EACS
European AIDS Clinical Society

Antiretroviral Therapy for HIV Prevention

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Question 1

- 32 year old heterosexual male
- HIV positive
- CD4 count 580; viral load 12,000
- Regular female partner is HIV negative

- Would you recommend starting ART?

Question 2

- 32 year old MSM
- HIV positive
- CD4 count 580; viral load 12,000
- Regular male partner is HIV negative

- Would you recommend starting ART?

Question 3

- 32 year old MSM
- HIV positive
- CD4 count 580; viral load 12,000
- No regular male partner but frequent casual partners of unknown status

- Would you recommend starting ART?

Question 4

- 32 year old MSM
- HIV negative
- Regular male partner is HIV positive
  - CD4 count 580; viral load 12,000
  - Declines to start ART
- Would you recommend starting PrEP?

Question 5

- 32 year old MSM
- HIV negative
- No regular male partner
- Frequent casual male partners

- Would you recommend starting PrEP?

Outline

- **Post Exposure Prophylaxis (PEP)**
- **Pre Exposure Prophylaxis (PrEP)**
- **Treatment as Prevention (TasP)**
  - ***Summary of evidence-base***
  - ***Most recent data***
  - ***Current guidelines***
  - ***Clinical implications***

PEP

- Biological plausibility
  - “window of opportunity” in 72 hours
- Animal model studies
  - Tenofovir effective if given within 72 hours
- Case-controlled study (AZT)
  - 81% protection in health-care workers
- No RCT powered for effect on transmission
- One published controlled trial for sexual exposure (PEPSE)….

PEPSE

- **"Praca Onze" Study**
  - **MSM in Rio, Brazil**
  - **Given PEP pack to start after risk exposure**
  - **N=200, follow-up 24 months**
  - **10 seroconversions in "non-PEP users" (4.2%); 1 seroconversion in "PEP user" (0.6%); p<0.05**
  - **However…overall HIV incidence 2.9/100py compared to 3.1/100py expected; p>0.97**
  - ***"PEP did not appear to substantially affect HIV transmission"***

Schechter M et al; JAIDS, 2004

PEP

- **Guidelines continue to recommend PEP**
  - Occupational and sexual exposure
  - No plans for any RCT of effectiveness
- **Guidelines beginning to embrace viral load and ART status**
  - e.g. UK guidelines no longer recommend PEPSE if viral load undetectable
- **Variation in timing**
  - e.g. EACS 48 hours, WHO and UK 72 hours, NYC 24 hours
- **Opportunities to improve tolerability**
  - Truvada, darunavir, raltegravir, maraviroc
- **Opportunity for more-effective prevention strategies? PEP may be an “indicator” for PrEP?**

Pre Exposure Prophylaxis

- **Biological plausibility**
  - **Presence of ARVs should be able to prevent productive infection**

- **Animal model studies have shown:**
  - **Efficacy of tenofovir**
  - **Efficacy of tenofovir and emtricitabine**
  - **Vaginal and rectal exposure to SIV**
  - **Protective against multiple exposures**
  - **Requires pre and post exposure therapy**

Pre Exposure Prophylaxis (PrEP) RCTs

Trial	Population	Location	PrEP agent	Protective Effect
iPreX	MSM and transgender	USA, South Africa, Thailand, South America	TDF/FTC	44% (15-63%)
Partners PrEP	Discordant Hetero Male and female	Kenya Uganda	TDF TDF/FTC	67% (44-81%) 75% (55-87%)
TDF-2	Hetero Male and Female	Botswana	TDF	62% (55-87%)
Fem PREP	Hetero Female	Kenya, South Africa, Thailand	TDF/FTC	6% (-52-41%)
VOICE	Hetero female	South Africa, Uganda, Zimbabwe	TDF TDF/FTC	-49% (-130-3%) -4% (-50-30%)
Bangkok TDF Study	IDUs	Thailand	TDF	49% (10-72%)

PrEP Studies: why different results?

- Statistical anomaly
- Gender difference
- Pharmacokinetics of genital tracts
- Serodiscordant versus casual partners
- Biological co-factors and higher risk for acquisition
- *Adherence*

Pre Exposure Prophylaxis (PrEP) RCTs

Trial	Population	Location	PrEP agent	Protective Effect	Adherence
iPreX	MSM and transgender	USA, South Africa, Thailand, South America	TDF/FTC	44% (15-63%)	51%
Partners PrEP	Discordant Hetero Male and female	Kenya Uganda	TDF TDF/FTC	67% (44-81%) 75% (55-87%)	81%
TDF-2	Hetero Male and Female	Botswana	TDF	62% (55-87%)	79%
Fem PREP	Hetero Female	Kenya, South Africa, Thailand	TDF/FTC	6% (-52-41%)	26-40%
VOICE	Hetero female	South Africa, Uganda, Zimbabwe	TDF TDF/FTC	-49% (-130-3%) -4% (-50-30%)	<50%
Bangkok TDF Study	IDUs	Thailand	TDF	49% (10-72%)	67%

Concerns about PrEP

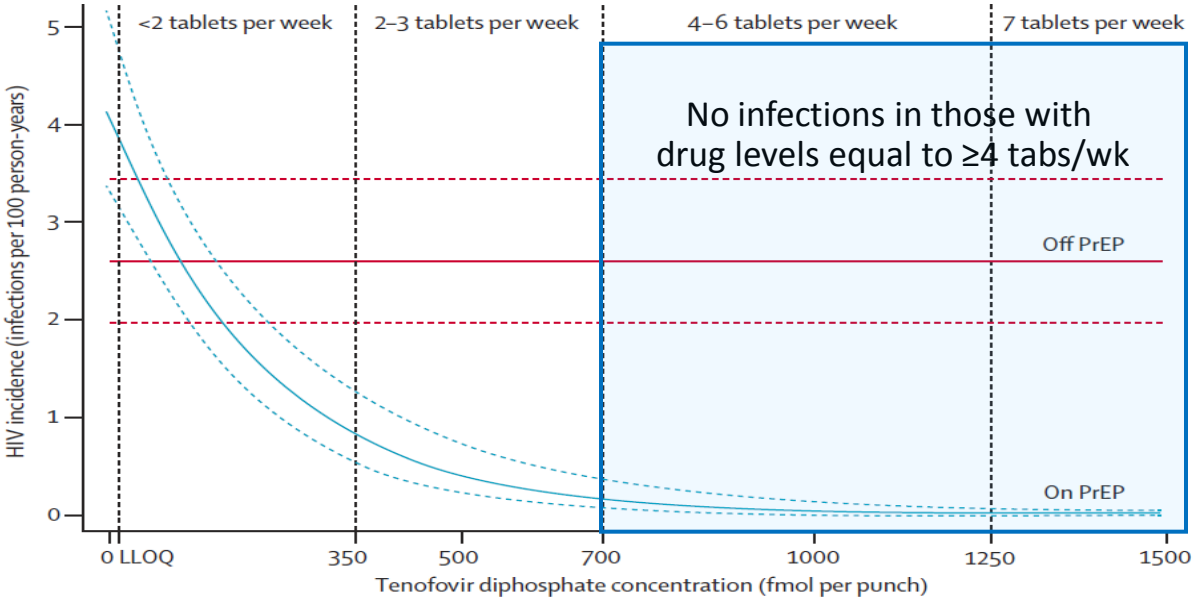
- Cost
- Toxicity
  - Decreased BMD seen in trials
- Healthcare utilisation
  - Who will provide?
- Regular HIV testing
  - How often?
- Adherence
  - How much is enough?
- Resistance
- Who to target?
- "Stopping rules" as well as starting rules
- *Awareness*
- *Willingness*

What will adherence be like if people know they are on active drug?

iPrEx Open-Label Extension (iPrEx OLE)[1]

HIV Incidence and Drug Concentrations

Participants in randomized placebo-controlled iPrEx, ATN 089, or US PrEP Safety trials were enrolled in the 72-week open label extension (iPrEx OLE); ***76% of those offered elected to take PrEP***



Drug Concentration	none	<2 pills/week	2-3 pills/week	≥ 4 pills/week	7 pills/week
HIV Incidence per 100 PY (95%CI)	4.7 (2.99-7.76)	2.25 (1.19-4.79)	0.56 (0.00-2.50)	0	0
Risk Reduction (95%CI)		44% (-31-77)	84% (21-99)	**100% (86-100)**	
Follow-up %	25%	26%	12%	21%	12%

Note: Recommended dose of TVD for PrEP in HIV-1 uninfected adults: One tablet once daily taken orally with or without food[2]

1. Grant R, et al. IAC 2014. Melbourne, Australia. #TUAC0105LB
2. Grant R. et al. *Lancet published on line 22 July 2014* **http://dx.doi.org/10.1016/S1473-3099(14)70847-3**
3. Truvada ® (FTC/TDF). US Prescribing Information. Gilead Sciences Inc. December 2013

iPrEx Open-Label Extension (iPrEx OLE)
Correlates of Drug Concentrations in Dried Blood Spots

Predictor of Drug Concentration	Adjusted OR	*P* Value
Non-condom Receptive Anal Intercourse at entry	1.69	<.0001
≥5 sexual partners in the past 3 months	1.57	<.0001
Known HIV-Positive Partner	1.40	.03
Age		
18-24	Ref	
25-29	1.08	.19
30-39	2.02	.0002
40+	3.16	<.0001
Education		
< Secondary	Ref	
Secondary	1.89	<.0001
Post-secondary	2.40	<.0001
Transgender	0.72	.02
Alcohol ≥5 drinks a day on drinking days	0.81	.07
Cocaine use in the past 30 days	1.07	.60
Methamphetamine use in the past 30 days	.78	.42

Grant R, et al. IAC 2014. Melbourne, Australia. #TUAC0105LB

Intermittent PrEP

Fixed / Time-based dosing

Event-based dosing

Fixed dosing with event-based supplementation

Periodic PrEP

Patient preference: daily > event-based

- **But adherence patterns in trials….**

50% MSM last AI "planned"; but……

Concerns regarding pharmacokinetics

- **?need to achieve steady-state before intermittent dosing**

– ***Buchbinder, CROI 2012 #68***

ipergay
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

- High risk MSM
- Condomless anal sex with ≥ 2 partners within 6 m
- eGFR > 60 mL/mn

→ **Full prevention services* TDF/FTC before and after sex (n=950)**

→ **Full prevention services* placebo before and after sex (n=950)**

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

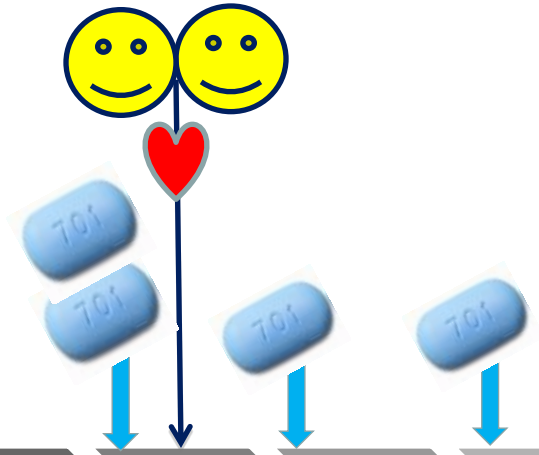
Molina; IAC Melbourne July 2014

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

Ipergay : Event-Driven iPrEP

- ✓ **2 tablets (Truvada® / placebo) 2-24 hours before sex**
- ✓ **1 tablet (Truvada® / placebo) 24 hours later**
- ✓ **1 tablet (Truvada® / placebo) 48 hours later**



Friday | Saturday | Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday | Sunday

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

Study Population

- 129 participants randomized (Feb 22, 2012 to Feb 26, 2013)
- 79.2 pt-years of follow-up, median follow-up: 8.3 months

Baseline Characteristics	N=129
Age (years, median, IQR)	35 (29-43)
Bisexual (n,%)	5 (4%)
Caucasian (n,%)	123 (95%)
Circumcised (n,%)	22 (17%)
Nb sexual intercourses/week (median, range)	2 (0-31)
Nb sexual partners/2 months (median, range)	10 (0-84)

Adherence Assessed by CASIs

- PrEP use during the last sexual intercourse

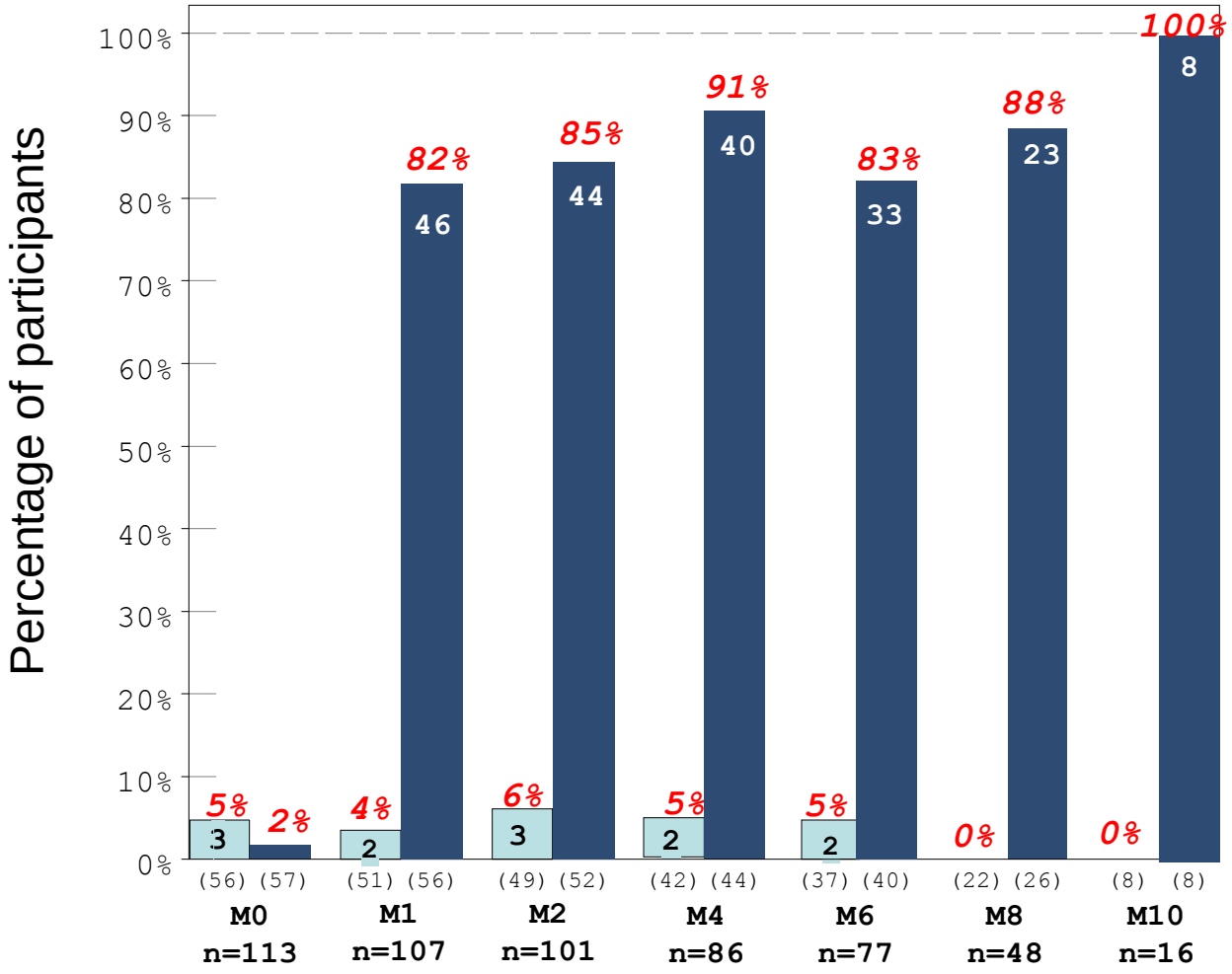
  - 126 participants, 543 sexual intercourses (all visits from M1 to M12)

PrEP Use	% (min-max)
Perfect use	**53% (44-66%)**
Suboptimal use	**28% (15-38%)**
No PrEP	**19% (15-23%)**

- Only 4 (3%) participants used daily PrEP

Detection of TFV in Plasma

% of participants with TFV detected in plasma (548 samples from 113 participants)



Placebo

TDF/FTC

Overall detection: 86% in theTDF/FTC arm vs. 4% in the placebo arm

Public Health England

PROUD

MRC Clinical Trials Unit

PRe-exposure Option for reducing HIV in the UK: an open-label randomisation to immediate or Deferred daily Truvada for HIV negative gay men

David Dolling, Monica Desai, Vanessa Apea, Nicola Mackie, Alan McOwan, Elaney Youssef, Christine Bowman, Charles Lacey, Gabriel Schembri, Richard Gilson, Ann Sullivan, Iain Reeves, Jake Bayley, Julie Fox, Steve Taylor, Saye Khoo, Mitzy Gafos, Anthony Nardone, Noel Gill, David Dunn, Sheena McCormack
on behalf of the PROUD study

MRC | Medical Research Council

IAC, Melbourne, July 2013

PROUD Study (pilot)

MRC Clinical Trials Unit

MSM reporting UAI
Willing to take a pill now or in 12M

↓

Randomize 500 HIV negative eligible MSM
(exclude if on treatment for hepB)

↙ ↘

Risk reduction includes Truvada **NOW**

Risk reduction includes Truvada **in 12M**

↓

Follow **3 monthly** for up to 24 months

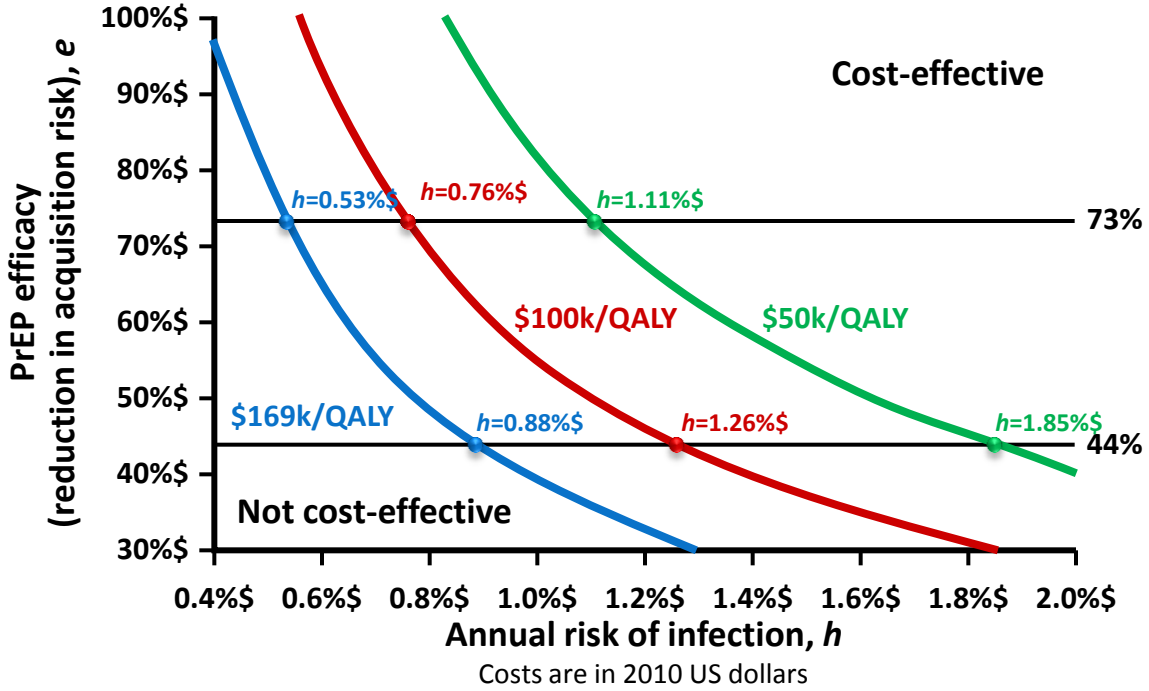
Main endpoints: recruitment and retention

Baseline Demographic Data

- N=443
- Median age 35.5 (29.4-42.3)
- Caucasian: 80%
- Educated to University or above: 59%
- Median no sex partners in past 3 months: 10 (4-20)
  - Condomless receptive sex 2 (1-5)
  - Condomless insertive sex 3 (1-6)
- PEP use in last 12 months: 40%
  - More than once: 21%

Analysing the Drivers of PrEP Cost Effectiveness

Cost effectiveness model of PrEP taking into account the cost of more frequent testing, early detection of HIV due to the frequent testing, and the costs saved and health benefits from HIV infections avoided due to PrEP



Costs are in 2010 US dollars

Cost-effectiveness of PrEP is dependent on

1. Risk of infection
2. Efficacy of PrEP
3. Annual cost of PrEP
4. Number of secondary HIV cases averted.

PrEP was shown to be cost effective in high risk groups even at lower adherence rates*

***Recommended dose of TVD for PrEP in HIV-1 uninfected adults: One tablet once daily taken orally with or without food**

Armbuster B, et al. IAC 2014. Melbourne, Australia. #THPE199

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE

CDC PrEP Recommendations 2014

- Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults; therefore,
- o PrEP is recommended as one prevention option for sexually-active adult MSM (men who have sex with men) at substantial risk of HIV acquisition **(IA)**1
- o PrEP is recommended as one prevention option for adult heterosexually active men and women who are at substantial risk of HIV acquisition. **(IA)**
- o PrEP is recommended as one prevention option for adult injection drug users (IDU) at substantial risk of HIV acquisition. **(IA)**
- o PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (i.e., HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and fetus **(IIB)**

World Health Organization

GUIDELINES

CONSOLIDATED GUIDELINES ON

HIV PREVENTION, DIAGNOSIS, TREATMENT AND CARE FOR KEY POPULATIONS

JULY 2014

KEY POPULATIONS

2014 World Health Organization (WHO)

PrEP: Guidelines on HIV Prevention, Diagnosis, Treatment and Care for Key Populations (Update July 2014)

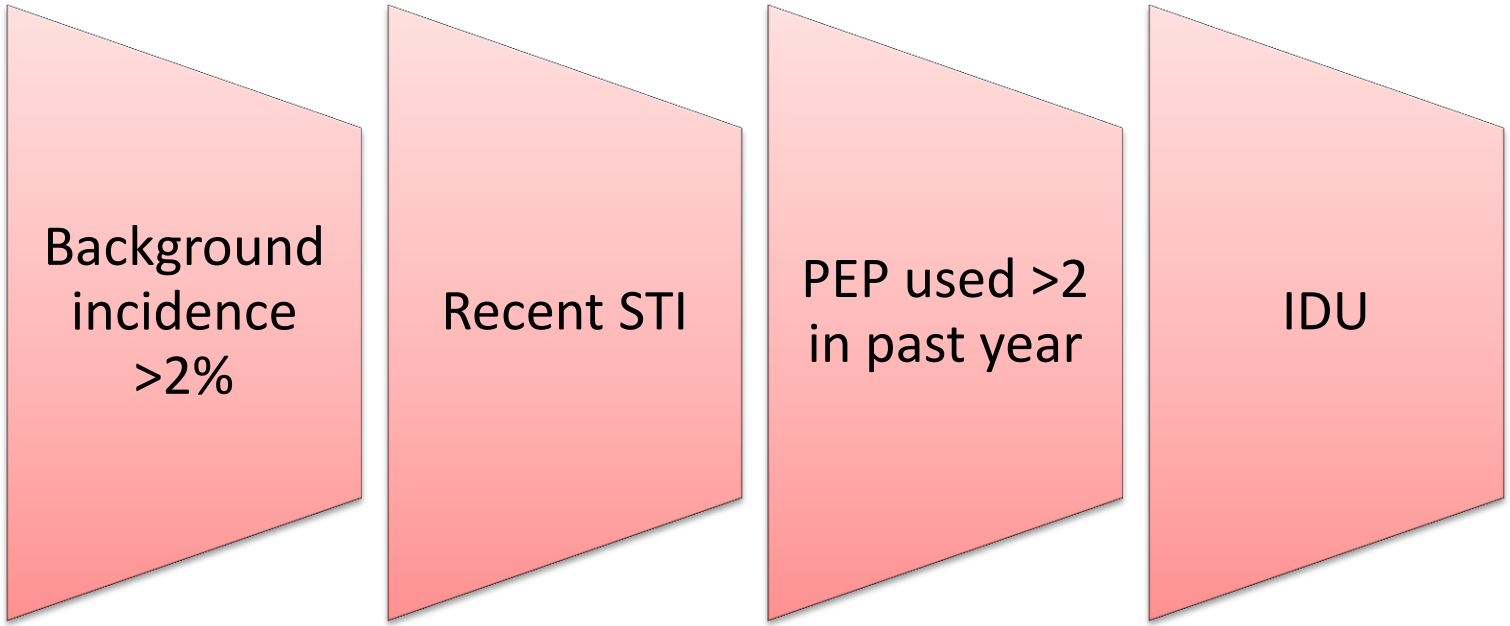
PrEP should be offered as a component of a comprehensive prevention intervention including unfettered availability of condoms and lubricants, routine HIV testing, risk reduction counseling and adherence coaching.

- **STRONG** Recommendation for **MSM**
- **CONDITIONAL** Recommendation for **Serodiscordant Couples**
  - Where additional HIV prevention choices are needed.
  - PrEP considered either FTC/TDF or TDF for this population
- **CONDITIONAL** Recommendation for **Transgender Women** who have sex with men
  - Only FTC/TDF recommended
- **NO** Recommendation for **People Who Inject Drugs** unless negative partner in serodiscordant relationship

WHO *Consolidated Guidelines on HIV prevention. Switzerland.* July 2014.

PrEP Prevention Recommendations (July 2014)

Possible Candidates for PrEP



"HIV prevention should not be considered as either behavioral or biomedical but rather as a combination intervention."

Marrazzo JM et al. JAMA. 2014;312(4):390-409.

ECDC : May 2014 – Statement on PrEP for HIV Prevention

- In response to US Recommendations on PrEP……

- "There is currently no consistent approach to PrEP across Europe"
- "Despite some encouraging results, a number of questions remain unanswered ….
  - Cost-effectiveness
  - Level of adherence required
  - Side-effects
  - Resistance
  - Impact on condom-use and HIV incidence rates
- "PrEP shows promising prospects for inclusion in HIV prevention…"
- ***"At present implementation data are lacking …. Makes it difficult to provide a clear recommendation to the EU"***

The British HIV Association/British Association for Sexual Health and HIV Position Statement on pre-exposure prophylaxis in the UK

S McCormack MSc FRCP*, **S Fidler** PhD MRCP† **and M Fisher** MBBS FRCP‡

*MRC Clinical Trials Unit, London; †Department of Medicine, Imperial College London, London; ‡Department of HIV/Genitourinary Medicine, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK

International Journal of STD & AIDS 2012; **23**: 1–4

BHIVA / BASHH Position Statement on PrEP in the UK

Fidler S, Fisher M, McCormack S

- *"It is imperative to gather evidence for the value of PrEP in the UK, in order to achieve universal access should it prove cost-effective as part of a combination prevention package. There are important concerns, and we recommend that ad-hoc prescribing is avoided, and that PrEP is only prescribed in the context of a clinical research study in the UK. Ideally this would be a randomised controlled trial, which is embedded in a broader concerted effort to intensify HIV prevention and implement the existing guidelines"*

Pre Exposure Prophylaxis - summary

- Undoubtedly works

… as long as it is taken

- How it will be taken and impact on behaviour in "real world" setting still unclear
- Guidelines / recommendations widely variable
- Cost / cost-effectiveness / affordability critical
- Truvada may not be the best option in the longer term
  - Longer acting agents: rilpivirine, GSK integrase inhibitor

Treatment as Prevention (TasP)

- Biological Plausibility
- Observational Data
- RCT data
- Ecological data
- Concerns
- Guidelines

Infectivity and Viral Load

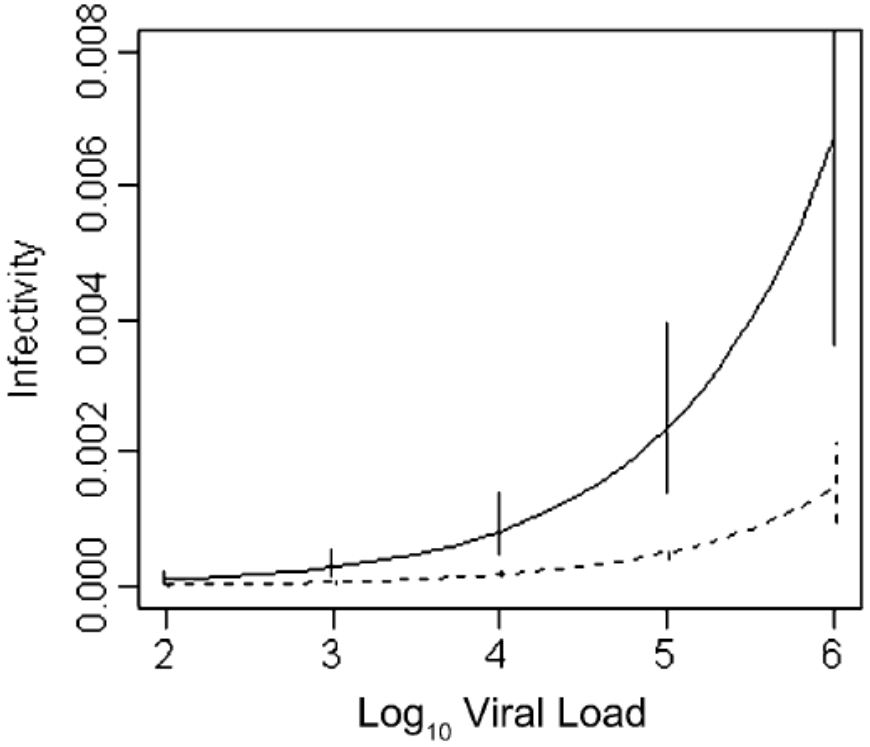


Figure 1. Per-act probability of transmission (infectivity) vs $\log_{10}$ plasma HIV-1 RNA (copies/mL) from a model that includes plasma human immunodeficiency virus type 1 RNA and condom use only. Solid line is without reported condom use and dashed line is with reported condom use. Vertical lines represent 95% confidence intervals.

Hughes et al, JID, 2012

Partners in prevention study

Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis

Transmission rate (per 100 years)

Initiated ART	Not initiated ART
0.37 (95% CI 0.09–2.04)	2.24 (1.84–2.72)

(p=0.004)

92% reduction in HIV transmission with ART

Donnell et al, Lancet 2010

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

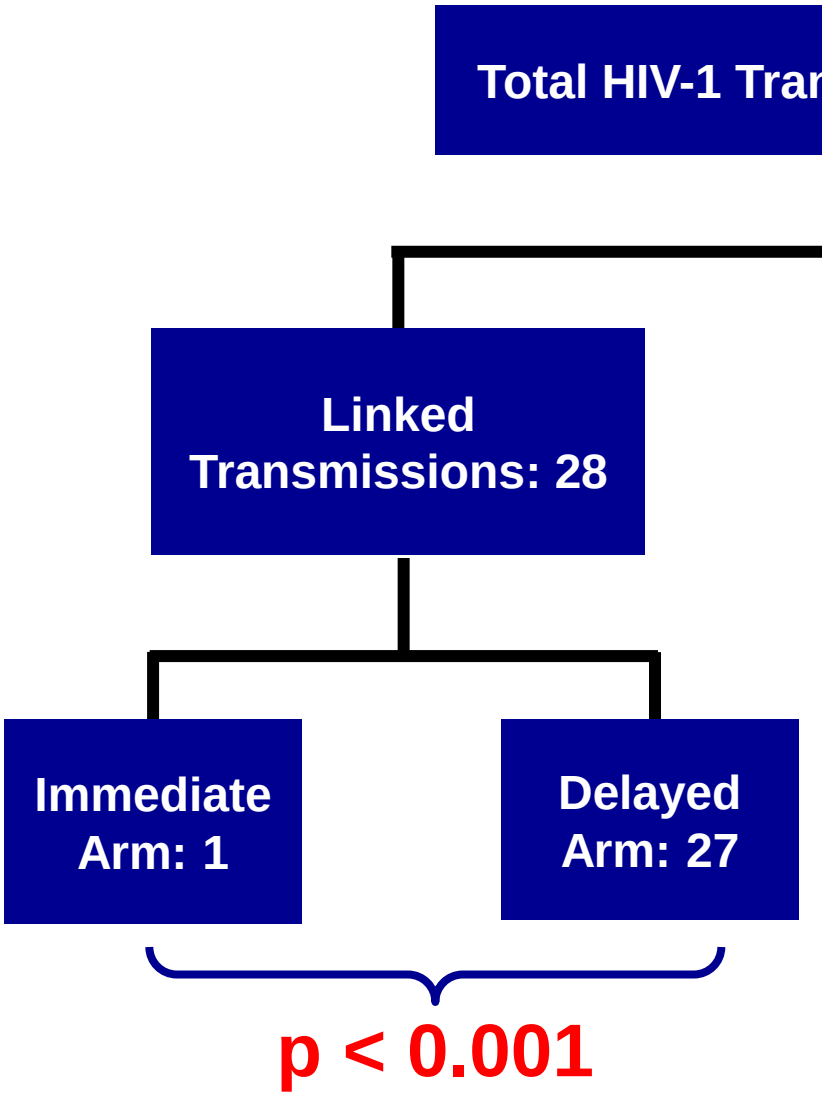
Primary Prevention Endpoint (in HIV-negative partner)

- Linked HIV transmission to HIV-1 negative partners

DSMB recommended study be stopped early on 28th April 2011

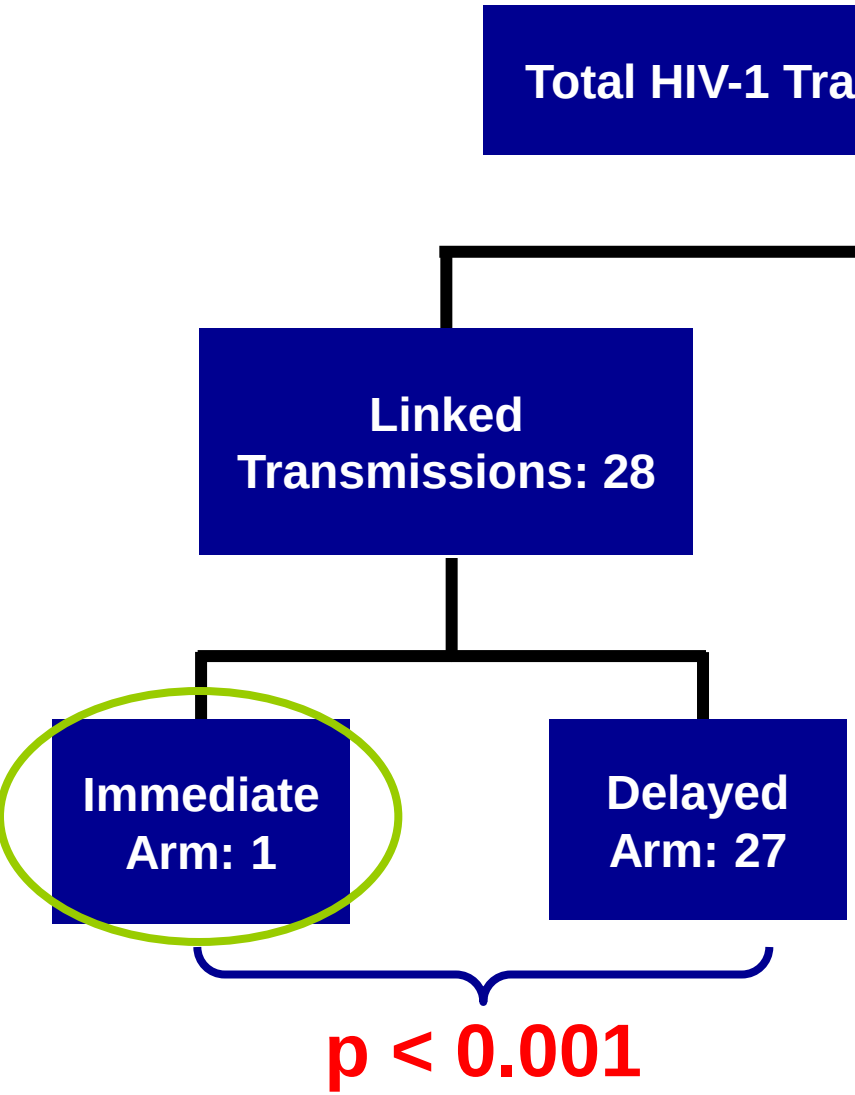
Adapted from Cohen MS, et al. N Engl J Med 2011;10.1056
Cohen M, et al. IAS 2011; Rome. Oral #MOSY0302
Grinsztejn B, et al. IAS 2011; Rome. Oral #MOSY0305
HPTN Study 052 Fact Sheet. Available at: http://www.hptn.org/web%20documents/IndexDocs/HPTN052FactSheet19Jul2011.pdf. Accessed 04 August 2011

HPTN 052: HIV-1 Transmission



- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm^3
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

HPTN 052: HIV-1 Transmission



- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm^3
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

HIV transmission risk through condomless sex if the HIV positive partner is on suppressive ART: PARTNER study

Rodger O 153LB

Taking all studies in serodifferent couples to date, cumulative couple-years of observation (CYFU) during which condomless sex was reported is around 330[1]There is no direct evidence at all for anal sex in men who have sex with men

Aim: To evaluate the risk of within-couple HIV transmission (HT and MSM) during periods where condoms are not used consistently and the HIV positive partner is on suppressive ART

HIV negative partners: Characteristics

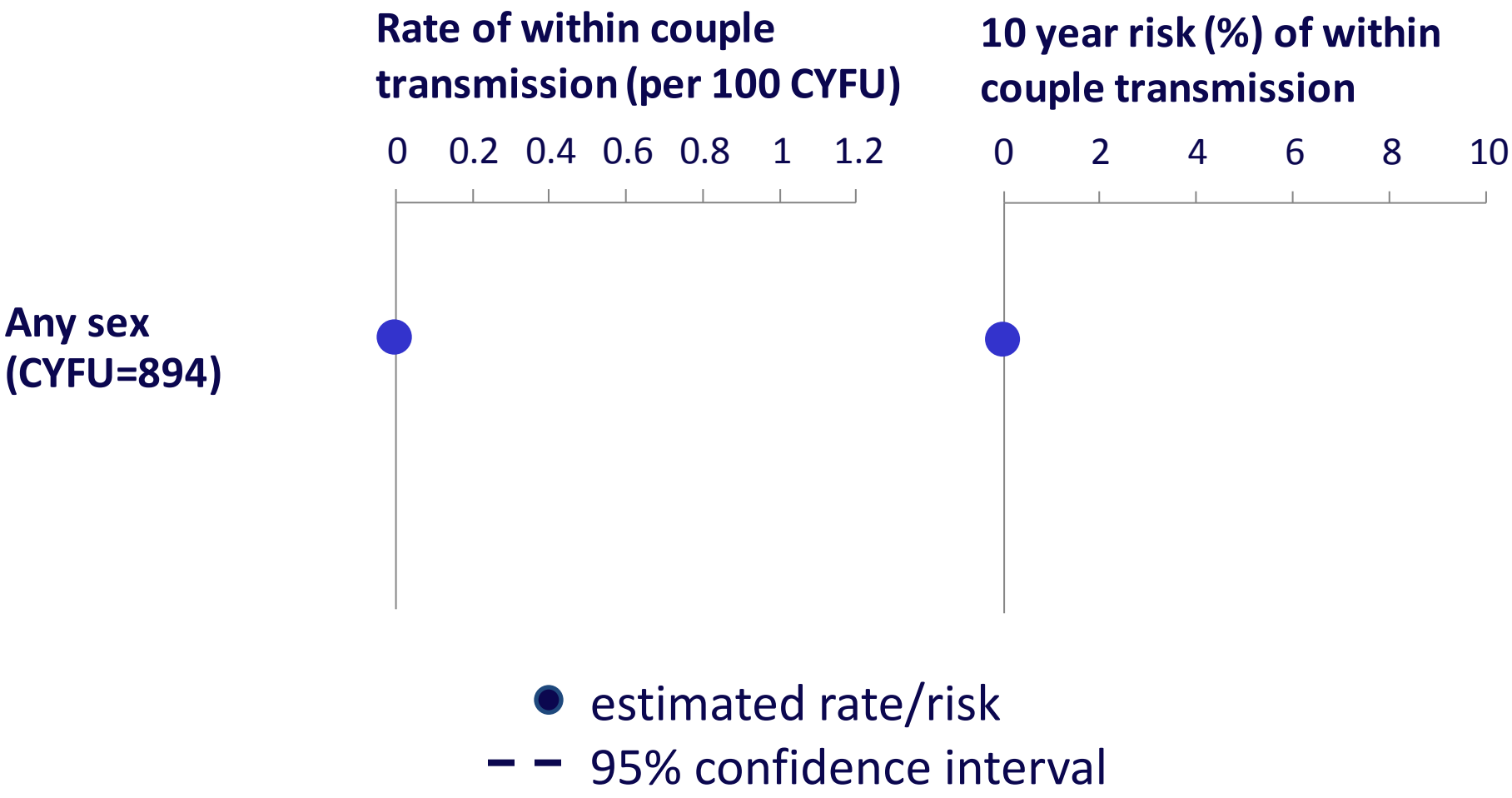
	MSM couples (n=282)	Heterosexual couples (n=445)	
		M -ve (n=245)	W-ve (n=240)
At study entry			
Age, median (IQR)	40 (32-47)	45 (37-50)	40 (34-46)
Yrs CL sex, median (IQR)	1.5 (0.5-3.5)	2.7 (0.6-6.9)	3.5 (0.7-10.6)
During follow up			
Years in the study, median (IQR)	1.1 (0.7-1.9)	1.5 (1.0-2.0)	1.5 (0.9-2.0)
Diagnosed with STI, %	16%	5%	6%
CL sex with other partners, %	34%	3%	4%
CL sex acts/year, median (IQR)	43 (18-79)	37 (14-77)	38 (14-71)
Estimated total number CL sex acts	16,400	14,000	14,000

HIV positive partners: Characteristics

	MSM couples (n=282)	Heterosexual couples (n=445)	
		W +ve (n=245)	M +ve (n=240)
At study entry			
Age, median (IQR)	42 (36-47)	40 (34-46)	45 (40-49)
Years on ART, median (IQR)	5 (2-11)	7 (3-14)	10 (4-15)
Self-reported adherence >=90%, %	97%	94%	94%
Self report undetectable VL, %	94%	86%	85%
CD4>350 cells/mm^3, %	90%	88%	84%
During follow-up			
Having missed ART for more than 4 consecutive days, %	2%	7%	4%
Diagnosed with STI, %	16%	4%	5%

British HIV Association
BHIVA

Rate of HIV transmission according to sexual behaviour reported by the negative partner



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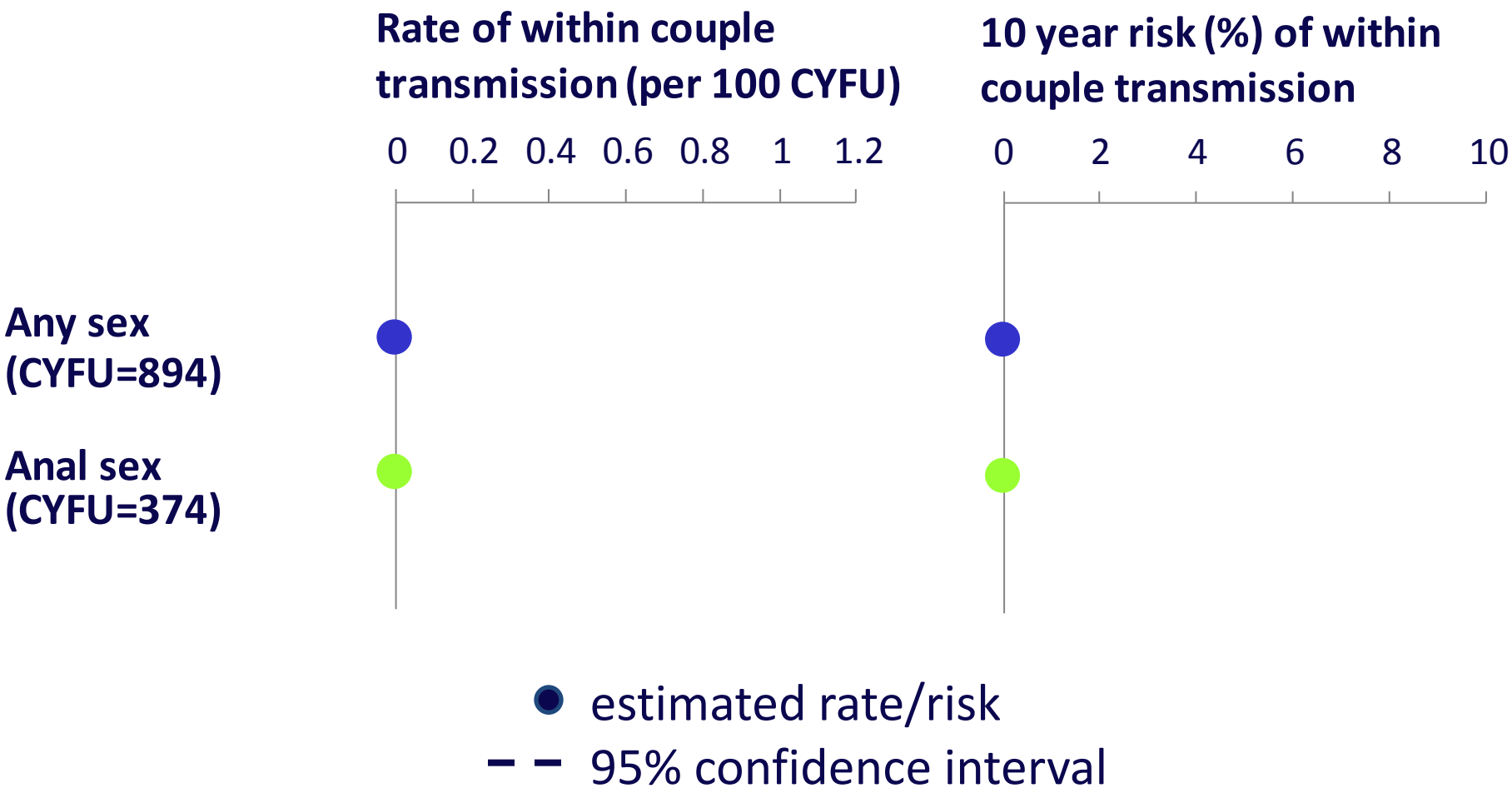

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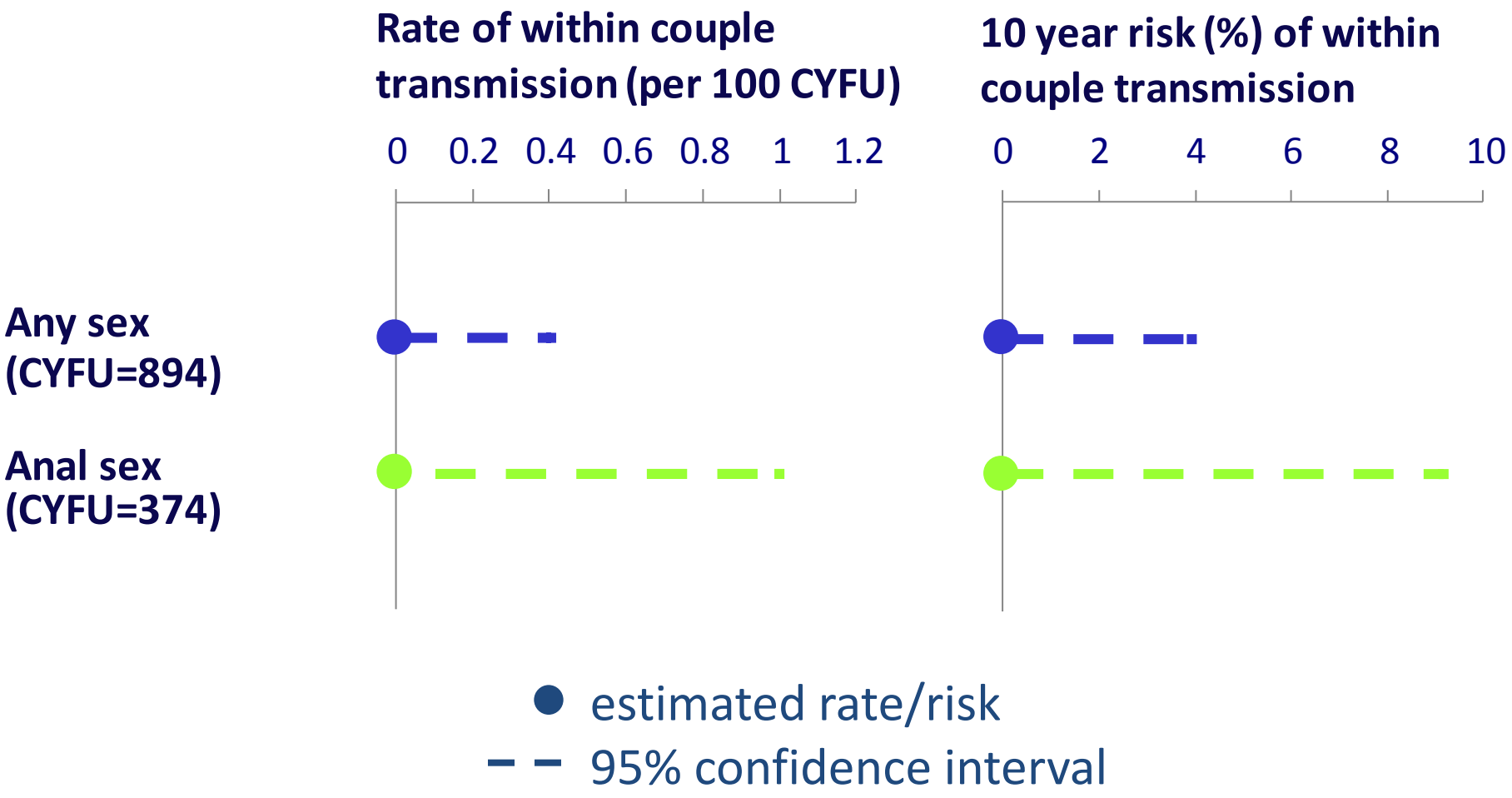

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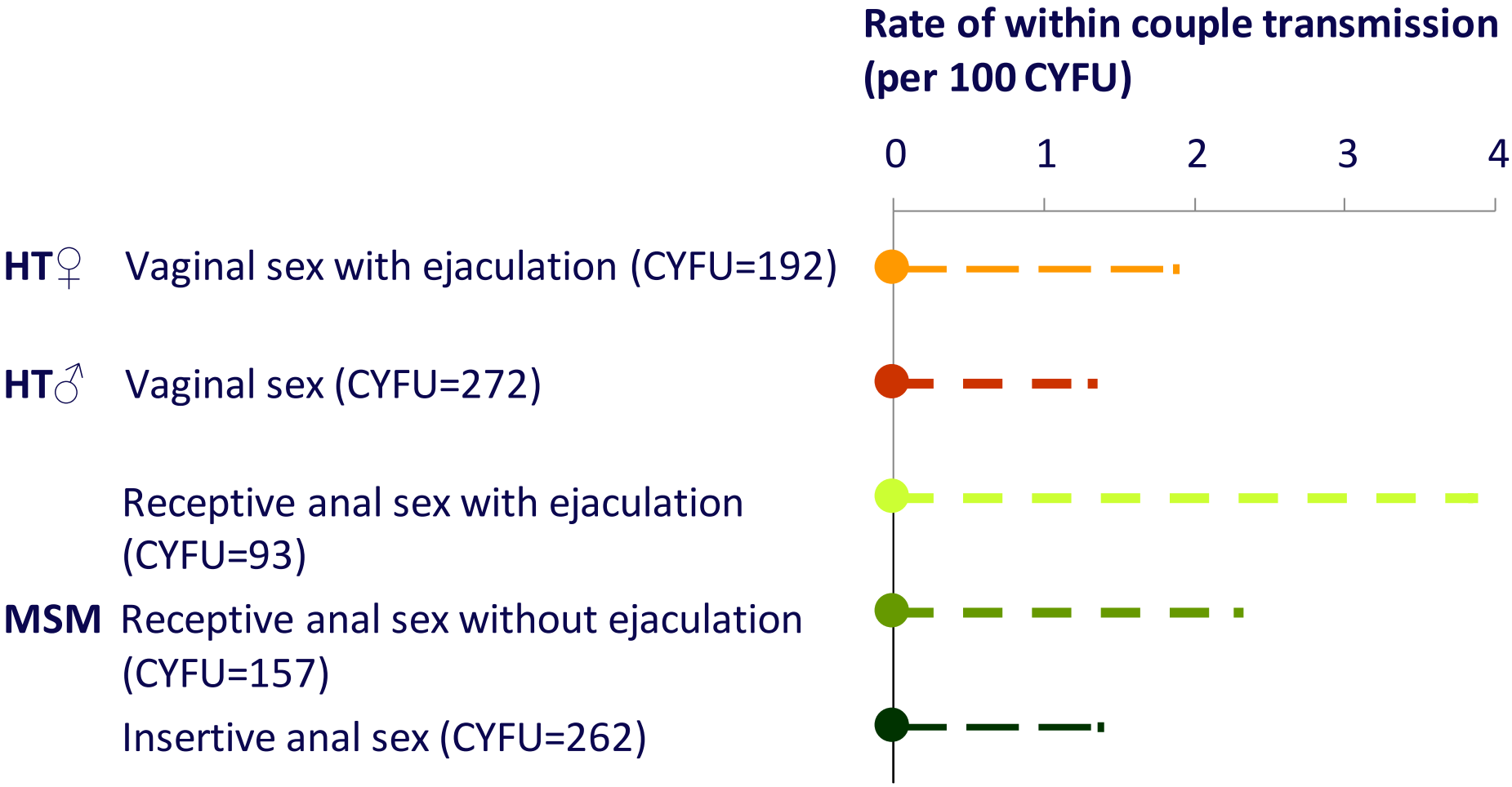


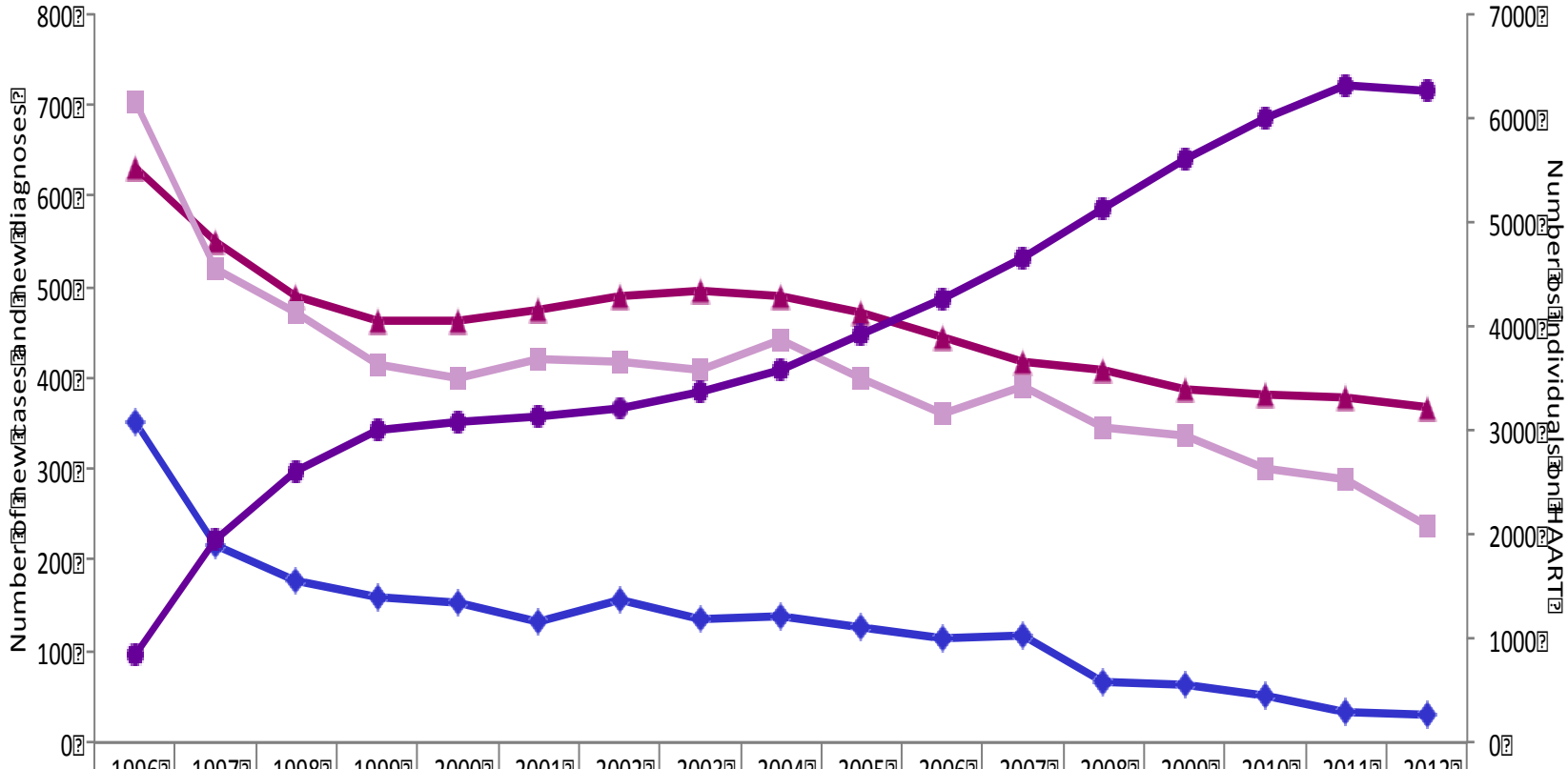
Conclusions

- Interim results after 894 eligible CYFU report an overall HIV transmission rate of zero through condomless sex with a plasma VL < 200 copies/mL on ART, despite a significant number of sexual acts.

- However uncertainty over the upper limit of risk remains, particularly over receptive anal sex with ejaculation

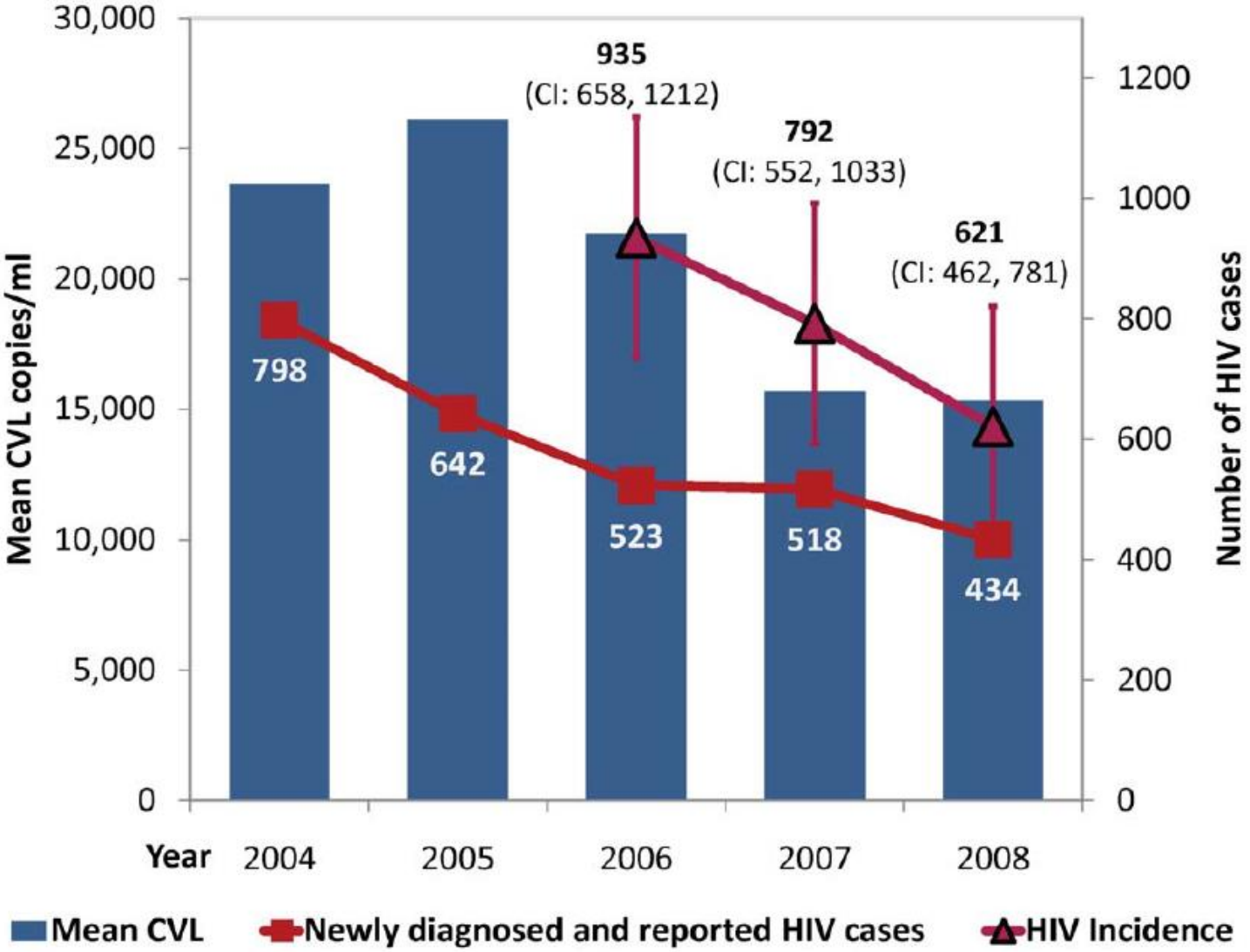
- Additional follow-up in MSM is needed through PARTNER2 (2014-2017) to provide more precise estimates for transmission risk to inform policy and also individual choice on condom use

HAART Use & New HIV Diagnoses for BC by year, 1996-2012



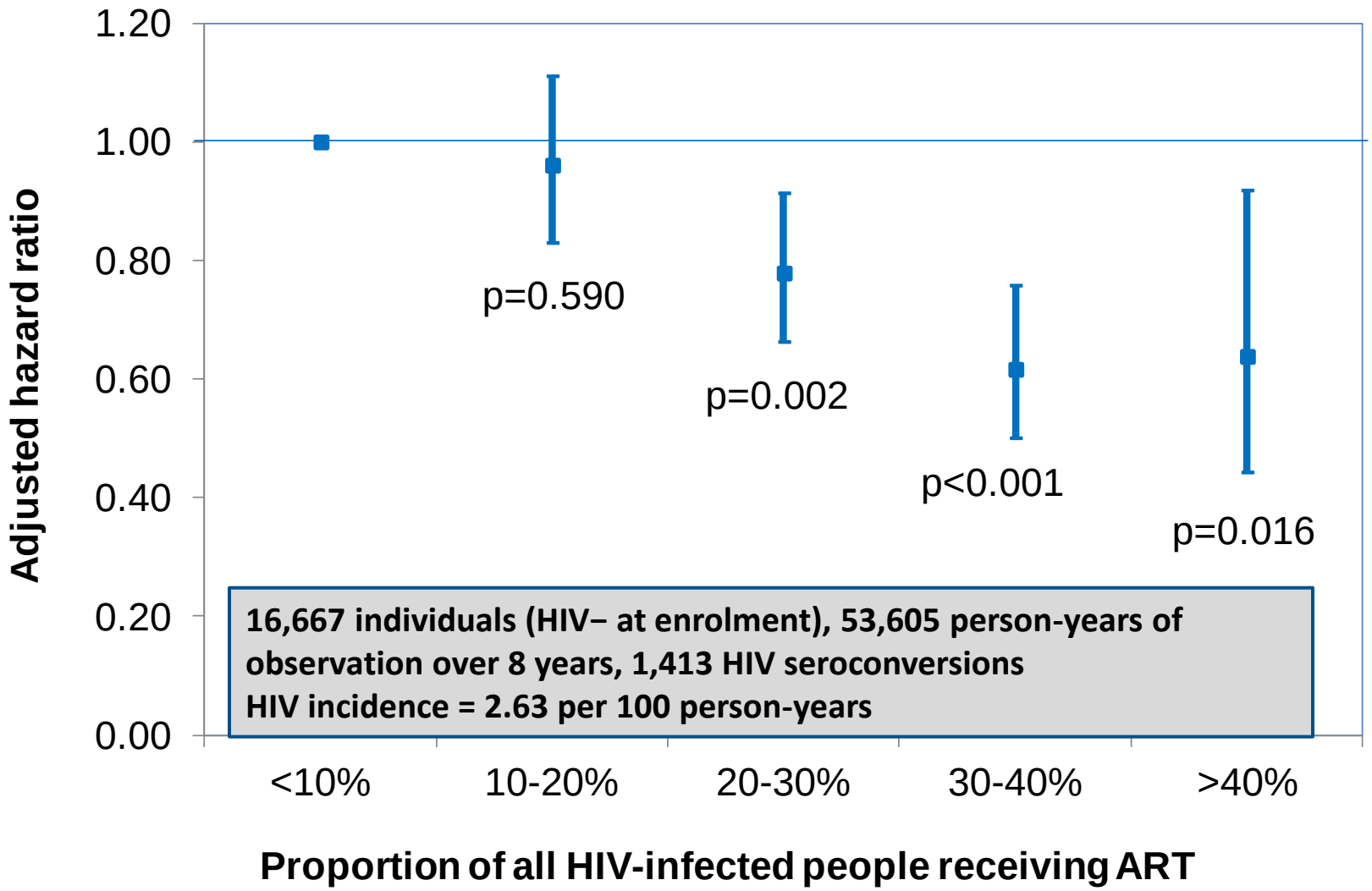
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
HIV Incidence	632	551	490	461	461	476	489	495	490	472	446	418	408	387	382	380	368
New HIV Diagnoses	702	519	471	416	400	420	418	408	442	400	361	391	345	337	301	289	238
New HIV Diagnoses (ever IDU)	352	215	177	159	152	132	156	136	137	125	115	118	65	64	52	34	29
Active on HAART	837	1960	2596	2994	3079	3120	3211	3356	3585	3913	4256	4654	5123	5595	5999	6298	6260
HIV Prevalence	7900	8228	8593	8933	9150	9408	9690	9936	10216	10398	10566	10790	11040	11280	11500	11700	11972

San Francisco: "Ecological Study"



Das, PLoS One, 2010

ART impact on HIV incidence



Tanser, Bärnighausen, Grapsa, Zaidi & Newell, Science 2013

HIV Infection Rates: Analysis of 51 Low and Middle-Income Countries

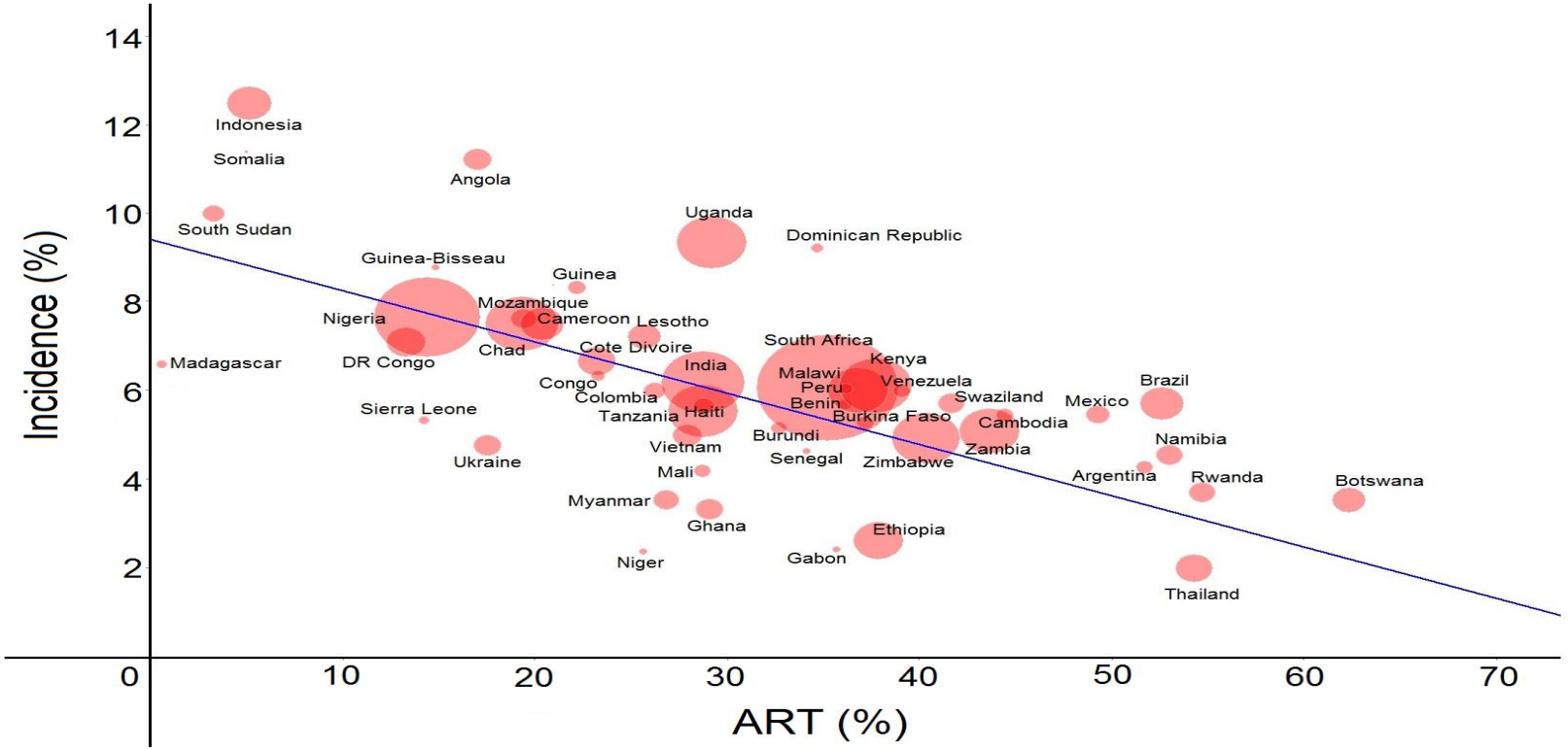
Higher ART Coverage is Significantly Correlated with Lower Incidence of HIV Infections and Annual AIDS-Related Deaths

UNAIDS country level estimates (2012) for number of people with HIV infections, receiving ART, new HIV infections and HIV-related death

- Analysis included 51 countries (36 African countries plus15 non-African low/middle income countries) with at least 50,000 HIV-infected individuals

- **Highly significant association between higher ART coverage and lower rates of HIV-related death and new HIV infection (p<0.00001 both cases)**

- **For each 10% increase in ART coverage: ~1% reduction in new infections and HIV-related death**



Hill A, et al. IAC 2014. Melbourne, Australia. #LBPE29

ART Coverage: Low/Middle- and High-Income Countries

Country Ranking of % of HIV-Infected Patients on ART (Abbreviated Table)

Ranking	Country*	No. HIV-Infected	No. on ART	% on ART
1.	United Kingdom	98,400	65,928	67.0
2.	Botswana	340,000	212,083	62.4
3.	Denmark	6,500	4,029	62.0
4.	France	149,900	89,940	60.0
5.	Netherlands	25,000	14,817	59.0
6.	Rwanda	210,000	114,978	54.8
11.	British Columbia	11,700	5,975	51.1
13.	Cambodia	110,000	48,913	44.5
18.	Ethiopia	760,000	288,137	37.9
26.	Australia	33,000	11,523	35.0
30.	United States	1,148,200	375,461	32.7

*High-income countries in red – ART coverage data extracted from published reports

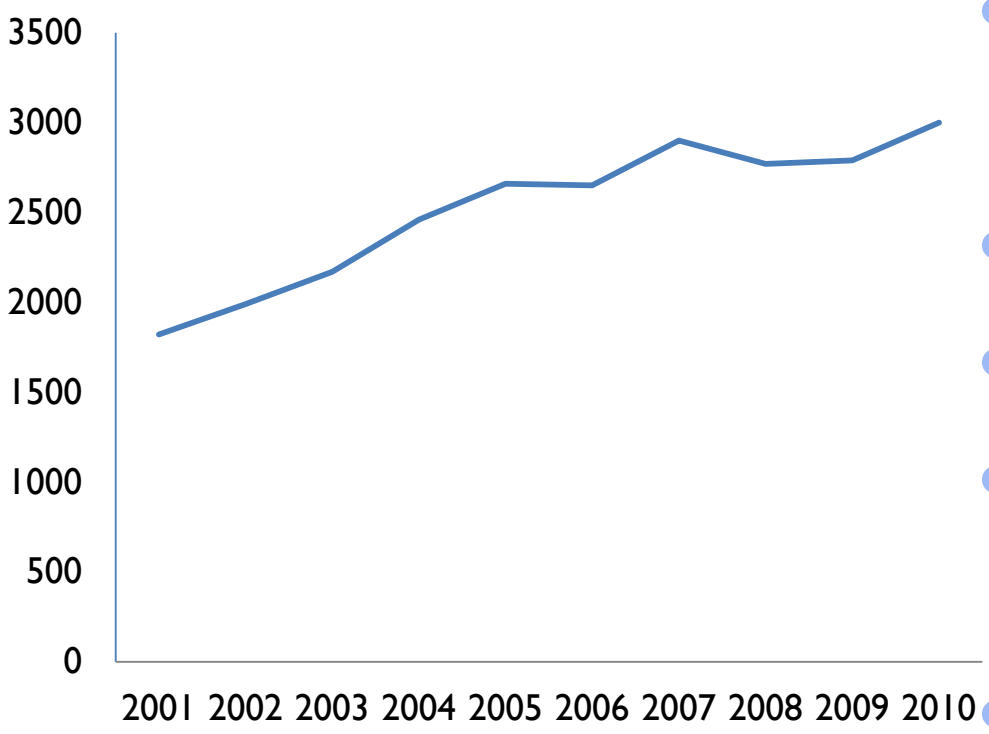
- **If all 51 countries had 62% ART coverage (Botswana): 1.2 million (65%) new infections and 1 million (70%) of HIV related deaths in 2012 could have been avoided**
- **Some low income countries now have higher ART coverage than high income countries, e.g. the USA (33%, ranked 30th out of 58)**

Adapted from Hill A, et al. IAC 2014. Melbourne, Australia. #LBPE29

Treatment as Prevention (TasP): Concerns

- Cost
- Risk compensation
- Increase in STIs
- Impact on different populations
  - Effect on MSM population incidence much less clear
  - Why is there no reduction in incidence in many countries?
- Where are new infections coming from?
- Acceptability and implementation issues
- Adherence to ART if not for personal benefit

HIV in MSM in UK



- Highest numbers ever
- >25% recently acquired
- >95% linkage to care
- >85% on ART
- >90% undetectable
- Improved testing policy
- Improved testing rates

OPEN ACCESS Freely available online

PLOS ONE

Increased HIV Incidence in Men Who Have Sex with Men Despite High Levels of ART-Induced Viral Suppression: Analysis of an Extensively Documented Epidemic

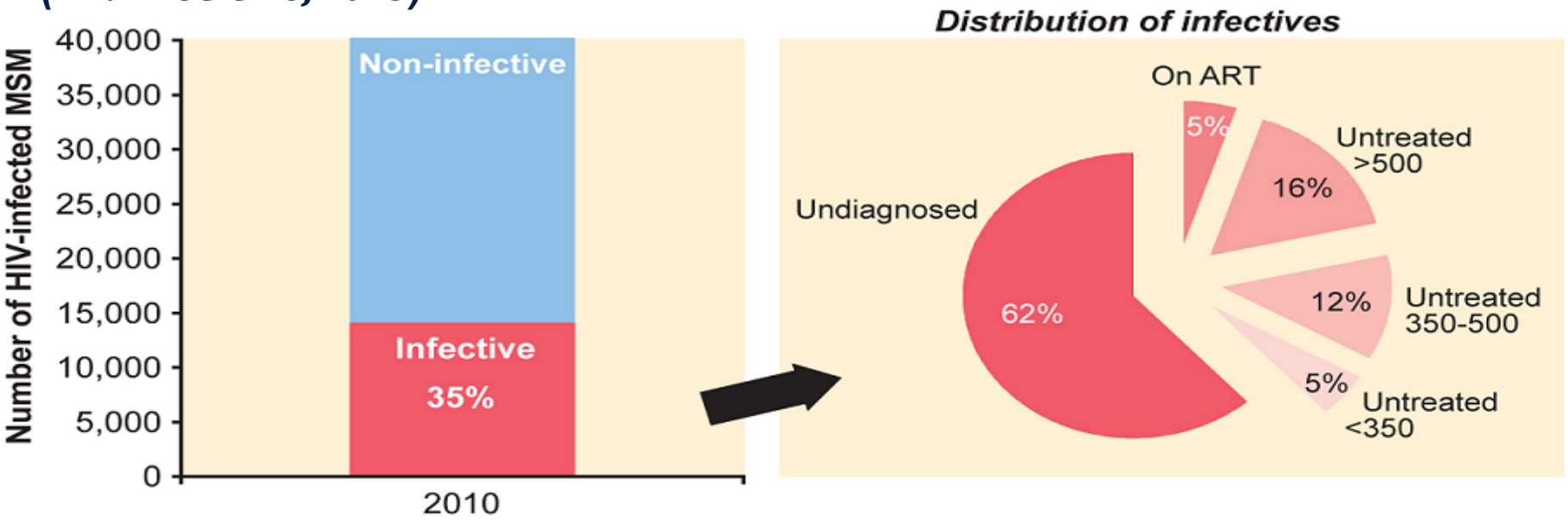
Andrew N. Phillips[1]*, Valentina Cambiano[1], Fumiyo Nakagawa[1], Alison E. Brown[2], Fiona Lampe[1], Alison Rodger[1], Alec Miners[3], Jonathan Elford[4], Graham Hart[1], Anne M. Johnson[1], Jens Lundgren[5], Valerie C. Delpech[2]

- **Source of new infections:**
  - **7% diagnosed, ART experienced**
  - **10% undiagnosed, ART naïve**
  - **34% undiagnosed in established infection**
  - **49% undiagnosed in PHI**

PLoS One, 2013

Distribution of infectives* among HIV-infected MSM, UK: 2010, *Brown et al*

(HIV Medicine, 2013)



* viral load >1500 copies/ml

Extending ART to all MSM with CD4 counts <500 cells/mm^3 would reduce infectivity from an estimated 35% to 29% and, in combination with halving the undiagnosed, to 21%.

HIV Treatment as Prevention in rural KwaZulu-Natal: progress and challenges in a cluster randomised trial

ANRS 12249; HIV prevalence 24%

12,910 individuals eligible

78% contacted

95% initially agreed to test for HIV; 82% actually tested

32% tested HIV positive (50% already known positive)

Of 50% new positives, 50% entered care

34% agreed to start ART (if high CD4 count)

Conclusion: achieving rates of ART coverage that will have an impact on incidence is challenging

Bordeaux School of public health ISPED Institut de Santé Publique d'Epidémiologie et de Développement

Iwuji et al; IAC Melbourne, July 2014

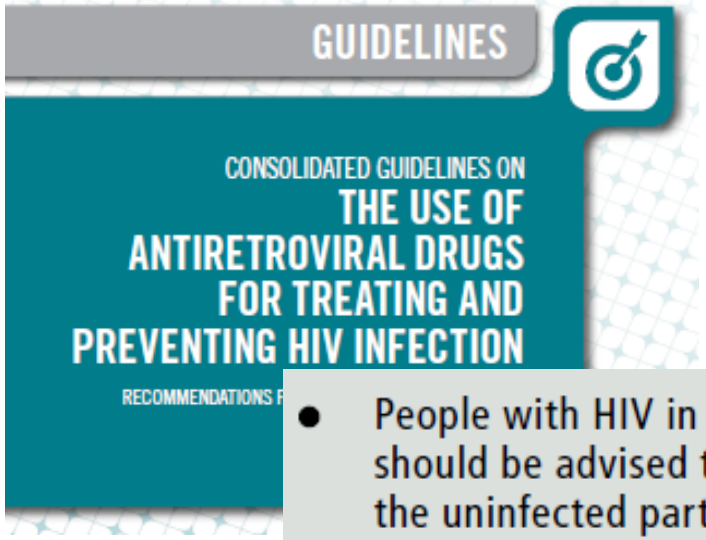
anRS French National Agency for Research on AIDS and Viral Hepatitis | An autonomous agency at Inserm |

AFRICA CENTRE FOR HEALTH AND POPULATION STUDIES

wellcome trust

UNIVERSITY OF KWAZULU-NATAL

World Health Organisation 2013 and March 2014 supplement

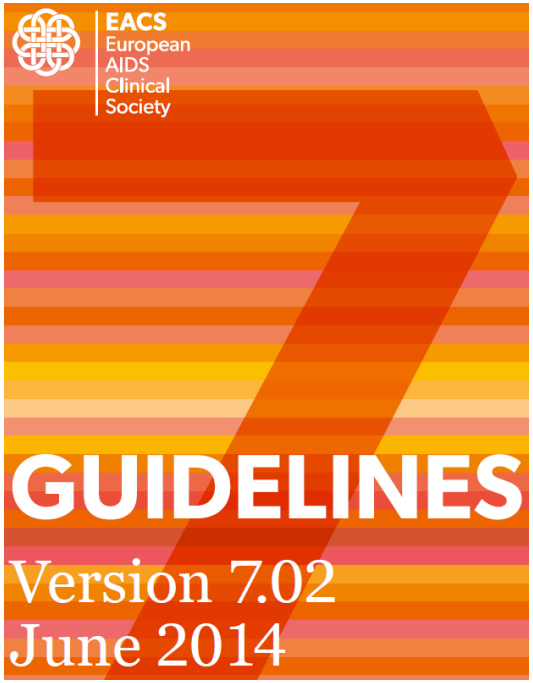


- **"public health approach to scaling up the use of ARV drugs for HIV treatment and prevention"**

- People with HIV in serodiscordant couples who start ART for their own health should be advised that ART is also recommended to reduce HIV transmission to the uninfected partner *(strong recommendation, high-quality evidence)*.
- HIV-positive partners with a CD4 count ≥350 cells/mm³ in serodiscordant couples should be offered ART to reduce HIV transmission to uninfected partners *(strong recommendation, high-quality evidence)*.

Population	Recommendation
Adults and adolescents (≥10 years)	Initiate ART if CD4 cell count ≤500 cells/mm³ • As a priority, initiate ART in all individuals with severe/advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm³
	Initiate ART regardless of WHO clinical stage and CD4 cell count • Active TB disease • HBV coinfection with severe chronic liver disease • Pregnant and breastfeeding women with HIV • HIV-positive individual in a serodiscordant partnership (to reduce HIV transmission risk)

EACS 2014



Recommendations for Initiation of ART in HIV-positive Persons without Prior ART Exposure[i]

Recommendations are graded while taking into account both the degree of progression of HIV disease and the presence of, or high risk for, developing various types of (co-morbid) conditions

Present condition/circumstance	Current CD4 count[i,ii,iii]	
	350-500	> 500
Asymptomatic HIV infection	C	C
To reduce transmission of HIV	C	C
Symptomatic HIV disease (CDC B or C conditions) incl. tuberculosis	R	R
Primary HIV infection	C	C
Pregnancy (before third trimester)	R	R

i,ii **ART is always recommended in a current CD4 count below 350 cell**
For persons with CD4 counts above ART should be individualized and co requesting ART and ready to start, h above and/or for any other personal to treat persons with CD4 counts be with higher CD4 counts if they suffe conditions before placing resources Time should always be taken to prep compliance and adherence.
Genotypic resistance testing is reco ideally at the time of HIV diagnosis; ART needs to be initiated before ge it is recommended to include a riton men. Before starting treatment, the be repeated to obtain a baseline to

iii R use of ART is recommended
C use of ART should be considered

In 2012: "In serodifferent partners, early initiation of ART as one aspect of the overall strategy to reduce HIV transmission should be strongly considered and actively discussed"

Position statement on the use of antiretroviral therapy to reduce HIV transmission January 2013. The British HIV Association (BHIVA) and the Expert Advisory Group on AIDS (EAGA) †

†Members of the Writing Group: S Fidler[1], J Anderson[2], Y Azad[3], V Delpech[4], C Evans[5], M Fisher[6], B Gazzard[5], N Gill[4], L Lazarus[4], R Lowbury[7], K Orton[8], B Osoro[9], K Radcliffe[10], B Smith[11], D Churchill[6], K Rogstad[12] and G Cairns[13]

[1]Imperial College London, [2]Homerton University Hospital, London, [3]National AIDS Trust, [4]Health Protection Agency, [5]Chelsea and Westminster Hospital, London, [6]Royal Sussex County Hospital, Brighton, [7]MEDFASH (Medical Foundation for HIV & Sexual Health), [8]Department of Health, [9]Positively UK, [10]University Hospital Birmingham Foundation NHS Trust, [11]Terrence Higgins Trust, [12]Royal Hallamshire Hospital, Sheffield, [13]NAM Publications/Aidsmap.com

What to do in the clinic (based upon BHIVA 2013)

- **Discuss the data on ART and transmission with *all* patients**
  - **At initial diagnosis**
  - **At subsequent visits (especially if known partner change)**

- **Consider starting ART earlier in patients if:**
  - **In serodiscordant relationship**
  - **Patient is concerned regarding onward transmission**
  - **Irrespective of risk group**
  - ***Irrespective* of whether in regular relationship**

What will you tell your patient the transmission risk is if their viral load is undetectable?

1. Zero
2. Almost zero
3. Extremely low
4. Very very low
5. Low
6. I don’t know

BHIVA and EAGA believe that giving an actual figure for the risk of transmission for one episode of sex in a serodiscordant couple is not currently meaningful for an individual and that any figure proposed would be misleading, for the reasons outlined below. In the absence of such a figure, BHIVA and EAGA have therefore adopted the term 'extremely low' whilst recognising the difficulty inherent in the imprecise nature of such a term.

BHIVA/EAGA TasP Statement

Additional Recommendations in WHO Prevention Guidelines

- The correct and consistent use of **condoms** with condom-compatible lubricants is recommended for all key populations to prevent sexual transmission of HIV and sexually transmitted infections (STIs).
- Voluntary medical **male circumcision** (VMMC) is recommended as an additional, important strategy for the prevention of heterosexually acquired HIV infection in men, particularly in settings with hyperendemic and generalized HIV epidemics and low prevalence of male circumcision.
- All people from key populations who inject drugs should have access to sterile injecting equipment through **needle and syringe programmes**.
- All people from key populations who are dependent on opioids should be offered and have access to **opioid substitution therapy**.

TasP: Summary

- At an individual level, undoubtedly works
- Growing evidence that works for anal sex as well as vaginal sex
- At a population / public health level, implications on HIV incidence less clear
  - Cluster randomised trials ongoing
  - May be different in different risk groups
- Knowledge of HIV status absolutely critical
  - Need to "scale-up" HIV testing
  - May need high rates of population ART coverage (>80%)
- All guidelines consistent: as clinicians we must be discussing with all patients at an individual level

Question 1

- 32 year old heterosexual male
- HIV positive
- CD4 count 580; viral load 12,000
- Regular female partner is HIV negative

- Would you recommend starting ART?

Question 2

- 32 year old MSM
- HIV positive
- CD4 count 580; viral load 12,000
- Regular male partner is HIV negative

- Would you recommend starting ART?

Question 3

- 32 year old MSM
- HIV positive
- CD4 count 580; viral load 12,000
- No regular male partner but frequent casual partners of unknown status

- Would you recommend starting ART?

Question 4

- 32 year old MSM
- HIV negative
- Regular male partner is HIV positive
  - CD4 count 580; viral load 12,000
  - Declines to start ART
- Would you recommend starting PrEP?

Question 5

- 32 year old MSM
- HIV negative
- No regular male partner
- Frequent casual male partners

- Would you recommend starting PrEP?