ART for HIV Prevention

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Global summary of the AIDS epidemic | 2012

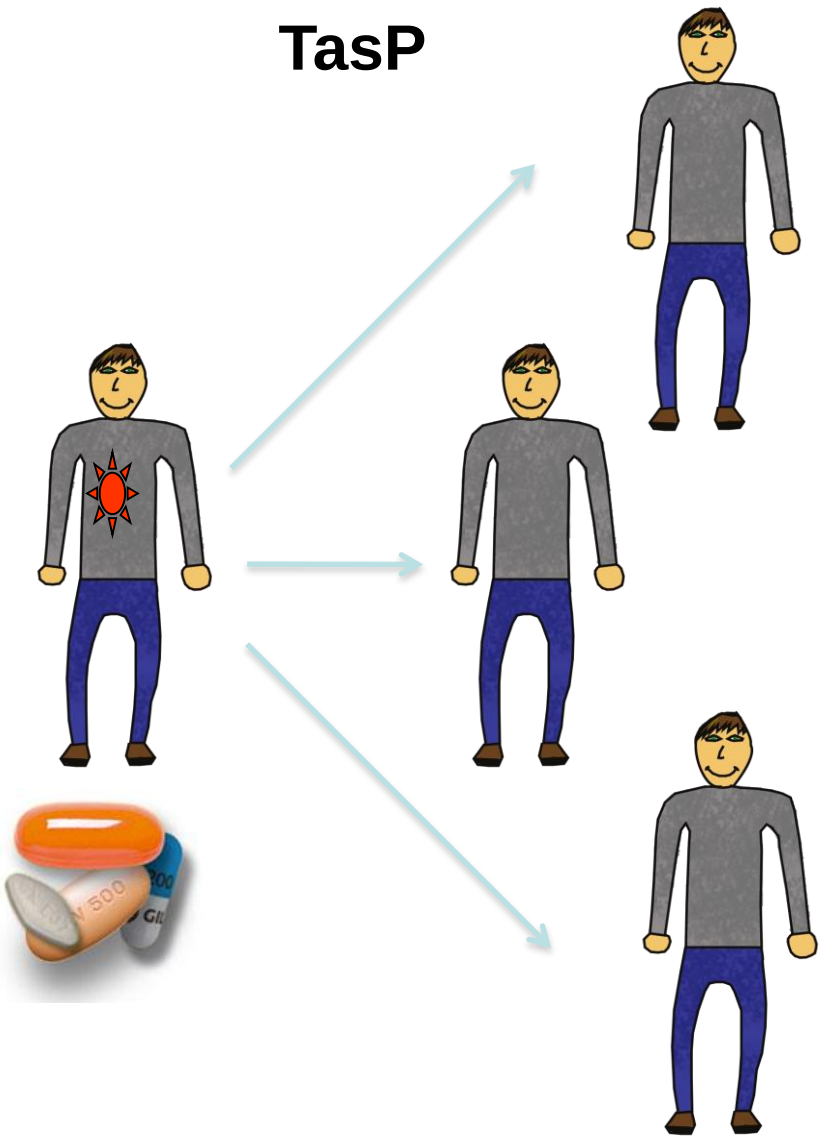
Number of people living with HIV	Total	35.3 million [32.2 million – 38.8 million]
	Adults	32.1 million [29.1 million – 35.3 million]
	Women	17.7 million [16.4 million – 19.3 million]
	Children (<15 years)	3.3 million [3.0 million – 3.7 million]
People newly infected with HIV in 2012	Total	2.3 million [1.9 million – 2.7 million]
	Adults	2.0 million [1.7 million – 2.4 million]
	Children (<15 years)	260 000 [230 000 – 320 000]
AIDS deaths in 2012	Total	1.6 million [1.4 million – 1.9 million]
	Adults	1.4 million [1.2 million – 1.7 million]
	Children (<15 years)	210 000 [190 000 – 250 000]

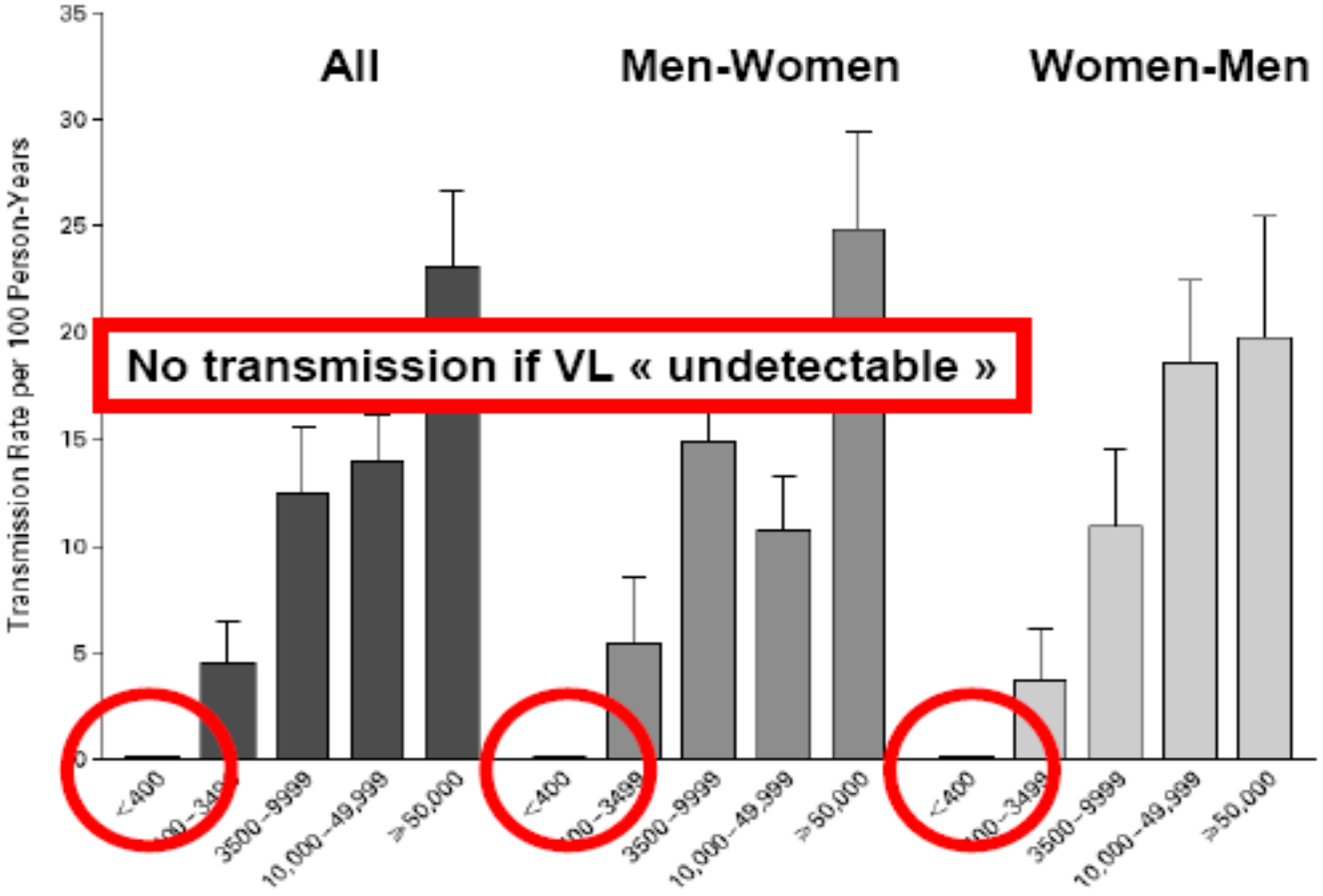
World Health Organization

UNAIDS

Treatment as Prevention

TasP

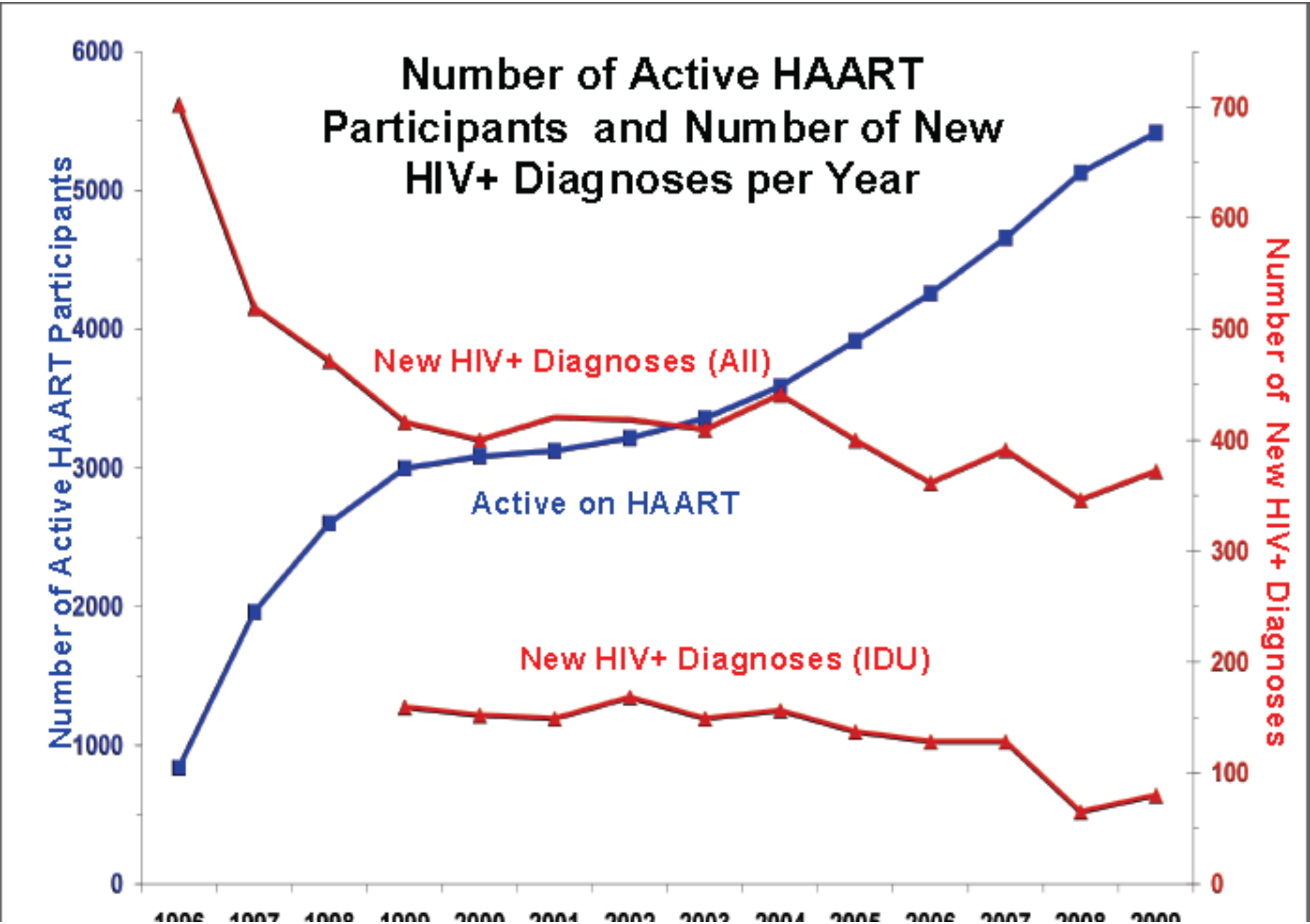




« Rakai » Study: Transmission risk as a function of viral load

Quinn et al. N Engl J Med 2000;342:921-9

Thai Study: no transmissions < 1049; Tovanabutra, JAIDS 2002


Number of Active HAART Participants and Number of New HIV+ Diagnoses per Year
Number of Active HAART Participants
Number of New HIV+ Diagnoses
6000
5000
4000
3000
2000
1000
0
700
600
500
400
300
200
100
0
New HIV+ Diagnoses (All)
Active on HAART
New HIV+ Diagnoses (IDU)

HPTN 052

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Multicenter, international, randomized, NIH-funded Phase III study

HIV serodiscordant adult couples
ART-naïve, HIV-infected partner
CD4 between 350-550
N=1,763 couples

HIV infected partner: 50% male

Early Arm (n=886)
Start ART when
CD4 between 350-550

Delayed Arm (n=877)
Start ART when
CD4 ≤250 or AIDS diagnosis

Primary Clinical Endpoint (in HIV-positive partner)

- Clinical Event: Pulmonary tuberculosis, severe bacterial infection, a World Health Organization stage 4 event, or death

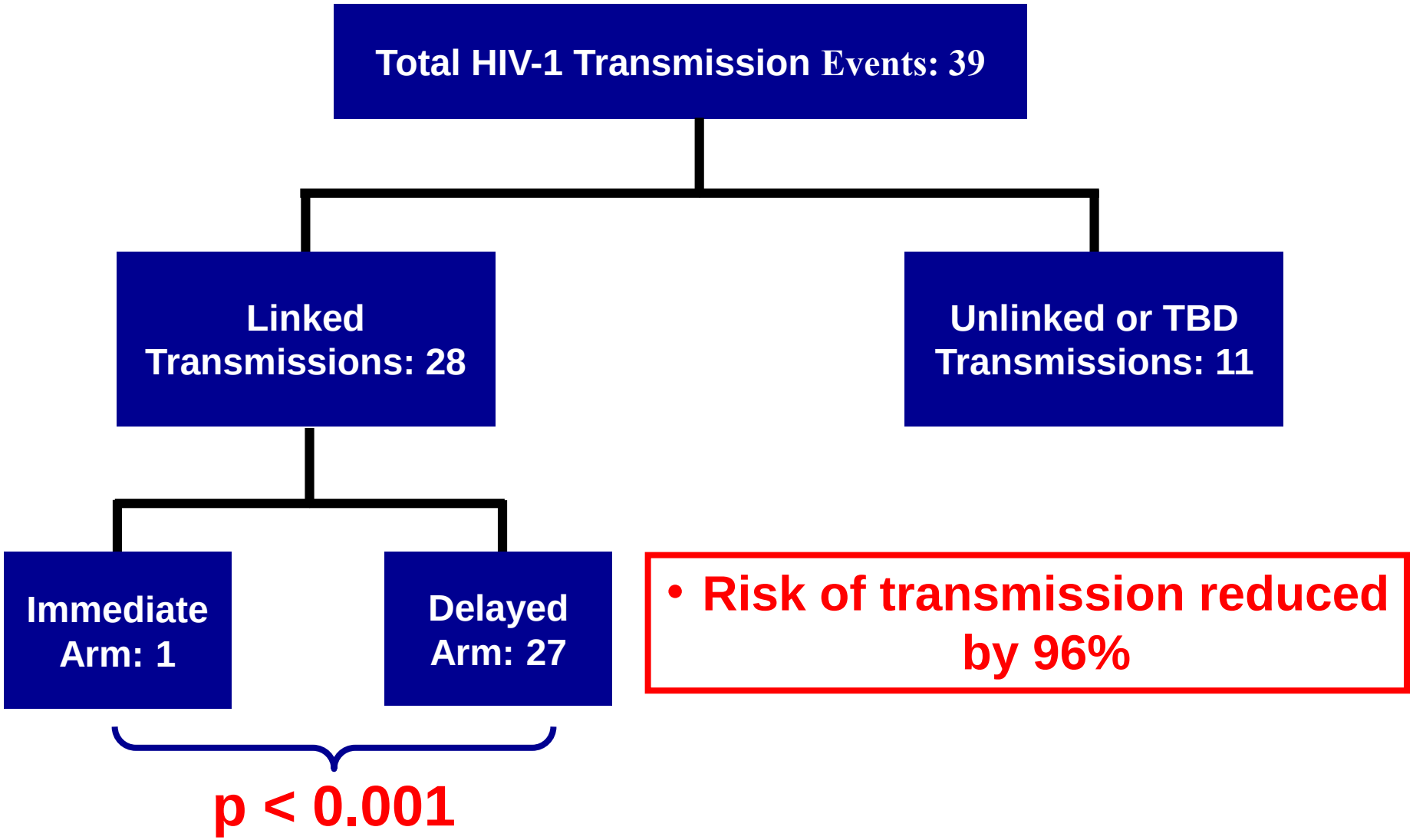
Primary Prevention Endpoint (in HIV-negative partner)

- Linked HIV transmission to HIV-1 negative partners

DSMB recommended study be stopped early on 28th April 2011

Adapted from Cohen MS, et al. N Engl J Med 2011;10.1056
Cohen M, et al. IAS 2011; Rome. Oral #MOSY0302
Grinsztejn B, et al. IAS 2011; Rome. Oral #MOSY0305
HPTN Study 052 Fact Sheet. Available at: http://www.hptn.org/web%20documents/IndexDocs/HPTN052FactSheet19Jul2011.pdf. Accessed 04 August 2011

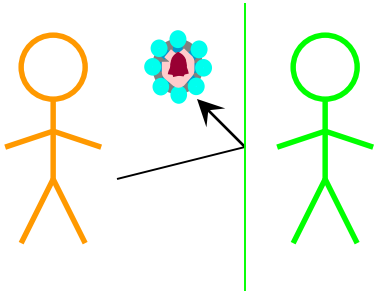
HPTN 052: HIV-1 Transmission



- **Risk of transmission reduced by 96%**

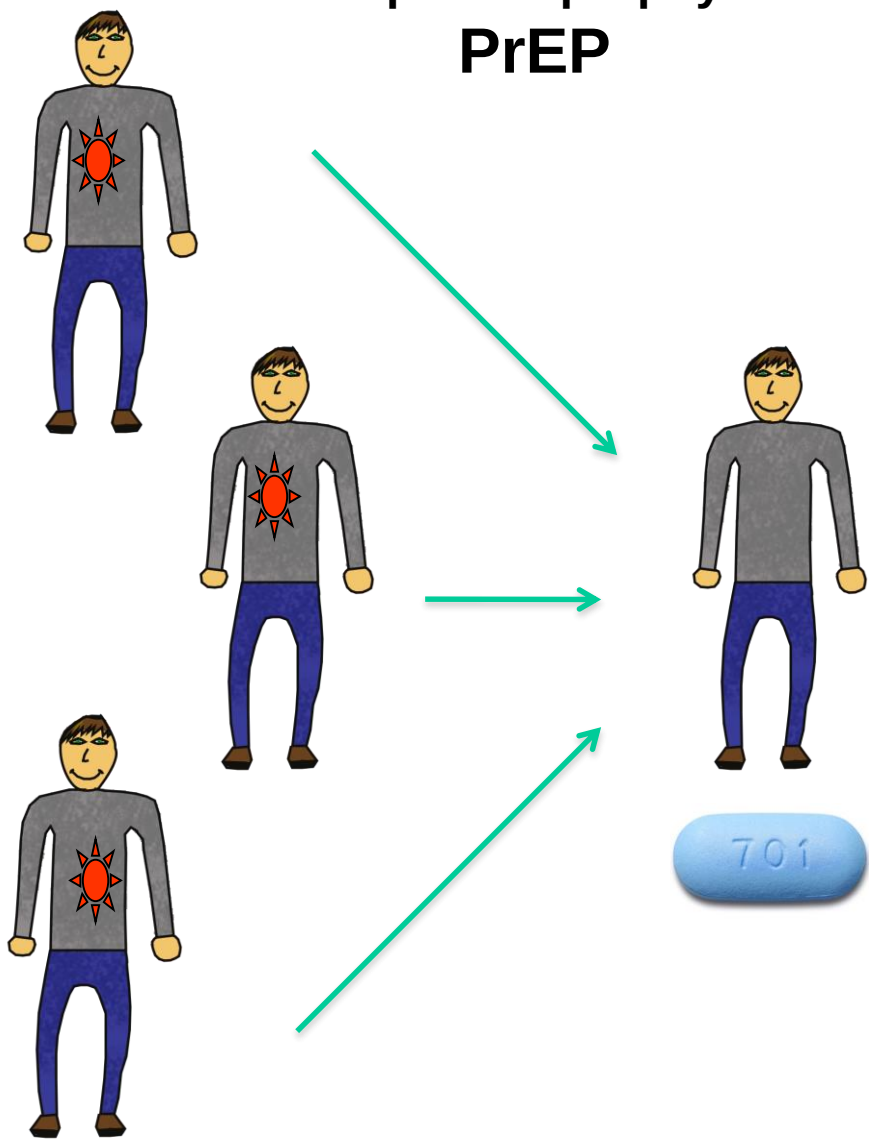
Pre-exposure prophylaxis (PrEP) for HIV prevention: the hypothesis

- Using an antiretroviral ahead of an HIV exposure (*i.e., PrEP*) will reduce the risk of becoming infected.
- In some ways, analogous to malaria prophylaxis for travelers
  - does not block exposure but may block pathogen
  - use is potentially time-limited



Pre-exposure prophylaxis

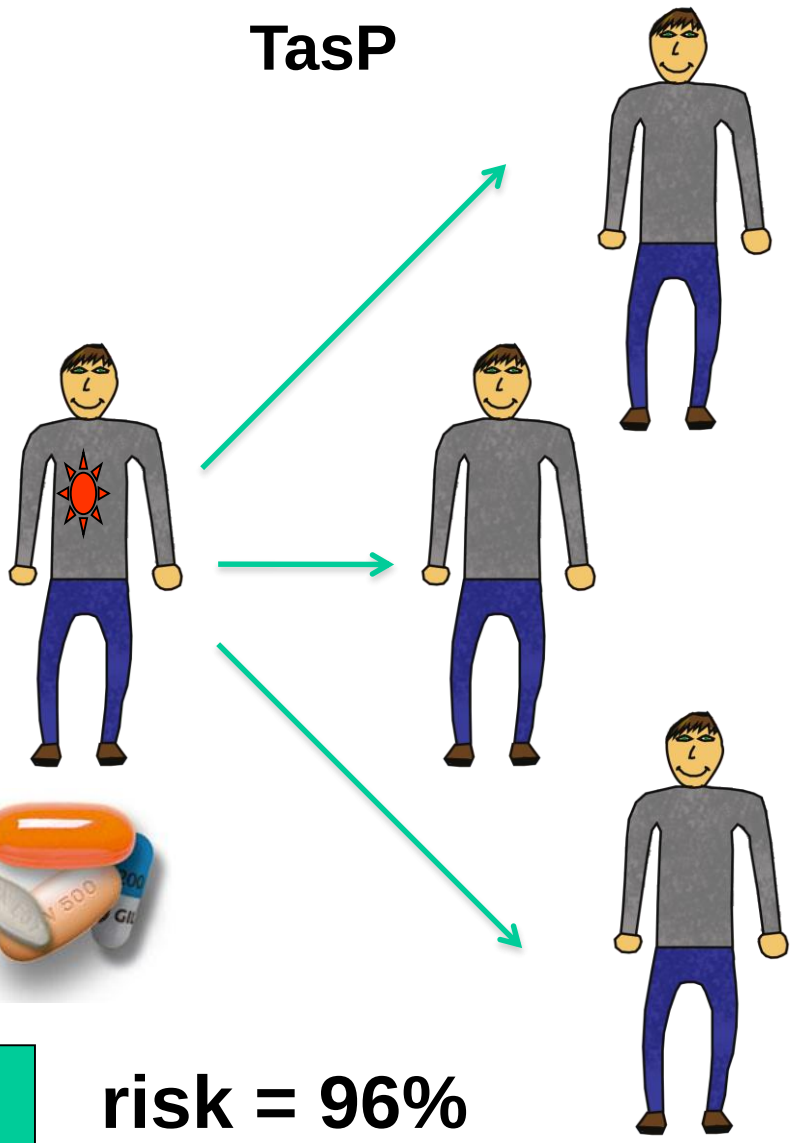
PrEP



Why use PrEP if TasP is so effective?

Treatment as Prevention

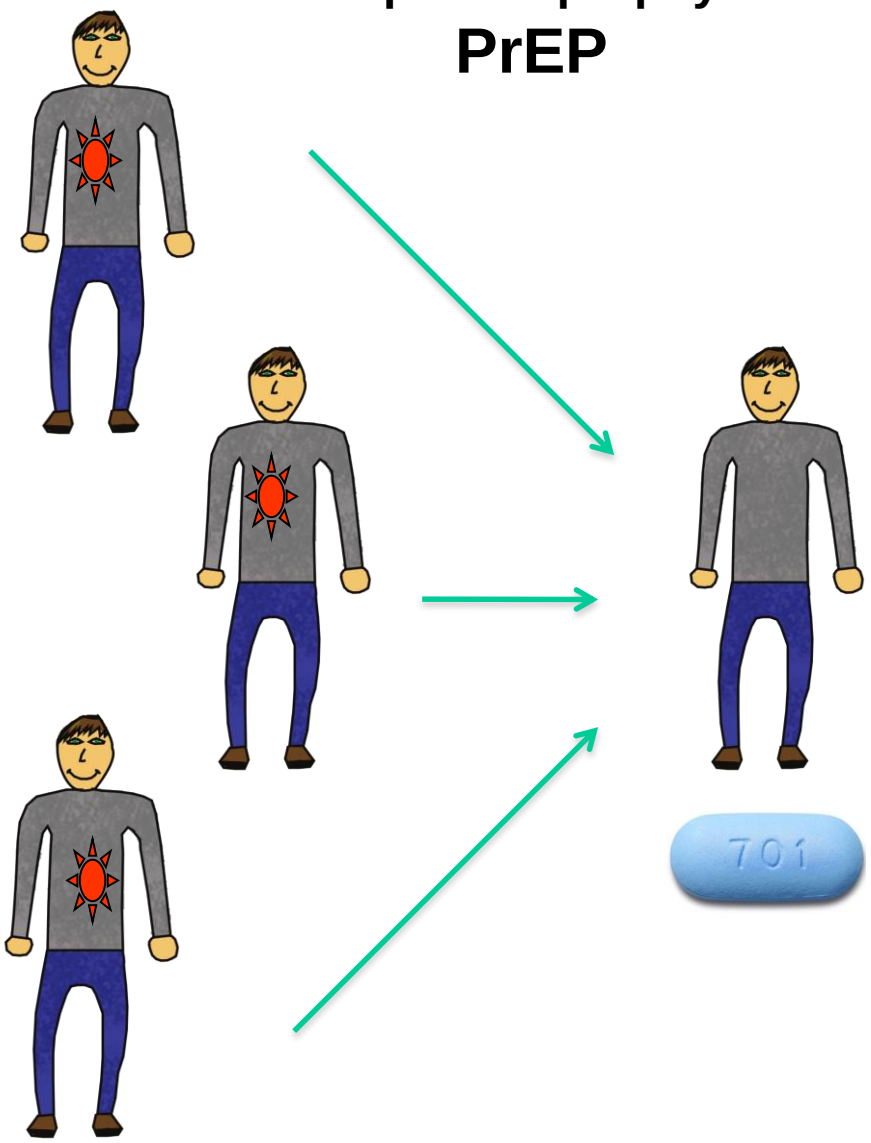
TasP



risk = 96%

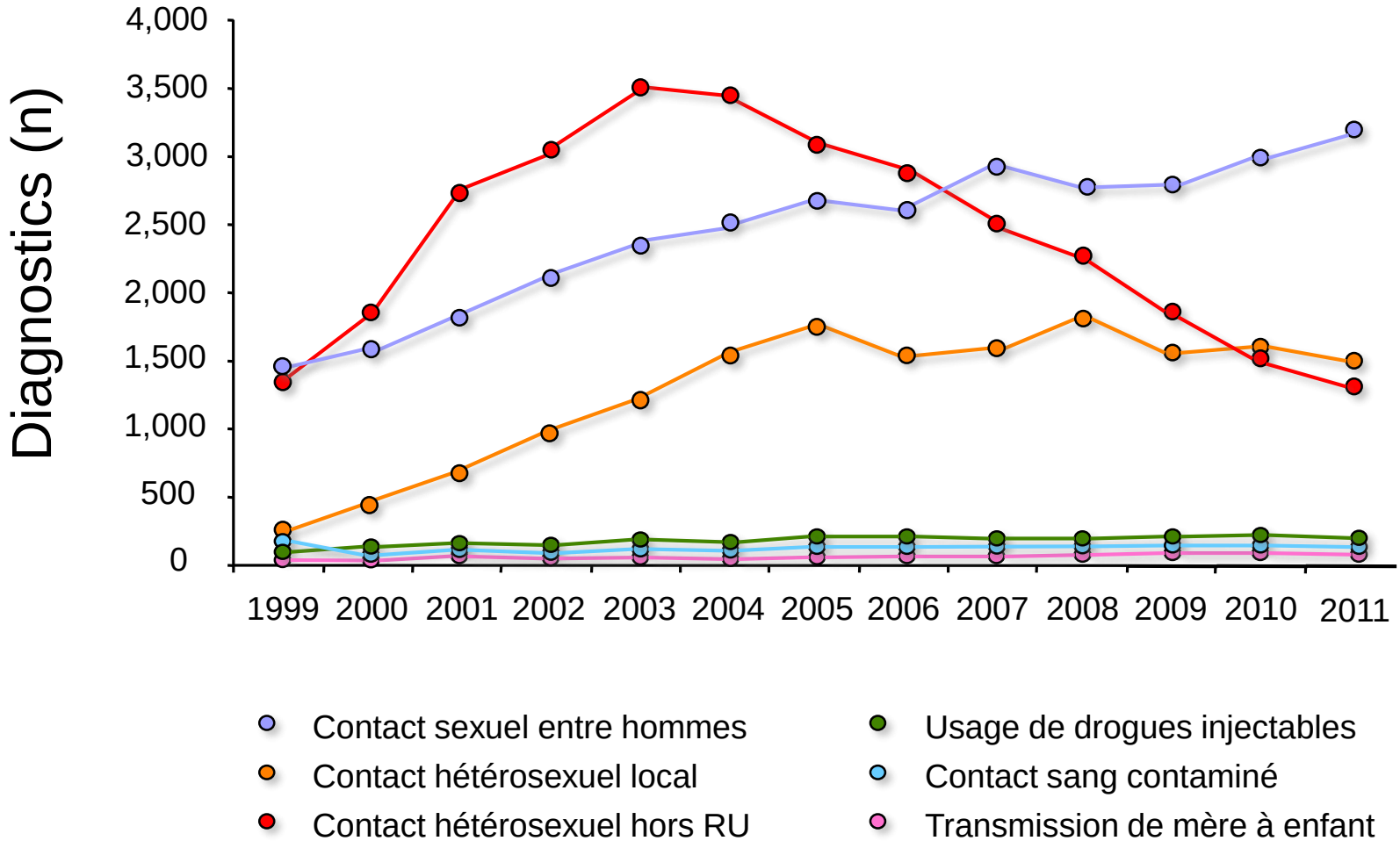
Pre-exposure prophylaxis

PrEP



Limitations of TasP

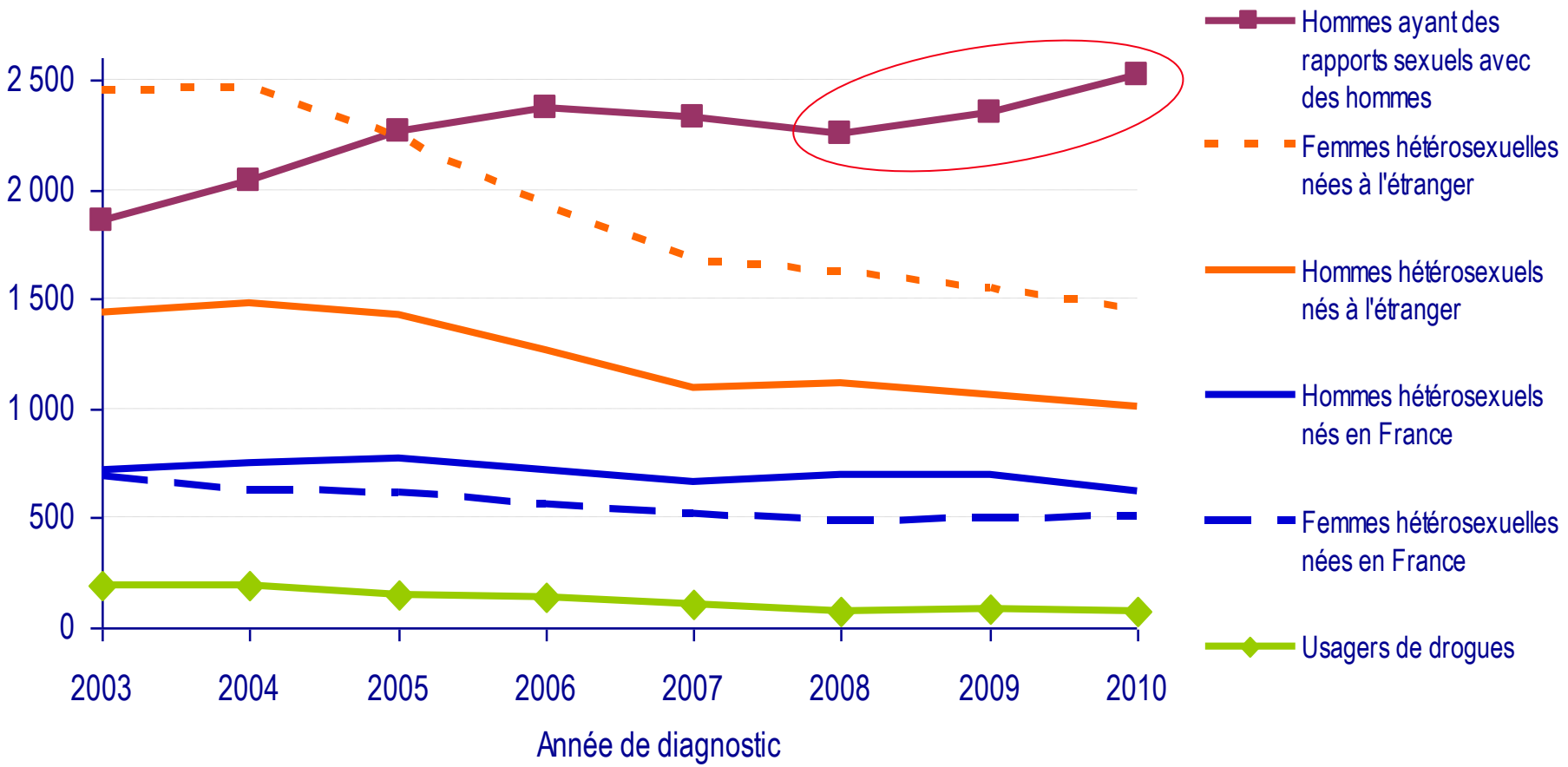
HIV incidence in the UK



Public Health England; 2012 Report

Quelles sont les personnes diagnostiquées pour le VIH en France?

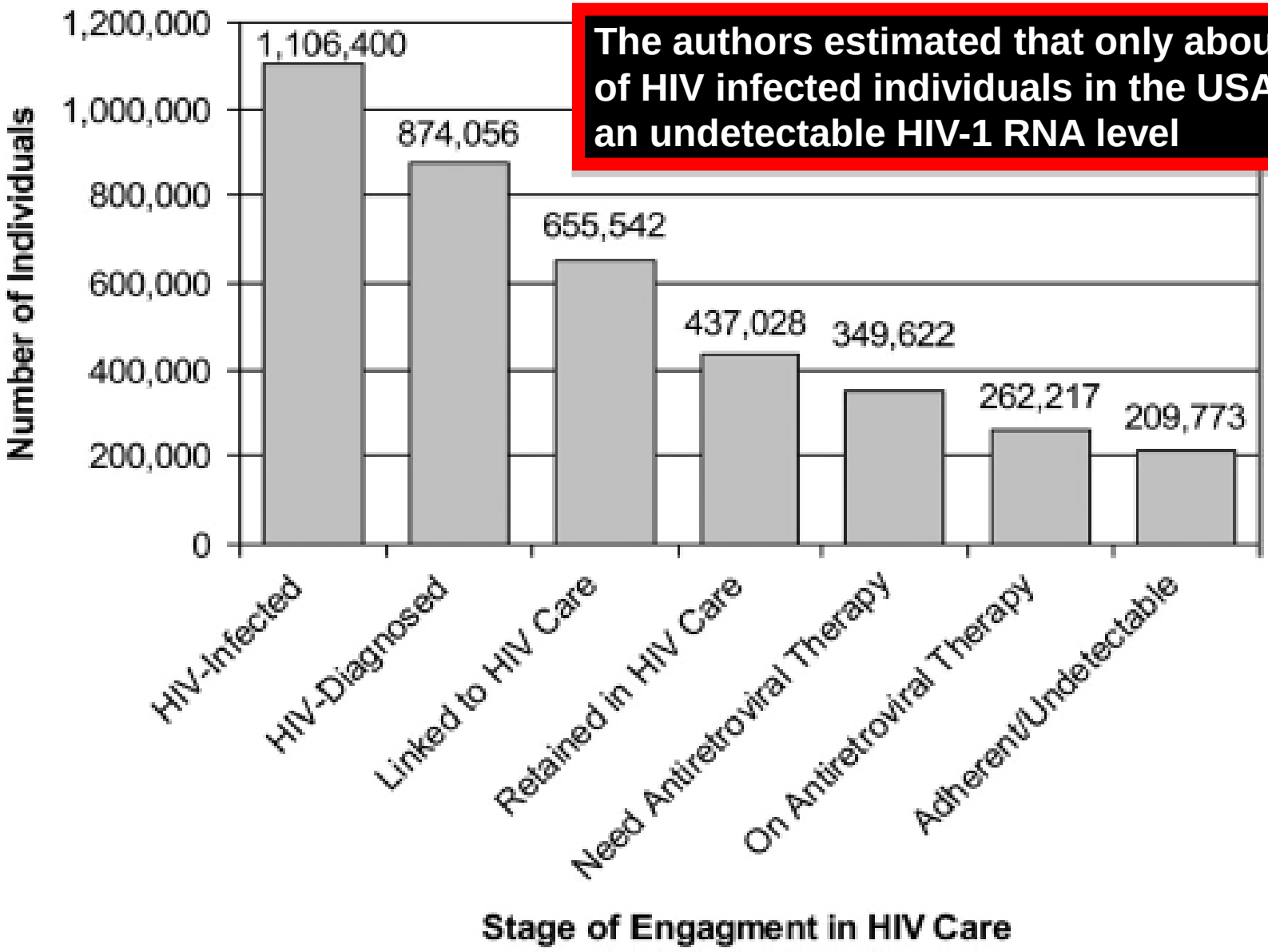
Augmentation des découvertes chez les homosexuels alors que les autres groupes sont stables



Source : InVS, données DO VIH au 31/12/2010 corrigées pour les délais, la sous déclaration et les valeurs manquantes

INSTITUT DE VEILLE SANITAIRE

Spectrum of Engagement in HIV Care - USA



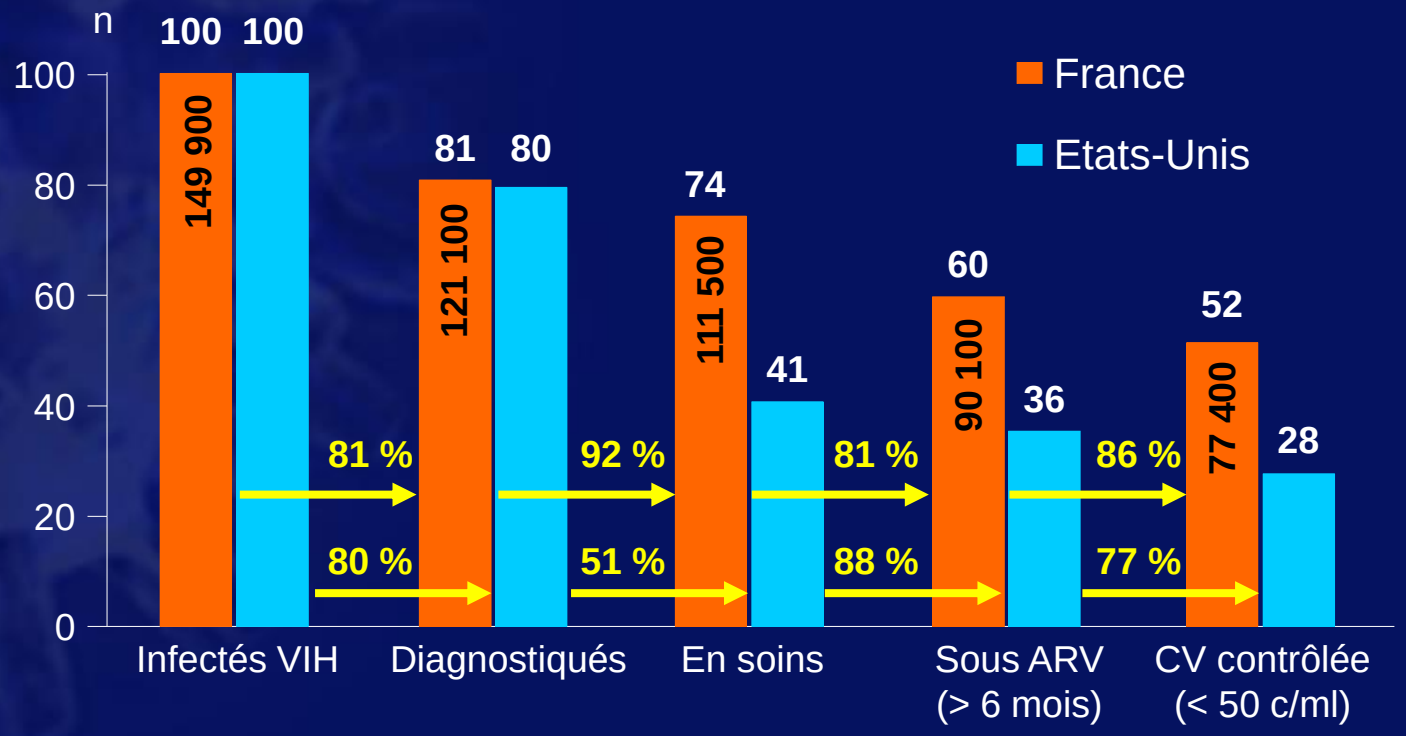
Gardner E, McLees M, Steiner J, del Rio C, Burman W, Clin Infect Dis. (2011) 52 (6): 793-800

le meilleur ...de la CROI 2013

Cascade de la prise en charge en France en 2010 (1)

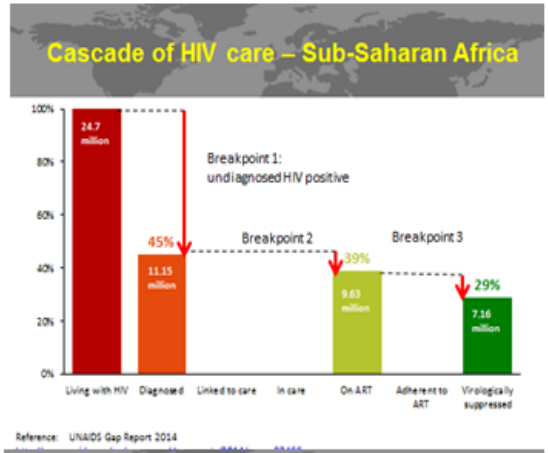
- Estimation du nombre et du pourcentage des personnes VIH+ engagées dans les différentes étapes des soins, à partir de :
  - Déclarations de nouvelles séroposivités (INVS)
  - Données de l'assurance maladie (CNAMTS)
  - Cohorte hospitalière française (FHDH – ANRS CO4)
- Comparaison avec données Etats-Unis *(Cohen SM, MMWR 2011,60:1618-23)*

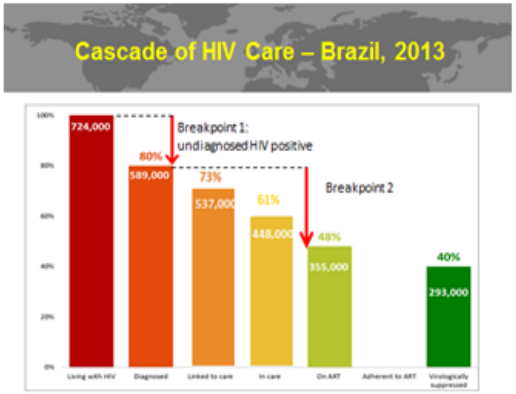
Cascade en France vs Etats-Unis

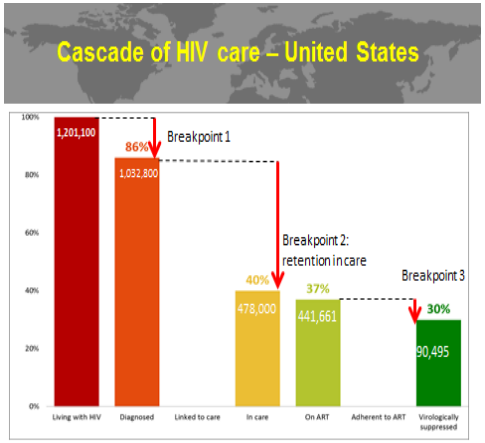


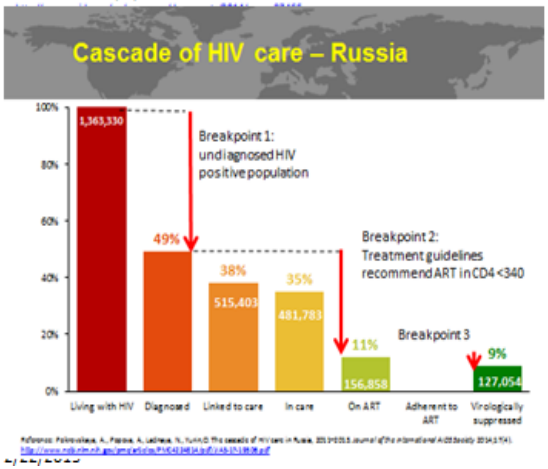
Supervie V, CROI 2013, Abs. 1030

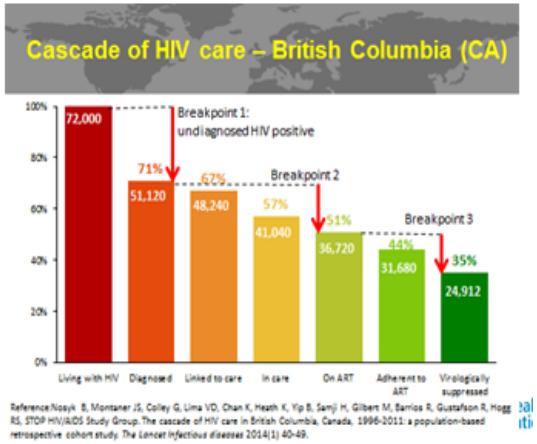
Même dans les contextes avec une bonne couverture du traitement antirétroviral, les cascades de traitement montrent des fuites importantes







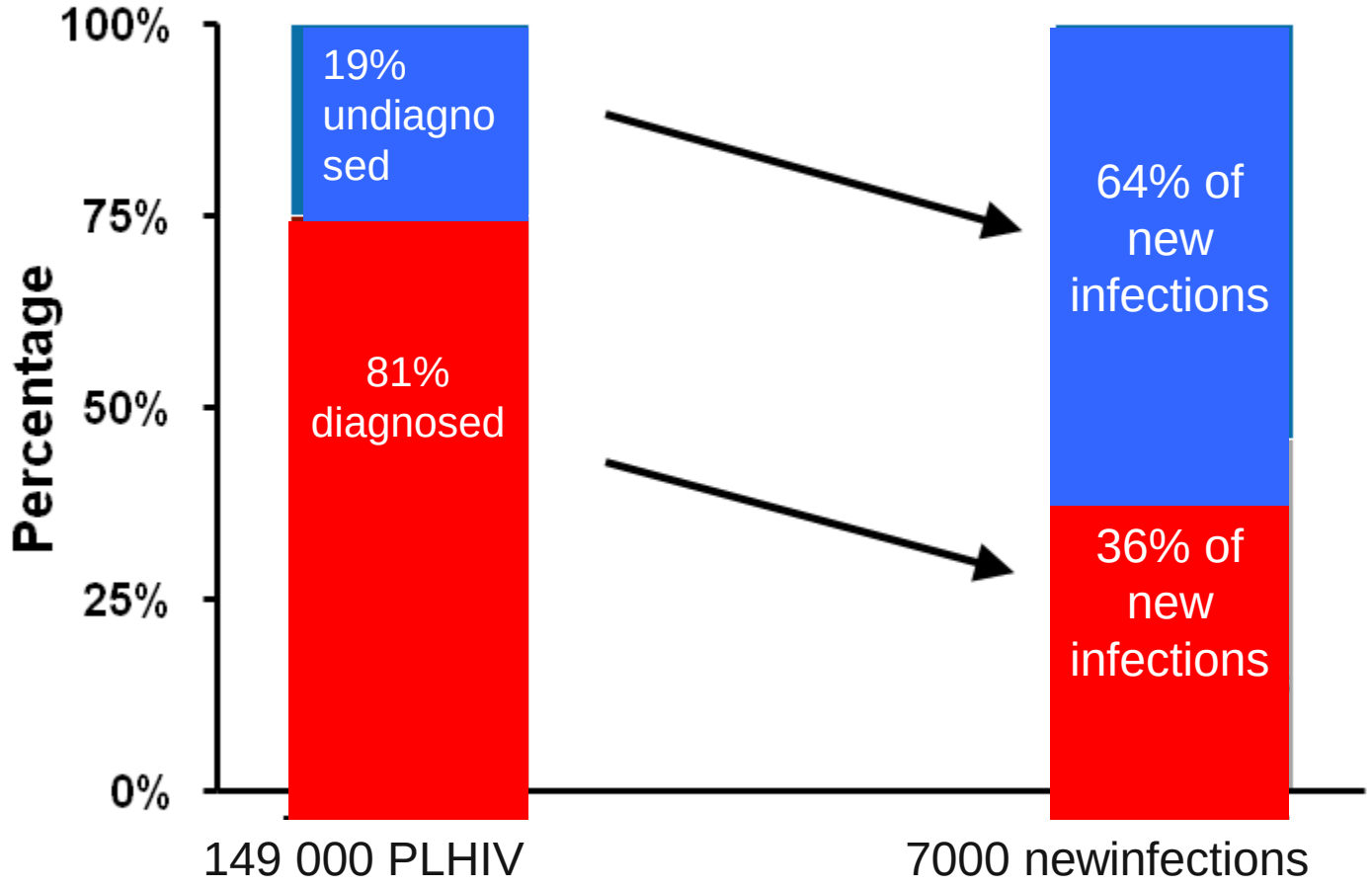




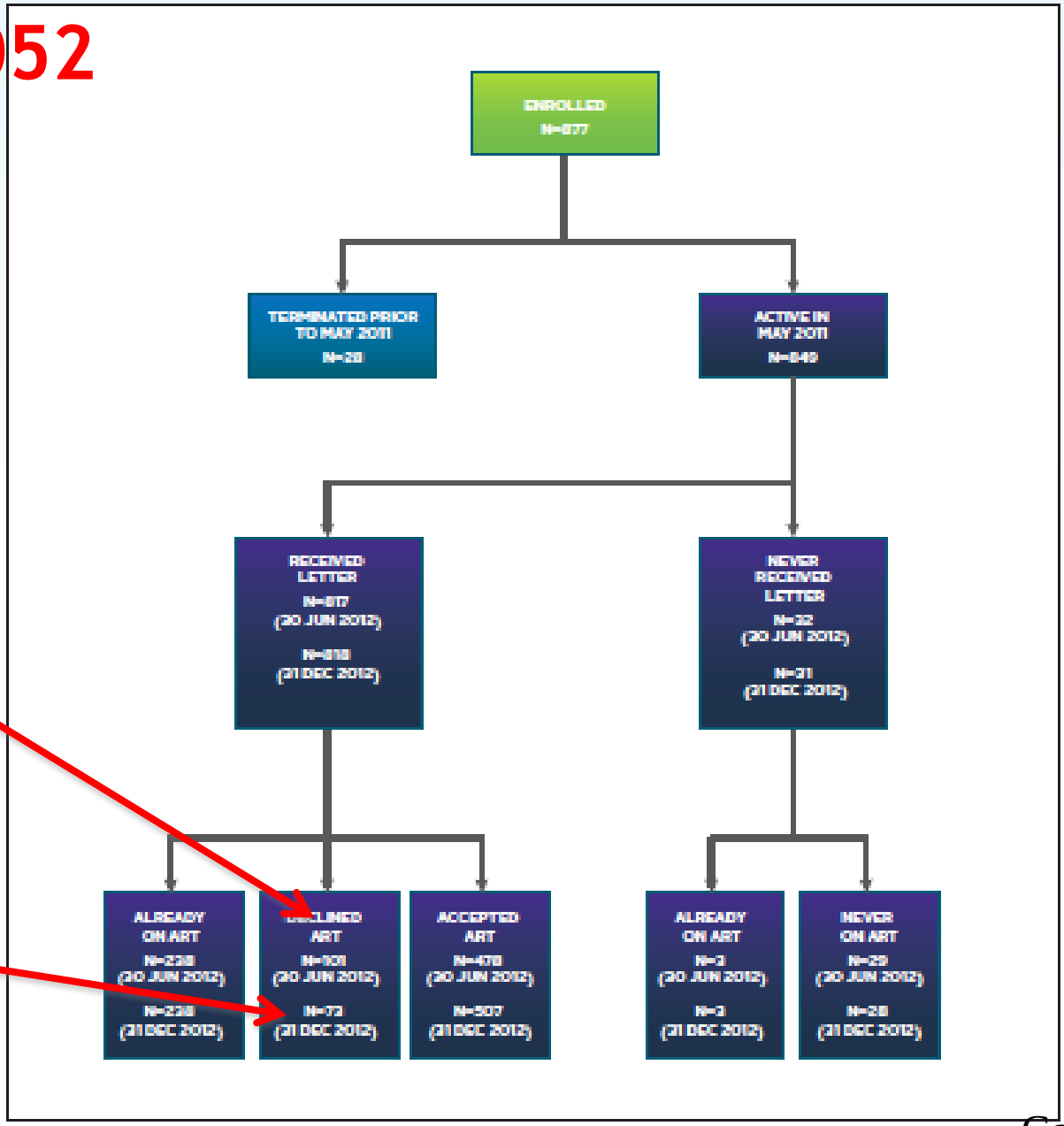
Hill et al. CROI 2015 [abstr 1118]

World Health Organization

The major source of new infections is the undiagnosed epidemic



HPTN 052



17% after 1 year

13% after 18 months

Gamble, CROI 2013

Role of Primary / Early HIV Infection

- Enhanced role of PHI in transmission
  - High viral load
  - Increased viral infectivity
  - Behavioural factors

- Models suggest PHI may account for 2-95% of onward transmissions
- Phylogenetic studies: 30-60%

- If PHI significantly driving transmission, then TasP may not work?

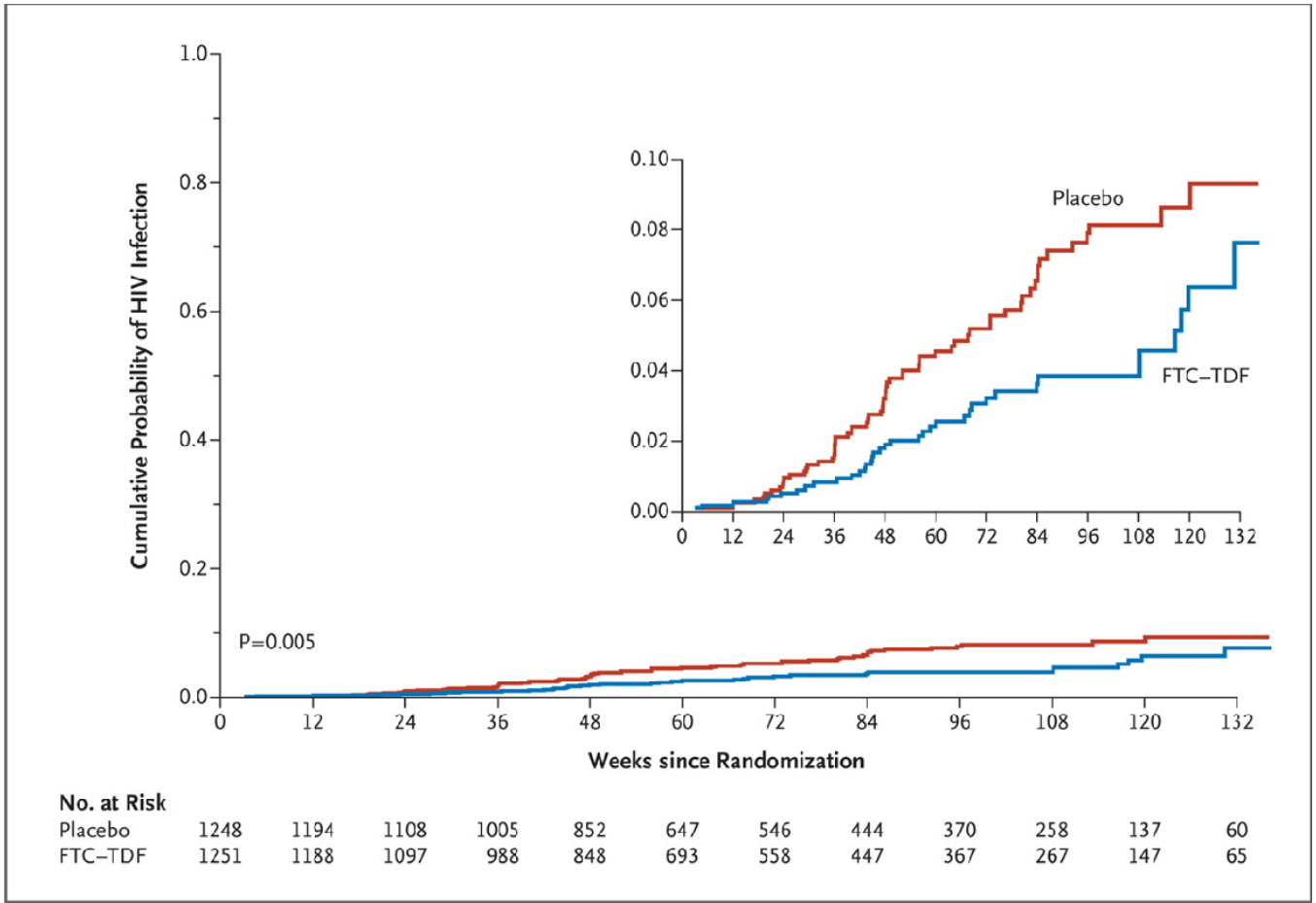
PrEP

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H.,
Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H.,



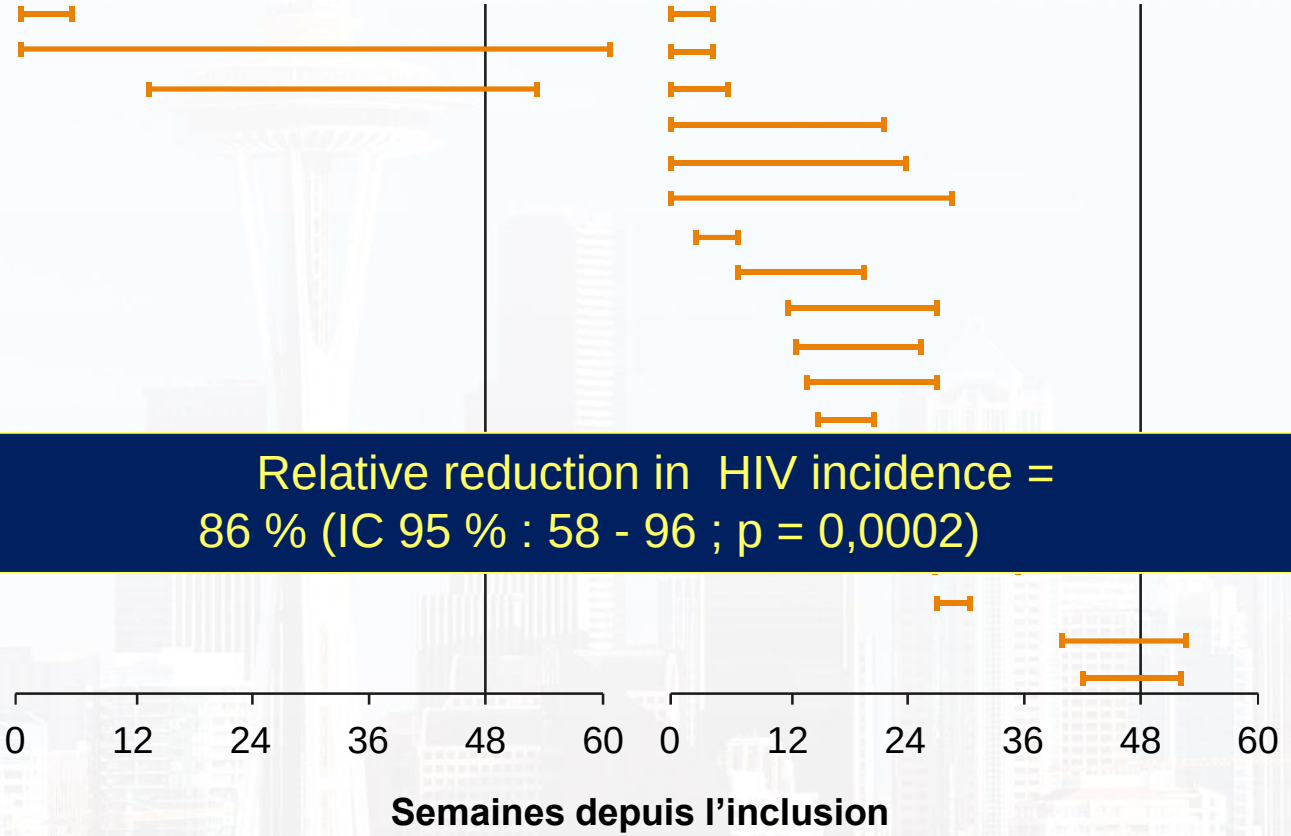
PrEP efficacy demonstrated in MSM and heterosexual men and women

Study, population	PrEP agent	# of HIV infections		PrEP efficacy (95% CI)
		PrEP	placebo	
iPrEx MSM Brazil, Ecuador, Peru, South Africa, Thailand, US (n=2499)	FTC/TDF	36	64	**44%** **(15-63%)** Grant et al. N Engl J Med 2010
Partners PrEP Study Heterosexual couples Kenya, Uganda (n=4758)	TDF	17	52	**67%** **(44-81%)**
	FTC/TDF	13		**75%** **(55-87%)** Baeten et al. N Engl J Med 2012
TDF2 Study Heterosexuals Botswana (n=1219)	FTC/TDF	10	26	**62%** **(16-83%)** Thigpen et al. N Engl J Med 2012

PROUD study : VIH seroconversions

immediate PrEP (n = 3)
1,3/100 patients.année

Differed PrEP (n = 19)
8,9/100 patients.année*



Relative reduction in HIV incidence =
86 % (IC 95 % : 58 - 96 ; p = 0,0002)

*Prescription de 174 prophylaxies post-exposition.

CROI 2015 - D'après Mc Cormack S et al., abstr. 22LB, actualisé

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 5, 2015 VOL. 372 NO. 6

Tenofovir-Based Preexposure Prophylaxis for HIV Infection among African Women

Table 3. Primary Efficacy Results.

Result	Oral TDF*		Oral TDF-FTC	Oral Placebo	TFV Gel	Placebo Gel
	Active Agent	Placebo				
Person-years	823	838	1284	1308	1024	1030
Number of HIV-1 infections	52	35	61	60	61	70
HIV-1 incidence — cases per 100 person-years (95% CI)	6.3 (4.7–8.3)	4.2 (2.9–5.8)	4.7 (3.6–6.1)	4.6 (3.5–5.9)	6.0 (4.6–7.6)	6.8 (5.3–8.6)
Hazard ratio (95% CI)	1.49 (0.97–2.29)	—	1.04 (0.73–1.49)	—	0.85 (0.61–1.21)	—
P value	0.07	—	0.81	—	0.37	—

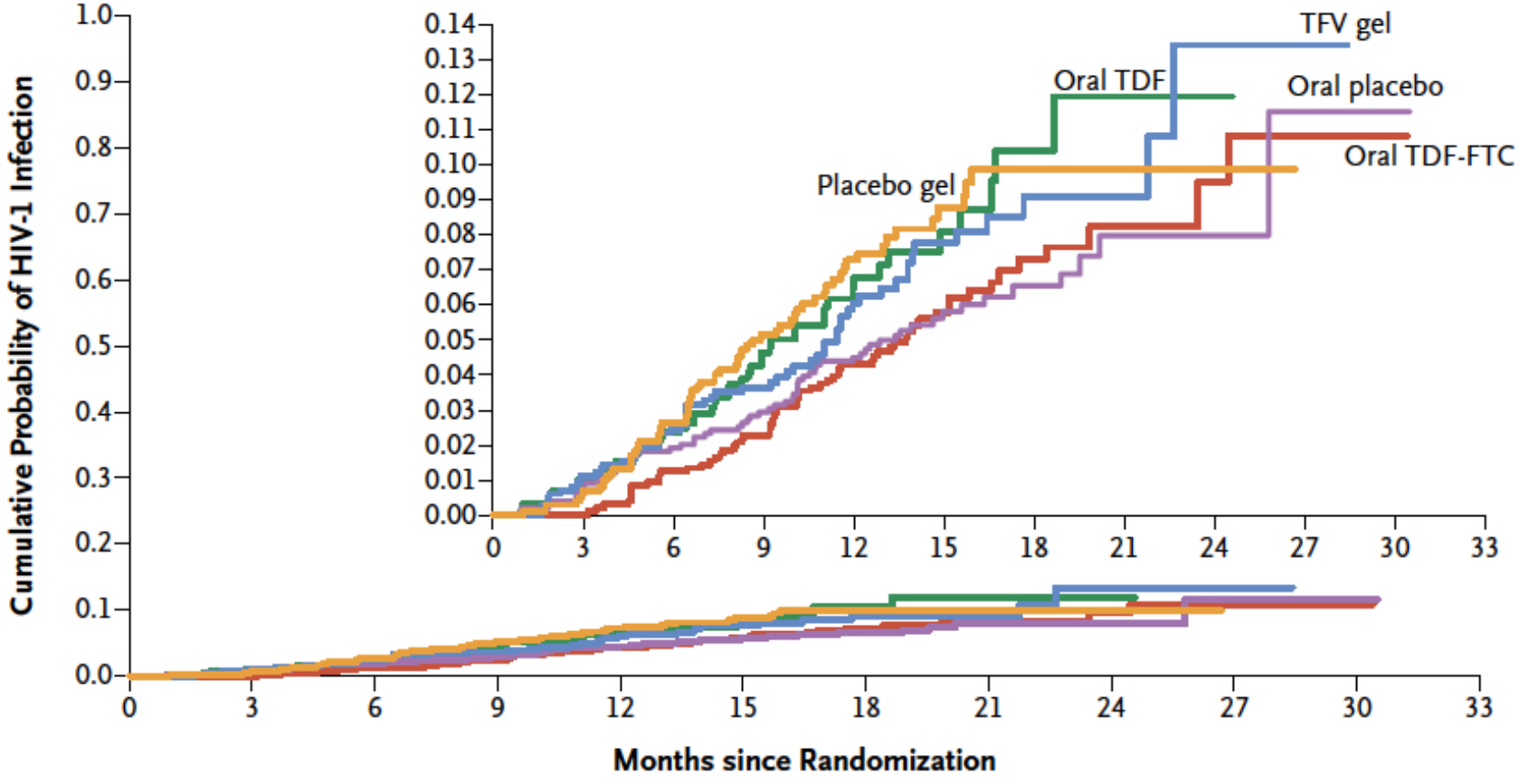


Table 2. Adherence to Study Products.*

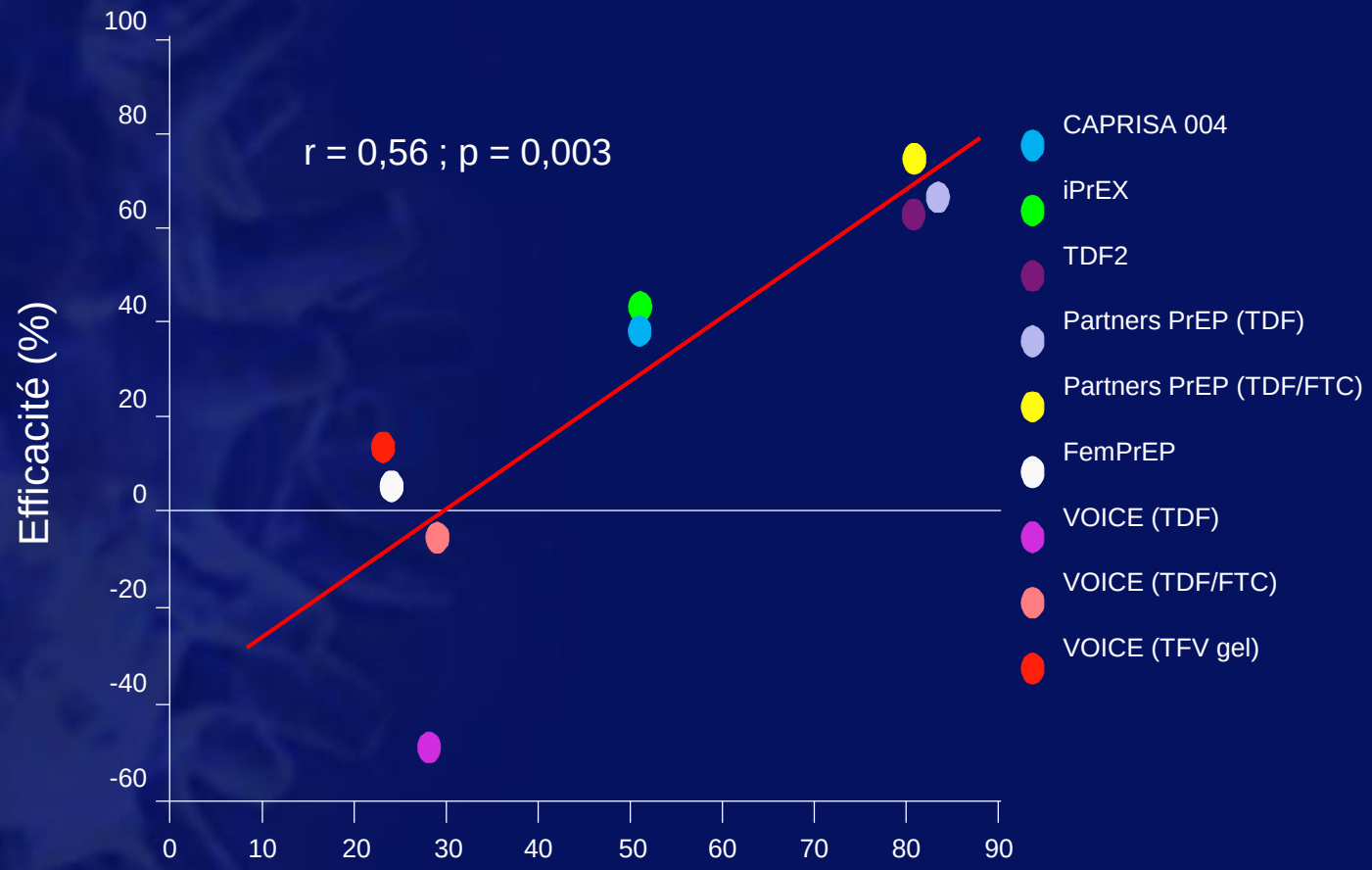
Measure of Adherence	Total (N=5007)	Oral TDF (N=1002)	Oral TDF-FTC (N=994)	Oral Placebo (N=1008)	TFV Gel (N=1003)	Placebo Gel (N=1000)
Mean rate of adherence (%)						
Assessed by clinic-based product count†	86	84	88	90	83	84
Assessed by face-to-face interview‡	90	91	90	91	90	90
Assessed by ACASI§	88	87	87	88	88	89
Mean proportion of quarterly plasma samples with TFV detected (%)¶	NA	30	29	NA	25	NA
Proportion of women with TFV not detected in any quarterly plasma samples (%)¶	NA	58	50	NA	57	NA
Mean proportion of vaginal swab samples with TFV detected (%)‖	NA	NA	NA	NA	49	NA
Proportion of women with TFV not detected in any vaginal swab samples (%)‖	NA	NA	NA	NA	41	NA

Challenges of PrEP

Adherence

PrEP

Strong correlation between efficacy and adherence



Landovitz RJ, CROI 2015, Abs. 20

What we've learned from PrEP trials: adherence → efficacy

	CASE-CONTROL / CASE-COHORT ANALYSES: DETECTION OF TENOFOVIR IN PLASMA	
	HIV seroconverters	**HIV uninfected**
iPrEx	9%	51%
Partners PrEP: TDF arm	35%	83%
Partners PrEP: FTC/TDF arm	25%	81%

Relative risk reduction associated with detectable tenofovir

iPrEx: 92% (95% CI 40-99%), p<0.001

Partners PrEP TDF: 86% (95% CI 57-95%), p<0.001

Partners PrEP FTC/TDF: 90% (95% CI 56-98%), p=0.002

How to Improve Adherence ?

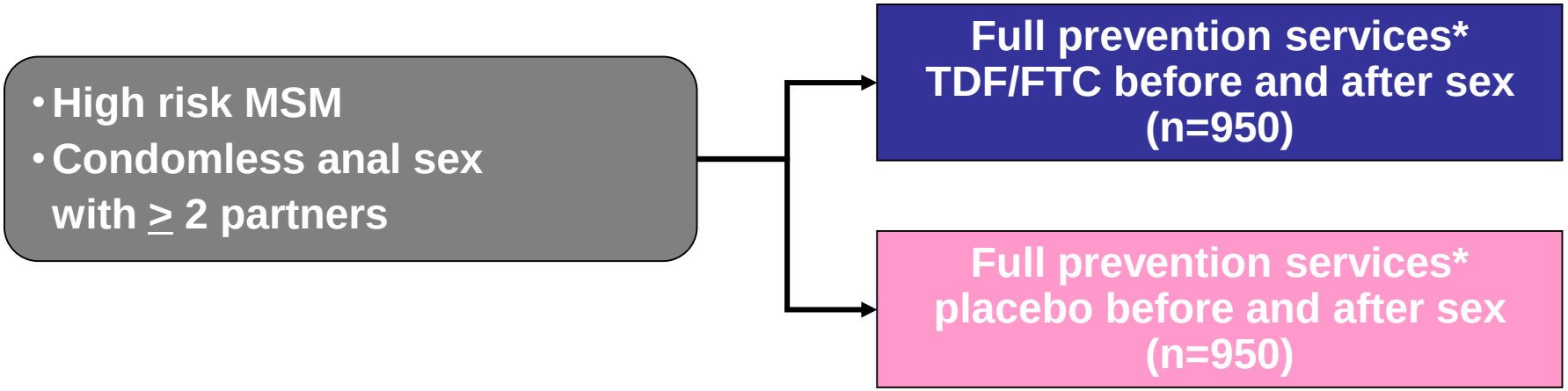
- Assess more friendly regimens for long-term use: “on demand” PrEP

IPERGAY
un essai ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les GAYS

www.ipergay.fr

IPERGAY
Study Design

Effectiveness of "on demand" PrEP
Randomized placebo-controlled trial



- Counseling, testing for STI, condoms, vaccination, PEP
- Primary endpoint : HIV infection, 64 events expected
- Incidence of HIV-infection: 3%PY, 50% efficacy, ~ 2000 pts

anrs
AGENCE NATIONALE DE RECHERCHES SUR LE SIDA
NATIONAL AGENCY FOR AIDS RESEARCH

GILEAD

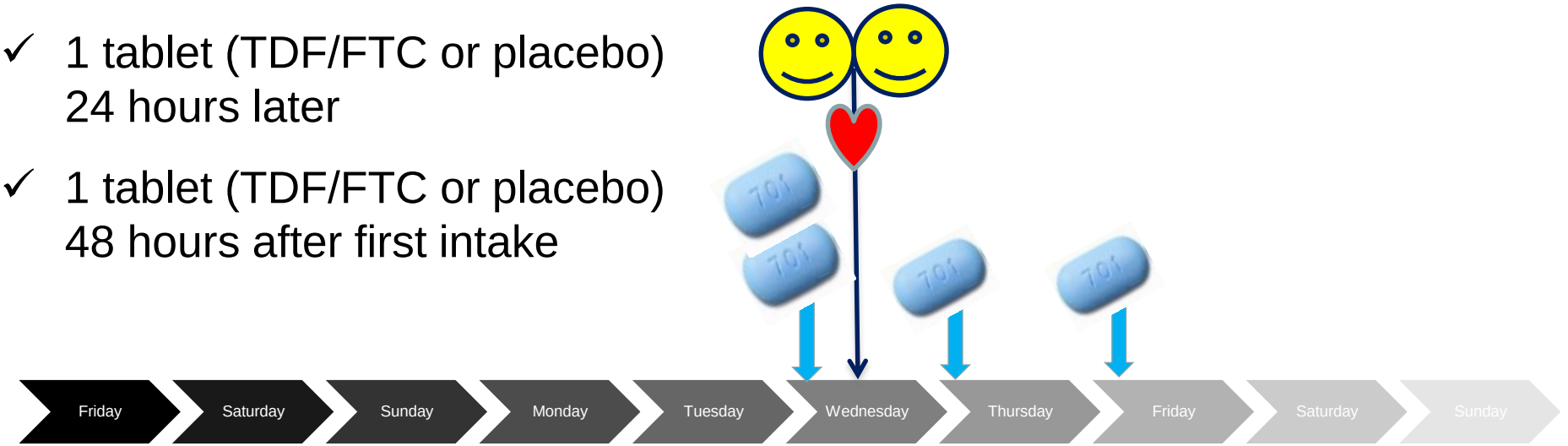
CANFAR
CANADIAN FOUNDATION FOR AIDS RESEARCH
FONDATION CANADIENNE DE RECHERCHE SUR LE SIDA

the CTN
CIHR Canadian HIV Trials Network

ipergay
ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les Gays

IPERGAY : Sex-Driven iPrEP

- ✓ 2 tablets (TDF/FTC or placebo)
  2-24 hours before sex
- ✓ 1 tablet (TDF/FTC or placebo)
  24 hours later
- ✓ 1 tablet (TDF/FTC or placebo)
  48 hours after first intake

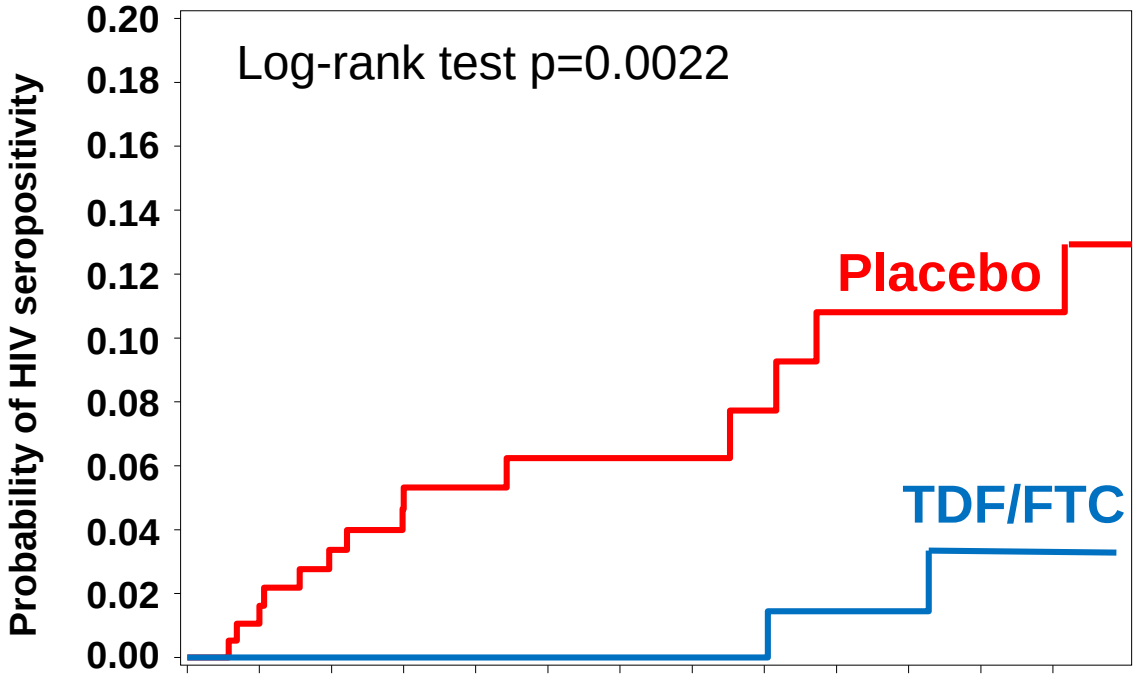


4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse

anrs France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm

ipergay
ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les Gays

KM Estimates of Time to HIV-1 Infection (mITT Population)



N at risk :	0	6	12	18	24
Placebo	201	142	74	55	42
TDF/FTC	199	141	82	58	43

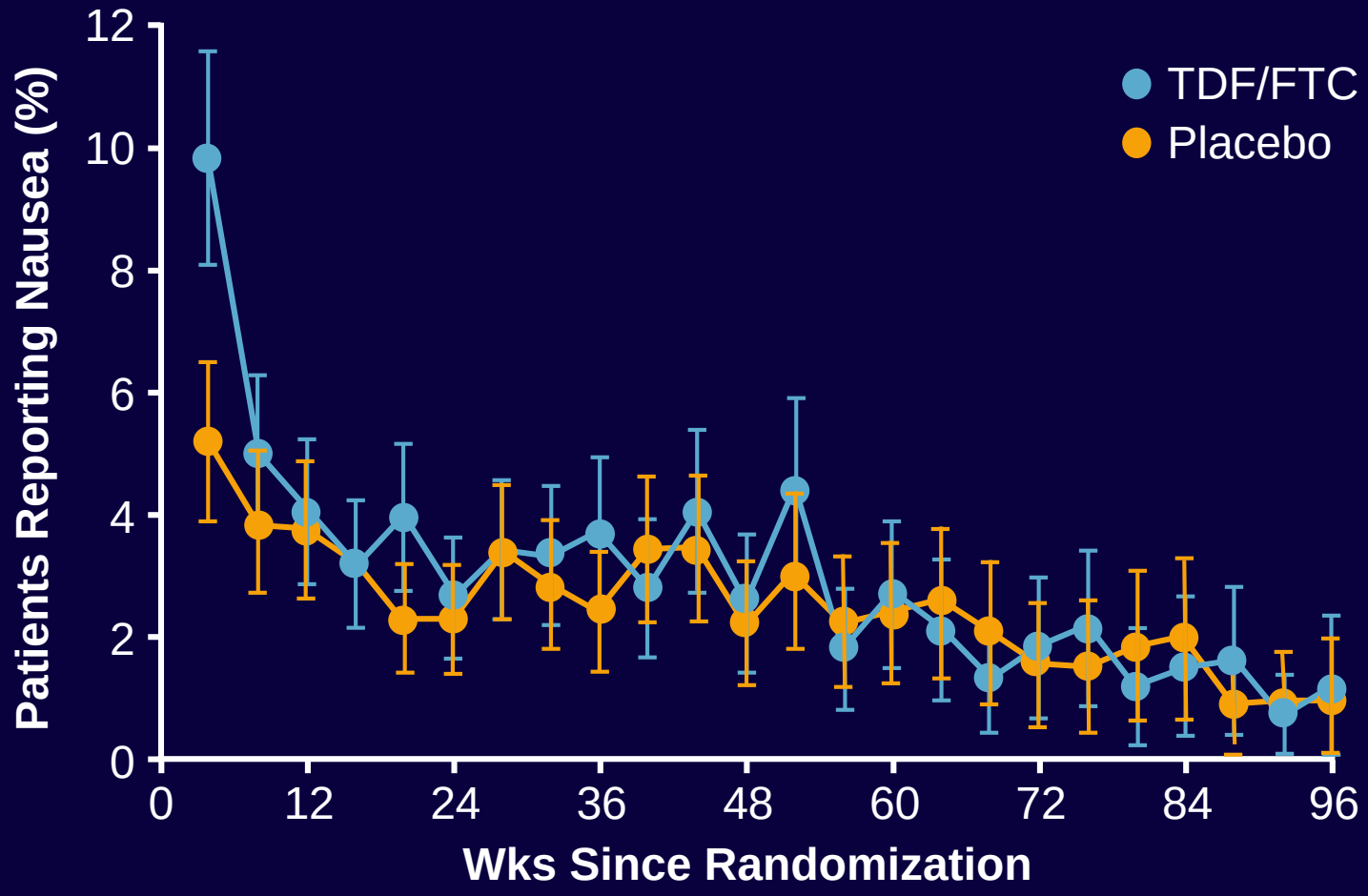
Mean follow-up of 13 months: 16 subjects infected

14 in placebo arm (incidence: 6.6 /100 PY) and **2 in TDF/FTC arm** (incidence: 0.9 /100PY)

86% relative reduction in the incidence of HIV-1 (95% CI : 40-98, p=0.0019)

Safety and Tolerability

iPrEx: Nausea on History



Grant RM, et al. N Engl J Med. 2010;363:2587-2599.

iPrEx: BMD Changes and Fracture Rates

- BMD changes were small (~1%); no evidence of negative effect on health[1]
- No differences in fracture rates between groups[1,2]
- All fractures were trauma related
- Need longer follow-up to evaluate effects on bone density and fracture risk over time

1. Liu AY, et al. PLoS One. 2011;6:e23688.2. Grant RM, et al. N Engl J Med. 2010;363:2587-2599.

Drug Resistance

PrEP and HIV Resistance

- Resistance was rare in clinical trials of PrEP, except for those with acute infection at baseline
- Resistance mutations seen: K65R (TDF) or M184V/I (FTC)

Number of HIV Seroconverters on *Active PrEP Arms* With HIV Resistance

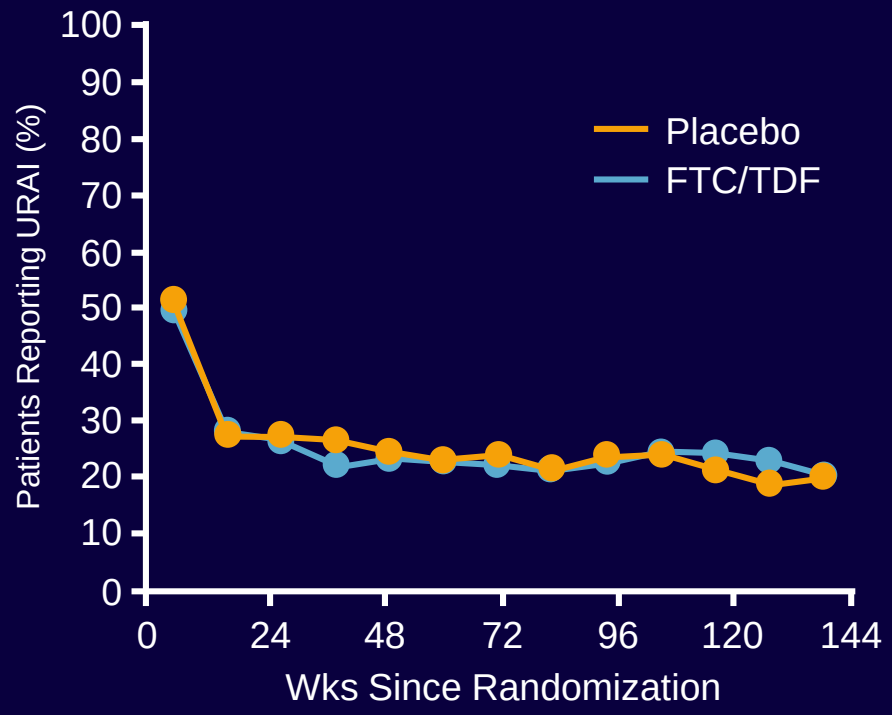
Trial	HIV Infected After Enrollment, n/N	Seronegative Acute HIV Infection at Enrollment, n/N	HIV Infections Averted, n
iPrEx[1,2]	0/36	2/2	28
Partners PrEP[3]	0/30	2/8	74
TDF2[4]	0/10	1/1	16

1. Liegler T, et al. CROI 2011. Abstract 97LB. 2. Grant RM, et al. N Engl J Med. 2010;363:2587-2599.
3. Baeten JM, et al. N Engl J Med. 2012;[Epub ahead of print] (supplementary appendix).
4. Thigpen MC, et al. N Engl J Med. 2012;[Epub ahead of print] (supplementary appendix).

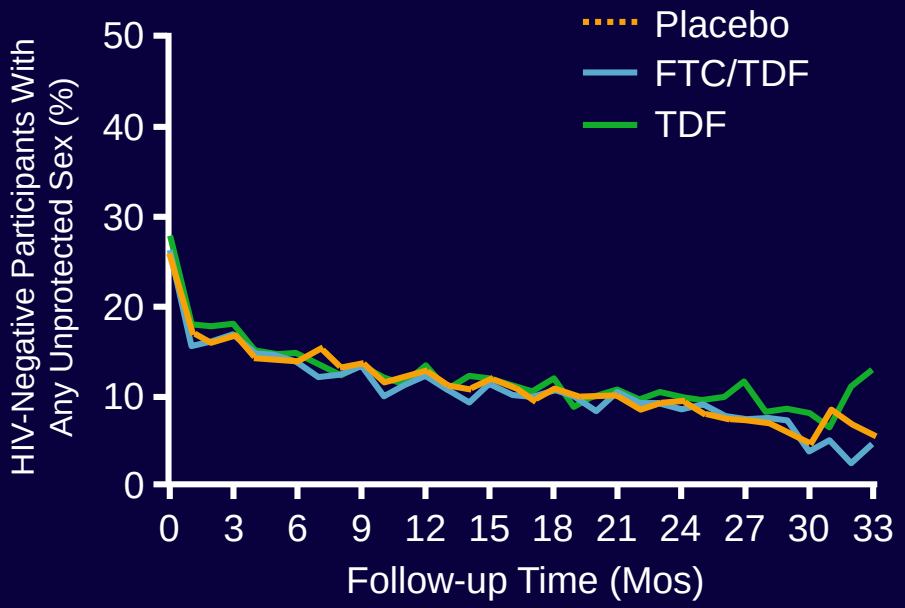
Risk Behavior

No Evidence of Risk Compensation in PrEP Clinical Trials

iPrEx[1]

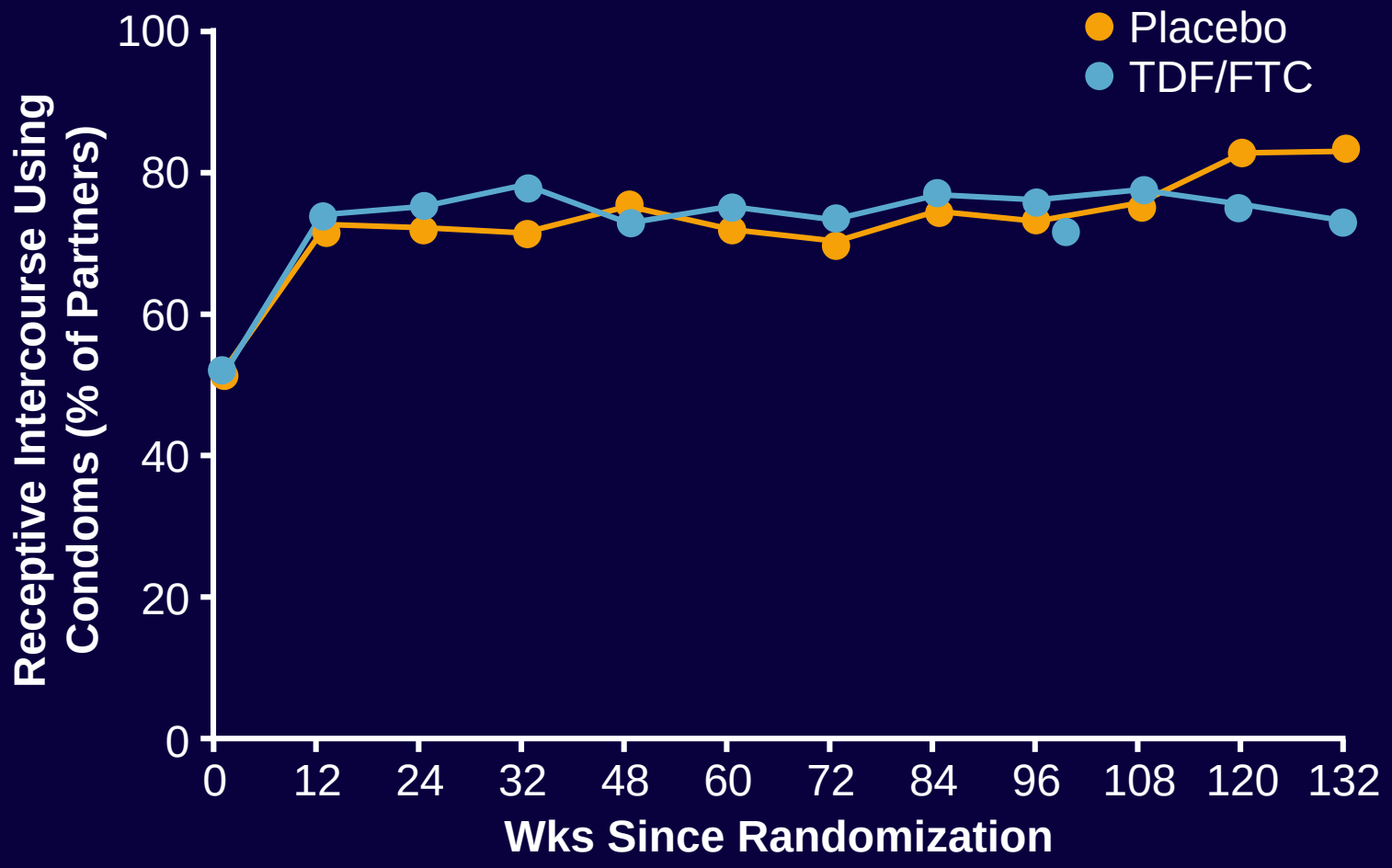


Partners PrEP[2]



1. Grant R, et al. CROI 2011. Abstract 92. 2. Baeten JM, et al. N Engl J Med. 2012;[Epub ahead of print].

iPrEx: Self-Reported Condom Use With High-Risk Sex



Grant R, et al. CROI 2011. Abstract 92.

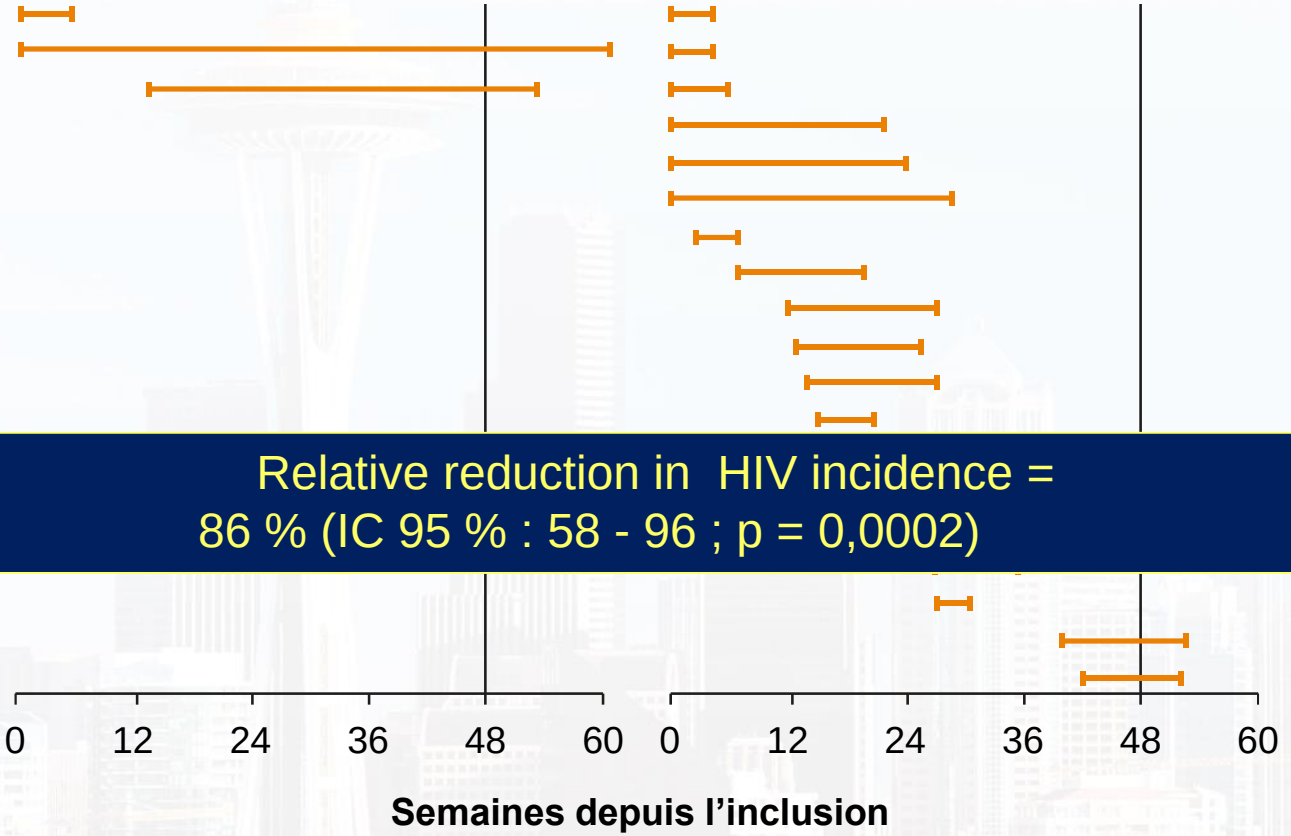
WARNING:

RCT versus placebo….

PROUD study : VIH seroconversions

immediate PrEP (n = 3)
1,3/100 patients.année

Differed PrEP (n = 19)
8,9/100 patients.année*



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CROI 2015 - D'après Mc Cormack S et al., abstr. 22LB, actualisé

Challenges and opportunities: reflections on PrEP and ART for prevention

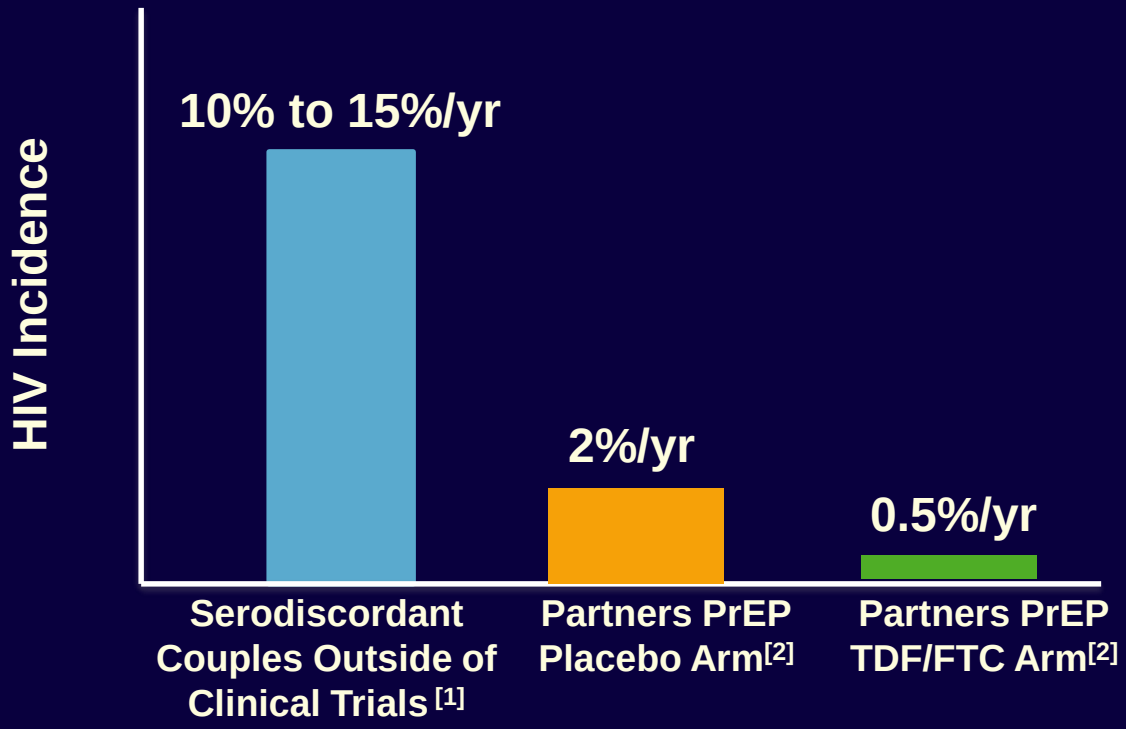
ART and PrEP: efficacy is clear

	Antiretroviral treatment for HIV prevention	**PrEP for HIV prevention**
HIV prevention effect with high adherence	**96%** (HPTN 052, near-perfect adherence)	**90-92%** (Tenofovir levels in iPrEx and Partners PrEP)

Two incredibly powerful prevention strategies

PrEP Works Together With Other HIV Prevention Strategies

- Ongoing HIV counseling and testing, condoms, risk reduction, male circumcision, treatment of STIs *plus PrEP* synergize to maximally reduce HIV risk



1. Quinn TC, et al. N Engl J Med. 2000;342:921-929. 2.Baeten JM, et al. N Engl J Med. 2012;[Epub ahead of print]. .

COMBINATION HIV PREVENTION

Microbicides for women

Abdool Karim Q, Science 2010

Male circumcision

Auvert B, PloS Med 2005
Gray R, Lancet 2007
Bailey R, Lancet 2007

Treatment of STIs

Grosskurth H, Lancet 2000

Treatment for prevention

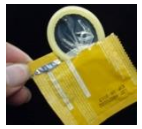
Donnell D, Lancet 2010
Cohen M, NEJM 2011

Female Condoms

Behavioural positive prevention

Fisher J, JAIDS 2004

Male Condoms



HIV Counselling and Testing

Coates T, Lancet 2000

Oral pre-exposure prophylaxis

Grant R, NEJM 2010 (MSM)
Baeten J , 2011 (Couples)
Paxton L, 2011 (Heterosexuals)

Behavioural Intervention

- Abstinence
- Be Faithful

Post Exposure prophylaxis (PEP)

Scheckter M, 2002

Vaccines

Rerks-Ngarm S, NEJM 2009

Key Questions

- Who needs what?
- Who wants what?
- Who gets what?

→ Personal

- How to deliver it?
- How to support adherence?

→ Programmatic

- Who pays?
- Who decides?

→ Policy

Conclusion

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The Uptake and Accuracy of Oral Kits for HIV Self-Testing in High HIV Prevalence Setting: A Cross-Sectional Feasibility Study in Blantyre, Malawi

Augustine Talumba Choko[1]*, Nicola Desmond[1,2], Emily L. Webb[3], Kondwani Chavula[1], Sue Napierala-Mavedzenge[4], Charlotte A. Gaydos[5], Simon D. Makombe[6], Treza Chunda[1], S. Bertel Squire[2], Neil French[4], Victor Mwapasa[1], Elizabeth L. Corbett[1,7]

"Whatever the next hottest, scientifically proven HIV treatment or prevention strategies are :

- PreP
- TasP

they will share a common denominator for implementation: **the HIV test.**

They all begin with learning one's HIV status."

Walensky et al. Plos Med 2011