated with decreased transmission, better immunological recovery and limitation of viral reservoir (VR) seeding. The aim of the study was to characterize VR dynamics in blood and rectal tissue and immunological recovery after initiating an intensified-5-drug ART regimen during very early PHI.
Method: We compared two groups: cases (Fiebig stages I-II) and controls (Fiebig stages III-V). Patients started an intensified ART consisting on abacavir/lamivudine/dolutegravir regimen during 48 weeks plus darunavir-r and maraviroc the first 12 weeks. Rectoscopies were performed at W0 and W48. Immunological recovery and viral reservoir in blood (VRb) and rectal tissue (VRr) were compared between W0 and W48. Clinical Trials NCT02588820.
Results: Seventeen patients were included, 6 were Fiebig stage II (cases), and 11 were Fiebig stages III-V (controls).

Main characteristics of included patients

Variable*		All patients	Cases (Fiebig I-II)	Controls (Fiebig III-V)	P Value
Fiebig stage		17 (100)	6 (35.3)**	11 (64.70)***	N/A
Gender and risk factor	MSM	16 (94.11)	6 (100)	10 (90.9)	1
	Trasgender woman	1 (5.88)	0 (0.0)	1 (9.09)	
Age		36 (28;44)	35 (32;44)	36 (24;48)	0.76
Ethnicity/origin	European	6 (35.29)	3 (50)	3 (27.27)	
	Hispanic-american	8 (47.05)	2 (33.33)	6 (54.54)	0.77
	Other	3 (17.64)	1 (16.66)	2 (18.18)	
HIV subtype B		11 (64.7)	3 (50)	8 (72)	0.32

*All variables expressed as N (%) or median (IQR)
**All cases were Fiebig II
***Including 2 Fiebig III, 4 Fiebig IV and 5 Fiebig V

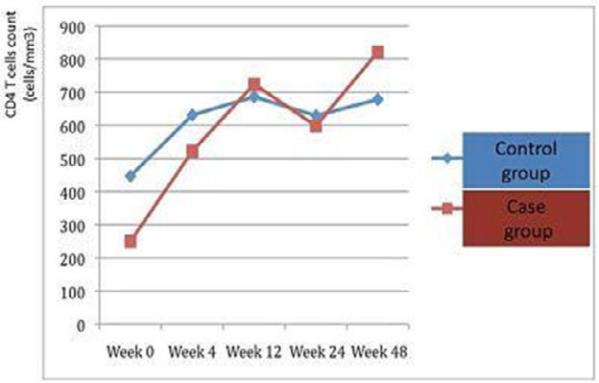
Tolerance of the intensified ART was good and no serious AE were reported. At W0 in cases group, median CD4 cells were 250/mm^3, VL= 3,128,000 copies/mL, VRb was 772.9 total and 55.9 integrated DNA copies/million CD4+ T cells. VRr was 7126.4 total and 1054.9 integrated DNA copies/million CD4+ T cells. In the control group, a trend to lower VL (1,086,350 copies/mL) and to higher CD4 cells (447/mm^3), VRb and VRr were observed at W0.At W48, all but one patient in the control group have undetectable VL in plasma. In the cases group CD4 cells increased to 821/mm^3, VRb decreased to 71.8 and 10 copies/million CD4+ T cells for total (p=0.02) and intregrated DNA (p=0.06), respectively, and VRr to 54.7 and 14 copies/million CD4+ T cells for total (p=0.04) and intregrated DNA (p=0.01), respectively. In the control group CD4 increase and VR decrease were less pronounced (p>0.05).

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Viral Reservoir dynamics in blood and rectal tissue at week 0 and week 48

Viral Reservoir in Blood (b) and rectal tissue (r)	All patients (N=17)	Cases (N=6)	Controls (N=11)	P Value
VRb* W0 (Total)	1475.2 (830.7; 7784.8)	772.9 (370.0; 2242.2)	2250.4 (1243.2; 8610.9)	0.47
VRb* W0 (Integrated)	94.6 (31.4; 612.2)	55.9 (27.5; 314.3)	244.3 (31.4; 920.3)	0.31
VRb* W48 (Total)	111.6 (85.3; 1026.1)	71.8 (31.8; 749.8)	242.4 (97.2; 1026.1)	0.96
VRb* W48 (Integrated)	30.7 (11.2; 197.6)	10.0 (6.5; 104.4)	36.4 (25.5; 251.0)	0.90
VRr** W0 (Total)	9912.0 (3885.9; 22857.5)	7126.4 (2435.3; 8393.9)	12620.2 (4199.3; 29580.0)	0.19
VRr** W0 (Integrated)	1351.7 (387.2; 3406.1)	1054.9 (225.4; 1793.5)	1373.7 (697.7; 3843.4)	0.14
VRr** W48 (Total)	59.8 (51.2; 133.4)	54.7 (53.9; 178.0)	70.6 (48.7; 119.0)	0.99
VRr** W8 (Integrated)	14.9 (7.1; 21.0)	14.0 (3.6; 81.1)	17.1 (10.1; 20.6)	0.96

All variables expressed as median (IQR)
*DNA copies/million CD4+ T cells
**DNA copies/million CD4+ T cells



CD4 T cell absolute count evolution in cases (Fiebig II) and controls (Fiebig III-V)

Conclusion: Starting intensified ART in very early PHI (Fiebig II) is associated with better immunological reconstitution and higher reservoir reduction in blood and tissues.

PE38/3

Lamivudine-based two-drug regimens are not associated with an increased risk of detectable rectal HIV-RNA

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Purpose: We aimed to assess whether lamivudine-based dual therapies (DT) are associated with a larger rectal HIV-RNA reservoir compared with standard triple therapy (TT) strategies.
Method: During routine proctological examination, consecutively-enrolled, HIV-positive MSM underwent anal swab for detection of mucosal HIV-RNA load. A cross-sectional analysis was conducted to test the association between detectable rectal HIV-RNA and the use of lamivudine plus either a boosted protease inhibitor or dolutegravir compared with TT through multivariable logistic regression.
Results: Data from 60 patients were analysed. Eighteen patients (30.0%) were on a lamivudine-based DT and forty-two (70.0%) on TT (2 NRTIs plus an InSTI or a NNRTI). Median age was 50 years, with 12 years since HIV diagnosis and 9 of cumulative exposure to antiretrovirals. The study groups differed for current CD4 count, treatment line and months since last plasma HIV-RNA≥50 copies/mL (see table 1). All patients except two (3.3%) had a plasma HIV-RNA< 50 copies/mL, but in fourteen cases (23.3%) residual viremia was detectable; nine patients (15.0%) had a detectable rectal HIV-RNA with a median of 84 copies/swab (IQR 50–120 copies/swab). No patients had concomitant sexually-transmitted diseases nor high-grade anal dysplasia. The agreement between plasma and rectal detectable HIV-RNA was minimal (Cohen's kappa: 0.26) even if statistically significant (p=0.034). After adjusting for current CD4 count and months since last HIV-RNA≥50 copies/mL, the use of DT had no effect on the risk of detectable rectal HIV-RNA (aOR: 1.79, 95% CI 0.28–25.40; p=0.389), whereas a larger number of treatment lines was associated with the outcome (per each line more, aOR 1.22, 95% CI 1.03–1.44, p=0.022). A stepwise forward model also including variables associated with the outcome at univariate analysis (plasma HIV-RNA, CDC stage and ethnicity) confirmed no effect of DT on rectal HIV-RNA.
Conclusion: Lamivudine-based DT, compared with TT, was not associated with increased detection of rectal HIV-RNA.

Table 1. Characteristics of study population according to antiretroviral therapy (N=60)

Variables	Two-drug regimens (N=18)	Other regimens (N=42)	p-value
Age	53 (44–58)	47 (39–53)	0.076
Non Caucasian ethnicity	1 (5.6)	7 (16.7)	0.246
CDC stage C	6 (33.3)	11 (26.2)	0.574
Years since HIV diagnosis	14 (9–22)	10 (4–22)	0.093
CD4 count (cells/μL): 1) Nadir 2) Current	1) 263 (25–313) 2) 630 (514–769)	1) 286 (52–452) 2) 774 (525–956)	1) 0.477 2) 0.048
Zenith HIV-RNA (log10 copies/mL)	4.69 (4.00–5.52)	4.77 (4.21–5.34)	0.974
Treatment line	7 (5–10)	5 (3–8)	0.047
Antiretroviral therapy: 1) Lamivudine + boosted protease inhibitor 2) Lamivudine + dolutegravir 3) 2NRTIs + integrase inhibitor 4) 2NRTIs + NNRTI	1) 7 (38.9) 2) 11 (61.1) 3) 0 (0) 4) 0 (0)	1) 0 (0) 2) 0 (0) 3) 26 (61.9) 4) 16 (38.1)	NA
Months since last HIV-RNA ≥50 cp/mL	120 (84–149)	41 (12–113)	0.001

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PE38/4

Comparison of HIV-1 viral load and drug resistance mutations between cerebrospinal fluid and plasma in patients with HIV and Cryptococcal meningitis co-infection in Botswana

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Purpose: To compare HIV-1 viral load (VL) and drug resistance mutations (DRMs) between cerebrospinal fluid (CSF) and plasma amongst individuals co-infected with HIV-1C and Cryptococcal meningitis in Botswana.
Method: This was a retrospective cross-sectional study utilising paired CSF and plasma samples from 60 participants enrolled in Ambition phase II Study conducted between 2014 and 2016. HIV-1 protease and reverse transcriptase fragments were sequenced using Big dye sequencing chemistry. Sequences were analysed for DRMs using Stanford HIV drug resistance database. Viral escape was defined CSF VL 0.5 log_{10} higher than plasma VL.
Results: HIV-1 VL was measured in 38/60 (63%) CSF and plasma paired samples. A total of 34/38 participants (89.5%) had detectable VL in both CSF and plasma with medians of 4.7 (IQR:3.6–5.0) and 5.2 (IQR:4.8–5.7) log_{10} copies/mL, respectively ($p \leq 0.001$). There was a statistically significant correlation between plasma and CSF VL (spearman $r=0.49$, $p=0.003$). The estimated prevalence of CSF viral escape was 2.9% [95% CI: 0.07–15.3]. A total of 30/45 (67%) paired samples were successfully sequenced and an overall of 9 and 11 different DRM was observed in the plasma and CSF samples respectively. The most predominant DRM in the plasma samples was K101E with a frequency of 2 whilst mutations in the CSF occurred at equal frequencies of 1. DRM discordance was present in 3/30 (10%) paired samples, of these, I84T and M46I were detected in CSF and absent in plasma in two patients.
Conclusion: Despite the elevated VL in these participants, CSF viral escape was not commonly observed. However, there were cases of DRM found in the CSF compartment only; this could be explained by compartmentalisation of HIV viral strains as a consequence of varying penetration effectiveness of some antiretroviral drugs through the blood-brain barrier or present in plasma at low frequency. Studies measuring the levels of antiretroviral drugs in both compartments are warranted.

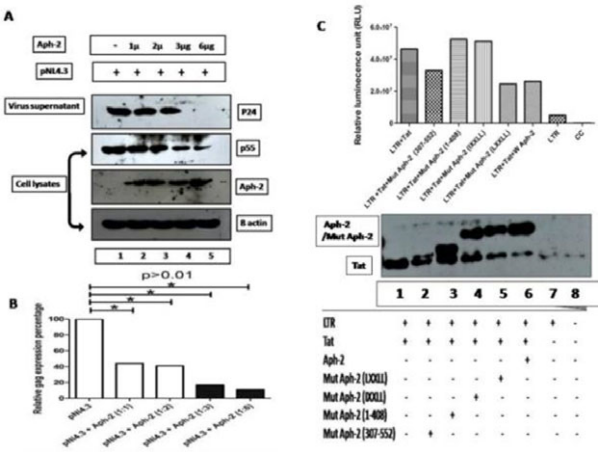
PE38/5

HTLV-II antisense protein Aph-2 negatively regulates HIV-1 transcription

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Purpose: Slower HIV-1 disease progression among HTLV-II/HIV-1 co-infected patients is well known. HTLV-II Aph-2 negatively regulates HTLV-II transcription. Given the common cellular factors orchestrating transcription of HTLV-II and HIV-1, we explored if HTLV-II Aph-2 coiled regulate HIV-1 transcription as well.
Method: HIV-1 molecular clone pNL4.3 and HA- tagged HTLV-II Aph-2 were co-transfected in 293T cells. Virus release in the culture supernatants and cell lysates was confirmed by HIV-1 p24 western blot. Expression of HA-Aph-2 was detected using anti-HA antibody. Simultaneously, effect of Aph-2 expression on HIV-1 transcription was assessed using quantitative PCR. The effect of Aph-2 on Tat mediated HIV-1 transcription was analyzed by co-transfecting, HA-Tat, HA-Aph-2 WT/mutants and HIV-1 LTR Luc plasmid in to 293T cells. The relative expression was measured using luciferase reporter assay.
Results: HIV-1 release was severely impaired with increasing concentrations of HA-Aph-2 (Fig. 1A). Moreover, concentrations of HA Aph-2 inhibiting HIV-1 release also impaired HIV-1 gag mRNA expression leading to reduced cellular gag protein (Fig. 1B). Further, Aph-2 over expression hampered ability of HIV-1 tat to transactivate expression of luciferase from HIV-1 promoter. Introduction of mutations in the IXXLL motif at the N-terminal domain of Aph2 reverted the inhibitory effect imposed by Aph2 (Fig. 1C).
Conclusion: HTLV-II Aph-2 protein may negatively regulate early events of HIV-1 life cycle, especially, transcription from LTR and the critical determinants required for this negative effect plausibly lie in its N-terminal domain. Deeper insights in this area necessary to may help in combating HIV-1 infection.



Effect of Aph-2 on A) HIV-1 release B) HIV-1 Gag expression and C) HIV-1 Tat mediated transcription

PE38/6

HIV compartmentalization between plasma and CSF and association with neurocognitive disorders

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Purpose: Evolution of HIV within the central nervous system (CNS) was associated with HAND and unique variants of HIV envelope gp120 (env) gene sequence can predict the CNS phenotype. Our aim was to evaluate HIV genetic divergence between plasma and cerebrospinal fluid (CSF) and to assess whether divergence is associated with cognitive domains impairment.
Method: V3 loop of env gene sequencing was performed in paired CSF/plasma HIV samples from patients diagnosed with HAND according to Frascati's criteria (10 NPS tests score) and with available viral tropism: Genetic divergence was evaluated as C/P ratio (ratio of nucleotidic variants detected in CSF by HXB2 sequence as a reference) or according to identity (aligning paired sequences using EMBOSS Needle software-derived identity score (http://www.ebi.ac.uk/Tools/psa/emboss_needle/nucleotide.html). Data are described as median (IQR).
Results: We included 48 patients: male 83.3%, age 45.6 (41.3–69.3) years, current and nadir CD4 were 67 (37–114) and 7 (4–14) cells/mm^3. Only 5 (10.4%) participants were receiving HAART. Plasma and CSF HIV-RNA was 5.55 (4.99–5.96) and 3.96 (3.20–4.65) log10 copies/mL. Thirty six (75 %) patients harboured a R5-tropic virus in plasma and 38 (79.2%) in CSF.
C/P ratio was associated with longer executive functions (Trail making B and StroopTests; p-values 0.051 for both, rho-values 0.949 and −0.949, respectively) and motor performances (non-dominant Grooved Pegboard Test; p-value 0.013, rho-value 0.483).
Higher viral identity was associated with worse long term memory (Immediate and Deferred Free and Cue Selective reminding test; p-values 0.032 and 0.018, rho-values −0.481 and −0.525, respectively; Sensitivity to Cues, p-value 0.028, rho-value −0.491) and better visuospatial abilities (Rey complex figure test, p-value 0.019, rho-value 0.497).
Conclusion: Genetic divergence between CSF and plasma within V3 loop of HIV-1 env gene could reflect viral compartmentalization and is associated with worse neurocognitive performance.

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PE38/7

Determinants of neurocognitive impairments in a Romanian cohort of young adults with chronic HIV infection

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Purpose: The Romanian cohort of young adults, parenterally infected with HIV subtype F1 in early childhood, offers a unique opportunity to explore the effect of chronic HIV-infection on the developing brain. The association between neurocognitive impairment (NCI), host and viral risk factors was evaluated in this cohort.
Method: 250 HIV+ subjects (median age: 24 years, females: 52%, median duration of HIV infection: 23 years; median lenghts of cART: 12 years) underwent neurocognitive testing using a comprehensive neuropsychological test battery. Pol and env gene sequencing was performed on plasma and available paired CSF samples with a viral load >1,000 copies HIV RNA/mL. Inflammatory biomarkers (IL-1β, IL-6, IL-8, TNF-α, CXCL10/IP-10, MCP-1, IL-8) were measured using multiplex assays (Meso Scale Diagnostics, Gaithersburg, MD).
Results: Viral suppression was achieved in 63% of the cases, severe immunosuppression was present in only 16% of the cases. 36% of the patients had mild cognitive impairment, without any association with age, CD4 cell count (actual or nadir), plasma and CSF viral load, AIDS-diagnosis, duration of HIV infection and cART exposure. A trend toward a higher impairment rate was identified in the group of subjects carrying resistant viruses, but did not reach statistical significance. No signs of virologic compartmentalization were observed based on CSF vs plasma viral load and on the profile of pol sequences. Multivariable logistic regression analyses showed that in plasma, higher levels of IL6 (OR=2.85) and TNF-α (OR=1.9), were associated with NCI (ps < 0.05), after controlling for HIV RNA level. Low plasma CXCL10 levels were positively correlated with CSF CXCL10 levels and with the degree of NCI (d=-1.44, p=0.01).
Conclusion: Chronic, sustained immune activation in the CNS might explain the relatively high level of neurocognitive impairment present in young adults with long term HIV infection, despite succesful antiretroviral therapy.

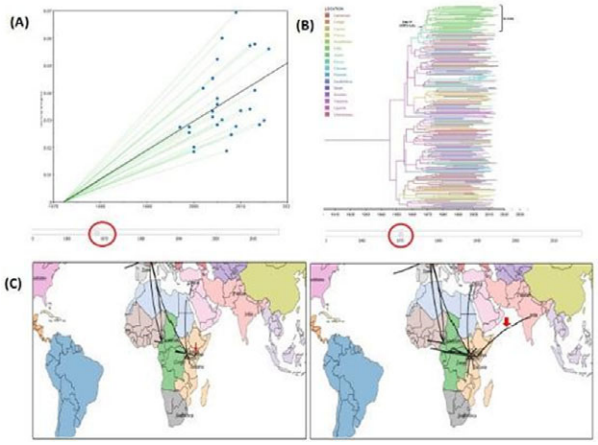
PE38/8

Reconstruction of phylogeography for Indian HIV-1 sub-subtype A1

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Purpose: Subtype A is second only to the infections caused by HIV-1 subtype C around the globe. Though Indian HIV-1 subtype A was shown to be monophyletic, there is no study addressing its ancestral roots with respect to its phylogeography. In this regard this study aims to estimate the spatio-temporal spread of HIV-1 sub-subtype A1 in India.
Method: Data-set included 28 Indian HIV-1 A1 and 186 HIV-1 A1 partial reverse transcriptase sequences from other countries retrieved from HIV sequence database. Root to tip analysis for molecular clockliness was performed by TempEst. Bayesian Evolutionary Analysis Sampling Trees (BEAST) analysis was performed to estimate the time to most recent common ancestor (tMRCA) for Indian HIV-1 A1. Maximum clade credibility (MCC) tree was generated using Tree Annotator and tree was visualized using FigTree v1.4.2. Phylogeographic reconstruction was performed with asymmetrical discrete trait using Bayesian stochastic search variable selection (BSSVS). Phylogeographic reconstruction was visualized with Spread D3 .Bayes factor (BF) test used as a measure of statistical support for locations.
Results: Root to tip analysis of Indian HIV-1 A1 sequences demonstrated positive correlation between genetic distance and divergence time (correlation coefficient=0.41; slope rate=1.065×10^{-3}). BEAST analysis estimated the mean tMRCA for Indian HIV-1 A1 to be 1967.71 (95% HPD -1978.47–1955.74). Time scaled MCC tree shows the monophyletic nature of Indian HIV-1 A1 and their possible evolution from Kenyan HIV-1 A1 sequences around 1967. Further, phylogeographic reconstruction of HIV-1 A1 migration to India inferred using BEAST locations annotated MCC tree indicated the migration of HIV-1 A1 to India from Kenya between 1967–1970, with strong statistical support of BF >10 (12.34).
Conclusion: Phylogeographic reconstruction indicates that HIV-1 A1 was introduced to India from Kenya between 1967 to1970.



(A) Temporal signal estimation (B) BEAST MCC tree (C) Phylogeography

PE38/9

Broad and potent neutralizing antibody responses in HIV-1 infected Angolan patients: implications for vaccine design and efficacy

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Characterizing the neutralizing antibody response and virus evolution in Central and West African countries with old HIV epidemics driven by highly divergent viruses may provide useful insights for vaccine design. Herein, we make the first detailed characterization of the neutralizing antibody responses and identify its determinants in Angolan patients infected with HIV-1.
A total of 204 plasma samples from Angolan patients were analysed against a reference cross-clade Env-pseudotyped tier 2 indicator virus panel (n=12). Binding antibody activity to polypeptides comprising the C2, V3 and C3 envelope regions from different HIV-1 clades was evaluated in ELISA assays. The envelope C2V3C3 region was sequenced in order to assess subtype, co-receptor use and virus evolution
Neutralizing antibody responses were positively associated with subtype C infection and patients' age, and negatively associated with CD4 counts. Patients infected with isolates more closely related to the viruses in the indicator panel had stronger neutralizing responses neutralization. However, few patients developed broad neutralizing antibody (bnAb) responses despite the high genetic distance to the pseudoviruses in the indicator panel. There was a strong and positive correlation between neutralizing responses and titer of antibodies binding to C2V3C3-polypeptides of all clades. Viruses from patients with bnAb responses had far less variability in C2V3C3, as measured by entropy analysis and number of positively selected sites, relative to patients without bnAb responses. Important V3 bnAb recognition sites and sites associated with resistance to neutralization in the C2V3C3 region were under positive selection in patients with elite neutralizing capacity.
In conclusion, binding antibody titer against the envelope C2V3C3 region was a good indicator of neutralization responses in HIV-1 infected individuals from Angola. Taking into consideration the neutralizing responses of certain HIV-1 infected Angolan patients the design of a pan-HIV vaccine might not be an utopic concept.

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PE38/10

The XbnAb cohort: a HIV-1 cohort of 304 bnAb inducers and matched controls tailored to study determinants of bnAb induction

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Purpose: Eliciting broadly neutralizing antibodies (bnAbs) capable of inhibiting infection with diverse variants of human immunodeficiency virus type 1 (HIV-1) is a key component of prophylactic HIV-1 vaccine strategies. Understanding pathways that promote HIV-1 bnAb induction is crucial to advance bnAb-based vaccines. We previously reported on the Swiss 4.5K Study [1, 2] where 4,484 HIV-1-infected individuals enrolled in the Swiss HIV Cohort Study and the Zurich Primary HIV Infection Study were screened for neutralization breadth to identify determinants of bnAb induction. We confirmed several factors that are strongly linked with the development of neutralization breadth in natural infection, namely duration of infection, high viral load, viral diversity, and black ethnicity. Virus genetic subtype was linked with induction of specific bnAb classes. The purpose of the current study was to create a bnAb-inducer cohort based on the Swiss 4.5K Study that allows detailed analysis of correlates of breadth.
Methods: We defined within the Swiss 4.5K Study the XbnAb cohort comprising 304 HIV-1-infected individuals with bnAb activity (cross to elite neutralization activity; neutralization score median 11 (IQR: 10–14)) and 304 matched controls without neutralization activity.
Results: The XbnAb cohort represents the largest bnAb-inducer cohort described to date. We provide a detailed analysis of demographic factors of the cohort that confirms its utility for deciphering factors linked with bnAb induction. Selected controls were matched for HIV-1 subtype, length of infection and host demographics permitting unbiased analyses. We demonstrate that the XbnAb cohort corroborates the definition of bnAb linked parameters previously identified in the Swiss 4.5K study [2].
Conclusion: The thorough characterization of the newly defined XbnAb cohort we present here underlines the enormous potential of this cohort in unraveling key factors of bnAb evolution.

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2. Kadelka, C., et al J Exp Med, 2018. 215(6).

PE38/11

Performance of 'Xpert® HIV-1 Qual assay' for diagnosis of HIV-1 infection using Dried Blood Spot specimens

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Purpose: Point Of Care (POC) assays are important for timely diagnosis and effective HIV management. In this study "Xpert® HIV-1 Qual assay" was evaluated for accuracy, specimen stability and limit of detection (LOD) using Dried Blood Spot (DBS) specimens from HIV exposed infants and adults.
Method: The study was conducted between May 2018–March 2019 at ICMR-National AIDS Research Institute, Pune, India on 100 DBS specimens (HIV-1 infected and HIV-1 uninfected, 50 each) collected from HIV infected adults and HIV exposed infants less than 18 month of age. Diagnostic accuracy of the assay was assessed using Abbott Real Time HIV-1 Qualitative test prior to test on Xpert® HIV-1 Qual platform.The specimen stability was assessed by testing each specimen at three time points; 2 weeks, 6 weeks and 12 weeks when stored at 25–30°C. The LOD was assessed using frozen plasma specimens (N=3) collected from HIV infected individual which were serially diluted using negative plasma and mixed with negative whole blood. Viral load of diluted samples was assessed using Xpert® HIV-1 Viral Load test and prepared DBS samples was tested on Xpert® HIV-1 Qual platform.
Results: The observed accuracy of the results of Xpert® HIV-1 Qual assay and Abbott Real Time assay was 100% for HIV uninfected specimens and 98% for HIV infected DBS specimens. DBS stored at 25–30°C could be used for testing up to 12 weeks with 100% concordance confirming the stability of DBS at ambient temperature and its utility for diagnosis using Xpert® HIV-1 Qual assay. The lowest viral load detected using this platform was observed to be 983cp/mL (range: 983–3330 copies/mL).
Conclusion: The "Xpert® HIV-1 Qual assay" can be utilized as POC for diagnosing HIV infection using DBS specimens. This can be useful for early initiation of treatment leading to achieve the second 90 of 90-90-90 goal.

PE38/12

HIV-1 infections belonging to transmission clusters originating in different countries are frequently detected in Spain among newly diagnosed individuals

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Purpose: To examine the spread into Spain of HIV-1 transmission clusters originating in other countries.
Methods: Plasma samples from newly diagnosed HIV-1-infected individuals attended at clinical centers from 10 Spanish regions, collected in 2016–2019, were used for RNA extraction and subsequent RT-PCR amplification and sequencing of HIV-1 protease-reverse transcriptase (PR-RT). Phylogenetic analyses were performed with FastTree2, including most similar sequences identified with BLAST searches at the Los Alamos HIV Sequence Database. Transmission clusters (TC) were defined as those comprising 4 or more individuals supported by a local Shimodaira-Hasegawa (SH)-like value ≥0.95. Clusters of ≥6 individuals including sequences from samples collected outside of Spain were analyzed with the Bayesian coalescent method implemented in BEAST v1.8.1, using the SDR06 evolutionary model, a lognormal relaxed clock model and the Bayesian Skyline Plot demographic growth model.
Results: Of 1905 PR-RT sequences from new HIV-1 diagnoses analyzed, 764 (40.1%) branched within TC of ≥4 individuals. Clusters frequently included sequences from samples collected outside of Spain, retrieved through BLAST searches at the Los Alamos HIV Sequence database. Bayesian coalescent analyses estimated the origin of 34 clusters in countries other than Spain: 11 in United Kingdom, 4 each in Romania and Argentina, 2 each in Portugal, Germany, Poland, Cuba, and Brazil, and 1 each in Thailand, Turkey, USA, Honduras, and Senegal.
Conclusion: Among new HIV-1 diagnoses in Spain, infections belonging to transmission clusters originating in other countries are frequently detected. These results indicate that, in contrast to some published studies, transnational propagation of HIV-1 clusters is relatively common.

Vulnerable groups

PE39/1

Boys having sex with boys: CD4 count as parameter to estimate the time of infection among HIV seropositive men having sex with men and its societal implications in the Philippines

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Purpose: CD4 count is a significant clinical parameter in the management of HIV, especially in staging and treatment. There is no parameter that predicts

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the time of contracting the infection. This aims to investigate the average time between testing positive for screening and time of initial infection based on rate of decay in CD4 count among seropositive MSM and to analyse its social implications.
Method: Total of 2491 MSMs who tested HIV positive were enrolled. The mean CD4 values were determined by age-groups. The mean interval between between infection and seropositivity was estimated based on the average annual CD4 decay rate. Data analysis was performed using SPSS.
Results: Upon diagnosis, the mean CD4 values were 372 cells/μL for those among those aged 20 and below, which was found to be significantly higher than 323 cells/μL for 21–30 group (p=0.007), 284 cells/μL for 31–40 group (p=0.0000), 279 cells/μL for 41–50 group (p=0.015). Thus, the significant difference among age groups and WHO CD4 staging (p< 0.000).

Average of age of diagnosis, time interval of infection, and estimated age at diagnosis

	Sample	Age at Diagnosis	Time Interval of Infection	Estimated Age at Infection
20 and below	204	19	5.8	13.2
21–30	1988	26	6.5	19.5
31–40	717	34	6.8	27.2
41–50	66	44	6.9	37.1
Above 50	5	56	5.8	50.2

The average time between infection and testing is 5.81 years among ages 20 and below and 6.49 among 21–30 age group, estimating an average infection age of 13.2 and 19.5, respectively, implicating that 73.5% of the sample likely had been infected 20 years and below.
Conclusion: Being diagnosed with a CD4 count of 200–499 cells/μL is common among all age group. It is consistent with the estimated count calculated from the average time of infection among all age groups. Three-quarters of the patients were likely to have been infected below the age of 20. It is consistent with the 8.1 person-years incidence density among 21 years and below in the 2012–2016 data from the same facility. This emphasises the need to empower the youth's and healthcare providers' positivity towards sexual health through legislation, education, and awareness.

PE39/2

Evaluating factors increasing the vulnerability of adolescent girls and young women to HIV/AIDS infection in selected communities, Akwa Ibom State

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Purpose: Adolescent girls and young women are particularly vulnerable to HIV/AIDS infection because of the risky sexual behaviour, the lack of access to accurate and personalized HIV information and prevention, and for a host of other social and economic reasons. Hence, this study identifies factors increasing vulnerability of adolescent girls and young women to HIV/AIDS infection.
Methods: A qualitative household survey was conducted through a random sampling with a a Computer Assisted Personal Interviewing to select adolescent girls and young women (13–18 and 19–24 years respectively), an HIV testing services in 3 rural communities in Akwa Ibom State, Nigeria. 350 household in each community participated. Data were collected with a questionnaire that asked information about the sources of HIV/AIDS, and sexual behaviour, self efficacy to refuse sex,and peer influence.
Results: The evaluating factors revealed that adolescent girls (especially half of the poorest girls) in Eket, Oron and Ik community of Akwa Ibom state, report that their first sexual encounter was coerced. Some of them are student, slum and street youth. This target group of adolescent and young women (ages 15–24) is highly vulnerable to HIV/AIDS infections and other sexual diseases as they have limited access to services such as HIV testing, prevention and treatment.
Conclusions: Adolescent girls and young women between the ages 15–24 are prone to the vulnerability of HIV/AIDS infection judged by the following life situations: out of school, especially very young adolescent (ages 10–14); those newly migrated to cities and in domestic service, girls acting as heads of households and pressured to earn income. Considerable data gap exist in our knowledge of HIV/AIDS among adolescent and young women, particularly because of the challenges in getting parent approval for their involvement in surveys. In parts, because of these gaps adolescent are often missing from National HIV Strategic plans.

PE39/3

Men's perspectives on HIV self-testing in sub-Saharan Africa: a systematic review and meta-synthesis

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Purpose: To synthesize evidence on men's perspectives on HIV Self-Testing in sub-Saharan Africa.
Method: The databases we searched include PubMed/MEDLINE; American Doctoral Dissertations via EBSCO host; Union Catalogue of Theses and Dissertations; SA ePublications via SABINET Online; World Cat Dissertations; Theses via OCLC; ERIC; CINAH; PsychInfo; Embase, Sociological Abstract, Scopus and Google Scholar. We search World Health Organization and The Joint United Nations Programme on HIV and AIDS. We extracted only qualitative information from the included studies, despite the research method used (qualitative or mixed methods). We used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. The Mixed Method Appraisal Tool version 2018 was used to determine the methodological quality of the included studies. NVivo version 11 was used for thematic analysis.
Results: A total of 2053 articles were identified by our initial search criteria. Only 12 articles were included to data extraction and quality assessment stage. The following key themes emerged: knowledge of HIVST; acceptability of HIVST; need for HIVST counselling; confidentiality of HIVST; convenience of HIVST; and accuracy of HIVST. The study shows that while HIVST provides men with an alternative confidential and convenient testing model, the potential for psychological and physical harm remain a challenge.
Conclusion: The introduction of HIVST strategy has a potential of improving men's uptake to HIV testing services, thereby contributing towards addressing the first cascade of the 90-90-90 strategy. While HIVST is aimed at addressing many men's barriers to attending clinic settings, such as, confidentiality and convenience, it hardly addresses the HIVST counselling and accuracy concerns. Empirical evidence on the risk-benefit analysis associated with HIVST testing strategy is still required, especially among men in Africa.

PE39/4

Molecular-biological methods of diagnostics in the investigation of the case of transmission of HIV-infection

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Purpose: Analysis of phylogenetic relationships of HIV isolates.
Method: The HIV infected blood plasma samples of 8 patients (5 women and 3 men) from Veliky Novgorod were used. The studied material is presented in two groups: clinical material from the intended source of infection (4 people, including 3 women (104 16 f,110 16 f, 112 16 f) and 1 man (109 16 m) who was the intended source of infection, then the target group), as well as clinical material from patients not known to be involved in the intended source of infection with HIV infection (4 people, including 2 women and 2 men), comparison samples. In the study we used genotyping by direct sequencing of the site of the polymerase gene (pol) length of 1285 nt., The gene encoding the protease (PR) length of 465 nt. and a portion of the reverse transcriptase (RT) gene length of 820 nt.
Conclusion: The study allows identifying HIV in clinical specimens, as well as in establishing phylogenetic relationships between virus isolates. During the epidemiological investigation of a case of HIV-1 group infection, it was determined that infection of women in the target group occurred from a single source. The results of phylogenetic analysis indicate the presence of an epidemiological link within the survey group. The unconditional commonality of HIV-1 isolates of patients of the target group and patients of the reg. № 1 14 f, previously not involved in the target group in this case. Nucleotide identity within the group was 97.25% Conclusion. Molecular phylogenetic analysis using routine methods for determining the resistance of HIV to antiretroviral drugs allows to investigate cases of HIV infection, identifying the source of infection.

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PE39/5

Implementation of demedicalized and decentralized HIV testing project in Brussels: action test, project for vulnerable populations at high HIV risk in Brussels, including Subsaharan African Migrants (SAM)

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Purpose: Facilitate access to rapid HIV testing for vulnerable populations.
Method: *Data collected from 01/2017 to 12/2018 with an anonymous electronic questionnaire during counseling.
*2 strategies used for screening: (1) inside community association office; (2) outreach bus prevention which proposes additional services like HTA and diabetes screening.
*TROD INSTI VIH1/2 was used and tests were offered by trained lay-providers.
*Descriptive analysis performed with Epi-info version 7.2.2.2.
Results: 835 people received HIV testing and 12% of them were MSM.
Overall, 73% are male, 50% are SAM and the median age is 32 years.
24% people don't have insurance coverage, among which 27% of them are not documented and 58% refused to give their administrative status.
9 including 5 men and 4 women, had a reactive screening result. Only two men received a confirmatory laboratory testing and three women were already known to be HIV positive.
62% had never been tested for HIV and 51% have done the test because they found a near opportunity for testing.
Among reasons evoked for testing, there is a significant difference between places of testing with more risks taken (24%) when it was at the office (24%) and more opportunity based in the bus (68%)
87% had unprotected sex with casual partner in the last years.
PEP and PrEP knowledge was low (15% and 11.6%).
Conclusion: Findings from this project indicate that offering rapid HIV testing in community settings, in particular through outreach activities, is an effective approach to increase access to testing and to reach previously untested vulnerable populations. To increase the acceptance of HIV testing, it is important to offer HIV testing along screening for other chronic diseases such as HTA, diabetis, etc. . .
A combination of testing on site and outreach activities should be promoted as both strategies reach different risk profiles of people.

Sociodemographic characteristics

	1. Association		2. Bus		Total		
	n	%	n	%	N	%	p value
median age (min-max)	32 (17–71)		32 (16–70)		32 (16–71)		
no health insurance	433	29%	259	17%	692	24%	<0.001
origin SAM	465	51%	361	48%	826	50%	
gender (male)	467	76%	364	70%	831	73%	0.036

Risk profile and awareness

	1. Association		2. Bus		Total		
	n	%	n	%	N	%	p value
never testing for HIV before	453	63%	288	61%	741	62%	0.69
had unprotected sex with casual patner	207	86%	96	89%	303	87%	0.75
MSM	349	11%	249	13%	598	12%	0.32
reason for testing	465		247		712		
risk taken		24%		10%		19%	<0.001
opportunity		41%		68%		51%	<0.001
other reason		35%		22%		30%	<0.001
know what PrEP is	254	11%	91	14%	345	12%	0.46

PE39/6

HIV prevalence, risk-taking behavior and self-testing potential among men who have sex with men and transgender people

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Purpose: Acceptability of oral self-testing among MSM and TG in five Russian cities.
Method: Quantitative and qualitative data collection was conducted from December 2016 to February 2018 as part of a campaign for free of charge HIV self-testing among MSM and TG in five Russian citiesl. As part of the project, all the MSM and TG who wanted had a chance to receive OraQuick express testing kits for HIV on condition of anonymity. The study presents an analysis of quantitative data collected as part of the project on HIV self-testing among MSM and TG in Russia. When interpreting the quantitative indicators, we also relied on the data of in-depth interviews with those who self-tested as part of the project.
Results: In the three years of the project, almost 24,000 people in five cities received self-testing kits, which indicates a high demand for alternative HIV testing methods in these groups. Out of 3,003 people who informed us of the self-test results, 14% received a reactive result, which corresponds to the percentages given in similar studies in the Russian conditions.
Conclusion: Self-testing for HIV has already proven itself as an accurate and reliable tool with high acceptability among MSM and TG, and its potential to encourage first-time and repeated testing even in highly stigmatized settings is underlined by multiple research. In our research, we asked MSM and TG about their previous testing. As it turned out, self-testing was the first ever HIV test for 13% of the research participants and one out of five had not tested for over a year before the project's self-test. These facts, combined with general demand for self-testing we saw in the project, show high efficiency of the self-testing approach that can help to expand coverage and increase the frequency of HIV testing among MSM/TG in Russia.

PE39/7

Political commitment matters in the elimination of the threat of HIV and HCV and TB among people who use drugs

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Purpose: Eleven years to reach the 2030 SDGs, infectious diseases are still serious health threat, with 71.1 million people living with chronic hepatitis C (1) and 36.9 million people living with HIV/AIDS (2). Higher mortalities and transmission rates are concentrated among key subpopulations such as drug users who, in many geographical settings, lack basic rights to health care (3–6). Despite the efforts, many people around the world continue to use drugs. Harm reduction strategies prove to be cost effective at reducing negative consequences associated with the use of drugs in people unable or unwilling to stop (7). Notwithstanding, harm reduction exists in only half of total countries in the world, whereas prevalence of HCV and HIV are still high among drug users if compared with general populations (3).
Method: Considering the role of parliamentarians to eliminate infectious diseases within this population, UNITE has taken action and organized the *Joint Action Policy Day 2019* entitled *Road to 2030: Concrete Actions to Scale up Human Rights-based approaches to Harm Reduction,*attended by 184 participants coming from 30 countries, across 5 continents: 15 parliamentarians, 37 community organizations, 12 donors, 22 government and law firms, and 8 scientists. Case-examples from Portugal, China, West Africa, France, Brazil and the US were discussed.
Results: Participants agreed that: good policies that are effectively implemented are needed to assure human rights-grounded services for people using drugs. Proved to be cost-effective, accessible harm reduction services that are human-centered, without causing financial hardship, have the potential to reduce the burden of Hepatitis C, HIV/AIDS and TB among people using drugs.
Conclusion: Recommendations include the following: drug use decriminalization, human rights-based approaches, community grounded outreach and peer support, prison health as public health, quality evidence and M&A, Universal Health Coverage, sustainable financing, new partnerships, and political will and leadership.

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PE39/8

Challeges in health and social care for migrant HIV patients in the Czech Republic

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Purpose: In the Czech Republic, about 30% of all HIV-positive persons are citizens of other EU and non-EU countries. However, needs of this group are not reflected in any governmental strategy or program. Our purpose was to identify challenges in health and social care for HIV-positive migrants and EU mobile citizens in the Czech Republic from the providers' perspective.
Method: A web-based questionnaire has been distributed among health care (hospitals, relevant outpatient facilities) and social service providers (NGOs assisting migrants, HIV positive persons or working with other vulnerable groups with higher HIV risk – drug users, sex workers). The survey included questions regarding barriers on different levels which providers of health or social services face while working with patients with HIV or other STIs who are not Czech citizens.
Results: At present, we received 48 responses (60.4% healthcare workers, 27.1% social workers). Based on our data, 51.2% of respondents have clients with HIV/STIs who are nationals of other countries and more than half of respondents (53.8%) find that services currently available for these clients are insufficient. The main barriers are: lack of information, discrimination in access to treatment, poor availability of free anonymous testing, language barrier, low adherence to treatment. As a key reason, 65.4% of respondents see the lack of coherence of the health and social care, 61.5% – the lack of attention from the state (no prevention and treatment programs) and 53.8% mentions the lack of finances. From other perspective, 53.8% of respondents claim that migrants underutilize existing (especially social) services.
Conclusion: According to this, first in our country, survey among providers of health and social services, there is a number of legal, institutional and individual barriers in access of migrants and EU mobile citizens living in the Czech Republic to HIV testing and treatment.

PE39/9

Integration of hepatitis C cure in housing facility Soleil Evant: health cost implications

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Purpose: The Soleil Levant is a psycho-social-medical housing foundation providing healthcare services to multimorbid and vulnerable adults with infectious diseases (HIV, viral hepatitis) as well as other chronic conditions associated with psychosocial disorders and/or addiction problems. http://www.levant.ch/soleil-levant.
Nurses and social workers are core care givers with weekly psychiatric, medical and physiotherapy interventions. A tight collaboration with the local pharmacy team allows treatment updates as needed. From 2017 treatment classes and cost monitoring are part of the annual quality care assessment.
Methods: Analysis of treatment classes and their cost due to medical management of residents from Soleil Levant between 2017 and 2018 based on annual pharmacist' reports.
Results: Overall, main health problems included HIV infection or AIDS defining criteria, chronic hepatitis C, social precariousness and chronic illness (cirrhosis, diabetes, renal failure, cancer, physical handicap, etc.) and recovery from addiction and/or psychiatric comorbidity. In summary 15 residents were followed during the 2 years period with an average age of 53 years. The main five treatment classes according to cost impact were DAAs/HIV antiretroviral (55%), opioid pain relievers (6%), opioid substitution (3%), antiepileptic drugs (~2%) and neuroleptics (~2%).
Conclusion: Chronic hepatitis C treatment with SVR-6 and HIV co-infection therapy represented half of the total pharmacy expenses for all residents during 2017–2018 and concerned one third of patients. DAA treatment was easily integrated in Soleil Levant housing facility and achieved hepatitis C cure in multimorbid patients.

PE39/10

The role of sexual partners of people who inject drugs in better uptake of retention in HIV services

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Background: PWIDs remain most vulnerable population in Georgia. Heterosexual transmission rate of HIV is increasing continuously during recent years and became the dominant 63% among new HIV registered cases, while IDU associated transmission decreased from 43% (2012) till 15% in 2017. 14 Harm reduction sites have been providing comprehensive services to 30,000 PWIDs annually within the GFATM-program since 2006. From 2016 the program covers sex partners of PWIDs with HIV prevention services to support safer behavior. Majority of sex partners of PWIDs (90–92%) are women.
Methods: The qualitative research methods were applied to identify attitudes, motivations and needs, barriers and facilitators and services needed for sex partners. The convenience sampling method was used to recruit PWIDs, sex partners and harm reduction service providers. The study was provided in 5 cities of Georgia.
Results: The following barriers were revealed for sex partners of PWIDs: fear of HIV testing and associated stigma; Low awareness of HIV transmission risks and importance of testing; PWIDs don't allow their sex partners to be tested on HIV; Low awareness about anonymous free HIV testing services; Feeling of shame to do HIV-testing, especially in small cities; Lack of women oriented services at harm reduction sites; Negative approach towards PWIDs from society and criminalization of drug consumption. The needed services were free HIV and HCV testing; medical consultations and referral to free treatment (HIV, HCV, Syphilis, TB, reproductive healthcare) programs.
Conclusions: More efforts are needed to address the barriers revealed by this study. Harm reduction program personnel should increase motivation of sex partners to do HIV testing; Risk counseling of couples should be enhanced for decreasing HIV associated risks and better utilization of harm reduction services; Besides, women oriented services should be developed and adjusted to needs of sex partners for better uptake of HIV Services of PWIDs.

PE39/11

Male sex workers and ICT: anthropological approach of male sex workers and the different practices online: bareback, PrEP and chemsex

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Purpose: PrEP, bareback, chemsex, are now firmly part of strategies gay and MSM men use in their sexual interactions/socialization in much of Europe.This was an exploratory study to assess the impact on working practices that bareback, chemsex, PrEP, have had on MSM sex workers, utilizing websites (such Hunqz, Rent.men, etc.) and mobile applications (Grindr, Scruff, etc.) to contact and interact with clients.
Method: Between February 2017/March 2019 these issues were discussed with 600 plus sex workers. This involved four face to face interviews with 10 different persons, 2 sex worker facebook groups (one of 536 and one of 71 people) created by and for sex workers. Issues explored were sex workers perception and using of PrEP, the frequency of requests for bareback services, and chemsex, as well as more generally how sex workers viewed. The use of mobile and internet platforms as good ways to offer services.
Results: Almost all of the sex workers participating in the research had experienced impacts upon their ability to successfully negotiate, maintain, and control the services they provided to clients.Often clients knowledge of PrEP and its availability was used to pressurize the workers into barebacking when they were not comfortable with this .
The availability and offers of 'chemsex' being provided by clients was also used to pressurize workers into sessions were it was difficult for workers to maintain the boundaries they felt were appropriate.
Conclusion: Specific interventions need to be in place for those using mobile and internet based platforms for sex work – to improve negotiation skills for sex workers, as well as to educate (as is always necessary) clients about the rights of sex workers in deciding upon the services they offer free from coercion.

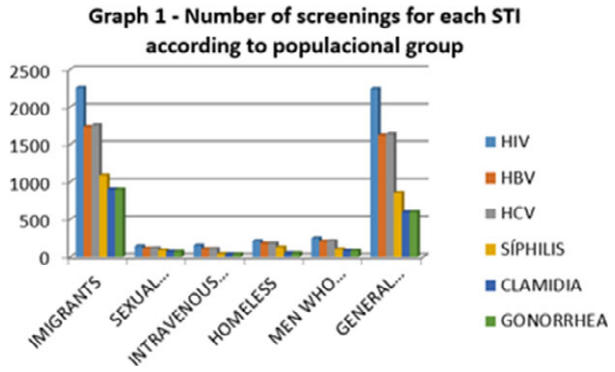
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PE39/12

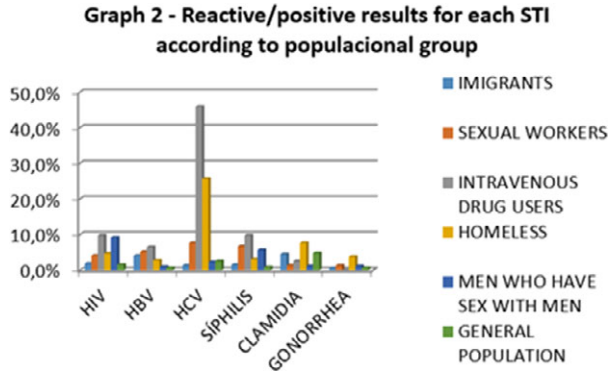
Portuguese League Against AIDS – mobile screening unit

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Purpose: The Mobile Screening Unit aims to facilitate access to testing, counseling, diagnosis, care and treatment of HIV and other Sexually Transmitted Infections (STI). The use of a MSU allows greater accessibility of populations enabling interventions in specific social and cultural contexts, particularly *vulnerable and most at risk populations* [sex workers and their clients, Man who have Sex with Men (MSM), intravenous drug users, migrants and homeless people]. The MSU offers free, voluntary, confidential STI screening services throughout Lisbon, Loures and Odivelas closely linked to local structures and health care services.
Method: The MSU has two mediators, a clinical psychologist, a doctor and a nurse. The mediators approach vulnerable populations, the psychologist conducts a survey to each patient collecting demographic information, sexual behavior data and to advise on healthier behaviours, the nurse performs the screenings and the doctor is responsible for STI appointments.
The sample for this analysis was collected from October 2014 to June 2019, in a total of 5334 screenings
Results:



Graph 1 shows the amount of screenings by population tested (2272 screenings were made to General Population, 2282 to Immigrants, 159 to Sex Workers, 156 to Drug Users, 220 to Homeless People and 253 MSM).



Graph 2 shows that the highest percentage of reactive/positive results are from Drug Users, followed by Homeless, both often diagnosed with HVC. The highest percentage of new cases of HIV is diagnosed on Drug Users and MSM.
Conclusion: Taking into account the results obtained (high prevalence of some STI), the good adhesion of the population and the close cooperation with the social partners and community structures, this type of strategy, in situations of outreach and proximity is an asset, as it facilitates access to vulnerable populations with high risk sexual behavior and in whom HIV and other STI screenings were never performed.

PE39/13

Detectable viraemia in the era of successful antiretroviral therapy; engagement with multi-disciplinary services

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Objectives: People living with HIV (PLWH) not willing to start and those on antiretroviral therapy (ART) who fail to suppress their viral load may require additional support. The aim of this study is to determine current utilisation of in-house support structures to facilitate uptake and adherence to ART.
Methods: Individuals attending a large urban HIV clinic June 2018-May 2019, diagnosed >1 year with at least one viral load>200 copies/mL regardless of ART status were included. Characteristics at time of detectable viral load were summarised. A notes review of a random subset of 30 individuals was conducted to assess need for additional support services; whether referral to services was offered, and patient uptake.
Results: Of 3184 people seen between June 2018-May 2019, 124(3.9%) ever had a viral load>200 copies/mL (median VL 5189 copies/mL); 47 (38%) female, 75 (60%) gay/bisexual men; median age 49 years. The majority (103/124, 83.1%) were receiving ART and 45 (21%) ever had an AIDS-defining illness. One or more in-house support services had been accessed by 89 (70%); 59 (48%) engaged with psychology/psychiatry services. The needs and usage of support services are shown in the Table 1.
Case note review indicated that all 30 individuals required support, predominately adherence support (80%) and psychological support (47%). Less than half (46%) were offered adherence support with 27% of those referred attending and 71% offered psychological support with 70% uptake.
Conclusions: Our findings indicate a requirement for support needs to be better identified and use of support services promoted to facilitate engagement if viral suppression is to be achieved for all.

Table 1. Documented need, linkage to and use of support services for individuals with detectable viraemia (n=30)

Support type	Need identified and documented	Service Offered	Support service uptake
Peer	1 (3%)	1 (100%)	0 (0%)
Adherence	24 (80%)	11 (46%)	3 (27%)
Assistance with transport (cost o arrangement)	1 (3%)	1 (100%)	1 (100%)
Psychological	14 (47%)	10 (71%)	7 (70%)
Psychiatric	7 (23%)	7 (100%)	5 (71%)
Drug and alcohol	9 (30%)	6 (67%)	2 (33%)
Support re housing, benefits or immigration	10 (30%)	9 (90%)	6 (67%)
Community Nursing	6 (20%)	6 (100%)	5 (83%)

PE39/14

Optimal HIV self-testing, potential strategies to increase HIV diagnosis in Tanzania

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Background: In Tanzania the testing gaps still remain large. An implementation science for HIVST was conducted since -May 2018 targeting KVP in 10 regions out of 26 regions in Tanzania. The objective was to understand uptake, acceptability of HIVST and linkage to other HIV services.
Methodology: HIVST is implemented by the Ministry of Health as demonstration project in collaboration with PEPFAR/T community partners. Oraquick kits were used and distributed to study participants in three modalities, assisted, unassisted. Three kits were provided to clients, one for him/herself, a sexual partner and their peers. A training package was

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developed, sensitization package and training of health care workers and peers from identified communities. By end of June 2019 a total of 17,692 kits were distributed.

Results: Two third of the clients opted unassisted approach of using the kits. The uptake was higher among female than males. The target population groups received kits are FSWs, PWID, MSM and AGYW. FSWs followed by PWID are the leading groups. In both cases the unassisted approach of using kits is more preferred by clients, except for PWID which shows that most opted the directly assisted approach. The proportion of primary and secondary distribution of kits is almost the same. Proportion of the kits' results returned is 64% with a positivity rate of 3% and 66% linkage to care. Among the FSW, ¾ of the clients opted to use HIVST kits for their own testing. Assisted approach was opted by 2/3 of clients in primary/direct distributed category. Among population types, 51% of kits were distributed to FSWs. 51% of all kits were taken up by FSWs.

Conclusion: Generally, we see higher yield among unassisted compared to directly assisted method. It is very possible that the higher yield among unassisted method reflects higher self-risk self-perception among these clients.

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