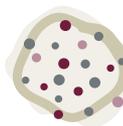




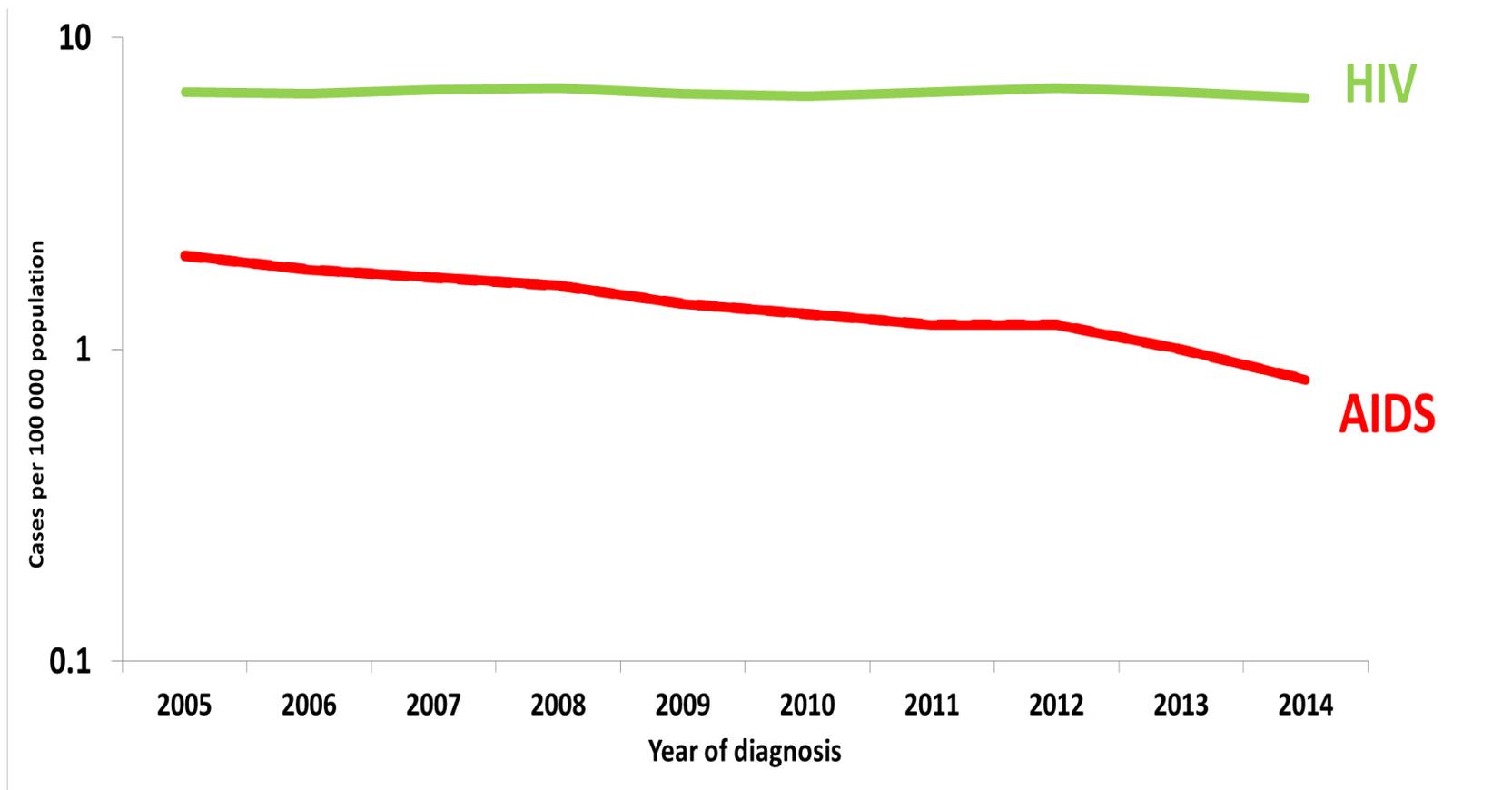
Intervenciones para evitar la Infección por VIH. Profilaxis Pre-Exposición

Santiago Moreno
Servicio de Enf. Infecciosas
Hospital Ramón y Cajal IRYVIS
Madrid



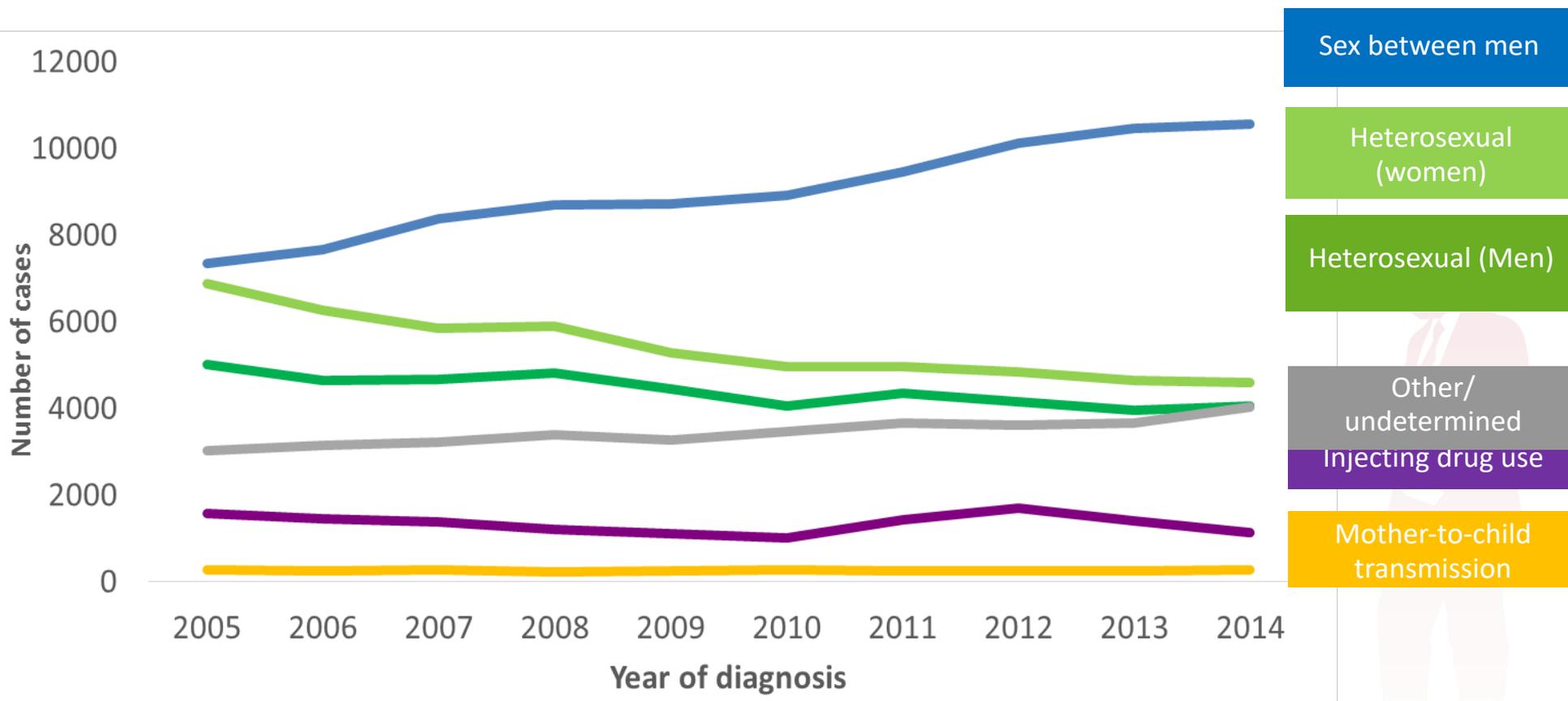


New HIV and AIDS diagnoses per 100 000, 2005-2014, EU/EEA





HIV diagnoses, by mode of transmission, 2005-2014, EU/EEA

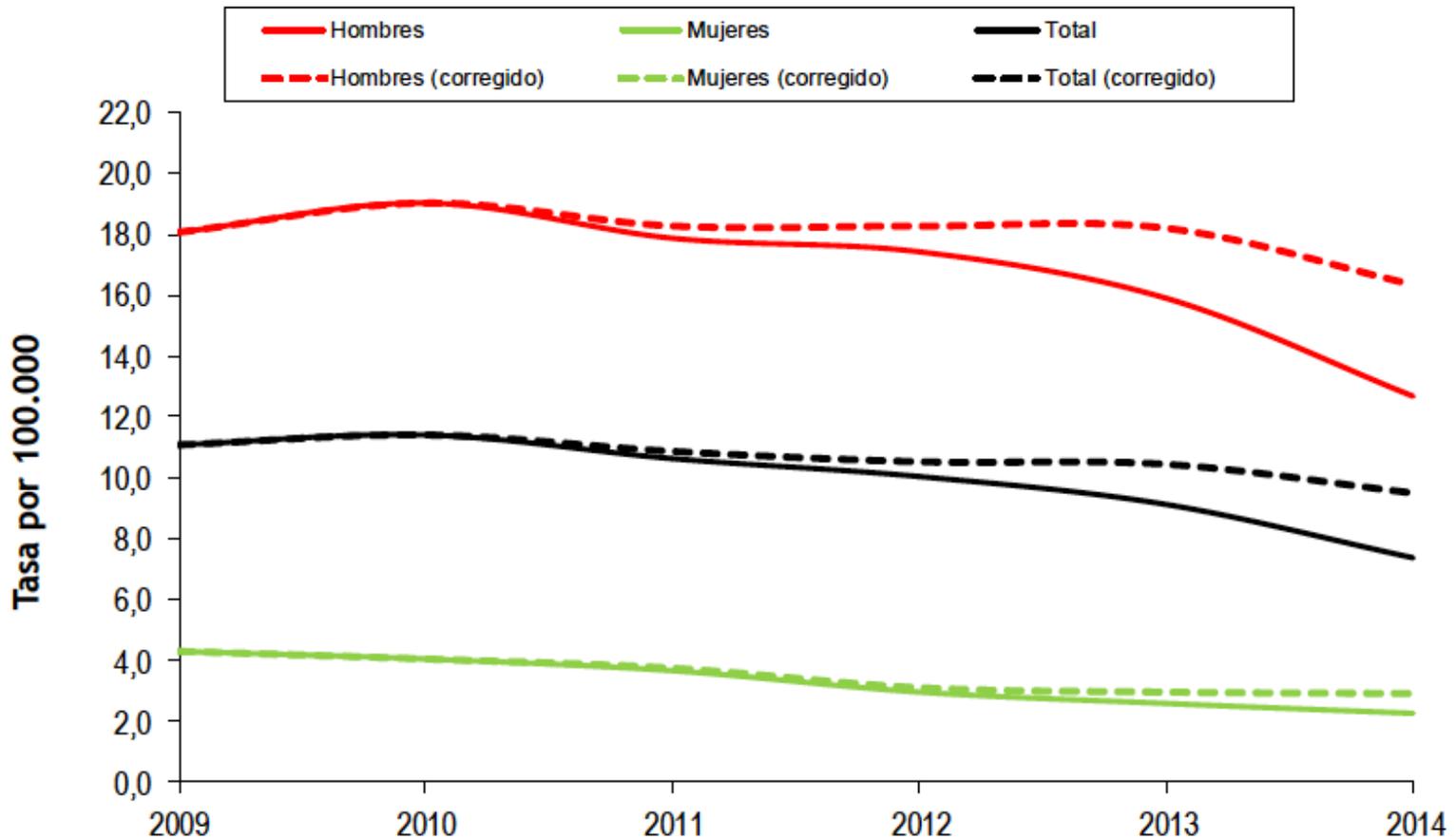


Data is adjusted for reporting delay. Cases from Estonia and Poland excluded due to incomplete reporting on transmission mode during the period; cases from Italy and Spain excluded due to increasing national coverage over the period.

Source: ECDC/WHO (2015). HIV/AIDS Surveillance in Europe, 2014



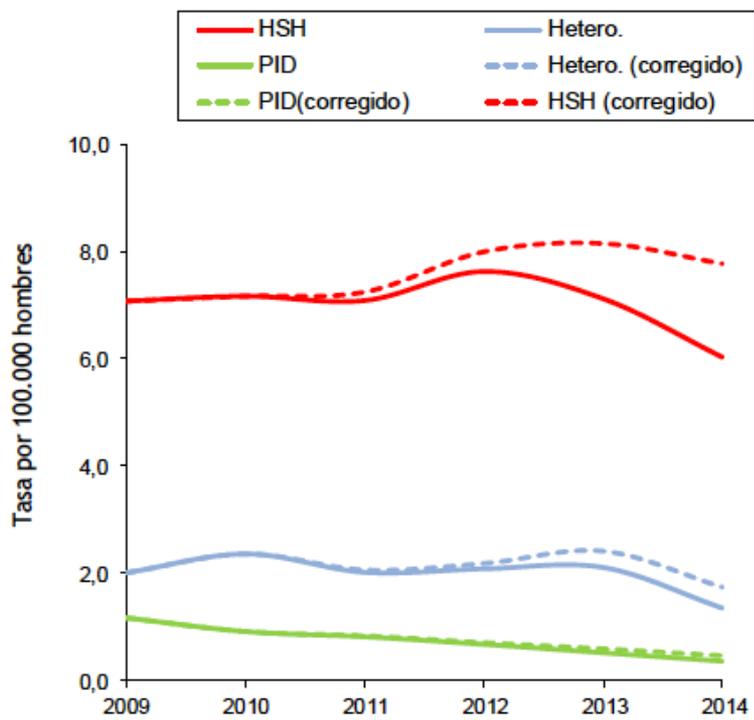
Tasas de nuevos diagnósticos de VIH anuales totales y según sexo. España, 2009-2014. Datos corregidos por retraso en la notificación.



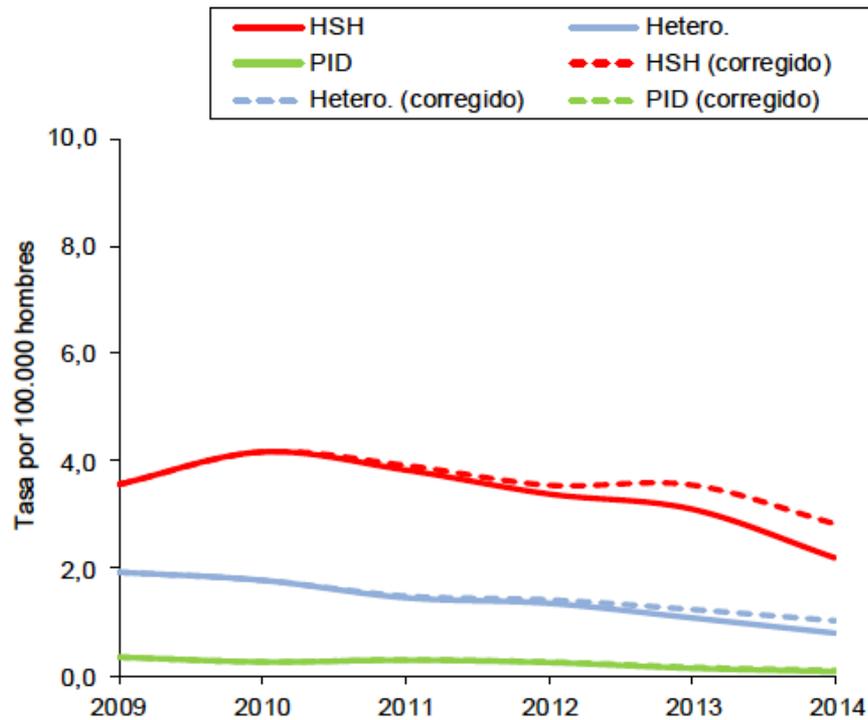


Tasas de nuevos diagnósticos de VIH anuales por modo de transmisión y lugar de origen. España, 2009-2014. Datos corregidos por retraso en la notificación.

HOMBRES



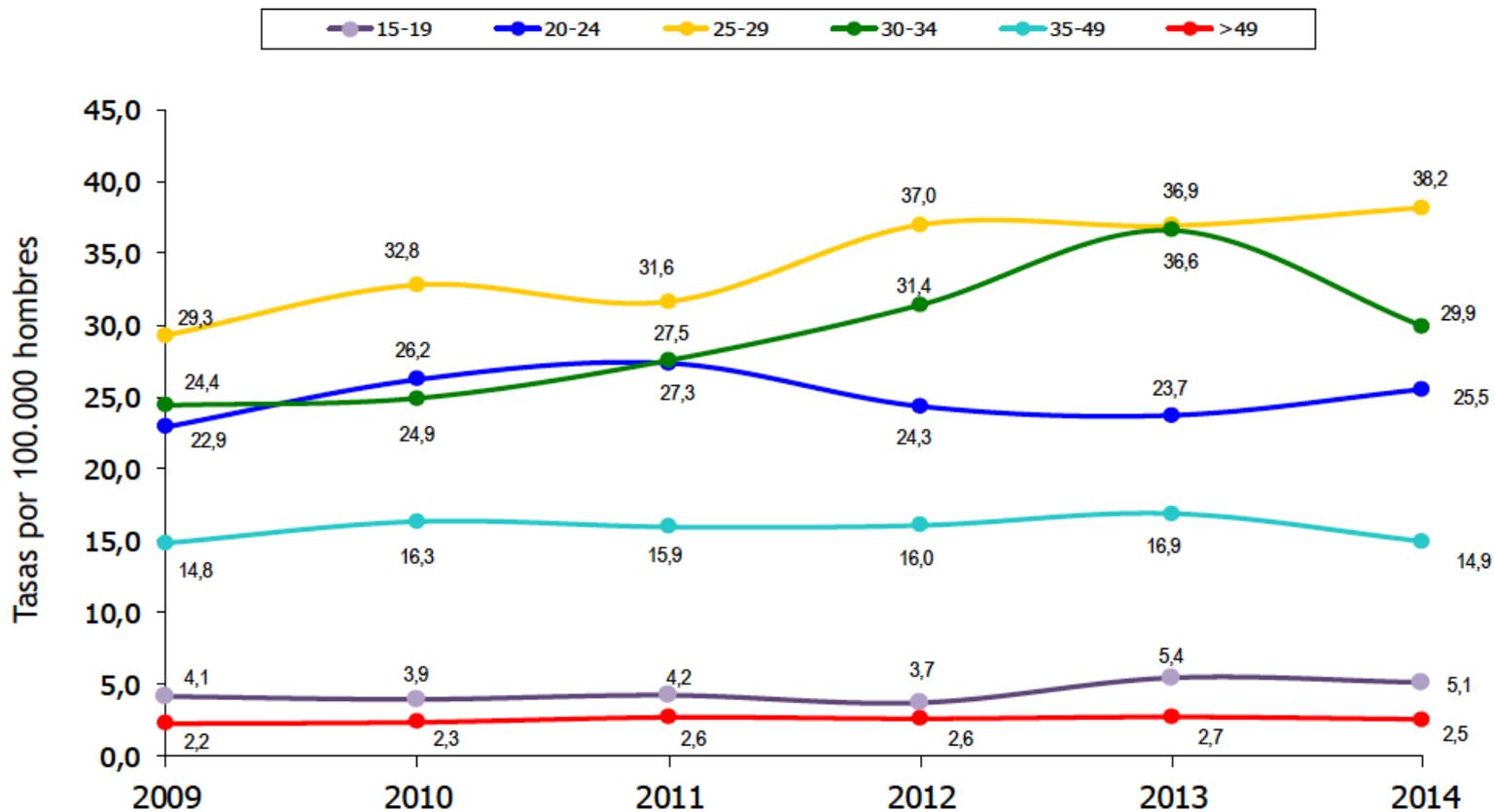
España



Otros países

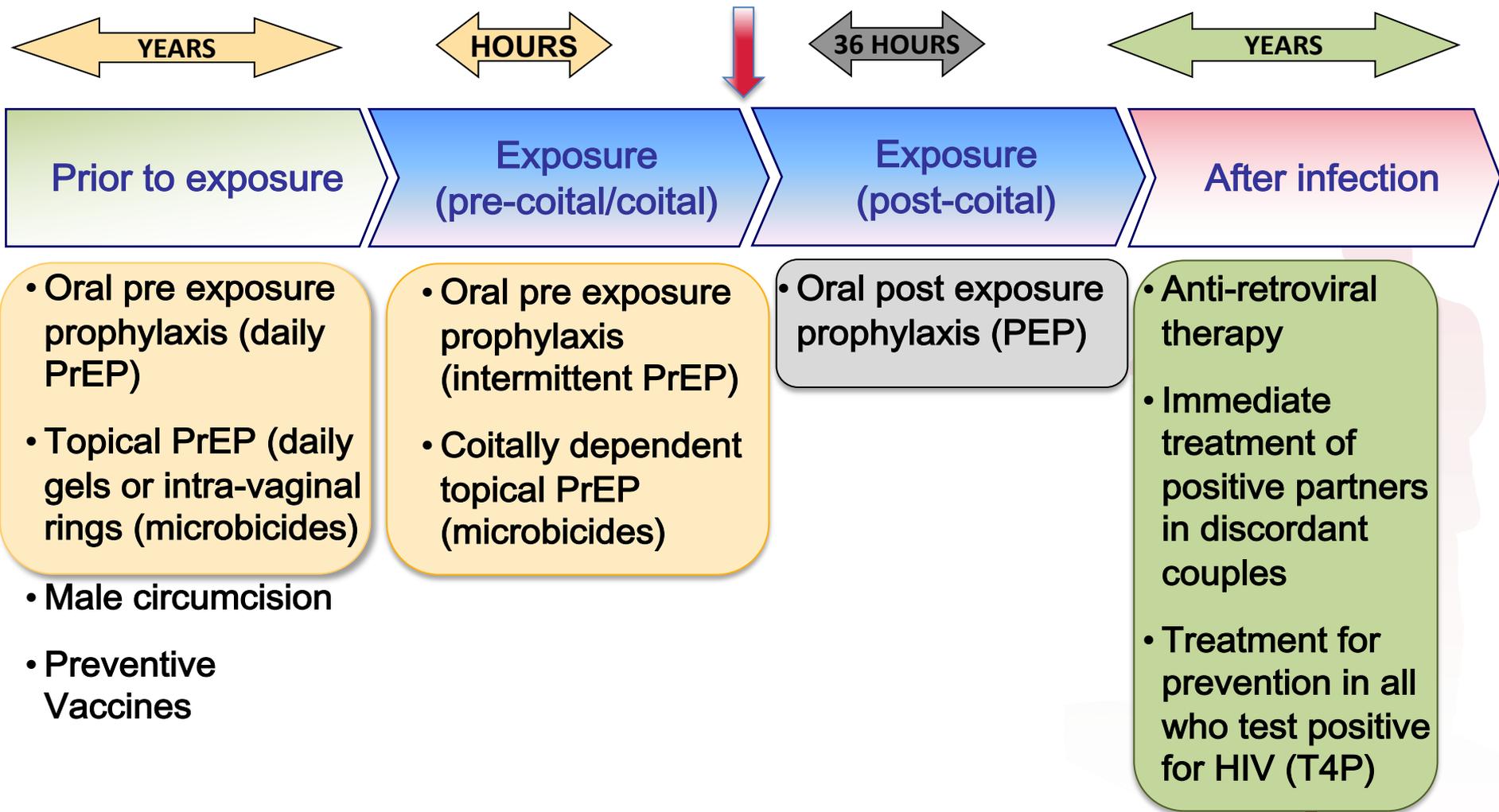


Tasas de nuevos diagnósticos de VIH en HSH por año de diagnóstico y grupos de edad. España, 2009-2014. Datos corregidos por retraso en la notificación.





HIV Prevention: Opportunities for biomedical interventions





What drives ongoing infections?

- Primary HIV infection¹⁻²
- Undiagnosed HIV infection³⁻⁶
- Untreated / poorly treated HIV infection^{4,7-8}





Sexual transmission of HIV by persons living with HIV status

	Daily census	Daily trans. rate (%)	Annual trans. rate (%)	Annual HIV infections (%)
Acutely-infected (unaware)	5370	0.1408	51.40	2760 (8.6%)
Nonacute, unaware	244,630	0.0174	6.35	15,524 (48.5%)
Nonacute, aware	750,000	0.0050	1.83	13,716 (42.9%)
Unaware	250,000	0.0200	7.31	18,284 (57.1%)
Overall	1,000,000	0.0088	3.20	32,000 (100%)

The transmission rate is the average number of transmission events, per PLWH, per unit time

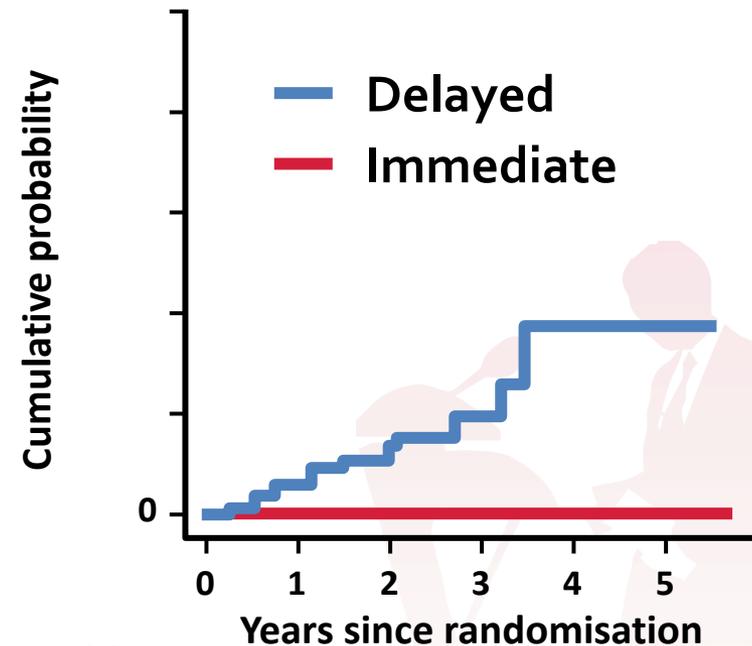
Pinkerton SD *et al. AIDS* July 31 2007;21(12):1625–1629

Treatment as prevention – TasP

- Internationally, HIV-positive population trends are declining¹⁻⁴
- For an individual, it has been demonstrated that the rate ratio of incidence of HIV infection is more favourable with the administration of ART⁵

“The early initiation of antiretroviral therapy reduced rates of sexual transmission of HIV-1 and clinical events, indicating both personal and public health benefits from such therapy”⁶

HPTN 052: Linked HIV transmission



No. at risk	0	1	2	3	4	5
Immediate	893	658	298	79	31	24
Delayed	882	655	297	80	26	22

1. Wood E, et al. *BMJ* 2009;338:b1649; 2. Montaner JSG, et al. *Lancet* 2010;376:532-9; 3. Das M, et al. *PLoS ONE* 2010;5:e11068; 4. Henard S, et al. *J Acquir Immune Defic Syndr* 2012;61:400-402; 5. Anglemeyer A, et al. *Cochrane Database Syst Rev* 2011;(8):CD009153; 6. Cohen MS, et al. *N Engl J Med* 2011;365:493–505



Partner Cohort Study: HIV Transmission Risk Despite Condomless Sex

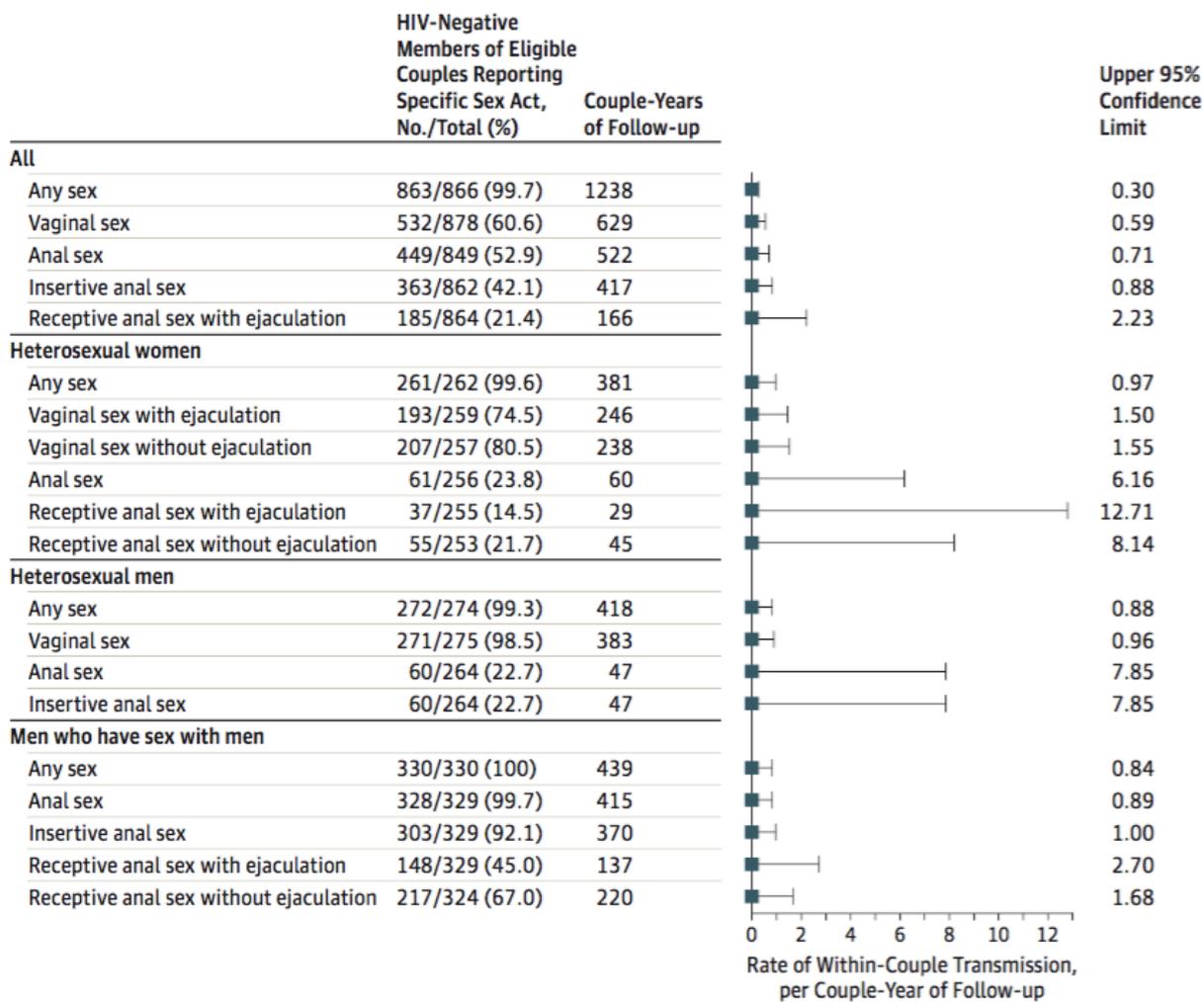
- International Observational Cohort Study of sero-discordant couples
- Analyzed transmission risk from HIV+ on ARVs with undetectable viral load from condomless sexual acts – no PEP nor PREP used in HIV-
- Analysis of transmissions linked to partner thru phylogenetic analysis

	Observed Transmissions	95% CI for 100 couple years
Overall	0	0-0.4%
Anal sex	0	0-0.96%
Receptive Anal, with or without ejaculation	0	0-1.97%

- Ten-year risk of HIV Transmission:
 - 0-3.9% overall
 - 0-9.2% for condomless anal sex



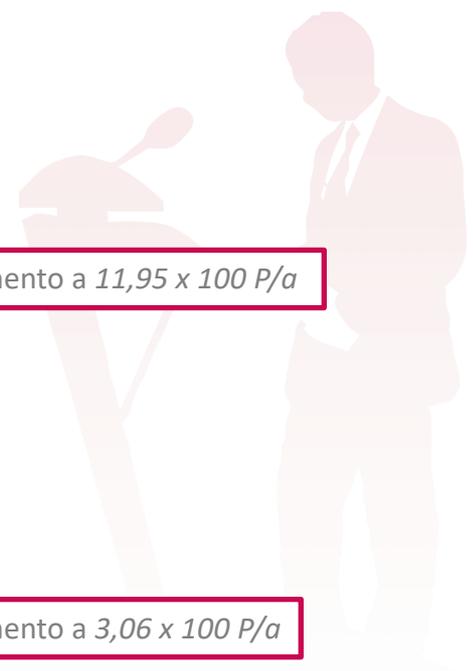
Tasa de transmisión del VIH según práctica sexual del sujeto VIH-



Aproximación jerárquica del riesgo

Incremento a 11,95 x 100 P/a

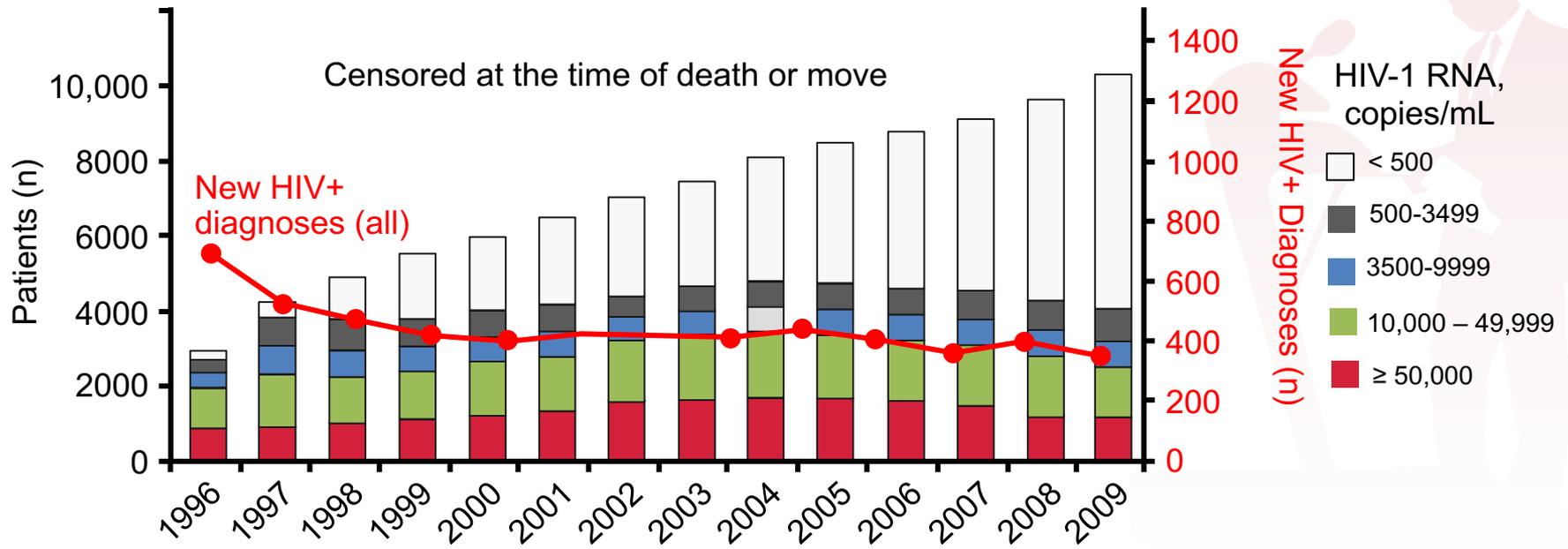
Incremento a 3,06 x 100 P/a





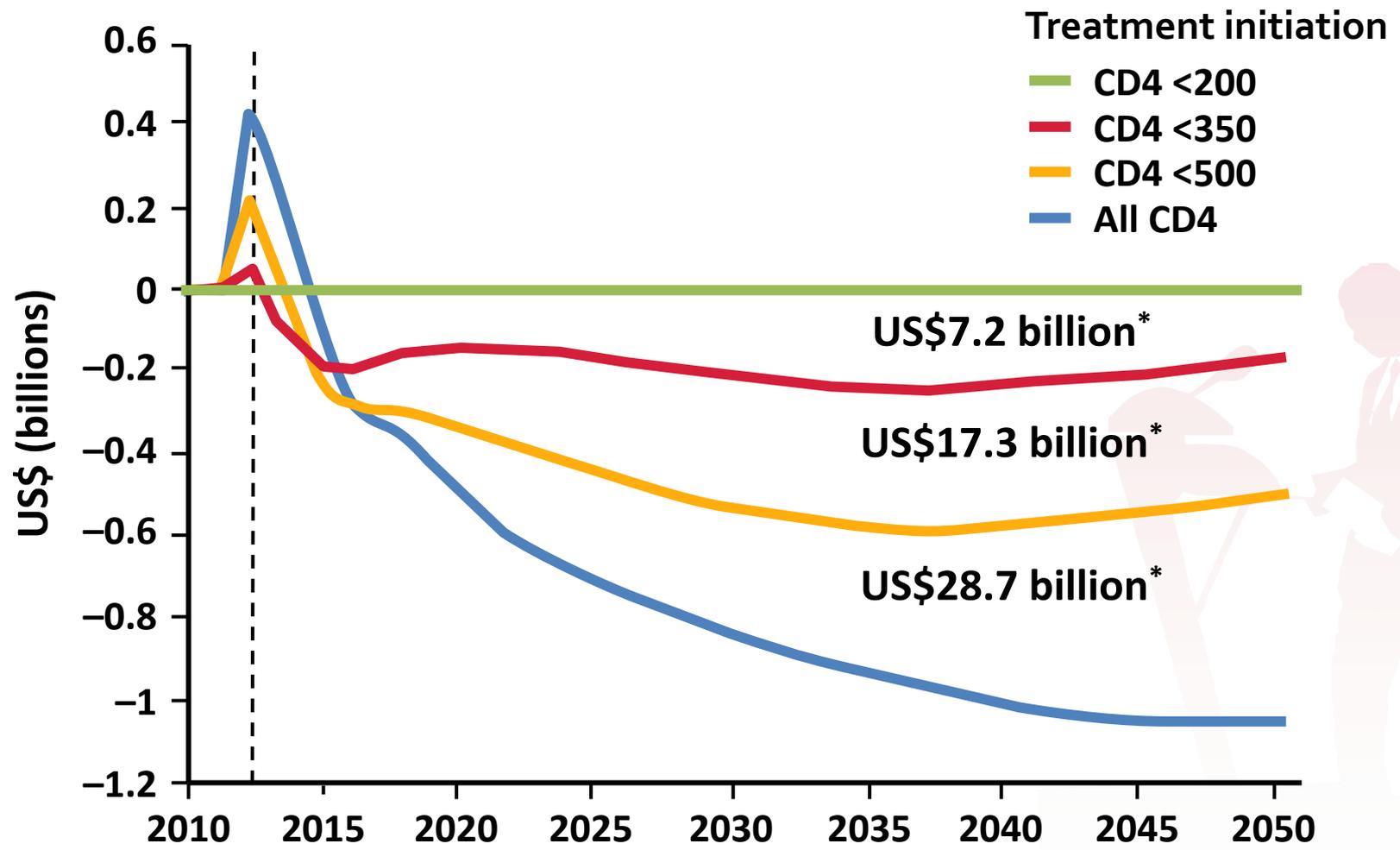
Reduction in New HIV Diagnoses in BC: Testing, HAART, and Community VL

- Period of declining new HIV diagnoses in BC coincident with increased HIV testing rates, increased uptake of antiretroviral therapy, and decrease in community viral load (1996-2008)
 - Decline in new HIV diagnoses despite increases in syphilis, gonorrhea, chlamydia





Potential cost savings of different ART initiation points (South Africa)



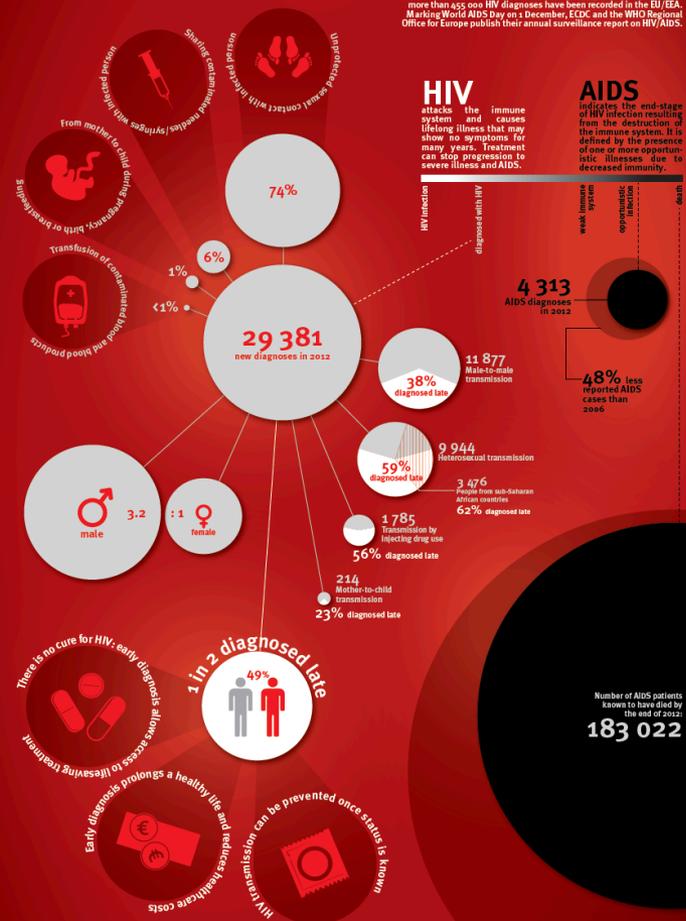
* Cumulative potential cost savings from 2010–2050 Granich R et al. PLoS ONE 2012; 7:e30216



HIV and AIDS in Europe



HIV infection remains of major public health importance in the European Union and European Economic Area (EU/EEA); there is no indication of a decline in transmission. Since the start of reporting on the HIV epidemic, more than 455 000 HIV diagnoses have been recorded in the EU/EEA. Marking World AIDS Day on 1 December, ECDC and the WHO Regional Office for Europe publish their annual surveillance report on HIV/AIDS.



Test & protect!

Early testing helps to prevent transmission and lowers the risk of severe health complications. More info: www.ecdc.europa.eu Follow us on twitter: @ecdc_HIVAIDS



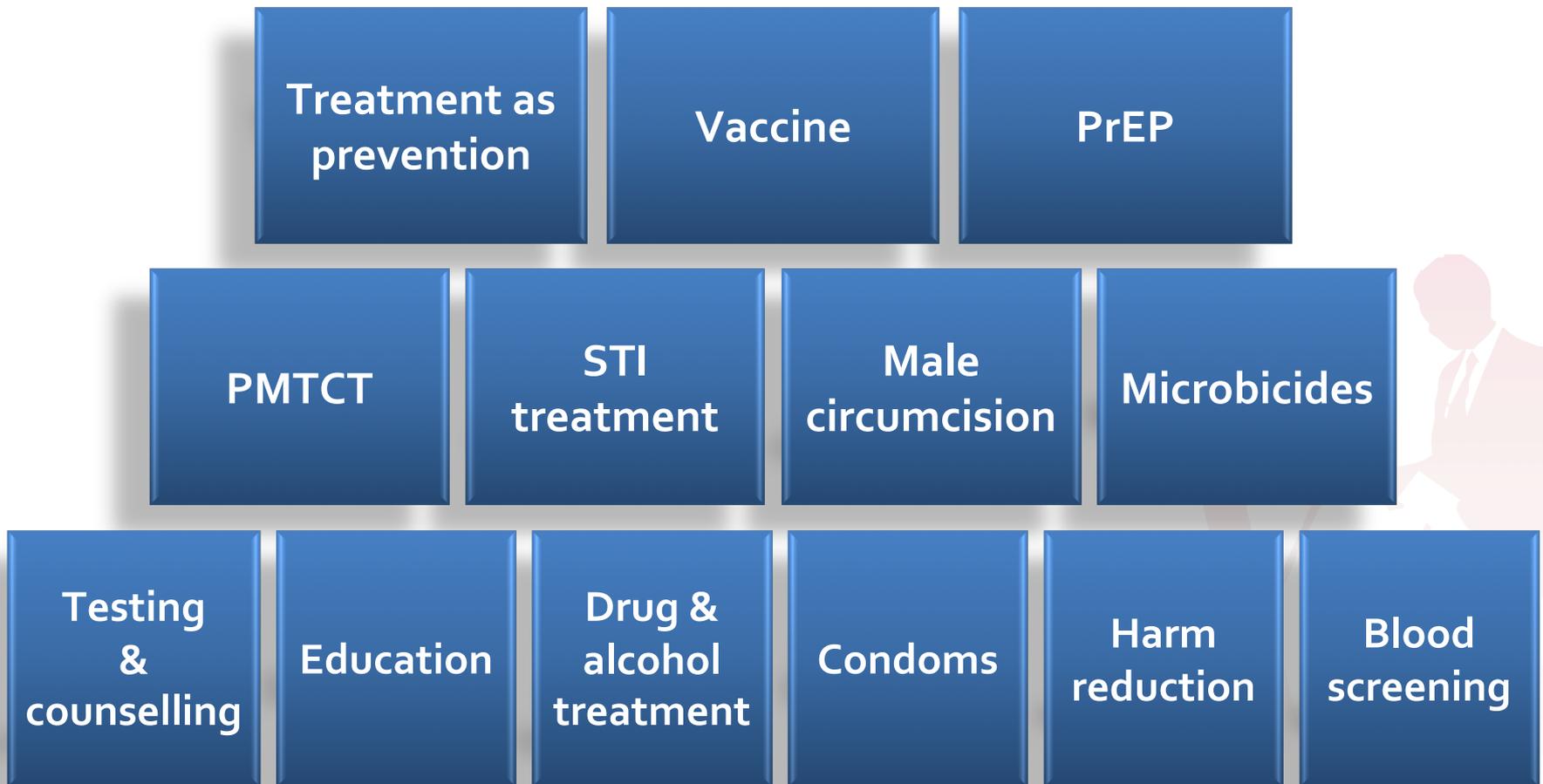


High levels of coverage with ART and PrEP would be needed for eradication

- A mathematical model was used to predict the effect of public health policies incorporating ART and PrEP on the basic reproductive number (R_0) of the HIV epidemic in South Africa
- The HIV eradication threshold was only reached in the scenario:
 - 96% effective ART + 75% effective PrEP (assuming 70% PrEP coverage)
- The eradication threshold was not reached assuming conservative estimates of effectiveness for ART (73%) and PrEP (55%)



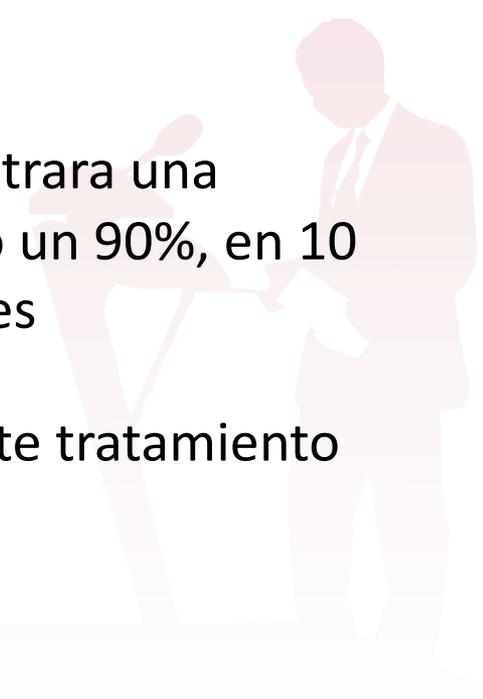
HIV prevention pyramid





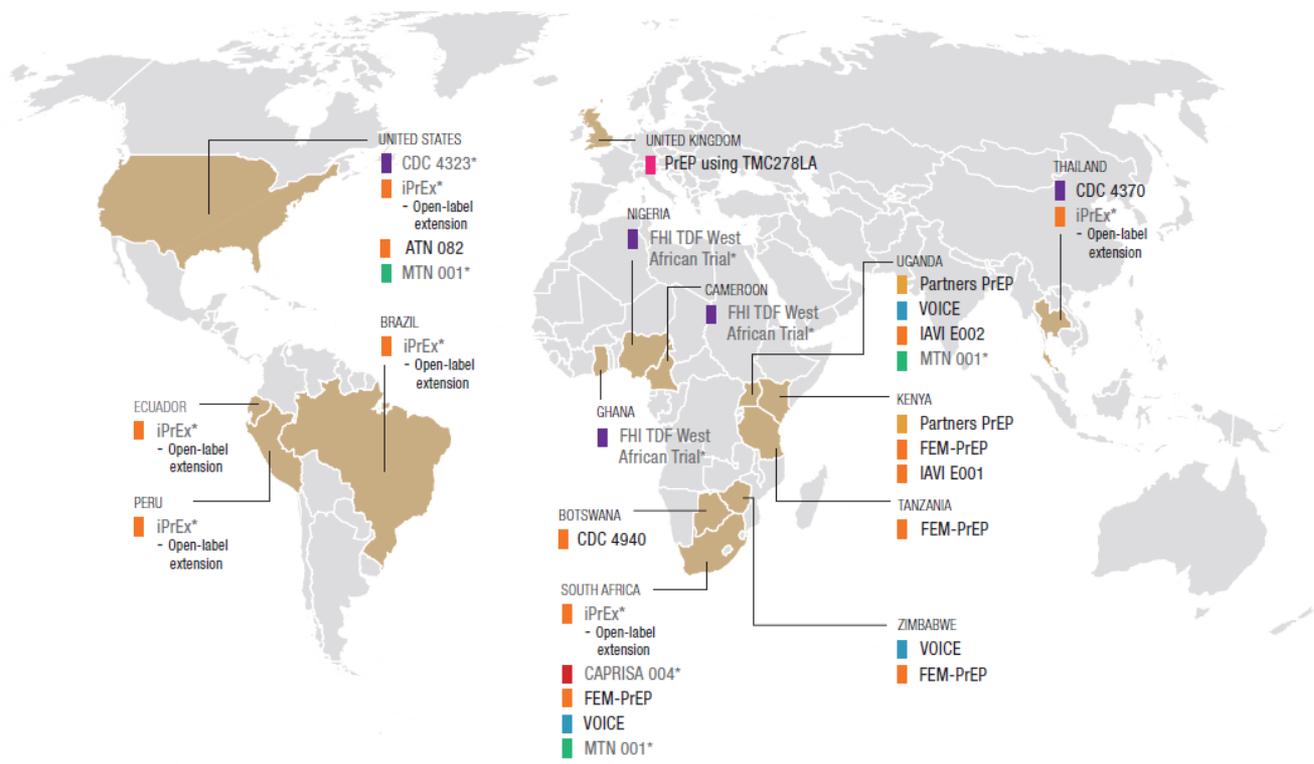
Profilaxis Pre-Exposición (Prep) Fundamentos

- Datos en primates no humanos
- Estudios farmacocinéticos que muestran que tenofovir y emtricitabina se concentran en secreciones genitales
- Modelos matemáticos que sugieren que, si se encontrara una profilaxis pre-exposición capaz de disminuir el riesgo un 90%, en 10 años se evitarían en África 3,2 millones de infecciones
- Éxitos previos en prevención de transmisión mediante tratamiento (prevención de transmisión vertical)





PrEP Trials Past and Present



Intervention arms:

- Oral TDF
- Oral TDF/FTC
- Vaginal tenofovir gel
- Oral TDF and TDF/FTC
- Oral TDF and vaginal tenofovir gel
- Oral TDF and TDF/FTC and vaginal tenofovir gel
- Injectable TMC278LA

ATN – Adolescent Trial Network; **CAPRISA** – Centre for the AIDS Programme of Research in South Africa; **CDC** – US Centers for Disease Control and Prevention; **FTC** – emtricitabine; **IAVI** – International AIDS Vaccine Initiative; **MTN** – Microbicide Trials Network; **TDF** – tenofovir disoproxil fumarate; **VOICE** – Vaginal and Oral Interventions to Control the Epidemic

* Completed trial



February 2011

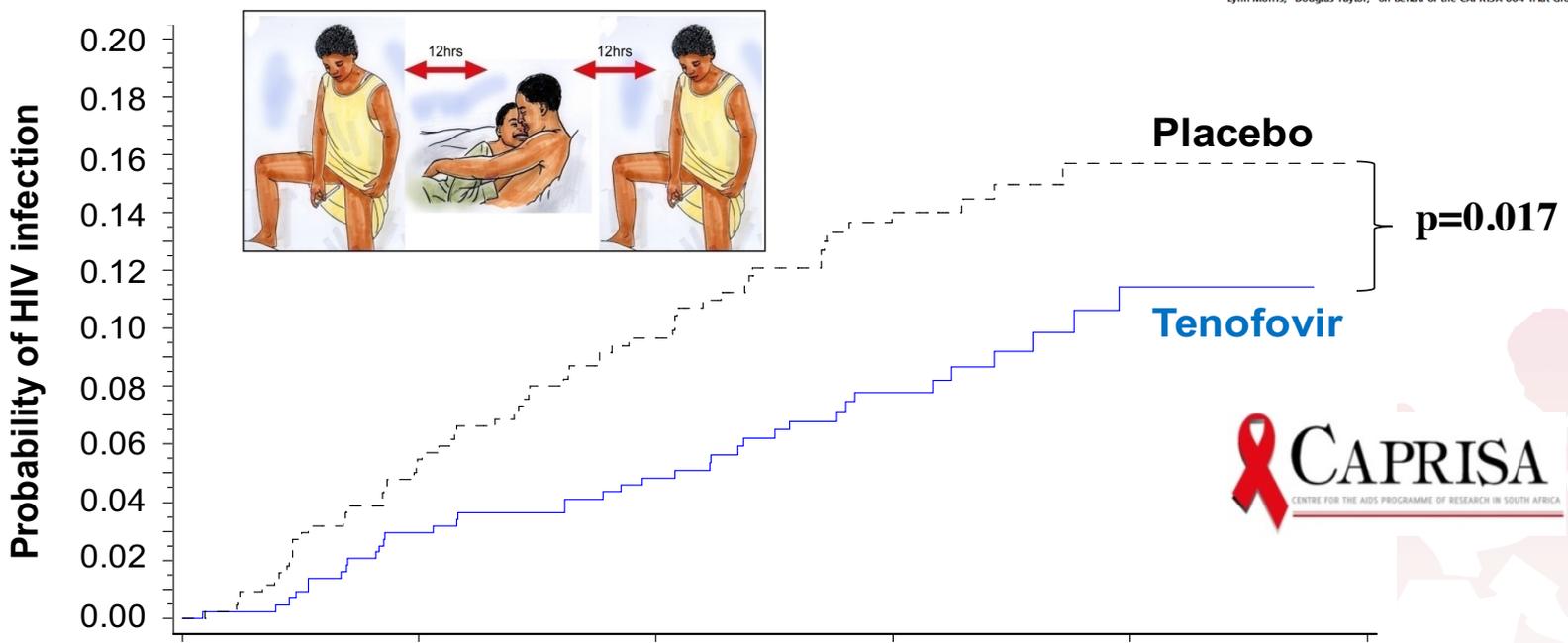




CAPRISA 004: HIV infection rates

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,^{1,2,3,4} Salim S. Abdool Karim,^{1,2,3,4} Janet A. Frohlich,¹ Anneke C. Grobler,¹ Cheryl Baxter,¹ Leila E. Mansoor,¹ Ayesha B. M. Kharsany,¹ Sengezwe Sibeko,¹ Koleka P. Mlisana,¹ Zahen Omar,¹ Tanaia N. Gengiah,¹ Silvia Maarschalk,¹ Natasha Arulappan,¹ Mukeleswe Motshwa,¹ Lynn Morris,⁴ Douglas Taylor,⁵ on behalf of the CAPRISA 004 Trial Group



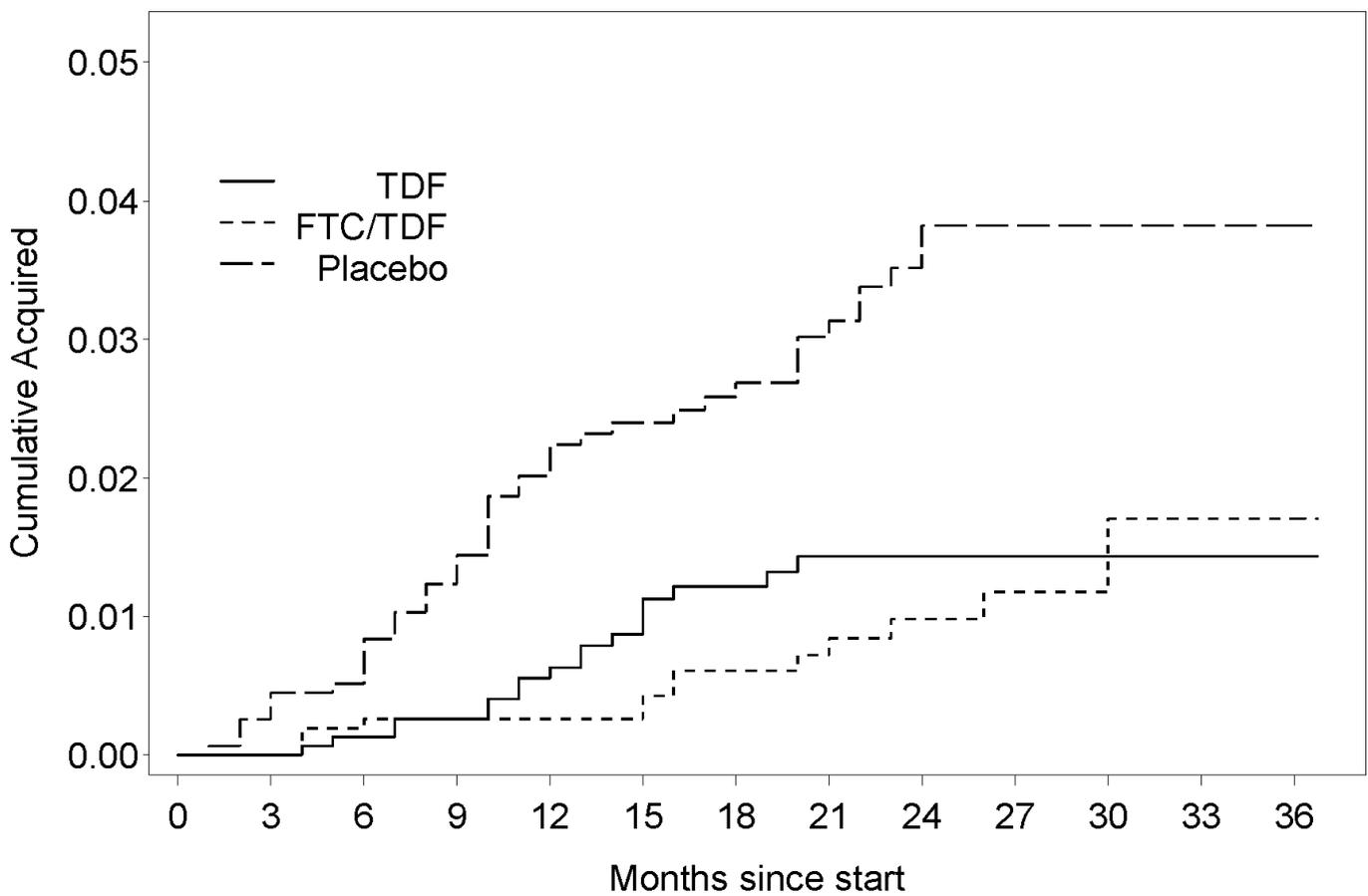
Months of follow-up	6	12	18	24	30
Cumulative HIV endpoints	37	65	88	97	98
Cumulative women-years	432	833	1143	1305	1341
HIV incidence rates (Tenofovir vs Placebo)	6.0 vs 11.2	5.2 vs 10.5	5.3 vs 10.2	5.6 vs 9.4	5.6 vs 9.1
Effectiveness (p-value)	47% (0.069)	50% (0.007)	47% (0.004)	40% (0.013)	39% (0.017)



Partners Study: Primary efficacy results



PARTNERS PrEP STUDY



No. at risk:	0	3	6	9	12	15	18	21	24	27	30	33	36
TDF	1573	1560	1546	1443	1292	1176	966	827	638	406	185	58	5
FTC/TDF	1567	1555	1544	1432	1303	1181	968	825	640	414	187	58	6
Placebo	1568	1557	1541	1431	1294	1164	970	829	637	405	203	62	6

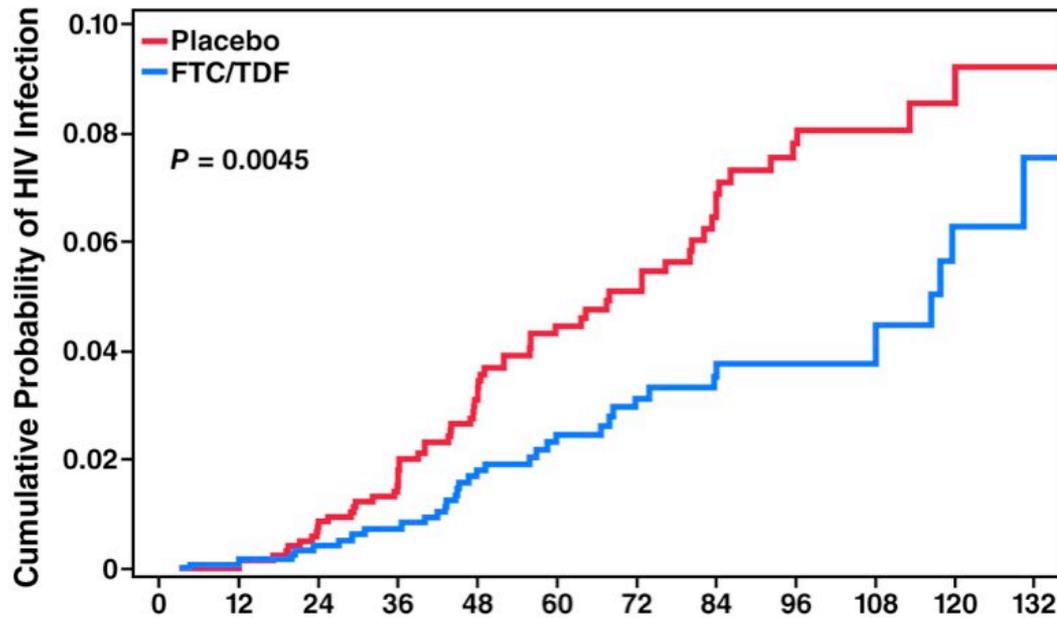




PrEP for HIV prevention in men who have sex with men



Efficacy (MITT) 44% (15-63%)
Infection Numbers: 64 – 36 = 28 averted



N =

Placebo:	1248	1194	1108	1005	852	674	546	444	370	258	137	60
FTC/TDF:	1251	1188	1097	988	848	693	558	447	367	267	147	65





Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men

BOX. CDC interim guidance for health-care providers electing to provide preexposure prophylaxis (PrEP) for the prevention of HIV infection in adult men who have sex with men and who are at high risk for sexual acquisition of HIV

Before initiating PrEP

Determine eligibility

- Document negative HIV antibody test(s) immediately before starting PrEP medication.
- Test for acute HIV infection if patient has symptoms consistent with acute HIV infection.
- Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection.
- Confirm that calculated creatinine clearance is ≥ 60 mL per minute (via Cockcroft-Gault formula).

Other recommended actions

- Screen for hepatitis B infection; vaccinate against hepatitis B if susceptible, or treat if active infection exists, regardless of decision about prescribing PrEP.
- Screen and treat as needed for STIs.

Beginning PrEP medication regimen

- Prescribe 1 tablet of Truvada* (TDF [300 mg] plus FTC [200 mg]) daily.
- In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected.
- If active hepatitis B infection is diagnosed, consider using TDF/FTC for both treatment of active hepatitis B infection and HIV prevention.
- Provide risk-reduction and PrEP medication adherence counseling and condoms.

Follow-up while PrEP medication is being taken

- Every 2–3 months, perform an HIV antibody test; document negative result.
- Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.
- Every 2–3 months, assess risk behaviors and provide risk-reduction counseling and condoms. Assess STI symptoms and, if present, test and treat for STI as needed.
- Every 6 months, test for STI even if patient is asymptomatic, and treat as needed.
- 3 months after initiation, then yearly while on PrEP medication, check blood urea nitrogen and serum creatinine.

On discontinuing PrEP (at patient request, for safety concerns, or if HIV infection is acquired)

- Perform HIV test(s) to confirm whether HIV infection has occurred.
- If HIV positive, order and document results of resistance testing and establish linkage to HIV care.
- If HIV negative, establish linkage to risk-reduction support services as indicated.
- If active hepatitis B is diagnosed at initiation of PrEP, consider appropriate medication for continued treatment of hepatitis B.





PrEP

Pre-Exposure Prophylaxis for HIV Prevention

PrEP is when uninfected individuals take HIV treatment medications PRIOR to exposure to protect against HIV infection.

In a recent study funded by the National Institutes of Health, it was determined that HIV negative gay men who took a daily dose of a drug called Viread, alone or in combination with Truvada over a period of 14 months, reduced their chances of contracting HIV by 44%.

Individuals who took their medication as recommended - 100% of the time - had a 92% reduction in their chances of contracting HIV.

It should be noted that the medication needs to be in the body at least 24 hours prior to any potential exposure. PrEP is not as effective if it is taken immediately prior to exposure.

For now, PrEP is a potentially important prevention approach being studied today. But it is important that we continue to promote HIV prevention education, consistently use condoms, regularly test for HIV, and have open dialogue with partners about their HIV status, to help end this epidemic.

For more information, please visit www.gmhc.org
or call the GMHC helpline at 1-800-243-7692.

GMHC
FIGHT AIDS. LOVE LIFE.





PROUD Pilot



GMSM reporting UAI last/next 90days; 18+;
and willing to take a pill every day



Randomize HIV negative MSM
(exclude if treatment for HBV/Truvada contra-indicated)



Risk reduction includes
Truvada **NOW**

Risk reduction includes
Truvada **AFTER 12M**

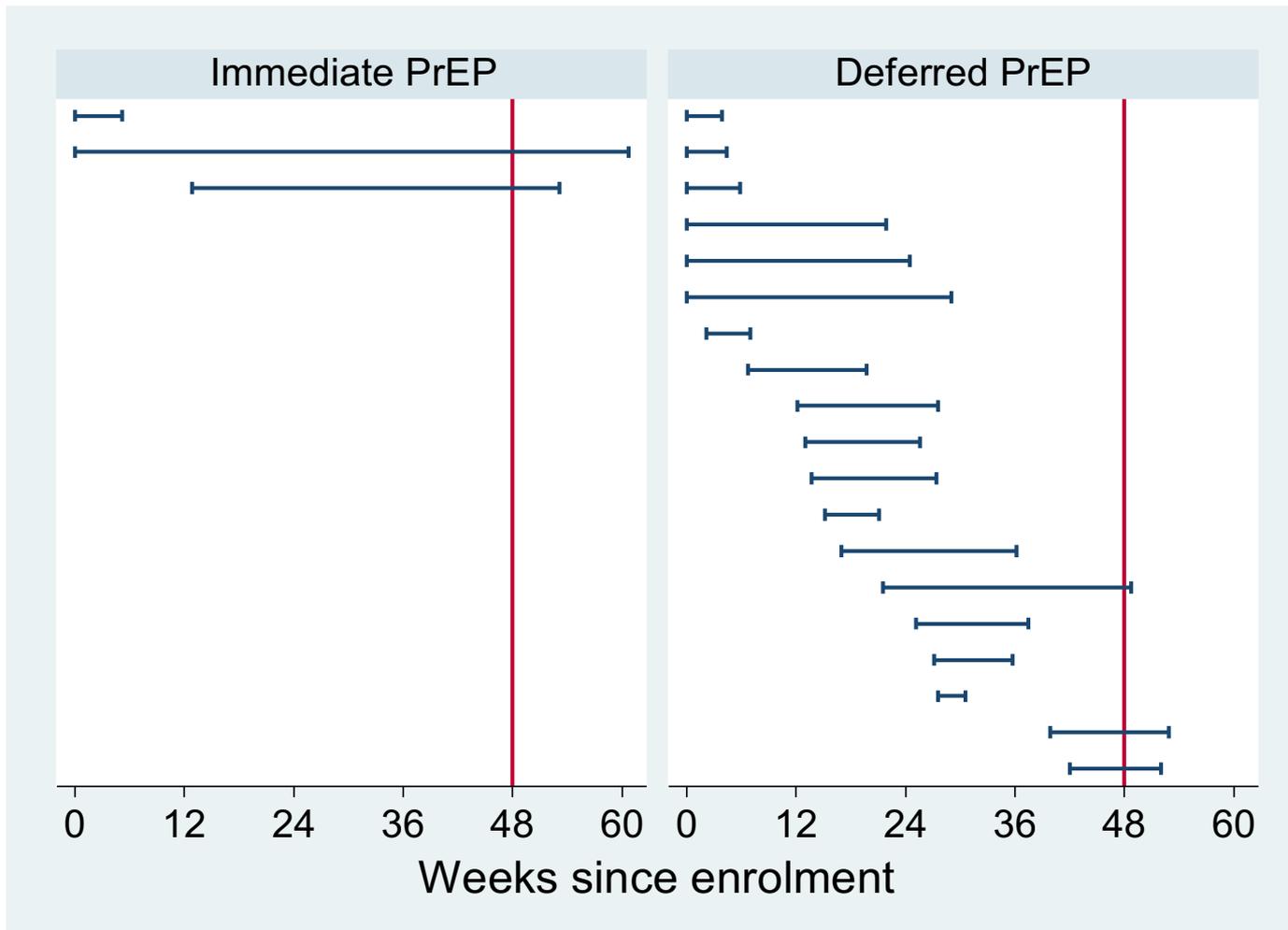


Follow **3 monthly** for up to 24 months

Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12 months



Individual incident HIV infections





HIV Incidence

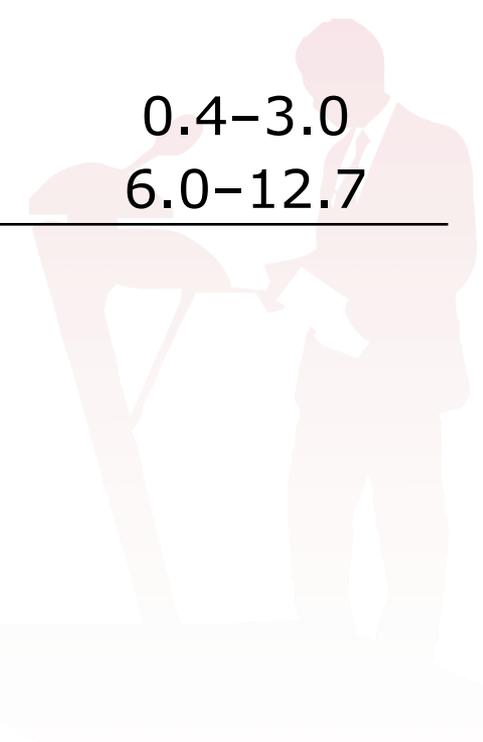
Group	No. of infections	Follow-up (PY)	Incidence (per 100 PY)	90% CI
Overall	22	453	4.9	3.4–6.8
Immediate	3	239	1.3	0.4–3.0
Deferred	19	214	8.9	6.0–12.7

Efficacy =86% (90% CI: 58 – 96%)

P value =0.0002

Rate Difference =7.6 (90% CI: 4.1 – 11.2)

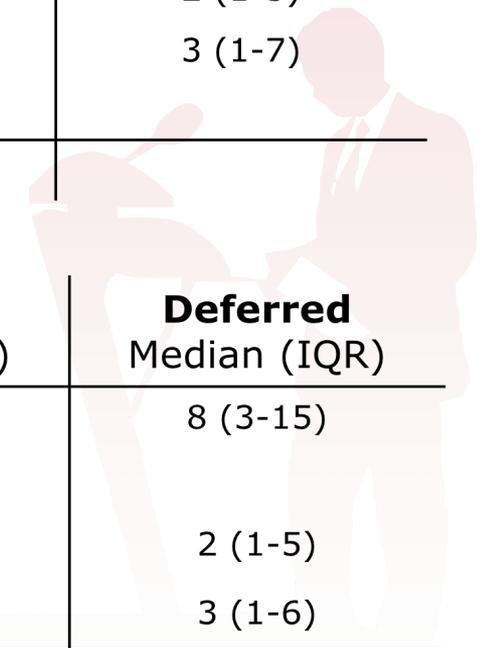
Number Needed to Treat =13 (90% CI: 9 – 25)





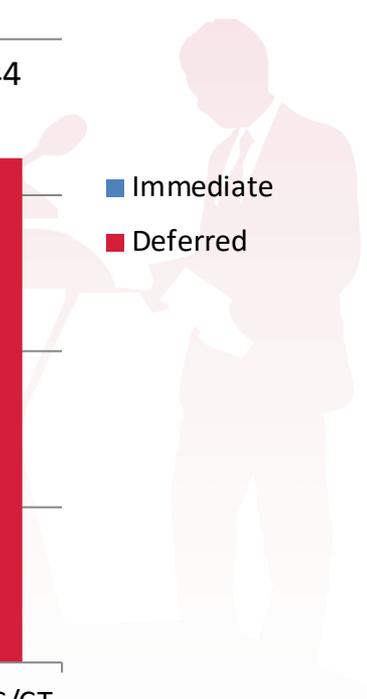
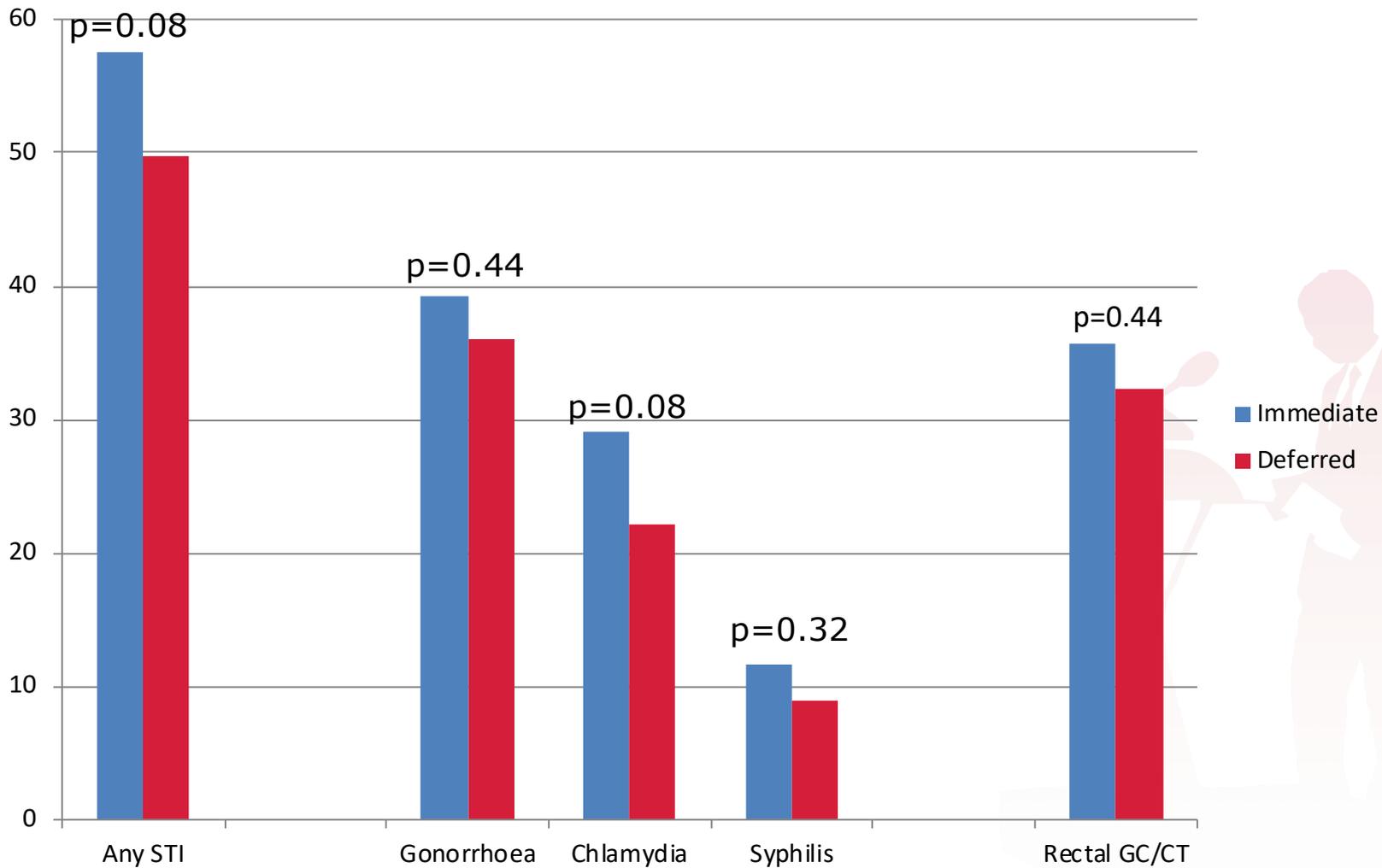
Reported sexual behaviour (preliminary)

Anal sex partners in last 90 days BASELINE n=539	Immediate Median (IQR)	Deferred Median (IQR)
Total number of partners	10.5 (5-20)	10 (4-20)
Condomless partners, participant receptive	3 (1-5)	2 (1-5)
Condomless partners, participant insertive	2.5 (1-6)	3 (1-7)
<hr/>		
Anal sex partners in last 90 days MONTH 12 n=349	Immediate Median (IQR)	Deferred Median (IQR)
Total number of partners	10 (3-24)	8 (3-15)
Condomless partners, participant receptive	3 (1-8)	2 (1-5)
Condomless partners, participant insertive	3 (1-8)	3 (1-6)



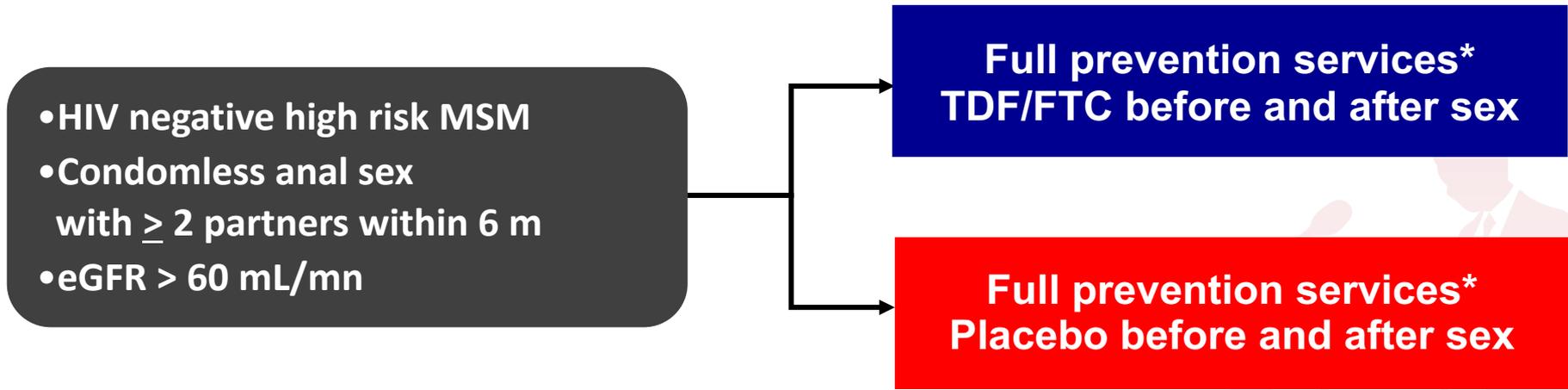


STIs



Ipergay: Study Design

Double-Blinded Randomized Placebo-Controlled Trial

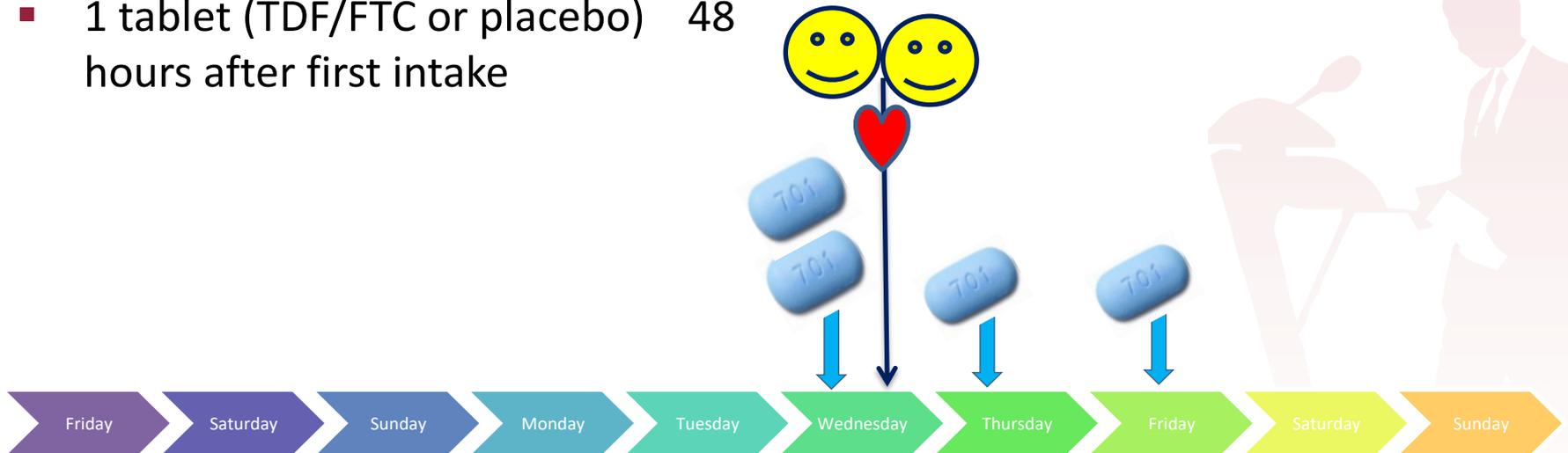


* Counseling, condoms and gels, testing and treatment for STIs, vaccination for HBV and HAV, PEP

- End-point driven study : with 64 HIV-1 infections, 80% power to detect a 50% relative decrease in HIV-1 incidence with TDF/FTC (expected incidence: 3/100 PY with placebo)
- Follow-up visits: month 1, 2 and every two months thereafter

Ipergay: Event-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





Baseline Characteristics

Characteristics (Median, IQR) or (n, %)	TDF/FTC n = 199	Placebo n = 201
Age (years)	35 (29-43)	34 (29-42)
White	190 (95)	184 (92)
Completed secondary education	178 (91)	177 (89)
Employed	167 (85)	167 (84)
Single	144 (77)	149 (81)
History of PEP use	56 (28)	73 (37)
Use of psychoactive drugs*	85 (44)	92 (48)
Circumcised	38 (19)	41 (20)
Infection with NG, CT or TP**	43 (22)	59 (29)
Nb sexual acts in prior 4 weeks	10 (6-18)	10 (5-15)
Nb sexual partners in prior 2 months	8 (5-17)	8 (5-16)

* in last 12 months: ecstasy, crack, cocaine, crystal, speed, GHB/GBL

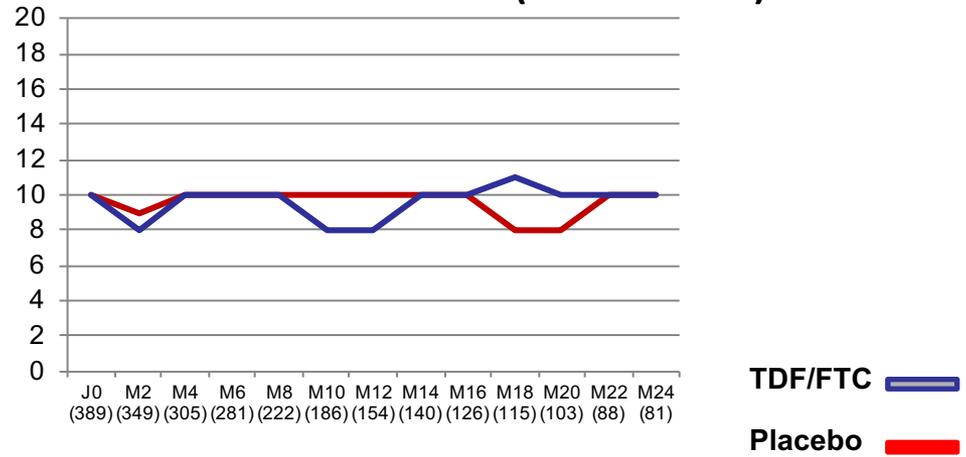
** NG: Neisseria gonorrhoeae, CT: Chlamydia trachomatis, TP: Treponema pallidum



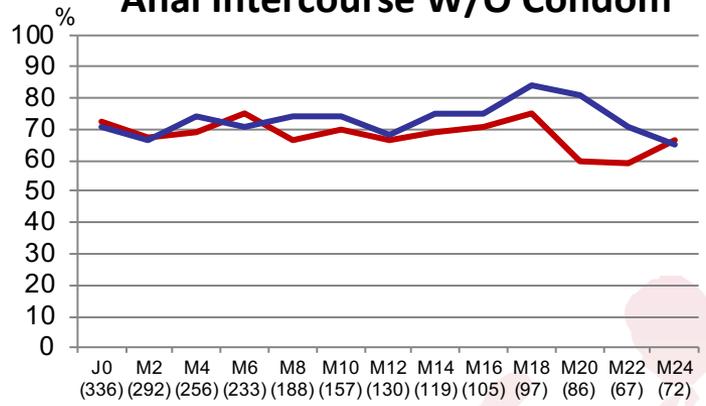
Sexual Behaviour



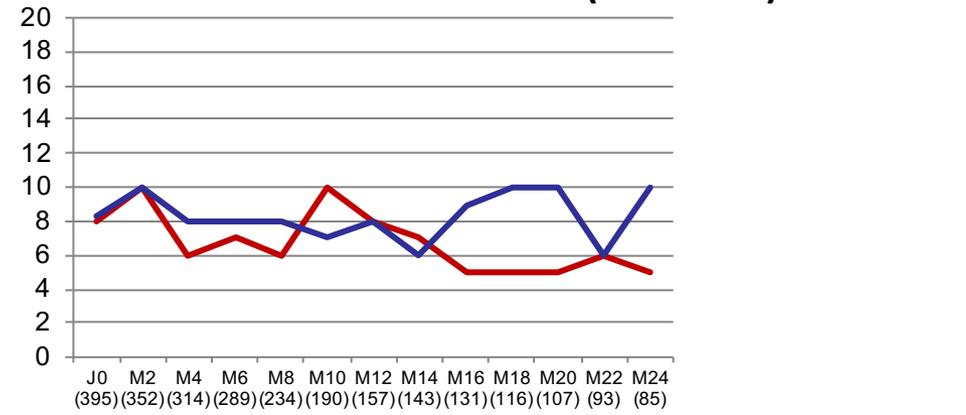
Median Nb of Sexual Acts (last 4 weeks)



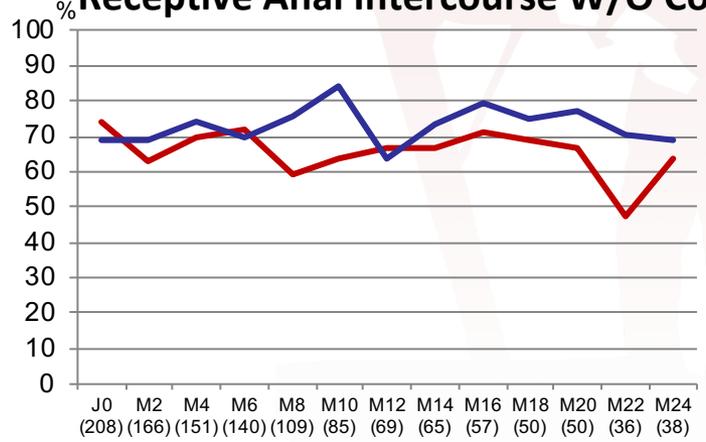
Anal Intercourse W/O Condom



Median Nb of Sexual Partners (2 months)

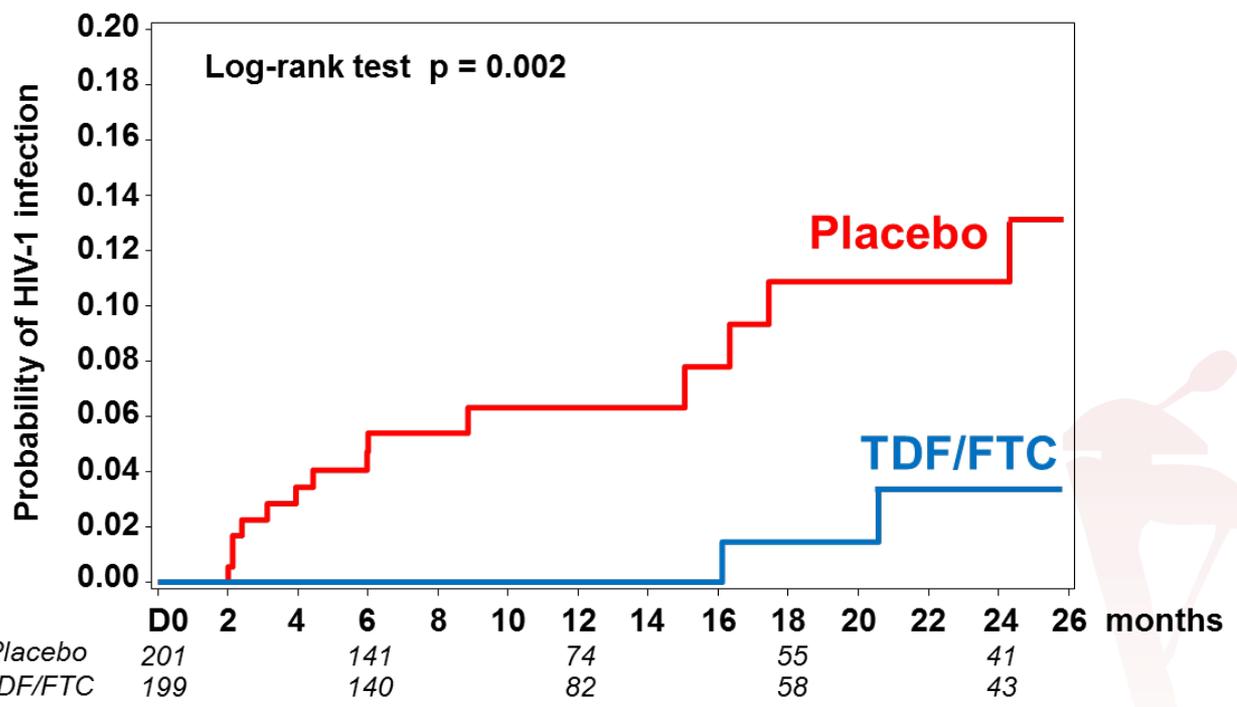


Receptive Anal Intercourse W/O Condom





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



Mean follow-up of 13 months: 16 subjects infected

14 in placebo arm (incidence: 6.6 per 100 PY), **2 in TDF/FTC arm** (incidence: 0.94 per 100 PY)

86% relative reduction in the incidence of HIV-1 (95% CI: 40-99, p=0.002)

NNT for one year to prevent one infection : 18



Cost-Effectiveness of PrEP Among MSM in the Netherlands





Four Prevention Opportunities

