

Prevention



Dr. Mark Nelson

Chelsea & Westminster Hospital
Executive Committee of the British HIV
Association (BHIVA)

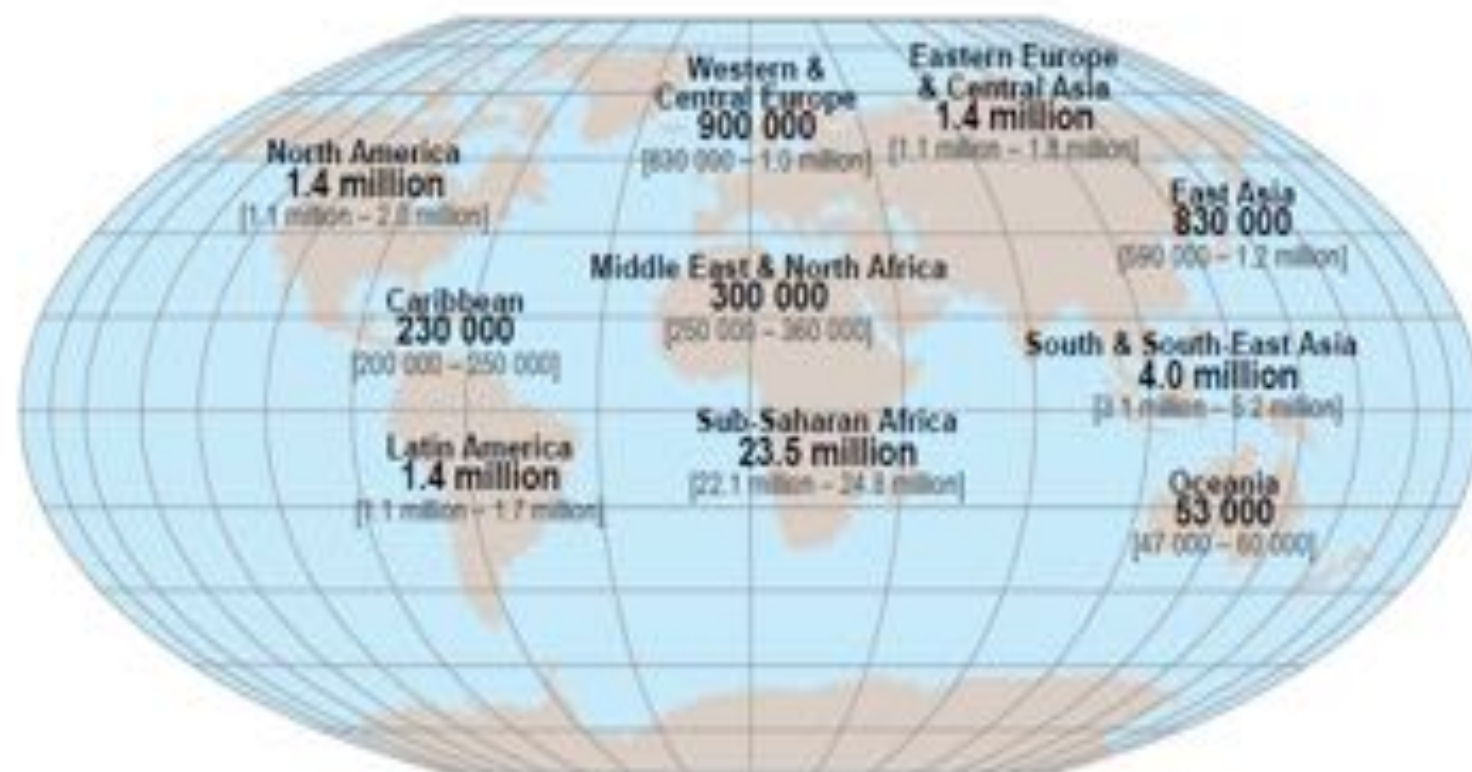


“Support needing populations through medical assistance and the transfer of knowledge to local medical practitioners.”

Our vision for the
Medical Assistance & Medical Education
(MAME) Programs

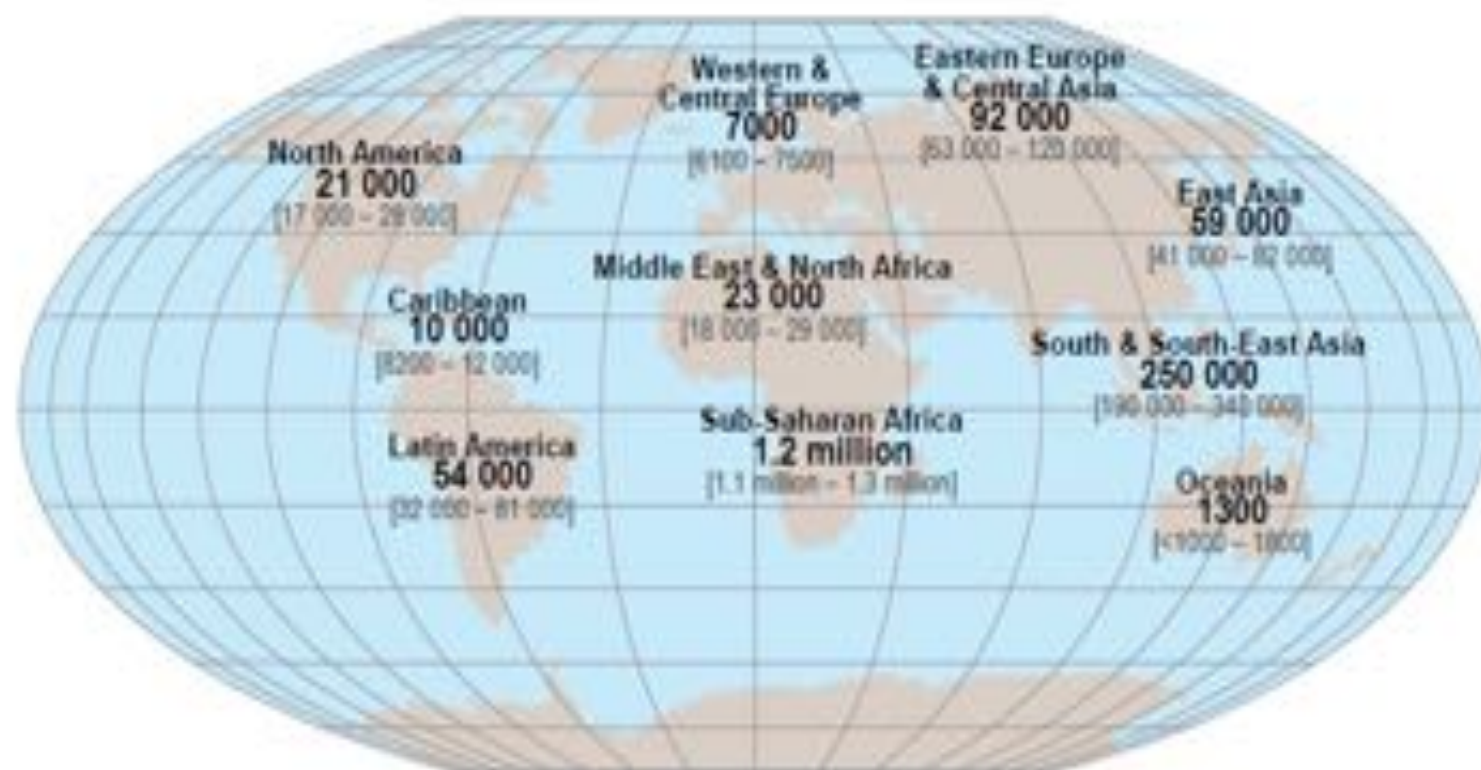


Adults and children estimated to be living with HIV | 2011



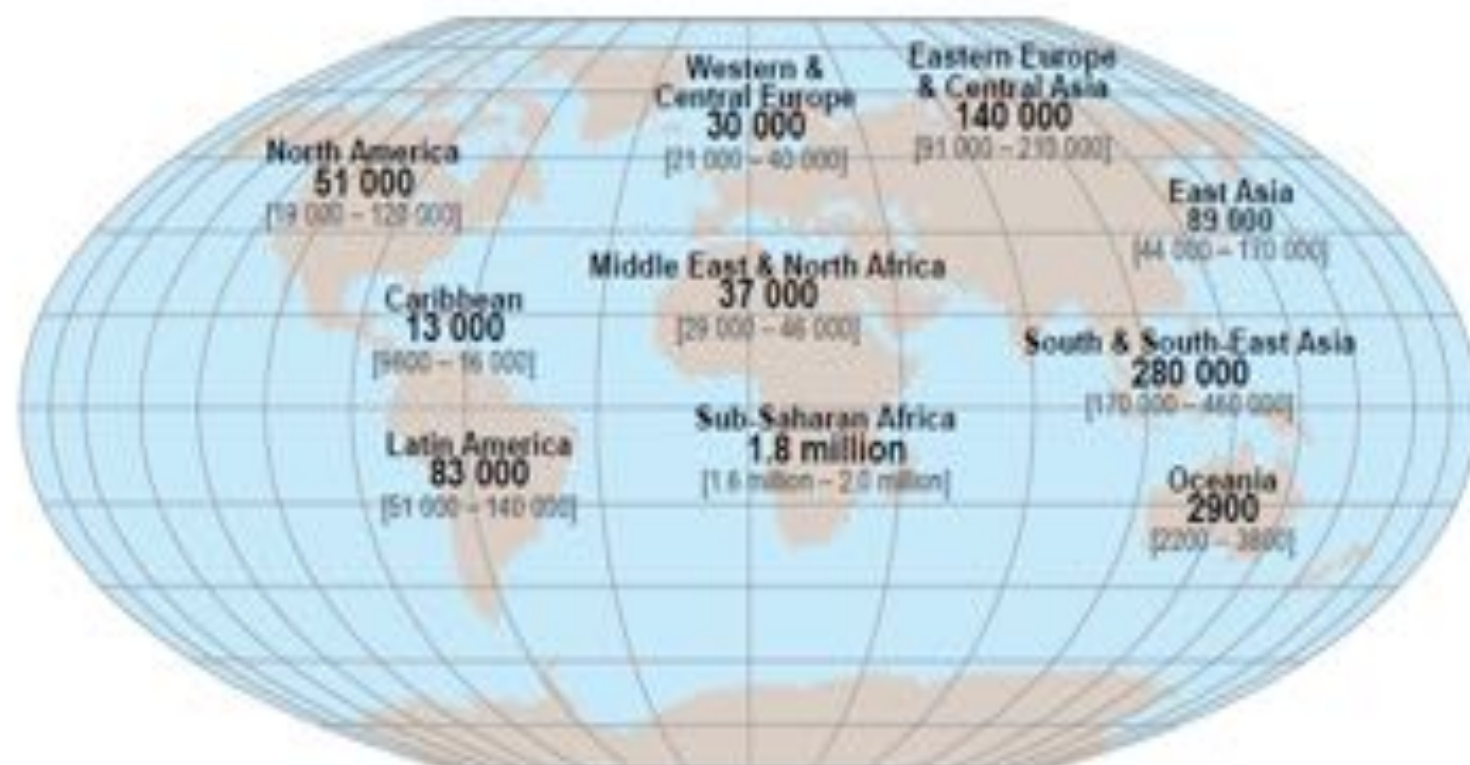
Total: 34.0 million [31.4 million – 35.9 million]

Estimated adult and child deaths from AIDS | 2011



Total: 1.7 million [1.5 million – 1.9 million]

Estimated number of adults and children newly infected with HIV | 2011



Total: 2.5 million [2.2 million – 2.8 million]

THE SEVEN RULES OF HEALTH

You and your family will stand a better chance of avoiding colds, influenza and other common ailments—as well as more serious diseases such as tuberculosis—if you follow these simple rules. The rules offer the best guidance on how to improve your health and increase your vitality.

FRESH AIR



Open your windows every day to get fresh air. Fresh air is one of the best things you can do to keep your family healthy.

EXERCISE



SLEEP



A GUIDE TO YOUR CHILD'S SLEEP

	INFANTS UNDER 1 Babies under 1 year old should sleep 12 to 14 hours a day.
	CHILDREN UP TO 4 Children up to 4 years old should sleep 10 to 12 hours a day.
	CHILDREN OF 4 TO 7 Children of 4 to 7 years old should sleep 9 to 11 hours a day.
	CHILDREN OF 7 TO 10 Children of 7 to 10 years old should sleep 8 to 10 hours a day.
	UP TO THE AGE OF 18 Teenagers and young adults should sleep 7 to 9 hours a day.

ABOUT CLOTHING

Let's be comfortable



KEEPING CLEAN



WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS
WASH YOUR HANDS

CONCERNING FOOD

A balanced diet



Keep your diet balanced with plenty of fruits, vegetables, and whole grains. Avoid too much sugar, salt, and fat.

HANDLING FOOD

Be sure to keep food safe. Wash your hands before and after handling food. Keep food covered when not eating.



Infected food causes illness

MILK FOR CHILDREN

...must be pure



LEISURE—enrich your life



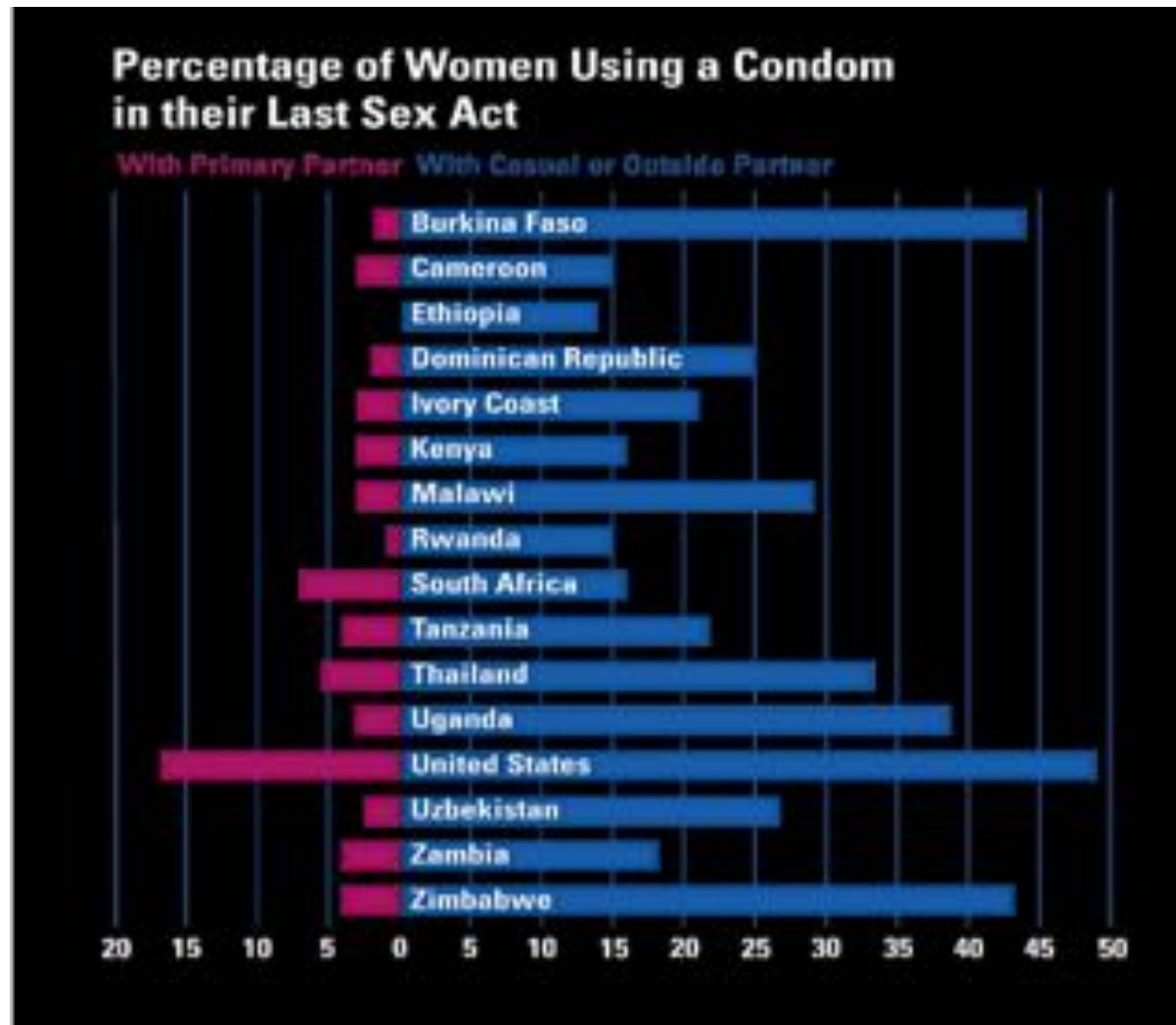
PREVENTION IS BETTER THAN CURE — LET THE RULES BECOME HABITS

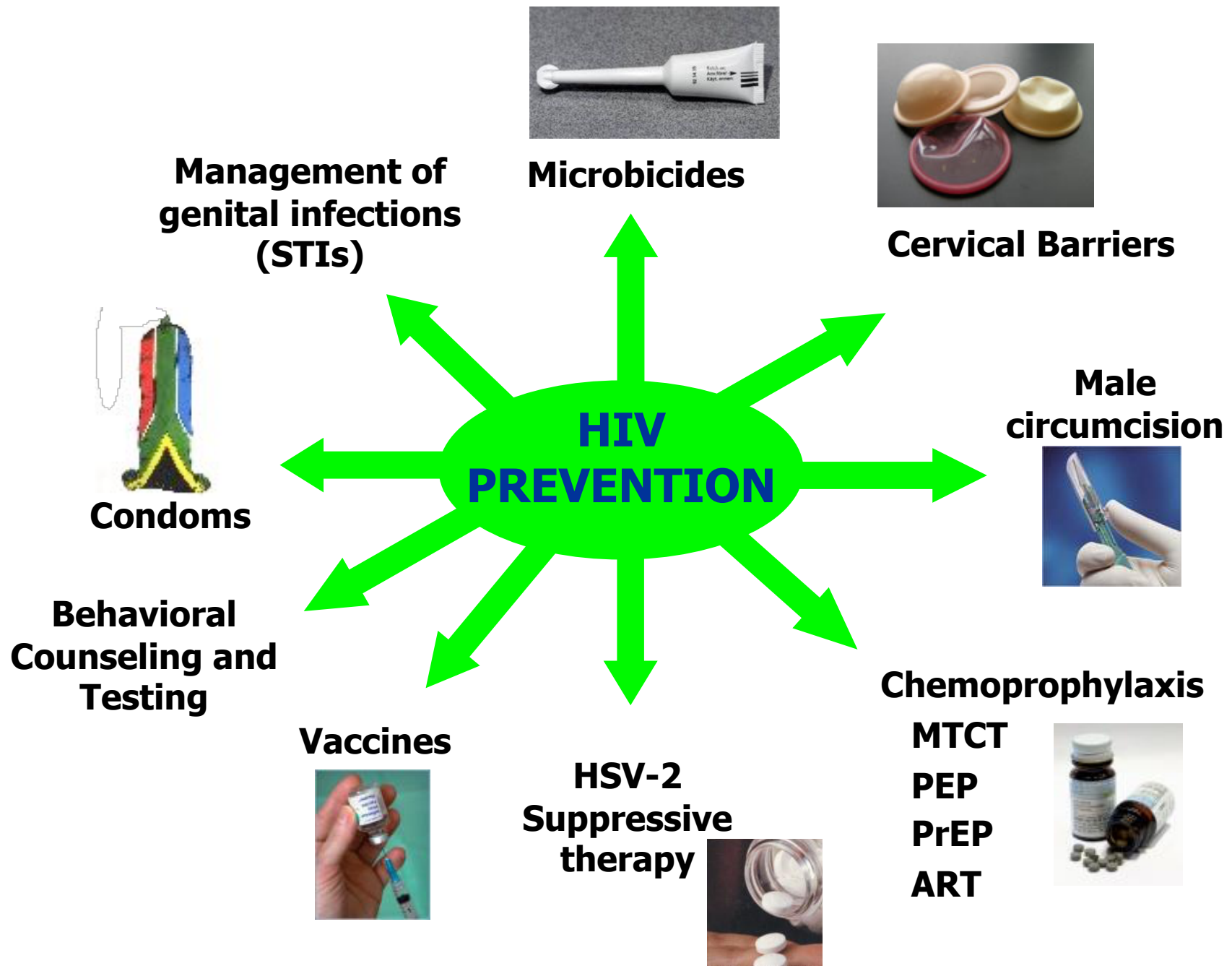


Why are Condoms Not Enough?

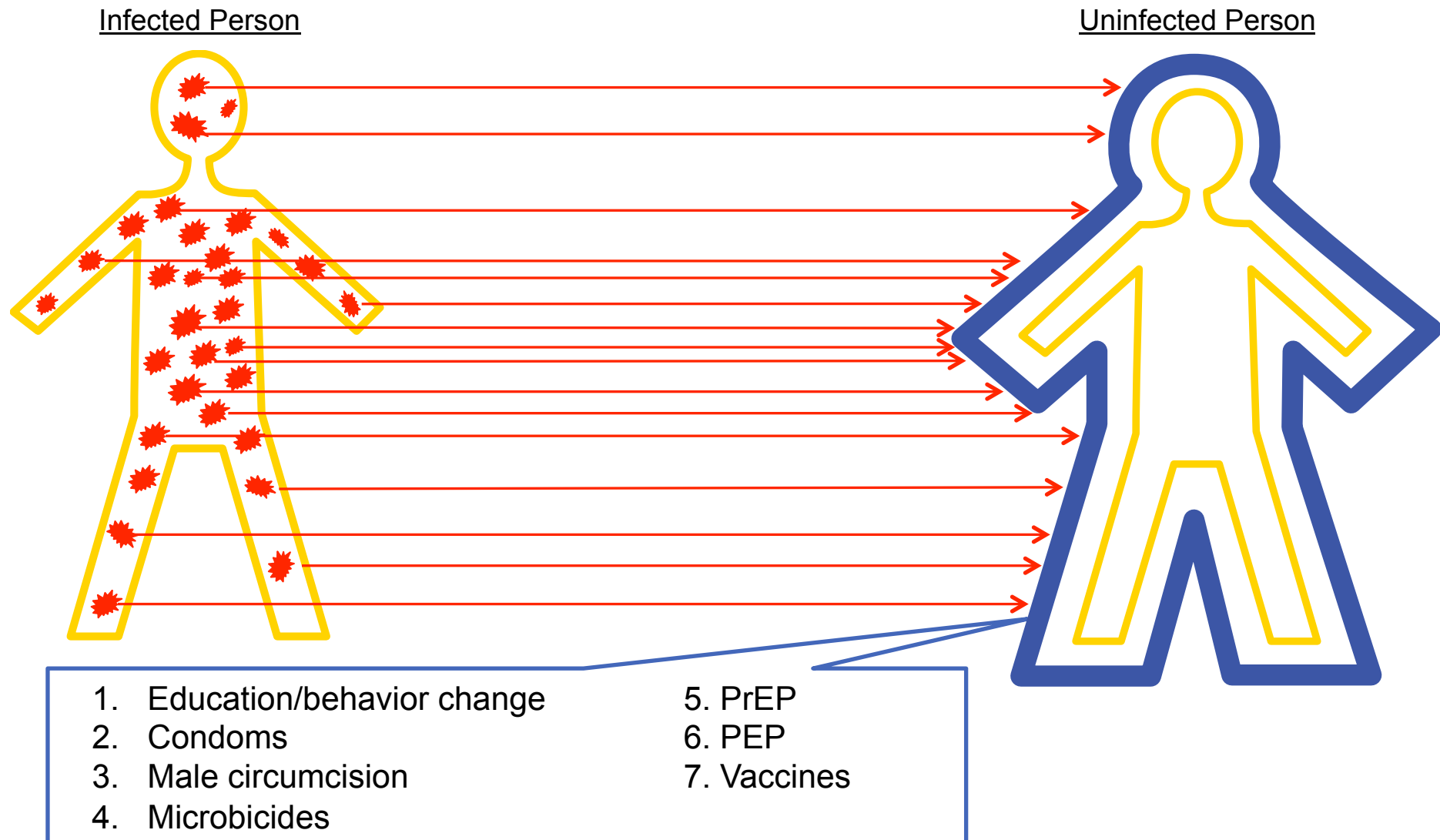


Why condoms are not enough





Strategies Based on Action by Uninfected Individual to Prevent Infection

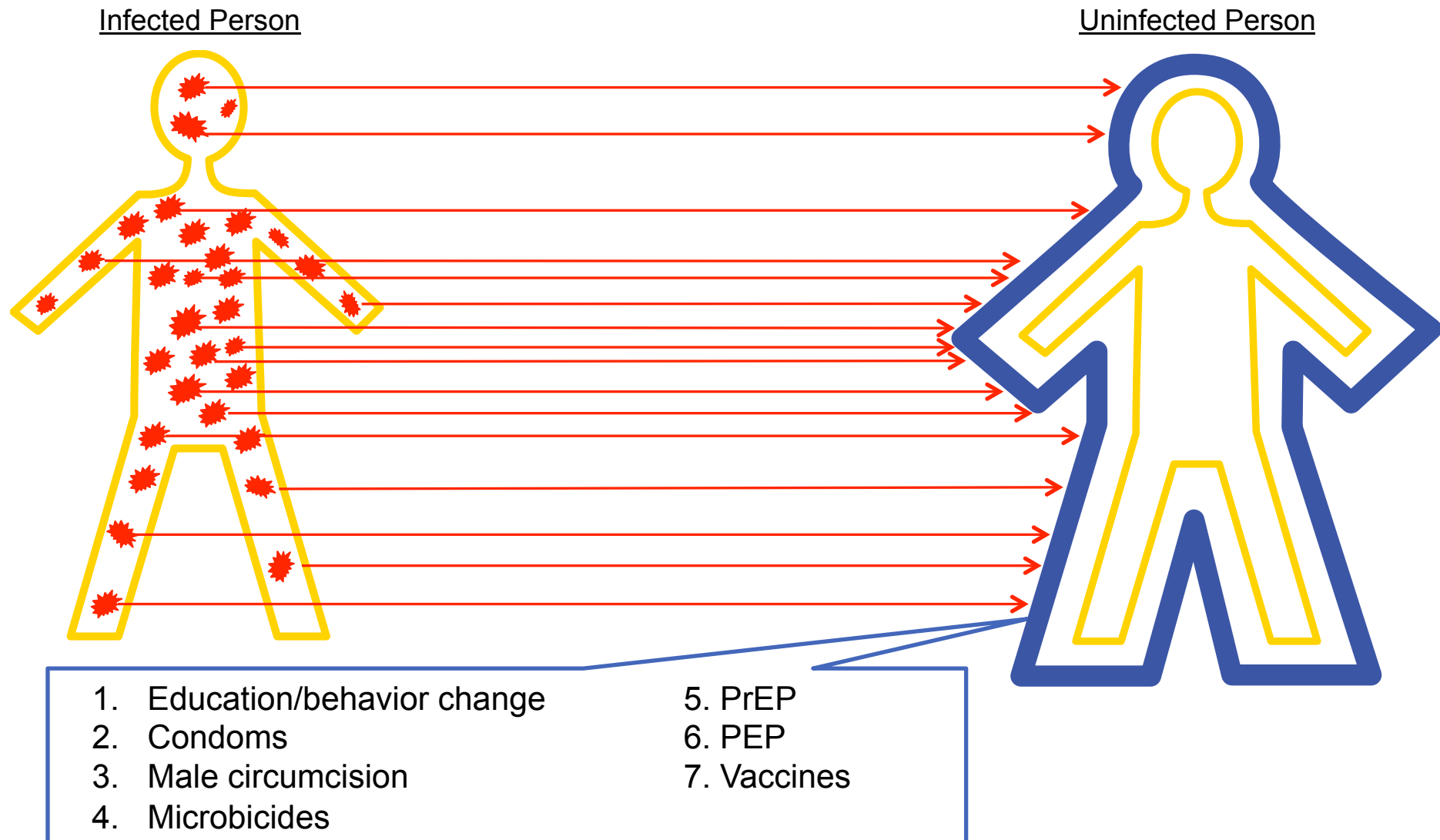


Biomedical Research Approaches to Prevention of HIV/AIDS

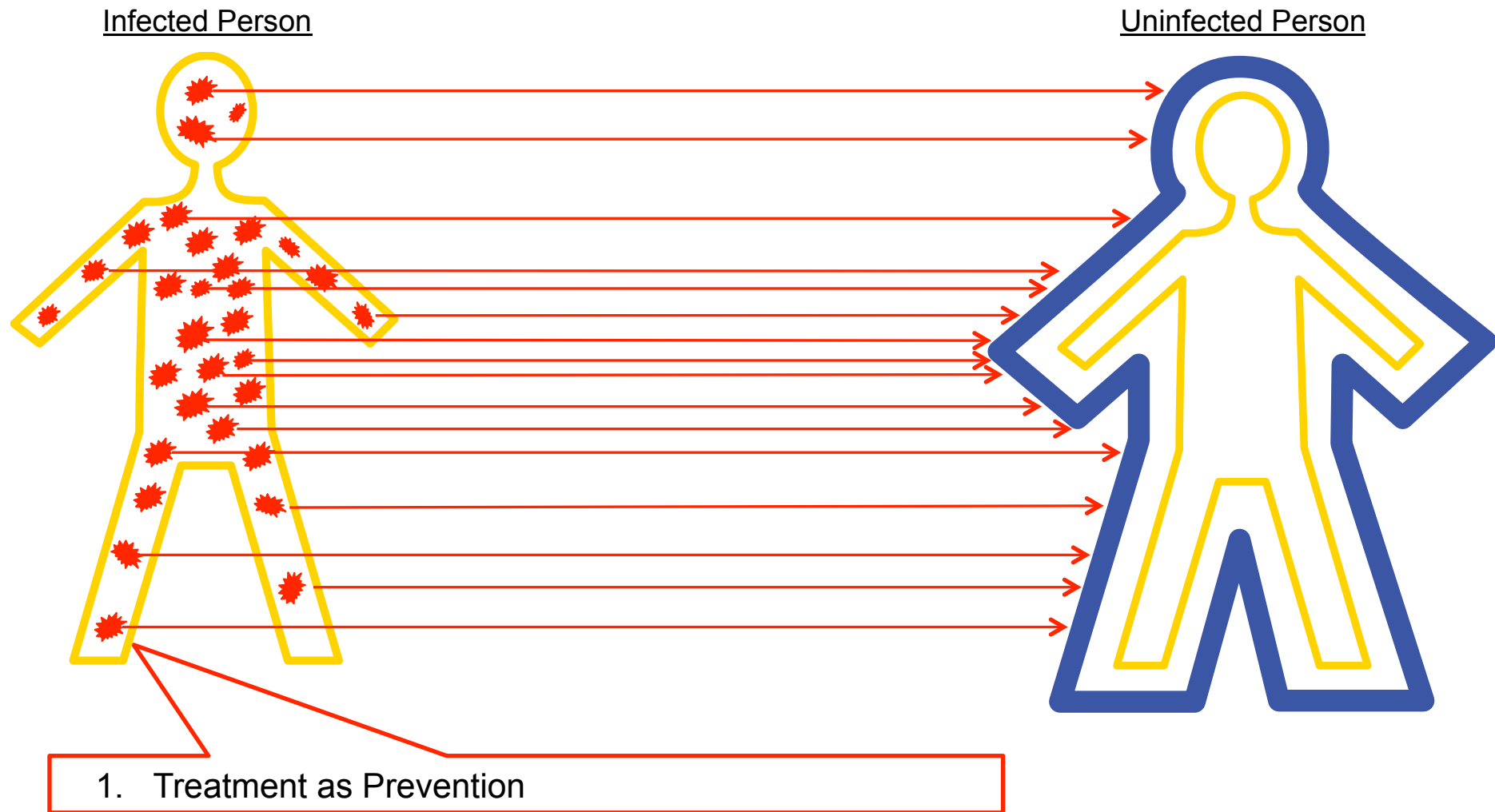
(1) No ARV

Category	Results	Comments
Vaccine	Generally poor	One recent design gave borderline efficacy; highly efficacious vaccine unlikely for at least a decade.
Treatment of venereal Herpes	No benefit	Control of Herpes replication in coinfecting individuals gave no benefit in reducing transmission of HIV.
Male circumcision	50–60% protection	Randomized controlled trials showed clear efficacy. Inexpensive.
Microbicides-broad spectrum disinfectants	No benefit	Some even showed increased risk for infection, presumably through damage to mucosal surfaces.

Strategies Based on Action by Uninfected Individual to Prevent Infection

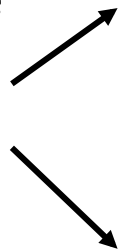


Strategies Based on Action by Infected Individual to Prevent Infection



HPTN 052: Immediate vs Delayed ART for HIV Prevention in Serodiscordant Couples

HIV-infected, sexually active
serodiscordant
couples; CD4+ cell count
of the infected partner:
350-550 cells/mm³
(N = 1763 couples)

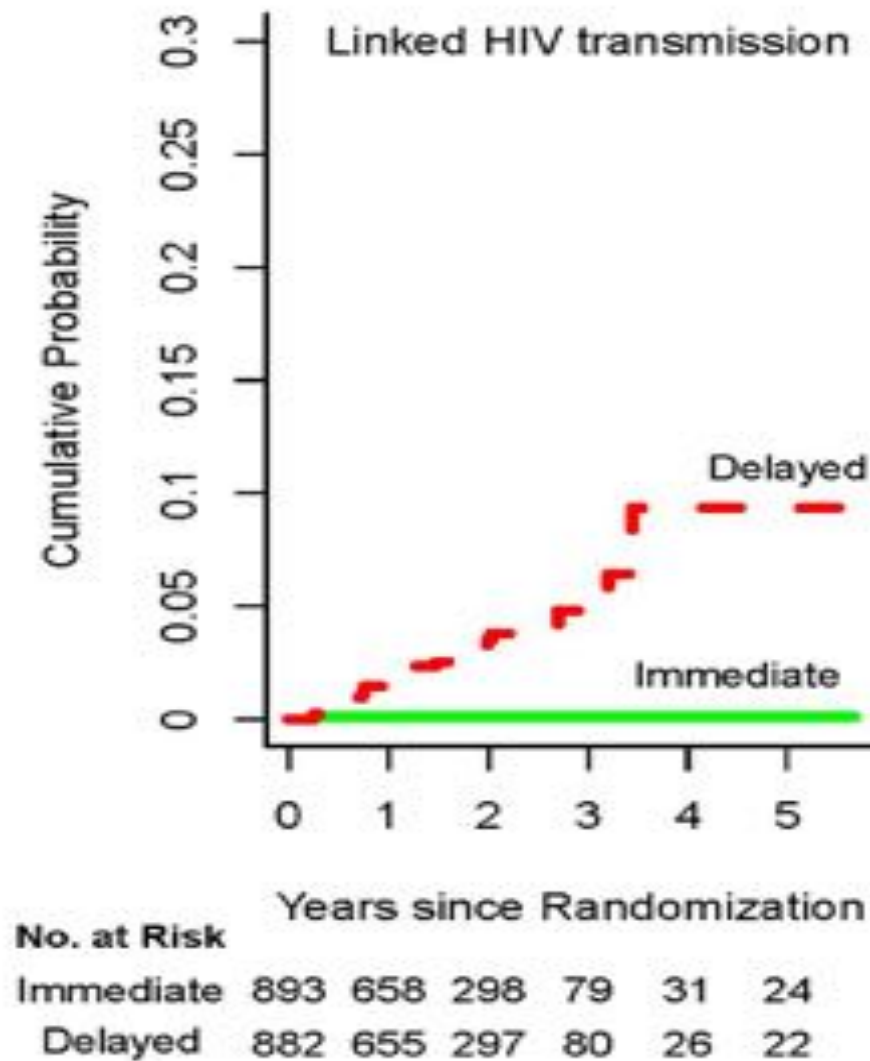


Immediate HAART
Initiate HAART at CD4+ cell count 350-550 cells/mm³
(n = 886 couples)

Delayed HAART
Initiate HAART at CD4+ cell count ≤ 250 cells/mm³*
(n = 877 couples)

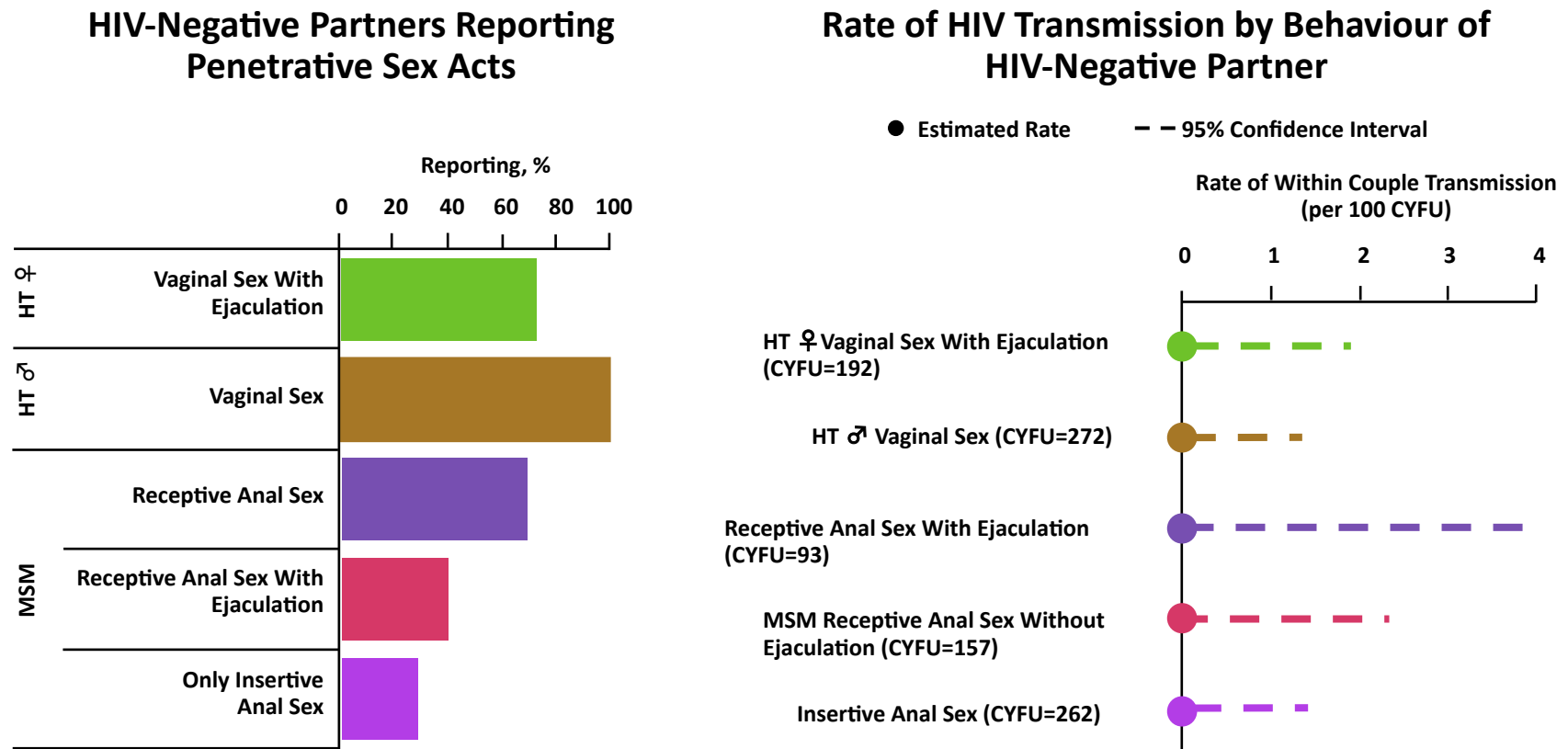
- Primary efficacy endpoint: virologically linked HIV transmission
- Primary clinical endpoints: WHO stage 4 events, pulmonary TB, severe bacterial infection and/or death
- Couples received intensive counseling on risk reduction and use of condoms

HPTN052: HIV-1 Transmissions





Condomless Sex Acts and Rate of HIV Transmission by Sexual Behaviour

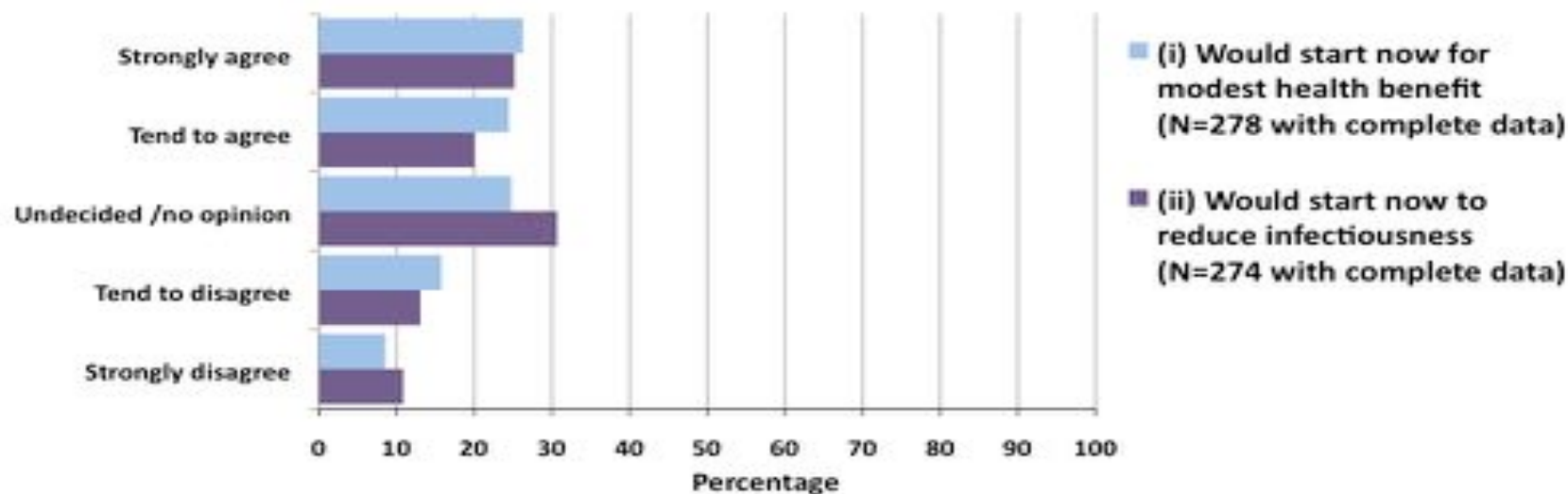


Suppressive ART resulted in zero linked transmissions to HIV-negative partners with condomless sex, despite a substantial number of sex acts. Unlinked transmissions did occur. Additional follow-up in MSM is forthcoming in the PARTNER2 study.

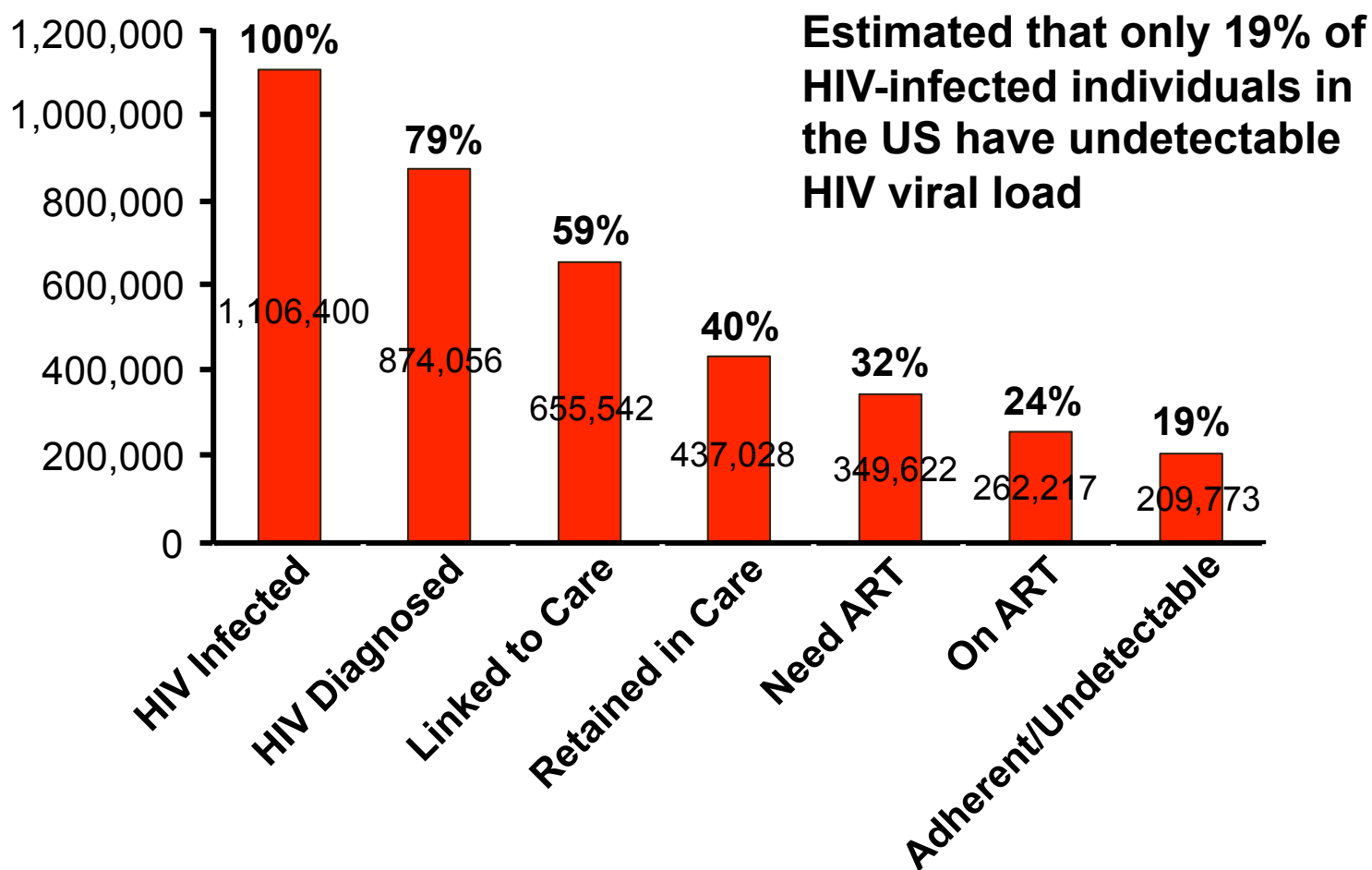


Treatment as Prevention: who wants it?

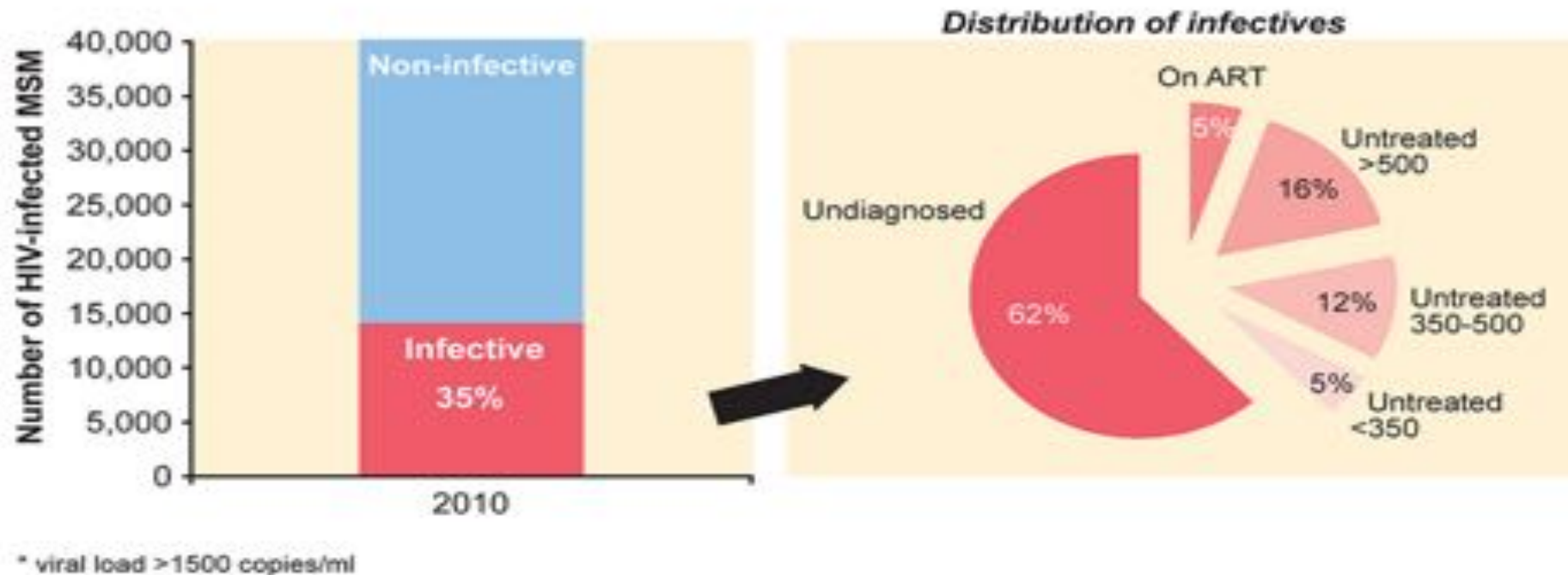
- Poster 1038 Rodger, A et al ASTRA UK
- Attitudes to early ART among 286 ART naïve individuals



Challenges in Linkage to Care and Successful Treatment



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

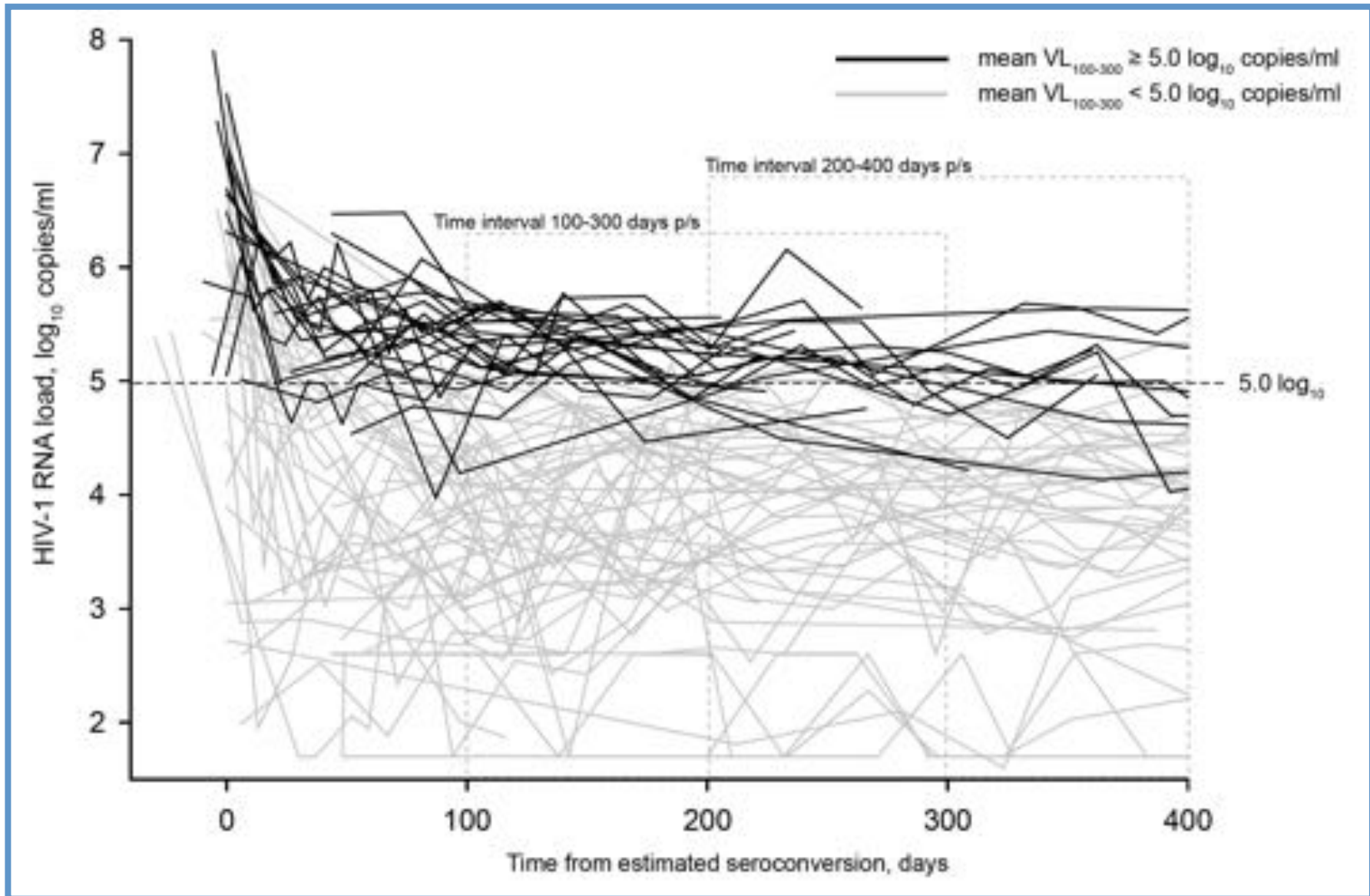


Extending ART to all MSM with CD4 counts <500 cells/mm³ would reduce infectivity from an estimated 35% to 29% and, in combination with halving the undiagnosed, to 21%.

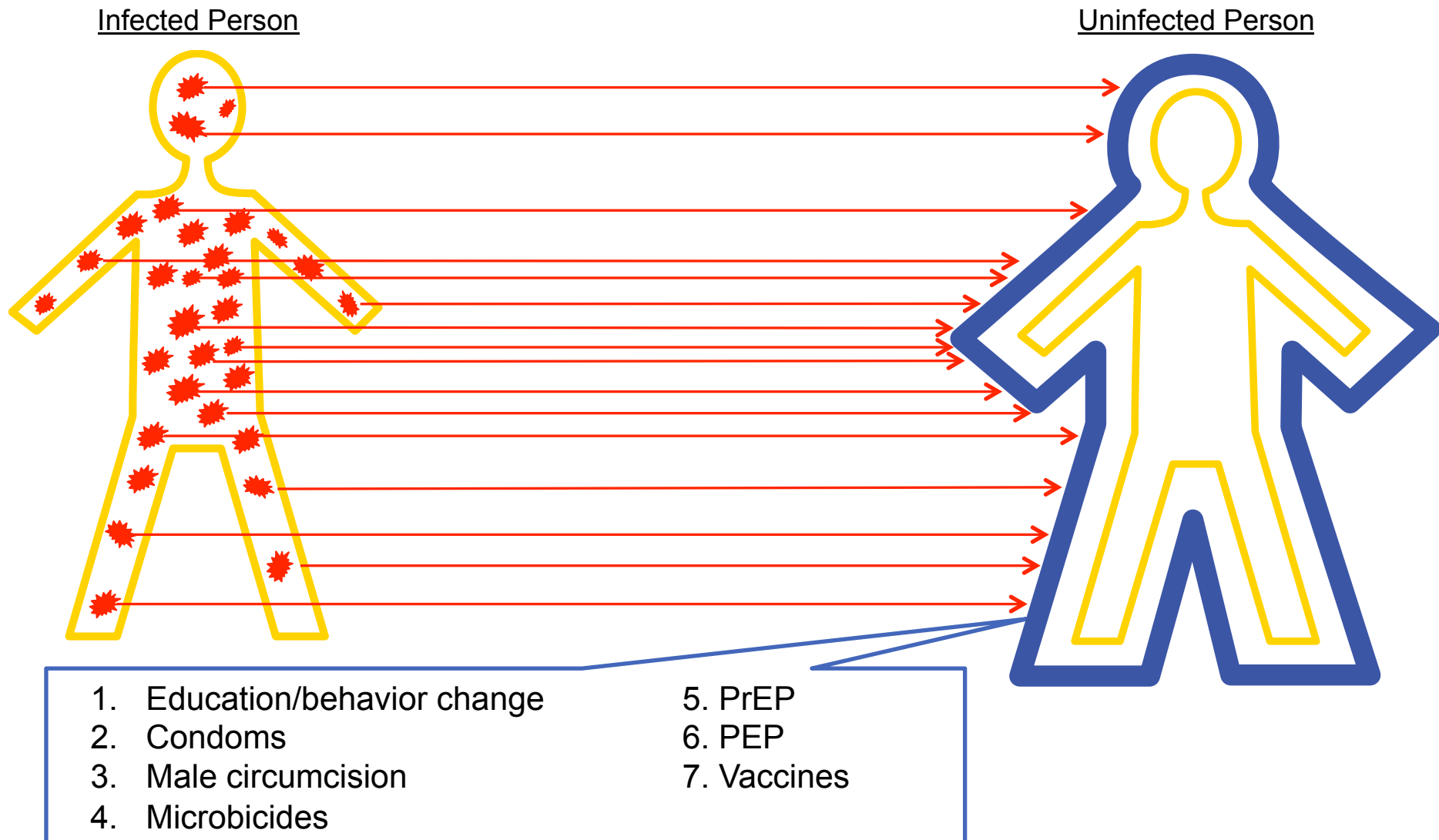
Source of new HIV Infections

- Phillips, UK, 2010 transmissions in MSM
- Source of new infections:
 - 49% undiagnosed in PHI
 - 34% undiagnosed in established infection
 - 10% diagnosed, ART naïve
 - 7% diagnosed, ART experienced
- Condom use more effective than ART in reducing incidence; combination of condom use AND ART most effective

Viral RNA Dynamics in Primary HIV-1 Subtype C Infection (n=75, pre-HAART data)



Strategies Based on Action by Uninfected Individual to Prevent Infection

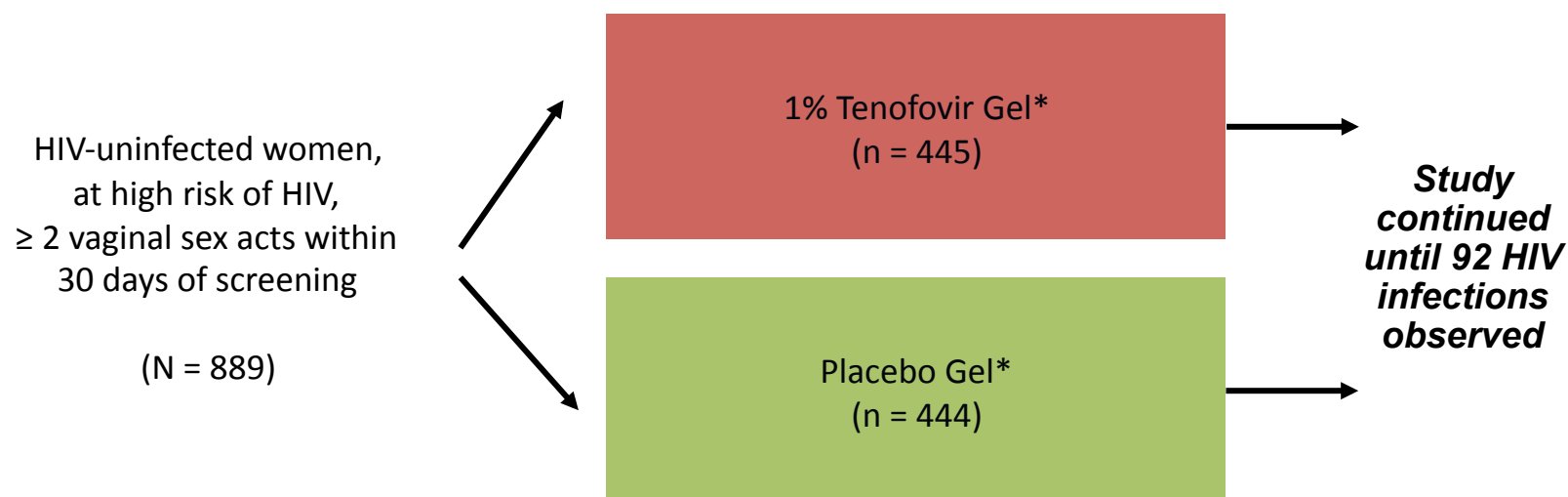


LOVE MAY HAVE ANOTHER PROTECTOR

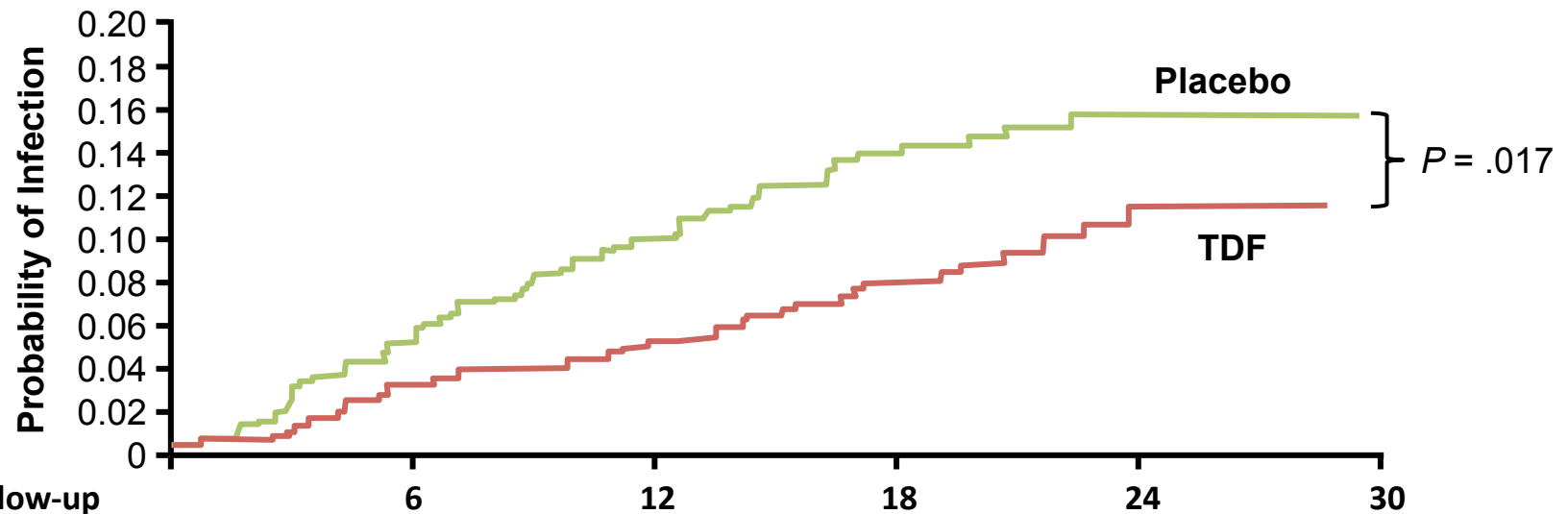


CAPRISA 004: 1% TFV Vaginal Gel for Prevention of HIV in Women

- Randomized, placebo-controlled, double-blind, proof-of-concept study conducted at 2 sites in South Africa



HIV Incidence in CAPRISA 004



Mos of Follow-up	6	12	18	24	30
Cumulative HIV endpoints	37	65	88	97	98
Cumulative women-ysrs	432	833	1143	1305	1341
HIV incidence rates (TDF vs placebo)	6.0 vs 11.2	5.2 vs 10.5	5.3 vs 10.2	5.6 vs 10.2	5.6 vs 9.1
Effectiveness, % (<i>P</i> value)	47 (.064)	50 (.007)	47 (.004)	40 (.013)	39 (.017)

- No K65R resistance mutations among seroconverters

Abdool Karim, Q, et al. Science. 2010;329:1168-1174.

iPrEx: Phase 3 Efficacy Study of Truvada



Can a pill a day
prevent HIV?

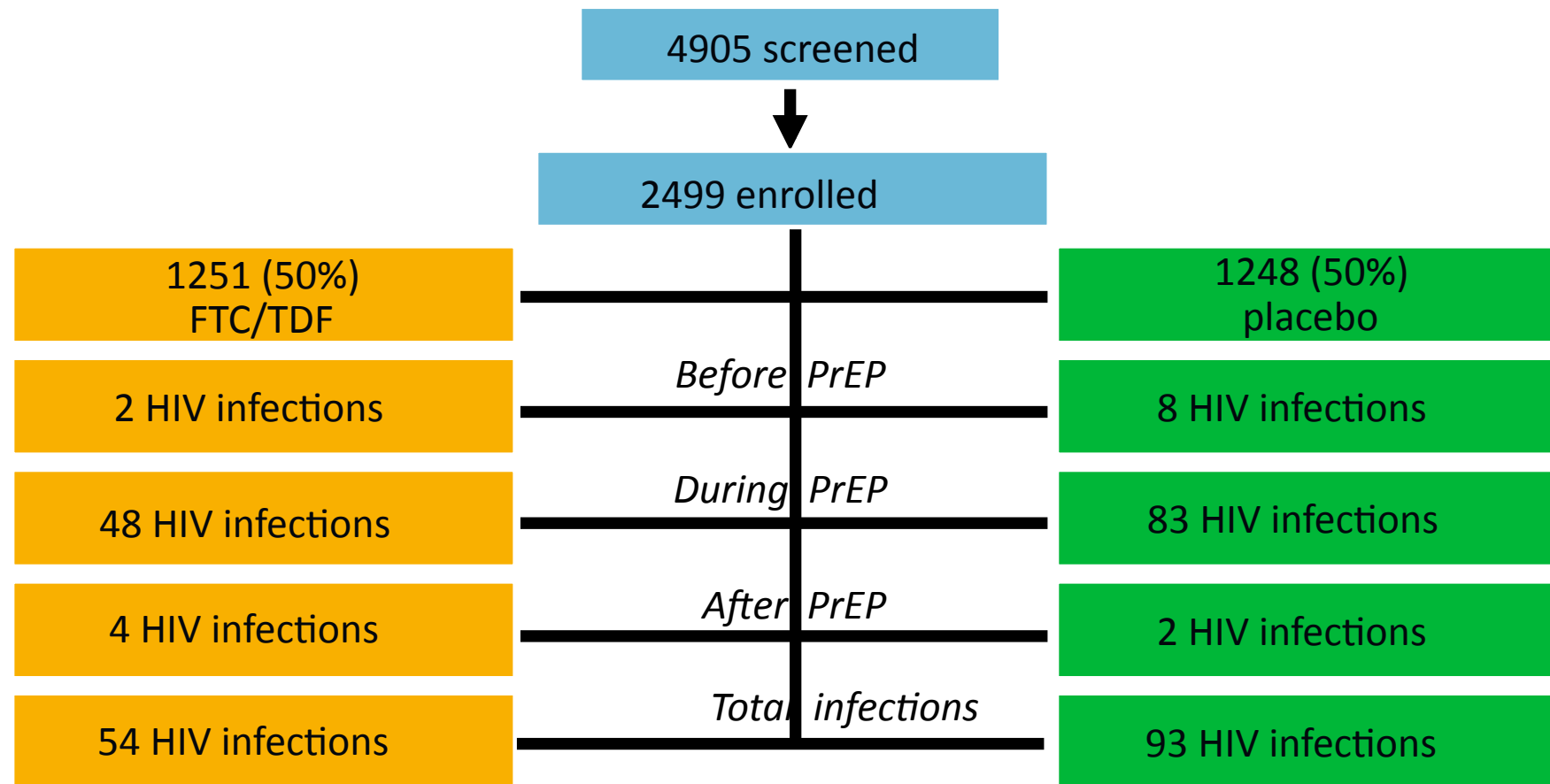
Help us find out.

415.554.8888
preparesf.org


prepare
san francisco

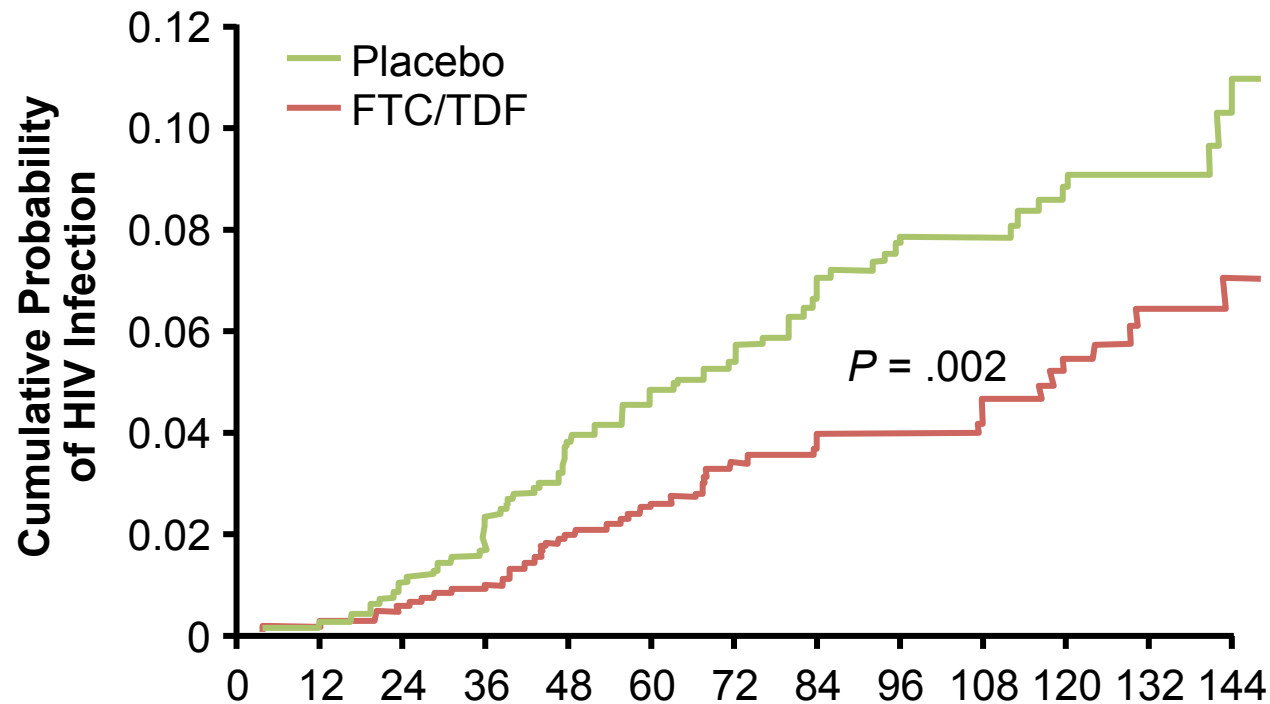
photo: steve the film photography.com

iPrEx: Enrollment and Follow-up



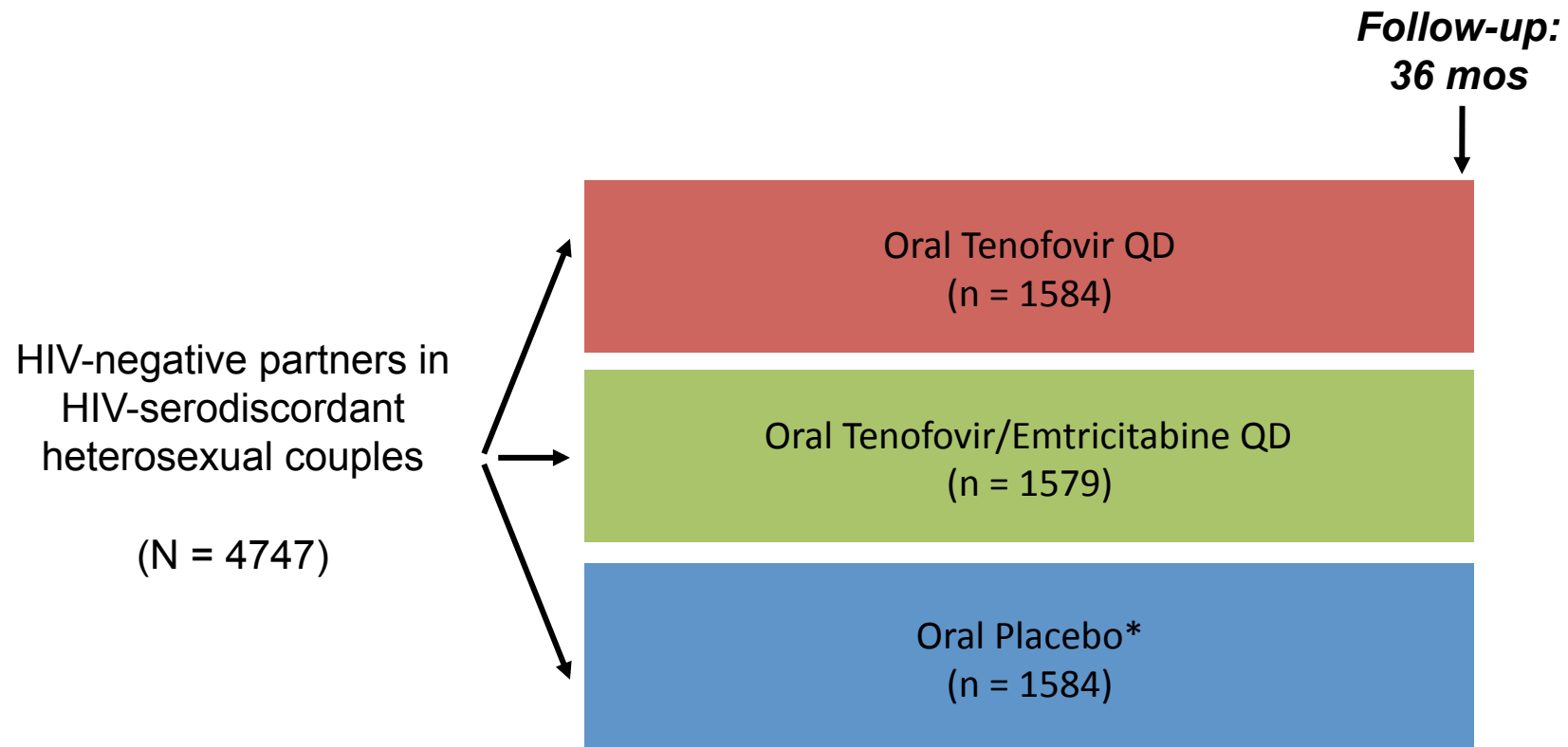
iPrEx: Efficacy

- Efficacy through study end (mITT): 42% (95% CI: 18% to 60%)



Placebo 1248 1198 1157 1119 1030 932 786 638 528 433 344 239 106
FTC/TDF 1251 1190 1149 1109 1034 939 808 651 523 419 345 253 116

Partners PrEP: TDF vs TDF/FTC vs Placebo in HIV-Serodiscordant Couples



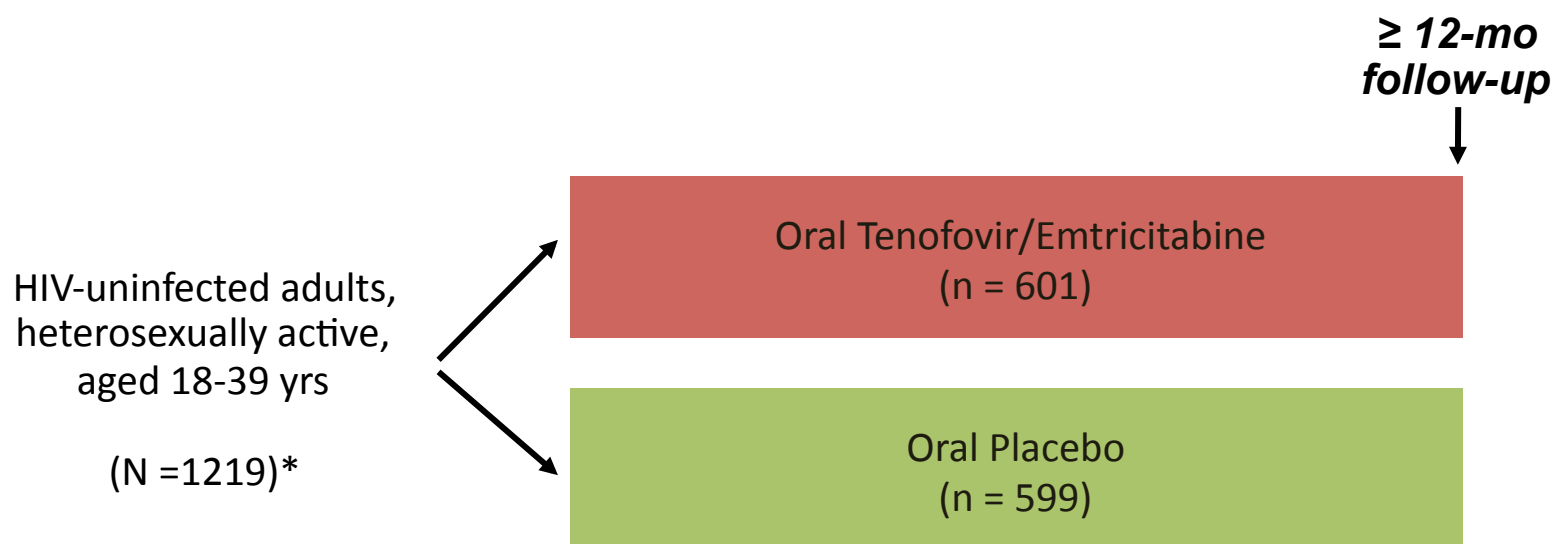
*Placebo arm terminated early on July 10, 2011, by data and safety monitoring board.

Partners PrEP: Both PrEP Strategies Significantly Reduce HIV Acquisition

Primary Efficacy Outcome, mITT Analysis	TDF (n = 1584)	TDF/FTC (n = 1579)	Placebo (n = 1584)
HIV acquisitions, n	17	13	52
HIV incidence/100 PY	0.65	0.50	1.99
Efficacy vs placebo, % (95% CI)	67 (44-81)	75 (55-87)	--
▪ <i>P</i> value	< .0001	< .0001	--

- Both PrEP strategies associated with significant reduction in HIV acquisition vs placebo in both men and women
 - TDF efficacy: 71% in women, 63% in men
 - TDF/FTC efficacy: 66% in women, 84% in men

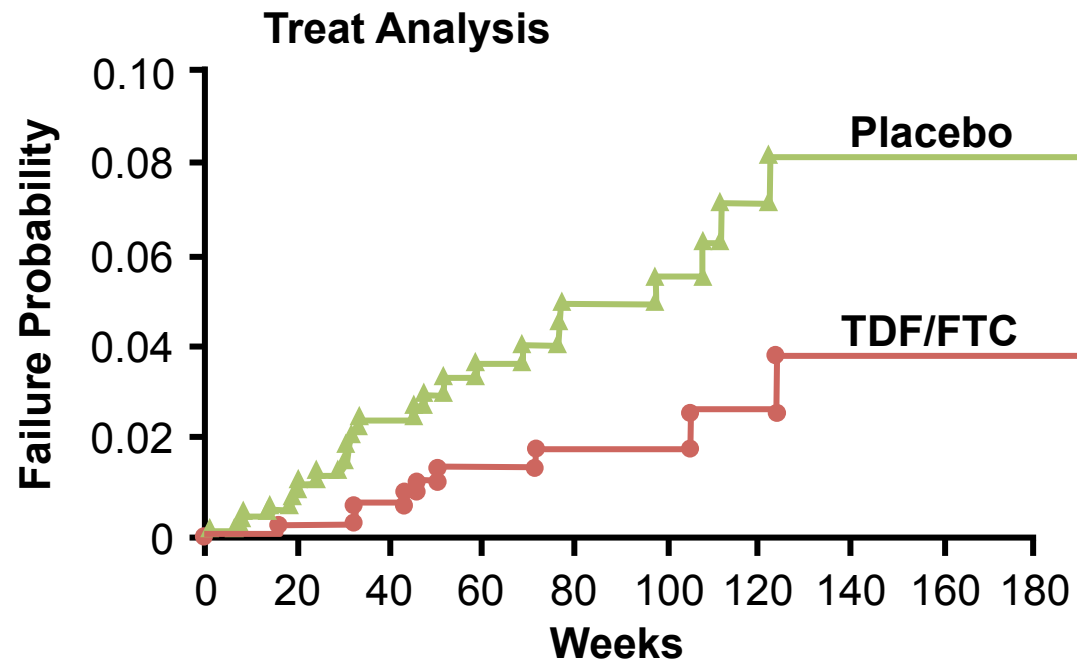
TDF2: PrEP With TDF/FTC in HIV-Negative Heterosexuals in Botswana



*n = 19 patients excluded for failure to start study medication or HIV infection.

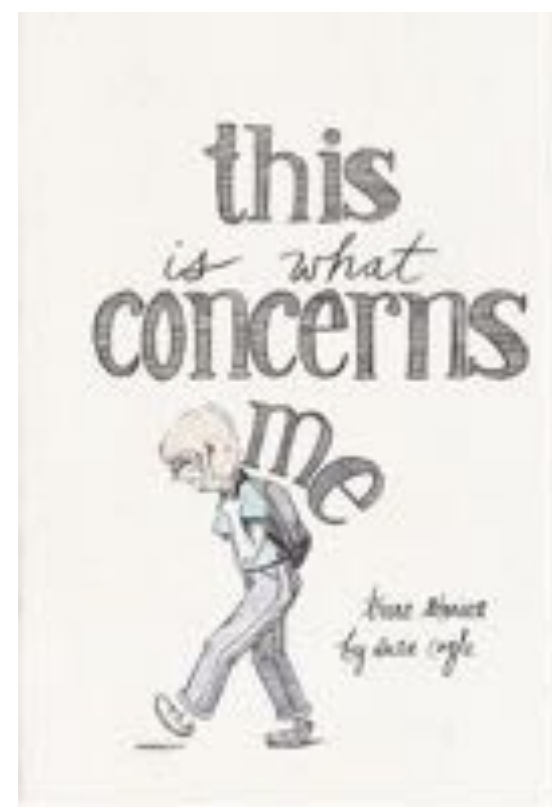
TDF2: PrEP With TDF/FTC Significantly Reduces HIV Acquisition

- 9 vs 24 patients seroconverted in TDF/FTC vs placebo arms, respectively
- Overall protective efficacy of TDF/FTC: 62.2% (95% CI: 21.5-83.4; P = 0.03)
- Reduction in HIV acquisition with TDF/FTC observed in both men and women but study underpowered to demonstrate sex-based differences in outcomes



Thigpen MC, et al N Engl J Med. 2012;[Epub ahead of print].



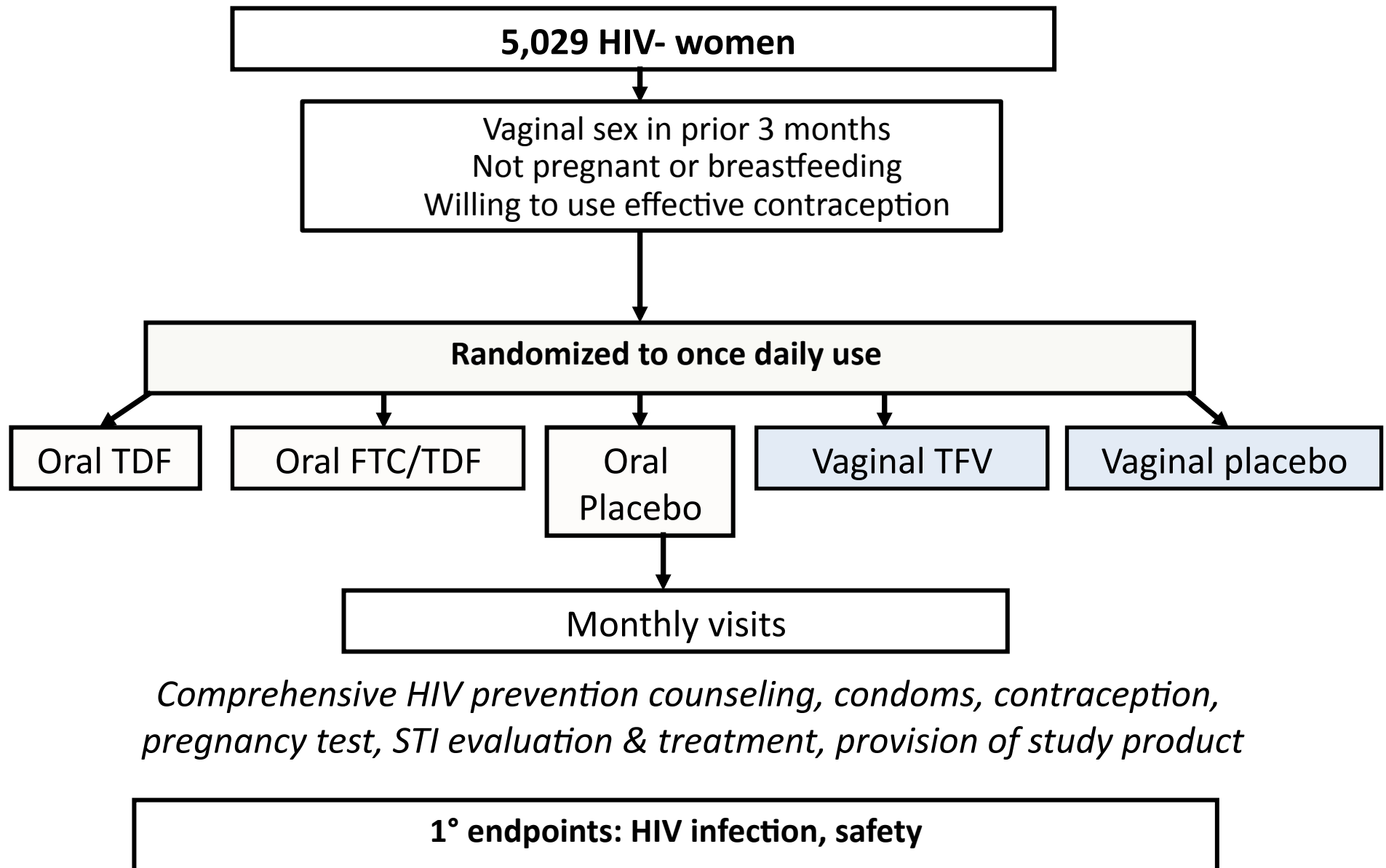




**Does it
Work?**



VOICE Design



Primary Efficacy Results (mITT)

	TDF*	Oral Placebo*	FTC/TDF	Oral Placebo	TFV Gel	Gel Placebo
Person-years	823	837	1285	1306	1026	1030
No. of HIV infections	52	35	61	60	61	70
HIV incidence per 100 p-y	6.3 (4.7, 8.3)	4.2 (2.9, 5.8)	4.7 (3.6, 6.1)	4.6 (3.5, 5.9)	5.9 (4.5, 7.6)	6.8 (5.3, 8.6)

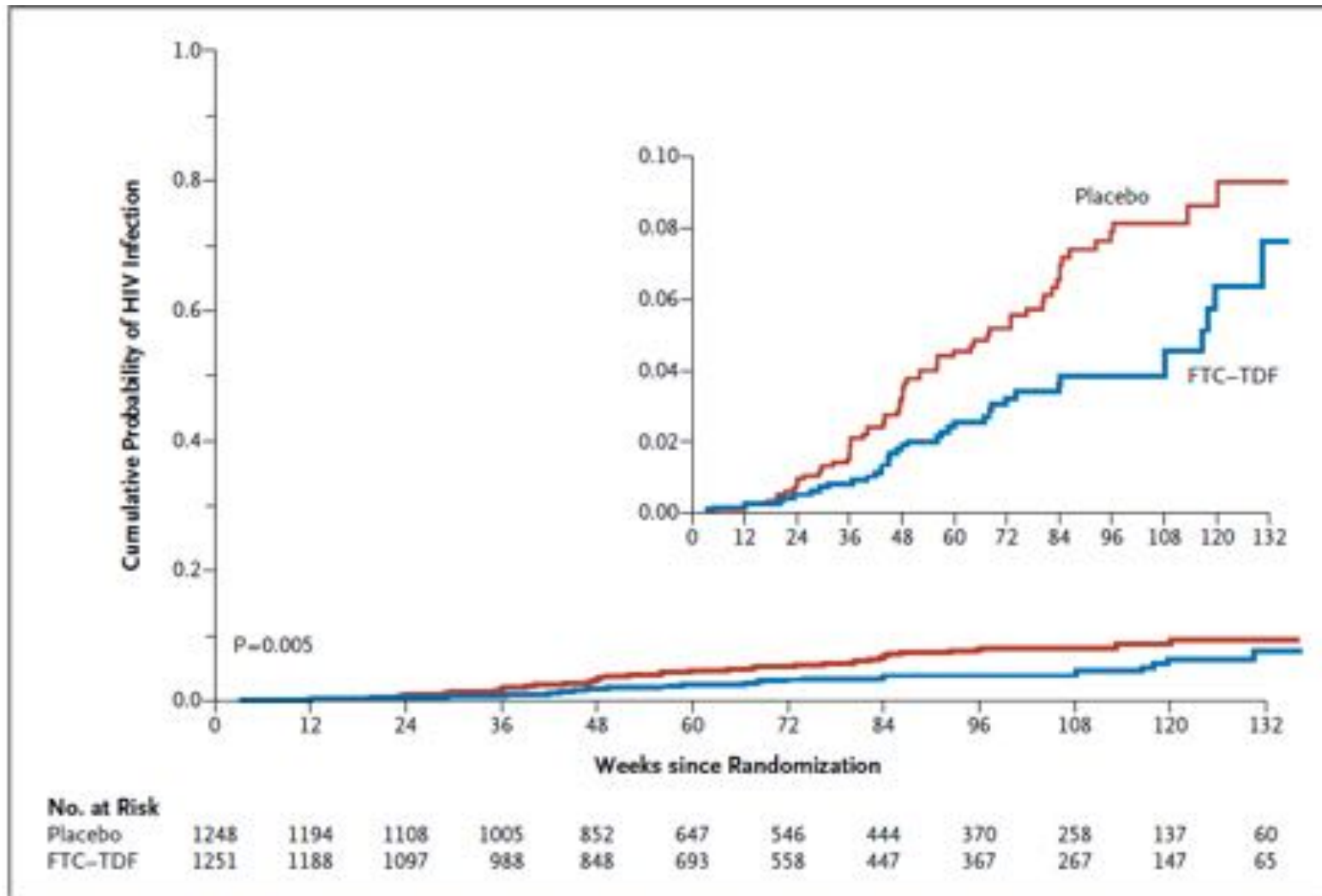
*Censored on date when sites were asked to take women off of TDF and TDF placebo pills

Primary Efficacy Results (mITT)

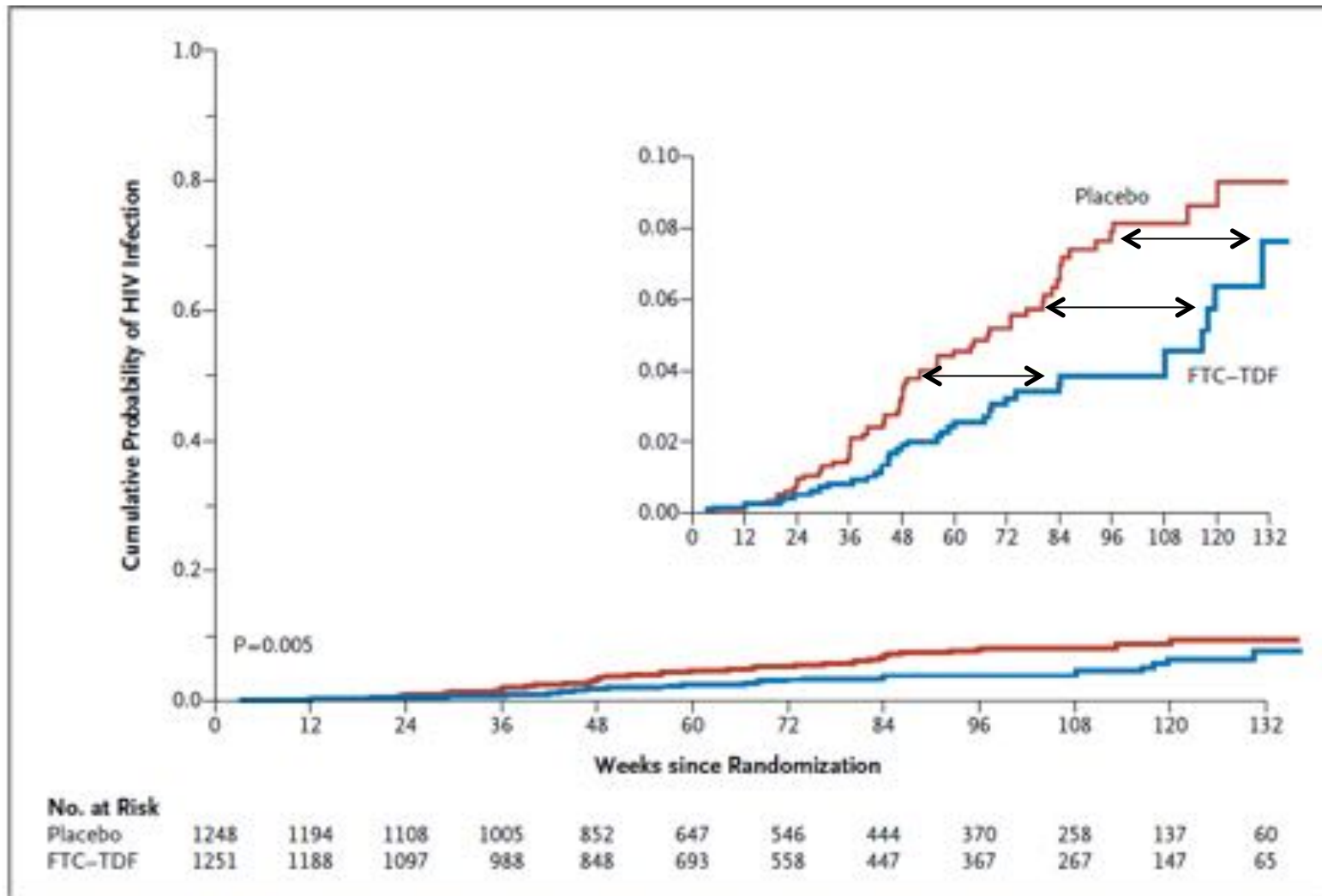
	TDF*		FTC/TDF		TFV Gel	
HIV protection efficacy vs. placebo						
HR 95% CI	1.49 (0.97, 2.3)		1.04 (0.7, 1.5)		0.85 (0.6, 1.2)	
P-value	0.07		>0.2		>0.2	

*Censored on date when sites were informed to take women off of TDF and TDF placebo pills

IPREX

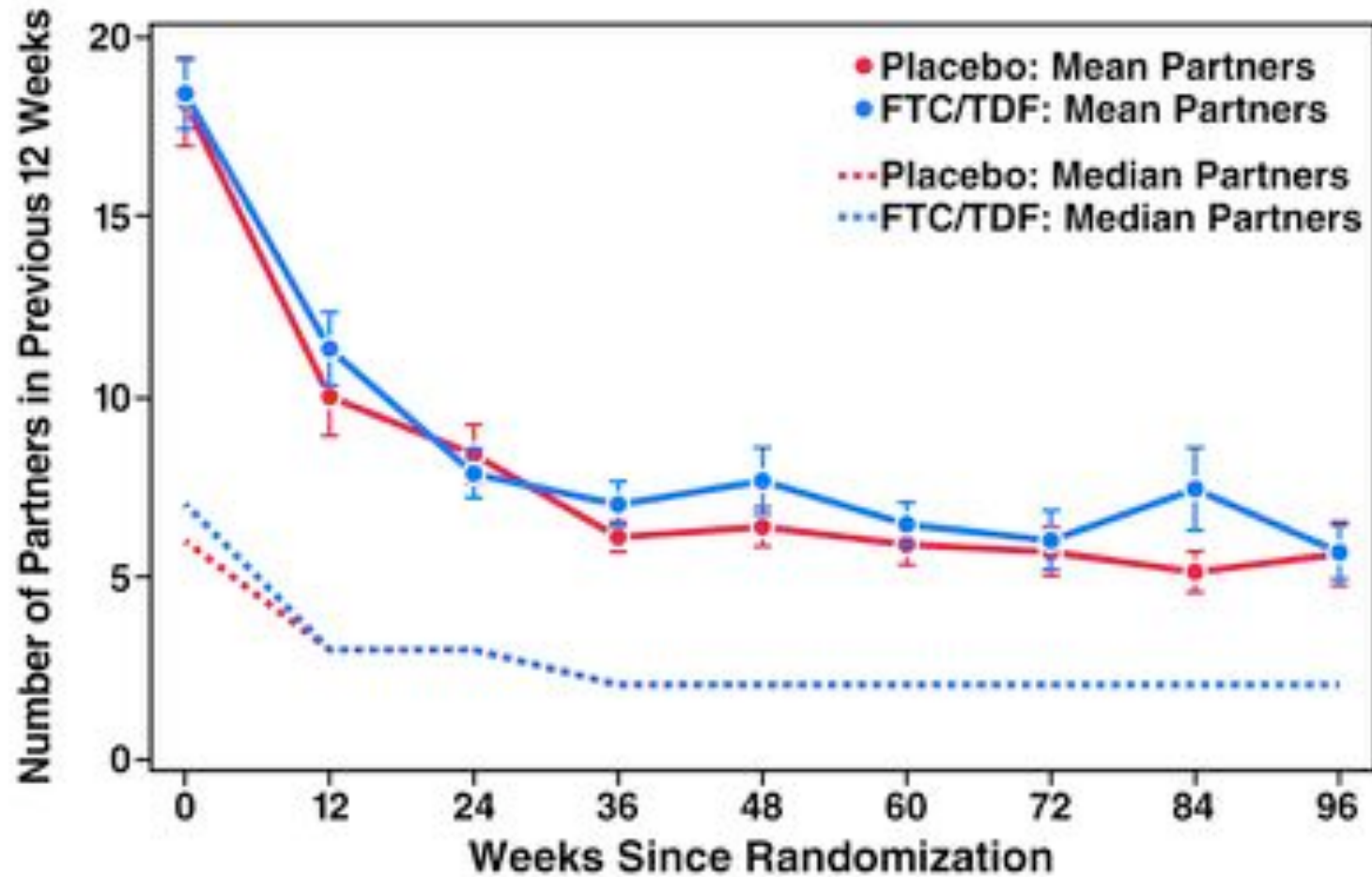


36 week delay

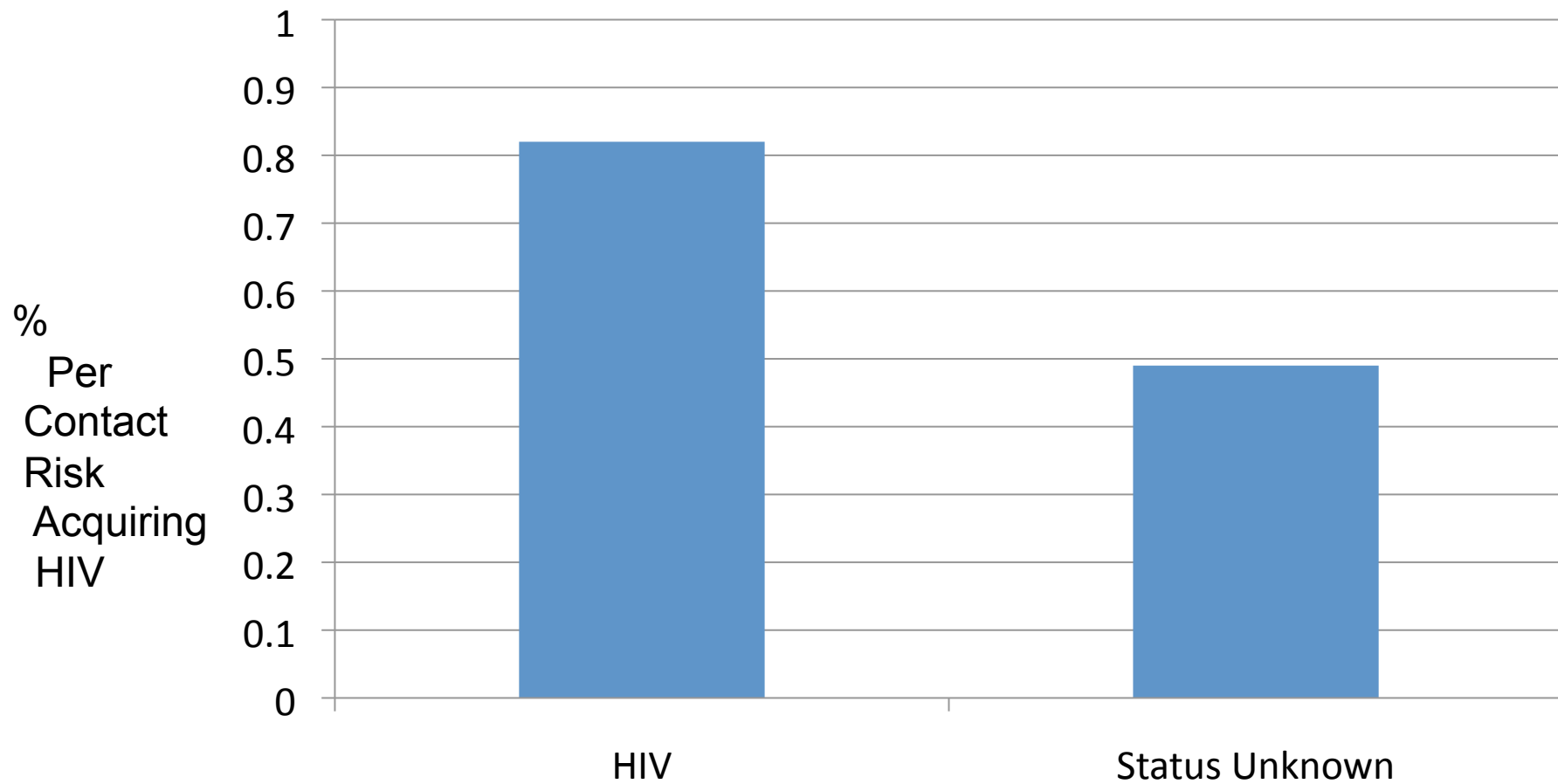


And what was happening before.....

Sexual Partners in iPrEx



And what was happening before.....











**IF HEP C WAS ATTACKING
YOUR FACE INSTEAD OF
YOUR LIVER, YOU'D DO
SOMETHING ABOUT IT.**

READY TO FIGHT BACK?

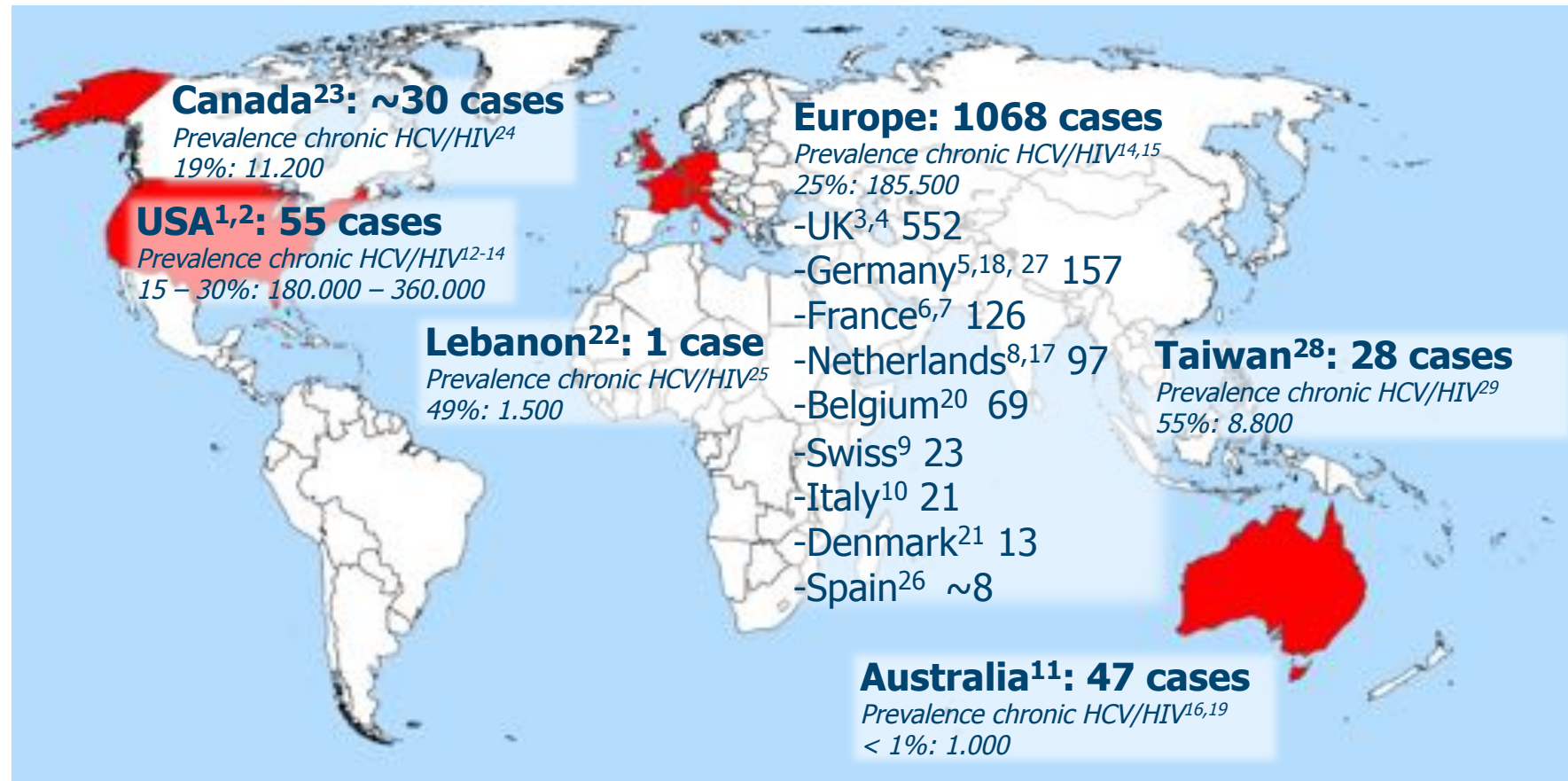
YOU'LL NEVER BE STRONGER THAN YOU ARE TODAY TO STOP THE DAMAGE HEP C IS DOING TO YOUR LIVER.
Talk to your doctor now about prescription treatment. Patients in clinical studies overall had a better than 50% chance
of reducing the Hep C virus to undetectable levels. Response to treatment may vary based on individual factors.
So log on or call, then talk to your doctor to find out if treatment is right for you. And help put Hep C behind you.

HepCSource.com

866-HepCSource

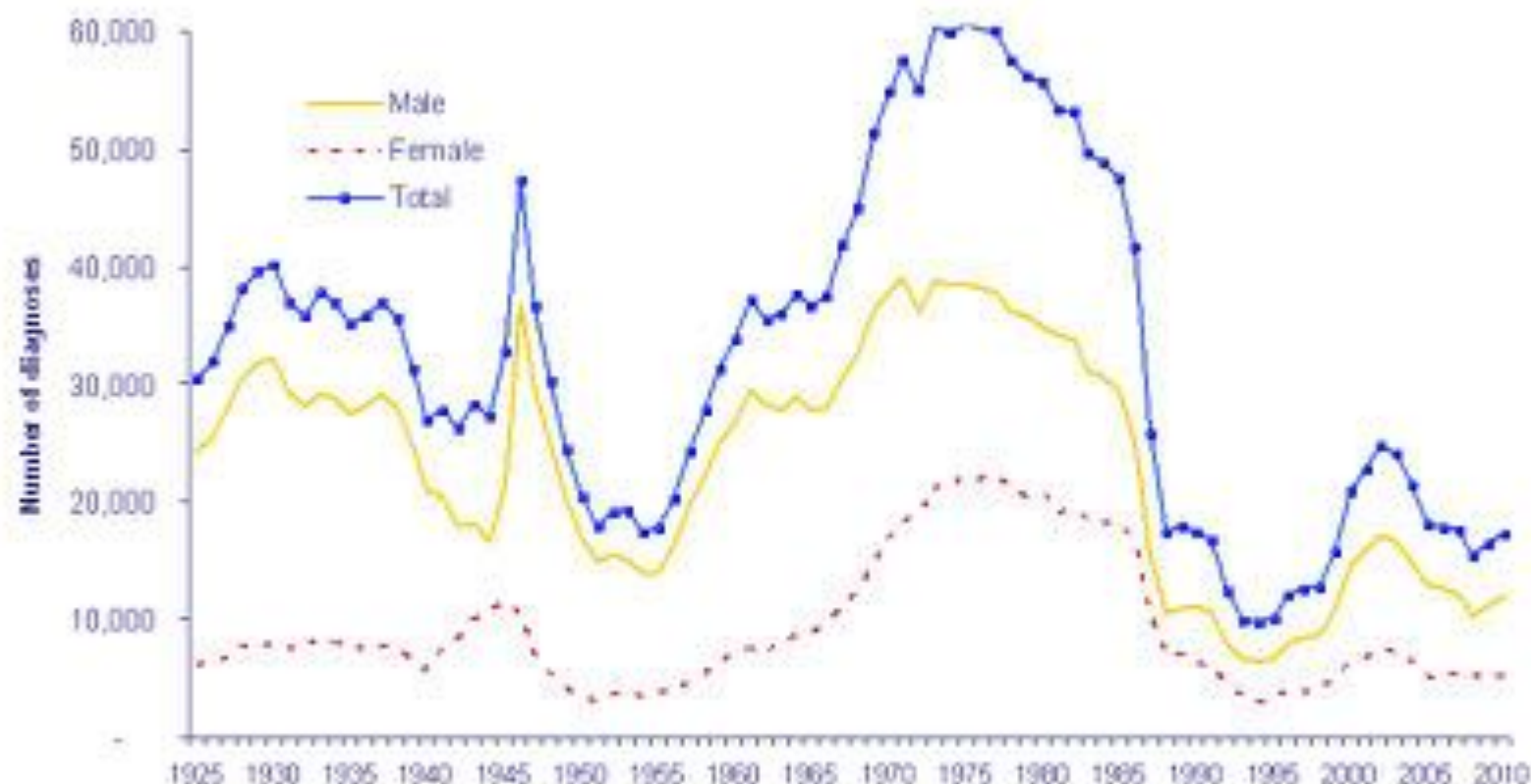
866-437-2768

Acute HCV among HIV+ MSM



1:Luetkemeyer JAIDS 2006; 2:Cox Gastroenterology 2008; 3:Giraudon Sex Transm Infect 2008; 4:Ruf Eurosurveill 2008; 5:Vogel CID 2009; 6:Gambotti Euro Surveill 2005; 7:Morin Eur J Gastro Hepat 2011; 8:Urbanus AIDS 2009; 9:Rauch CID 2005; 10:Gallotta 4th Works. HIV & Hep. Coinf. 2008; 11:Matthews CID 2009; 12:Sherman CID 2002; 13:Backus JAIDS 2005; 14:UNAIDS Report 2008; 15:Soriano JID 2008; 16:Matthews CID 2011; 17:Arends Neth J Med 2011; 18:Neukam HIV Med 2011; 19:Pfafferoth PLoS One 2011; 20:Bottieau Euro Surveill 2010; 21:Barford Scand JID 2011; 22:Dionne-Odom Lancet Infect Dis 2009; 23:Hull personal conversation 2011; 24:Remis Public Health Agency of Canada 2002; 25:UNGASS Country progress Report 2010; 26:Soriano personal conversation 2011; 27:Boesecke 18thCROI Boston 2011 abstract #113; 28:Sun Liver International 2011; 29:Lee J F Med Assoc 2008

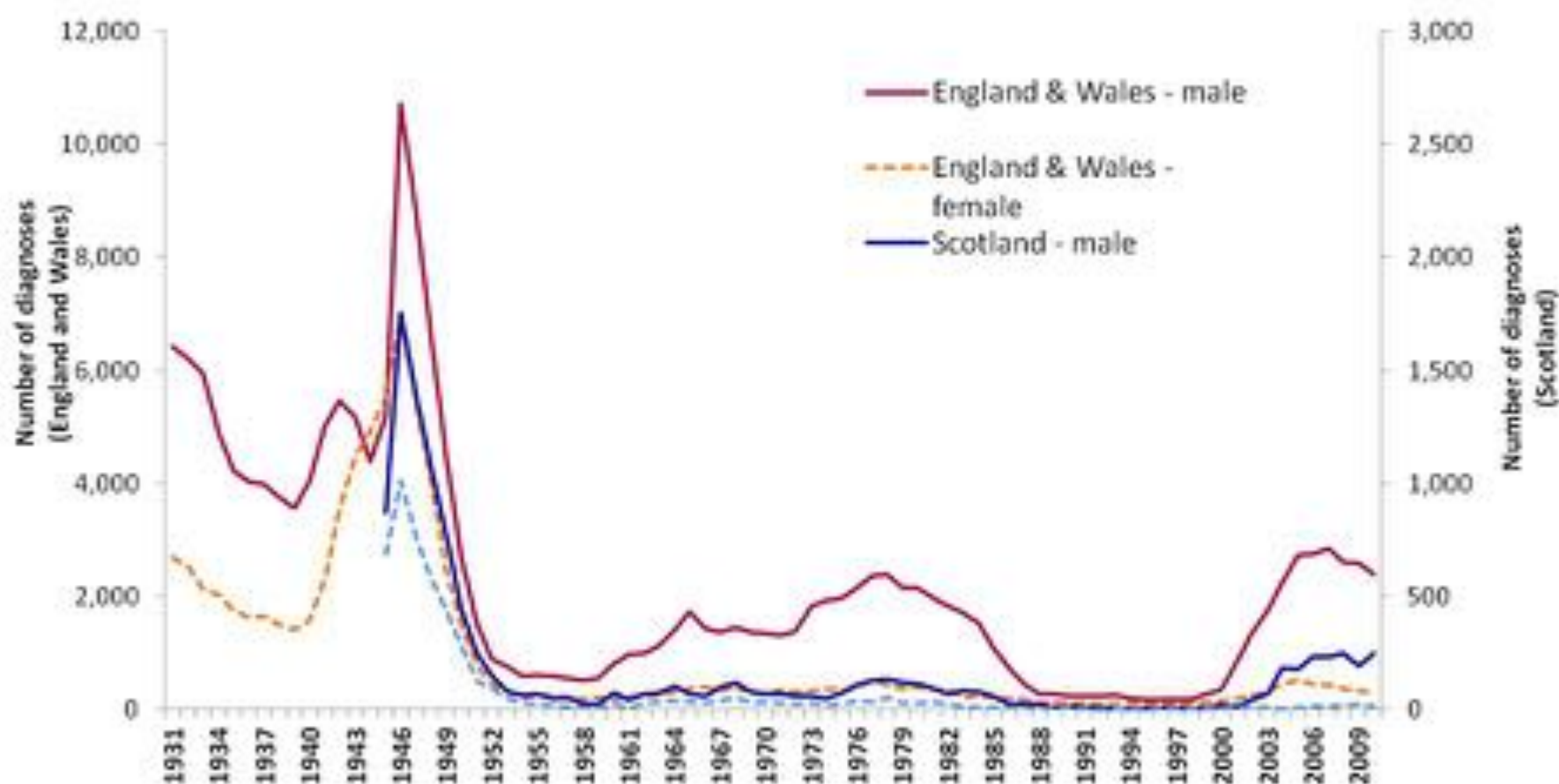
Number of diagnoses of gonorrhoea by sex, GUM clinics, England and Wales*: 1925 – 2010



* Scotland & Northern Ireland data are excluded as they are incomplete from 1925 - 2003

Routine GUM clinic returns

Number of diagnoses of syphilis (primary, secondary and early latent) by sex, GUM clinics, England, Wales and Scotland*:1931-2010



*Equivalent Scottish data are not available prior to 1945. Northern Ireland data from 1931- 2003 are incomplete, therefore, have been excluded.

Routine GUM clinic returns

Drug Resistance



iPrEX: Resistance

- **No resistance in those who acquired HIV after enrollment**
- **3 cases of resistance in 10 seroconverters at entry**

8 on placebo arm



1 with transmitted multi-resistant HIV

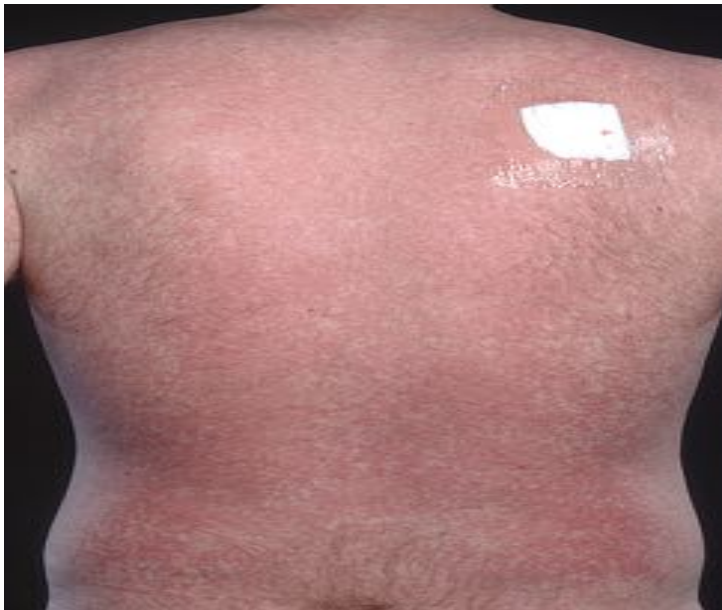
2 on FTC/TDF arm

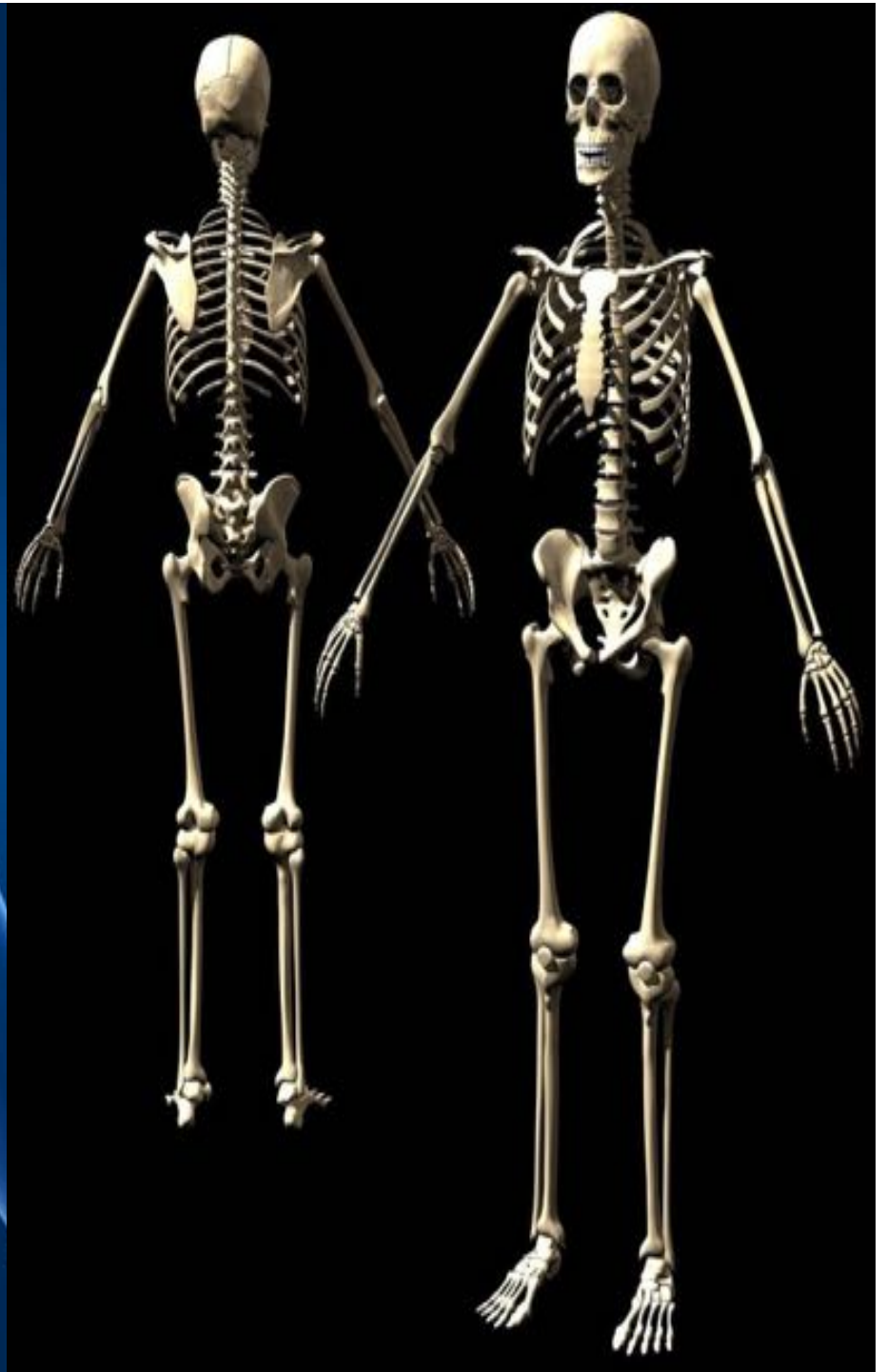
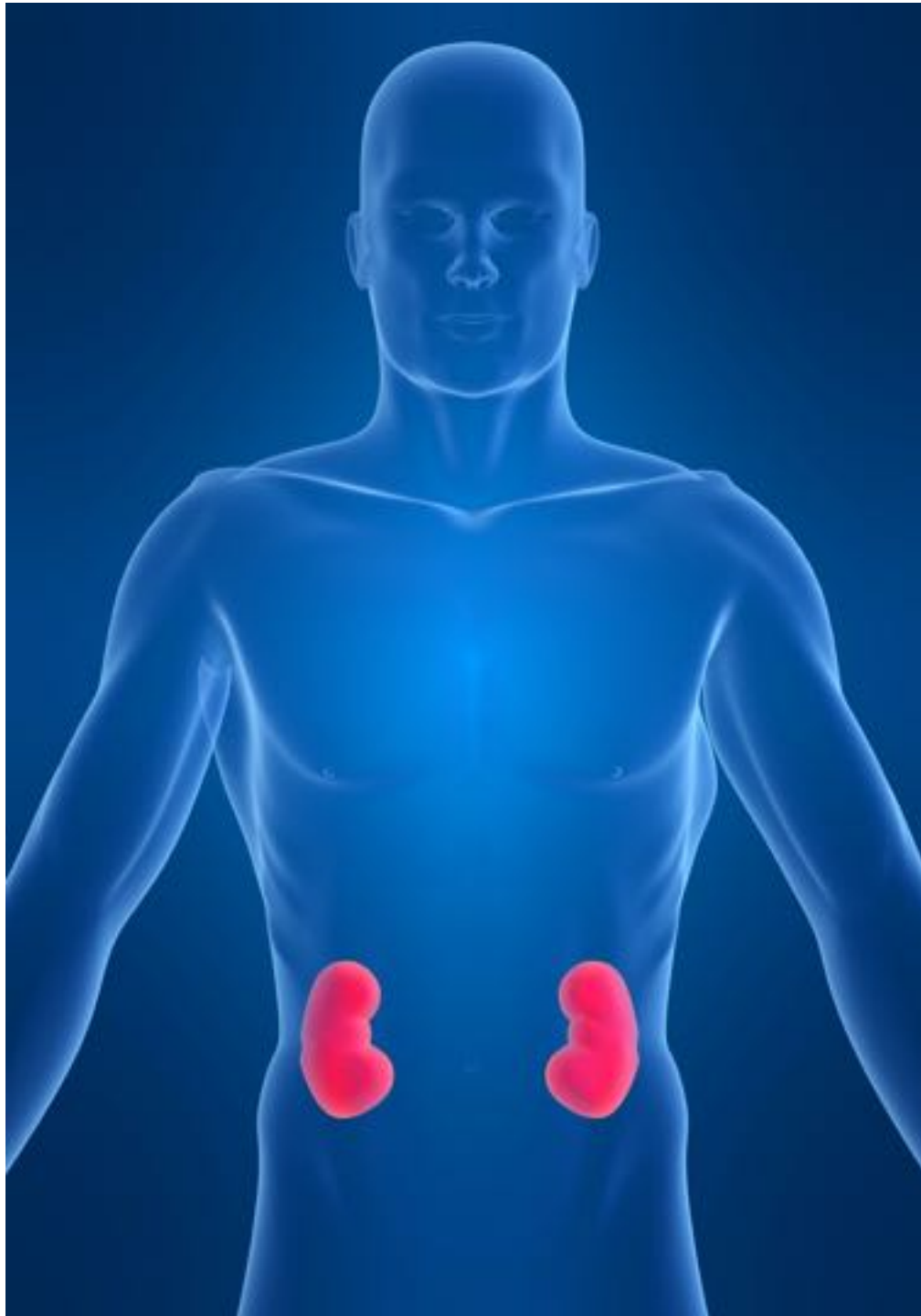


M184V & M184I (indeterminate)

iPrEX: Resistance

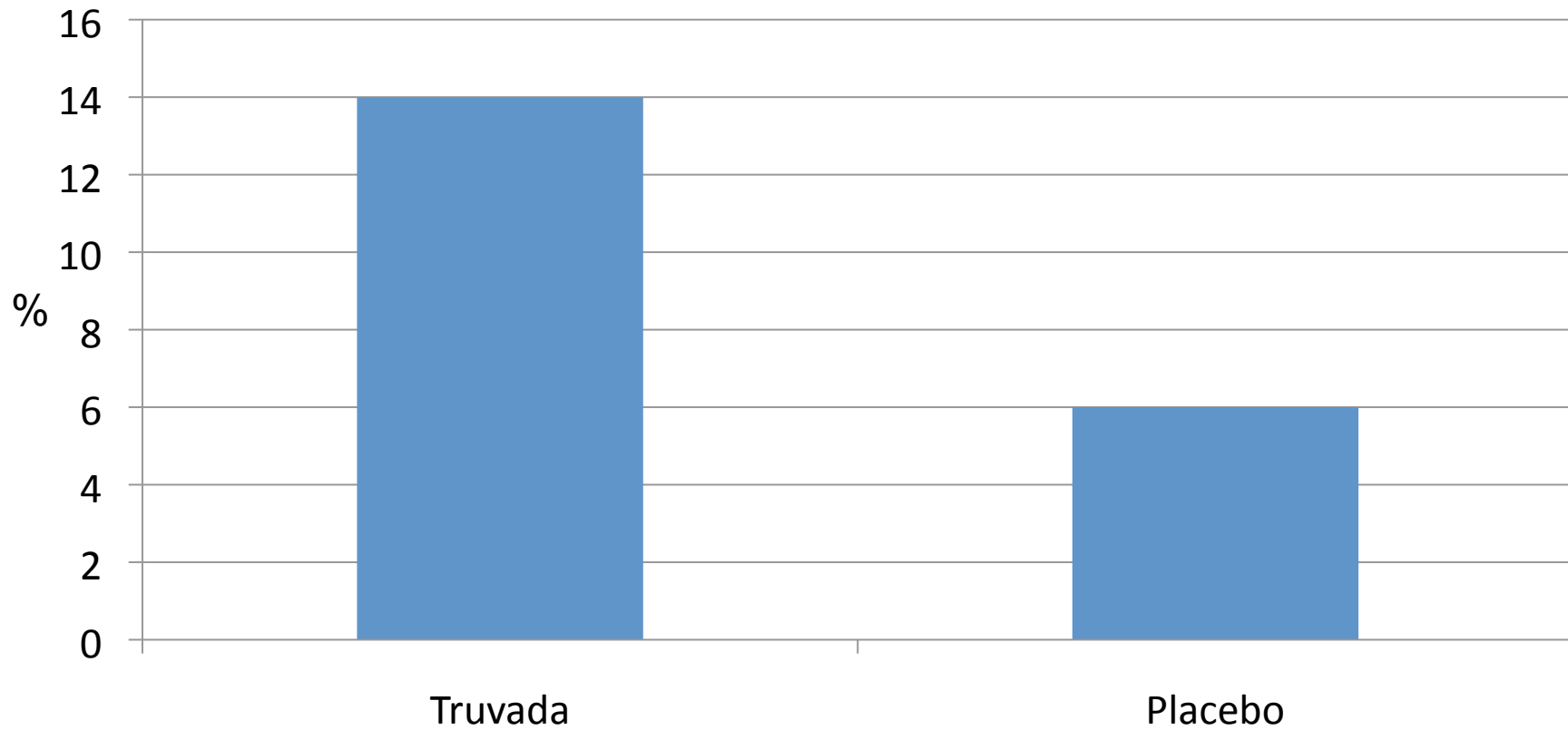
- **No resistance in those who acquired HIV after enrollment**
- **3 cases of resistance in 10 seroconverters at entry**





Reduction in BMD

Fall by 5% BMD from Baseline



Monitoring-The FDA says..

- Prior to starting measure renal function and serum phosphorus
- Assess risk factors for renal and bone toxicity
- Consider supplementing vitamin D and calcium
- Monitor renal function frequently
- Consider DEXA scans

Who will prescribe?

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.

Who will prescribe?

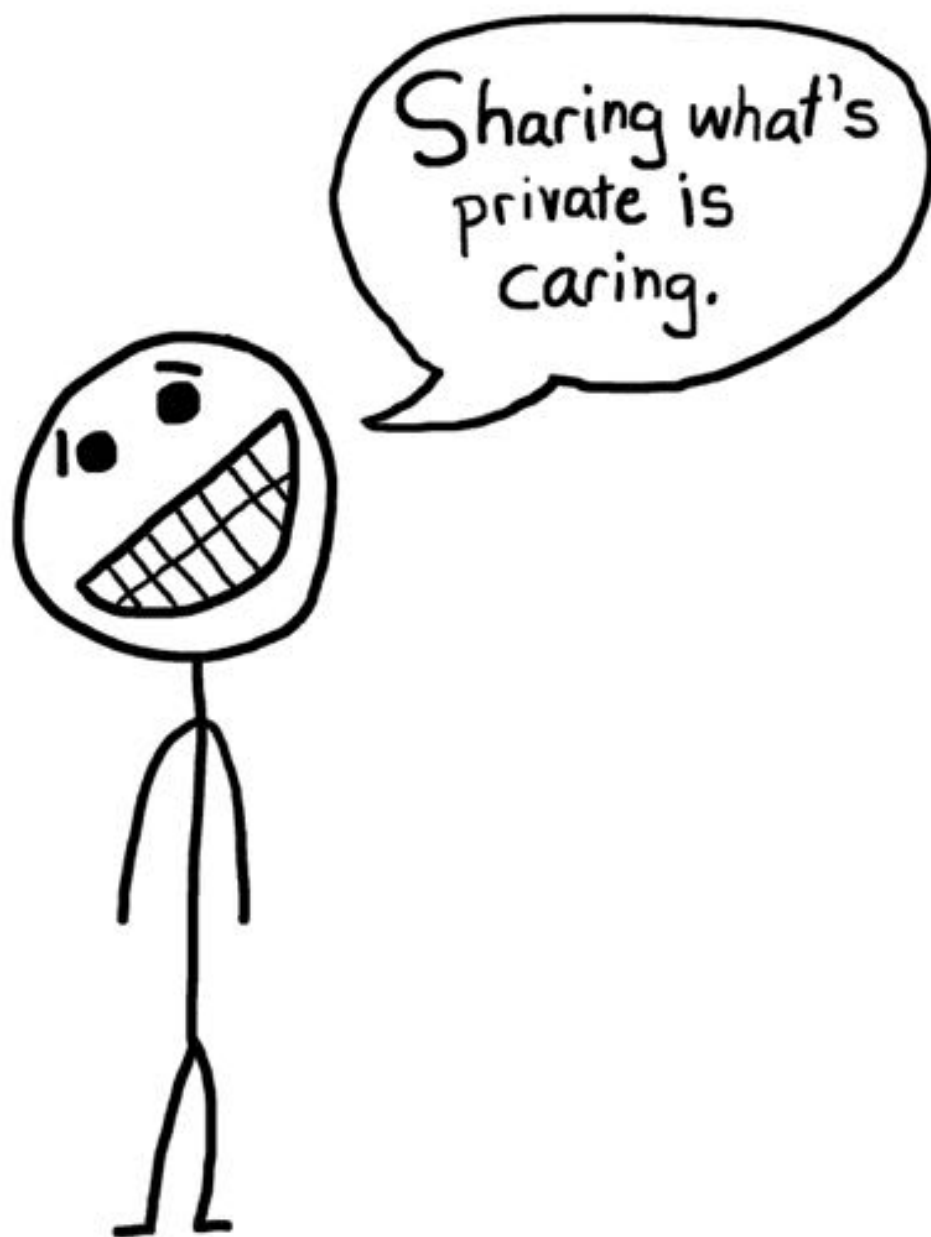


Who will prescribe?



Who will prescribe?





AIDS pill as party drug?

Some HIV-negative men are using tenofovir instead of condoms, hoping it provides protection. Physicians say the practice could lead to more infections.

By DANIEL COSTELLO
Times Staff Writer

"Taking a T." That's what HIV-negative gay men call the growing practice of downing the AIDS drug tenofovir and, with fingers crossed, hoping it protects them from the virus during unprotected sex.

It's being sold in packets along with Viagra and Ecstasy in gay dance clubs — and even prescribed by physicians, say doctors and AIDS prevention experts. The trend has alarmed

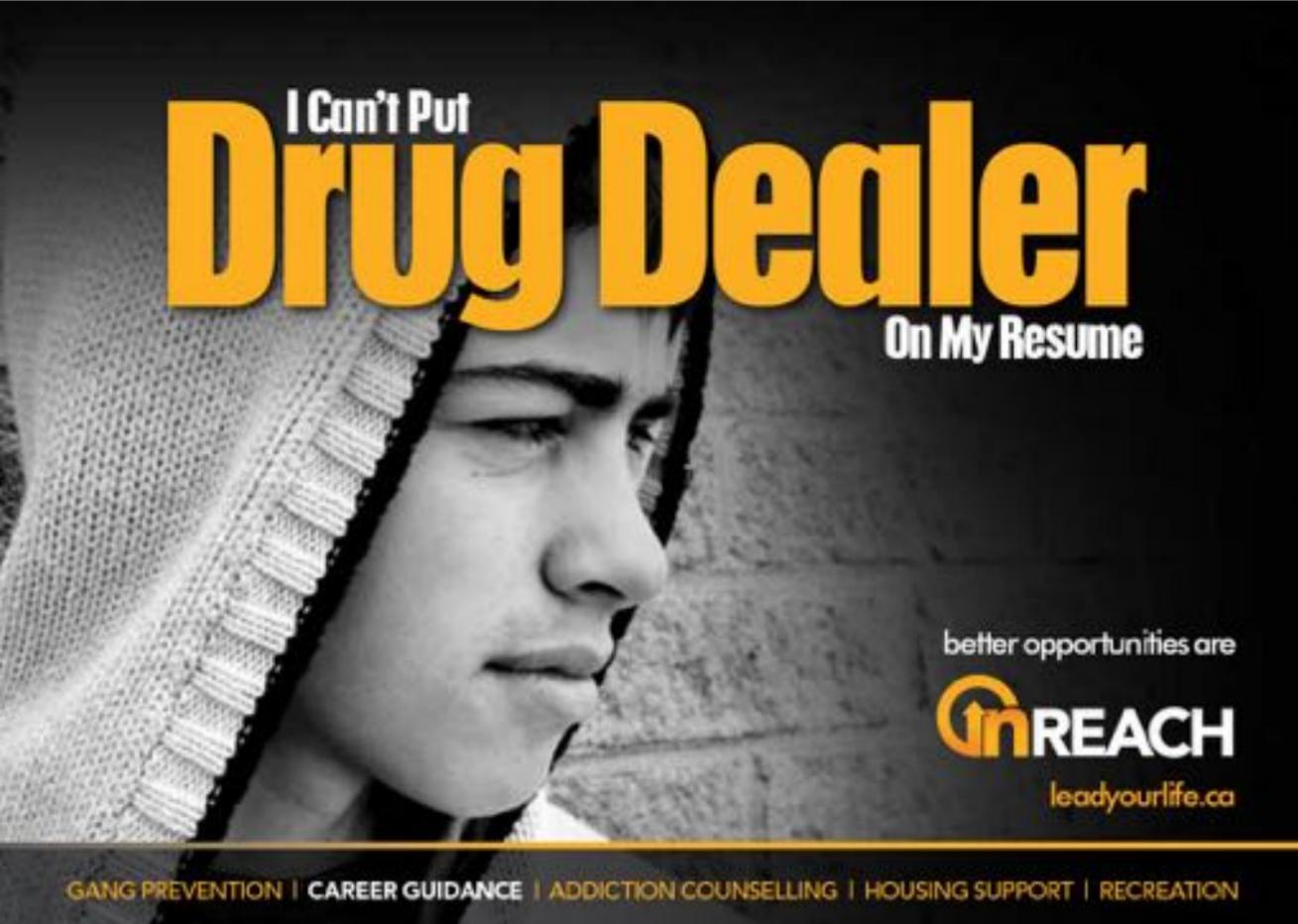
Los Angeles Times

Monday, December 19, 2005

SHAKEN OR



STIRRED?



I Can't Put
Drug Dealer
On My Resume

better opportunities are

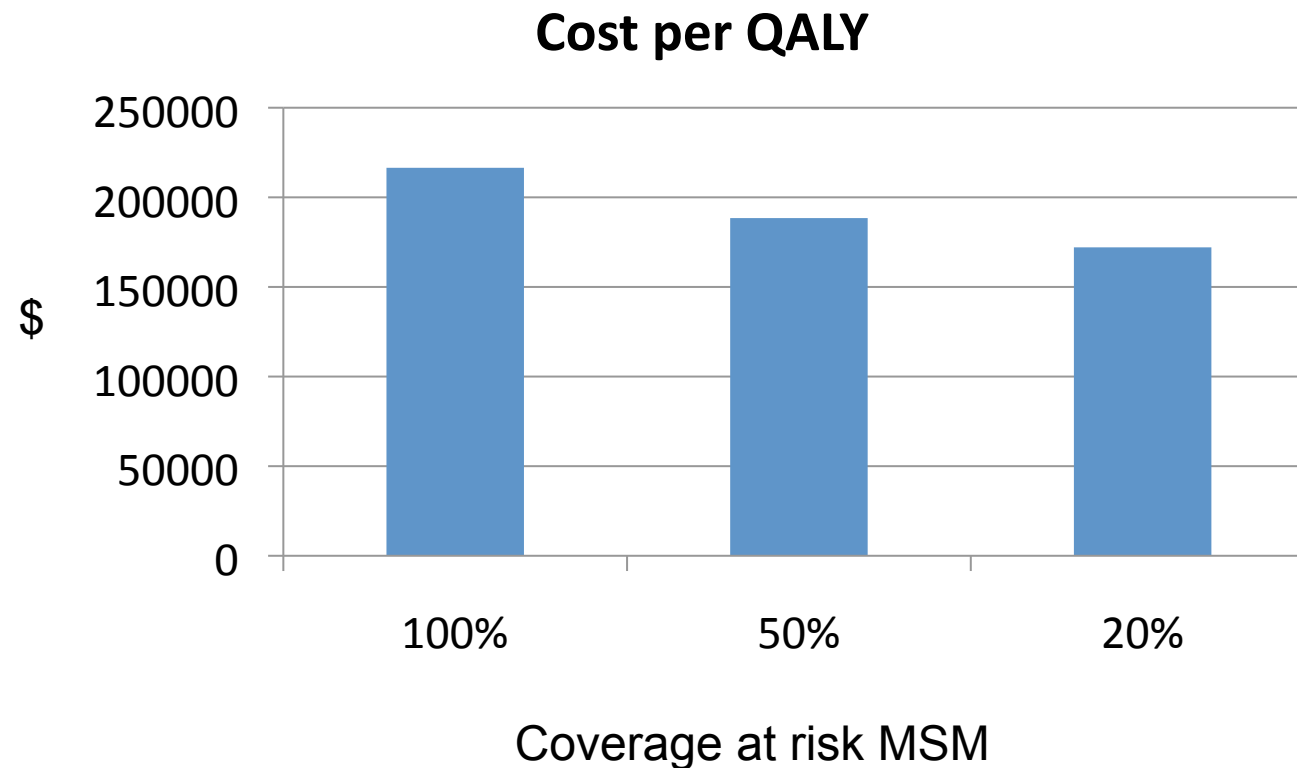
inREACH

leadyourlife.ca

GANG PREVENTION | CAREER GUIDANCE | ADDICTION COUNSELLING | HOUSING SUPPORT | RECREATION



- 75 billion dollars increase in health care related costs



To reduce below \$100,000 per QALY

- Daily cost less than \$15
- Efficacy greater than 75%

© Mike Baldwin / Cornered

BALDWIN



“Do a double-blind test. Give the new drug to rich patients and a placebo to the poor. No sense getting their hopes up. They couldn’t afford it even if it works.”

Can a pill prevent HIV?



Antiretroviral medication, Uganda

The Reality: PrEP Efficacy Trial Results, March 2012

Study	Population	N	Results
CAPRISA 004 South Africa	Women	889	39% efficacy vaginal TFV gel
iPrEx Brazil, Ecuador, Peru, S Africa, Thailand, US	MSM	2499	44% efficacy FTC/TDF
TDF2 Study Botswana	Young men women	1200	62% efficacy FTC/TDF
Partners PrEP Study Kenya, Uganda	Heterosexual couples	4758	67% efficacy TDF 75% efficacy FTC/TDF
FEM-PrEP Kenya, S Africa, Tanzania	Women	1950	FTC/TDF = futility
VOICE S Africa, Uganda, Zimbabwe	Women	5029	TDF = futility Vaginal TFV gel = futility FTC/TDF =futility
Bangkok Tenofovir Study Thailand	IDUs	2400	TDF ongoing
FACTS001 South Africa	Women	2200	TFV gel enrolling



CAPRISA: Impact of Adherence on Effectiveness of 1% TFV Vaginal Gel

Adherence Group	HIV Infections, n	HIV Incidence		Effect, %
		TFV	Placebo	
High (> 80% adherence) (n = 336)	36	4.2	9.3	54
Intermediate (50% to 80% adherence) (n = 181)	20	6.3	10.0	38
Low (< 50% adherence) (n = 367)	41	6.2	8.6	28

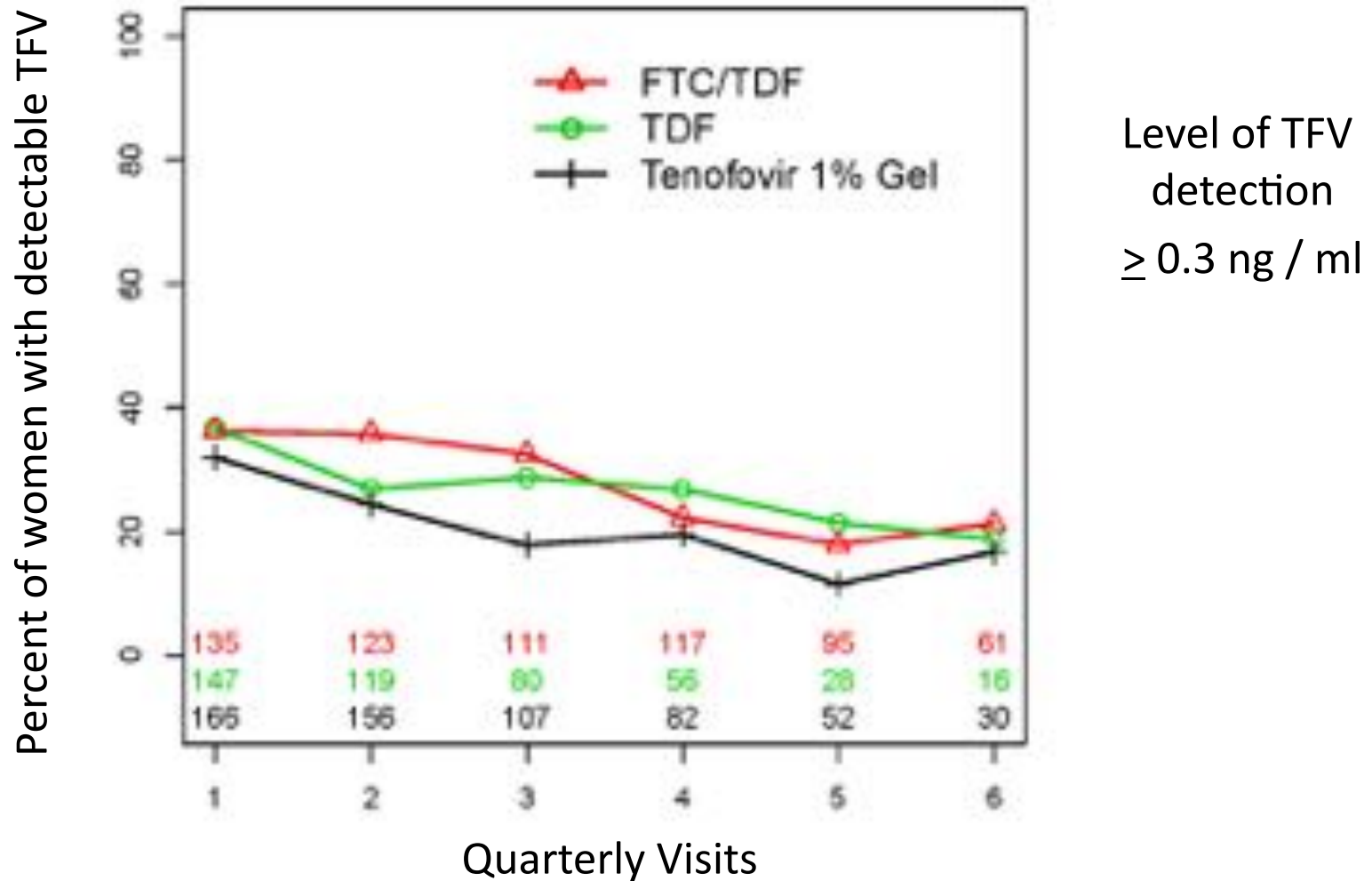
Adherence and HIV protection in oral PrEP trials

	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison
Partners PrEP FTC/TDF arm	81%	75%
TDF2	79%	62%
iPrEx	51%	44%
FEM-PrEP	26%	6%

**Clear dose-response relationship
between evidence of PrEP use & efficacy**

Baeten et al N Engl J Med 2012
Grant et al N Engl J Med 2010
Van Damme et al N Engl J Med 2012
Thigpen et al N Engl J Med 2012

Plasma Tenofovir Detection in Random Cohort Sample



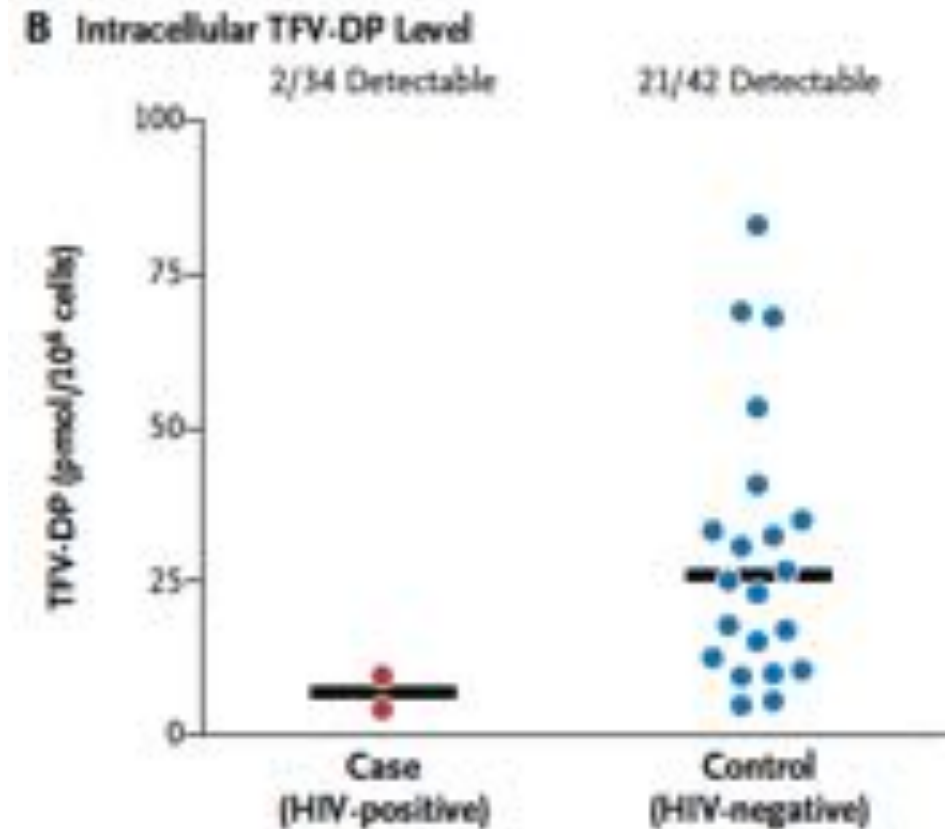
Tenofovir Detection During Study Participation*

	TDF	FTC/TDF	TFV Gel
Percent of <i>samples</i> with TFV detected averaged across women (mean)	30%	29%	25%
Percent of <i>women</i> with TFV not detected in <i>any</i> samples	58%	50%	55%

* At routine quarterly visits among participants in the random sample of active arms

iPrEX: Adherence is Critical

- High (> 90%) adherence
73% effective
- Intermediate
(50%-90%) adherence
50% effective
- Low (< 50%) adherence
32% effective



Tenofovir levels and HIV protection

- When PrEP was taken (detectable blood levels), high protective efficacy

	% of non-seroconverters with tenofovir detected in blood	HIV relative risk reduction: detection vs. no detection of tenofovir	
		Protection	p-value
iPrEx	51%	92%	<0.001
Partners PrEP FTC/TDF arm	81%	90%	0.002

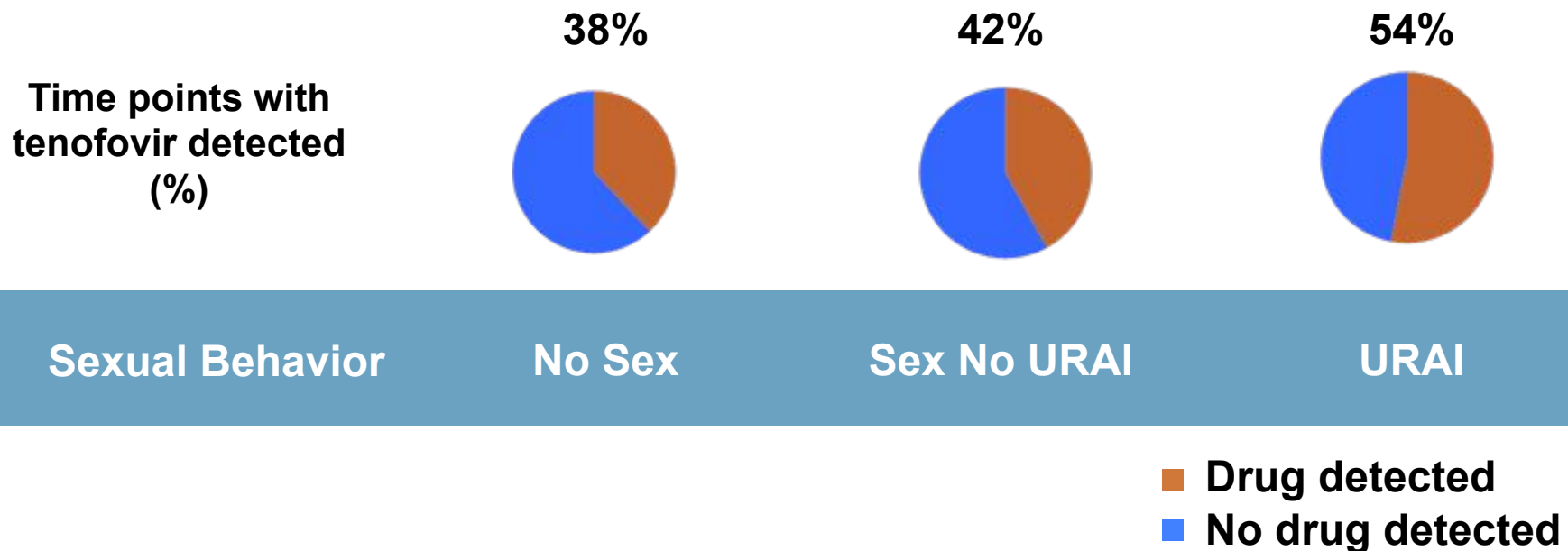
How much adherence is necessary?

iPrEx: imperfect adherence might still provide substantial HIV protection

	Estimated HIV risk reduction (95% CI)
2 doses/week	76% (56-96%)
4 doses/week	96% (90-99%)
7 doses/week	99% (96-99%)

Risk behavior and pill taking in iPrEx

- Men who practiced unprotected receptive anal intercourse (URAI) had higher PrEP use than other men
- Men not having sex were least likely to take PrEP





*“Drugs don’t work
if people don’t
take them”*

Former US Surgeon
General C. Everett Koop



- ***“Drugs do work if people do take them”***

Mark R. Nelson
UK Surgeon General



The Good News: Unprecedented momentum in the HIV prevention field

MICROBICIDES

- Microbicide gel (CAPRISA 004) reduces HIV infections in women

PRE-EXPOSURE PROPHYLAXIS

- Oral PrEP reduces HIV infections among MSM and transgendered women

VACCINES

- AIDS vaccine shows first efficacy in clinical trials
- Replicating viral vector effective in controlling SIV in animal studies
- Multiple new antibodies and targets on HIV discovered

Potent HIV-Blocking Proteins Raise Hopes for Vaccine

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.,
Thomas D. Van Ness, M.D., Vanessa McMahon, B.S., Albert Y. Liu, M.D., M.P.H.,
Thomas D. Van Ness, M.D., Vanessa McMahon, B.S., Albert Y. Liu, M.D., M.P.H.,

abc NEWS

Hope Found in First Vaccine to Stop HIV
After 20 Years of Dead Ends, a New Vaccine Can Protect Some From HIV

By MICHAEL SMITH
Sept. 24, 2009

For the first time, an investigational HIV vaccine has
For over 20 years, scientists have been trying to find
from... During the past million men, women

NewScientist

Discovery of HIV's weak spot boosts vaccine quest
...ies that bind to a hitherto unknown "weak spot" on HIV
...e within reach.

Vaccine first ever to help stop AIDS

By Marilyn Marchione and Michael Casey

BANGKOK, Thailand -- For the first time, an experimental vaccine has prevented infection
watershed event in the deadly epidemic and a surprising result. Researchers
might never be possible.
The World Health Organization
field of HIV

Breakthrough HIV gel earns applause in forum

July 20 2010 at 11:05pm

By Richard Ingham

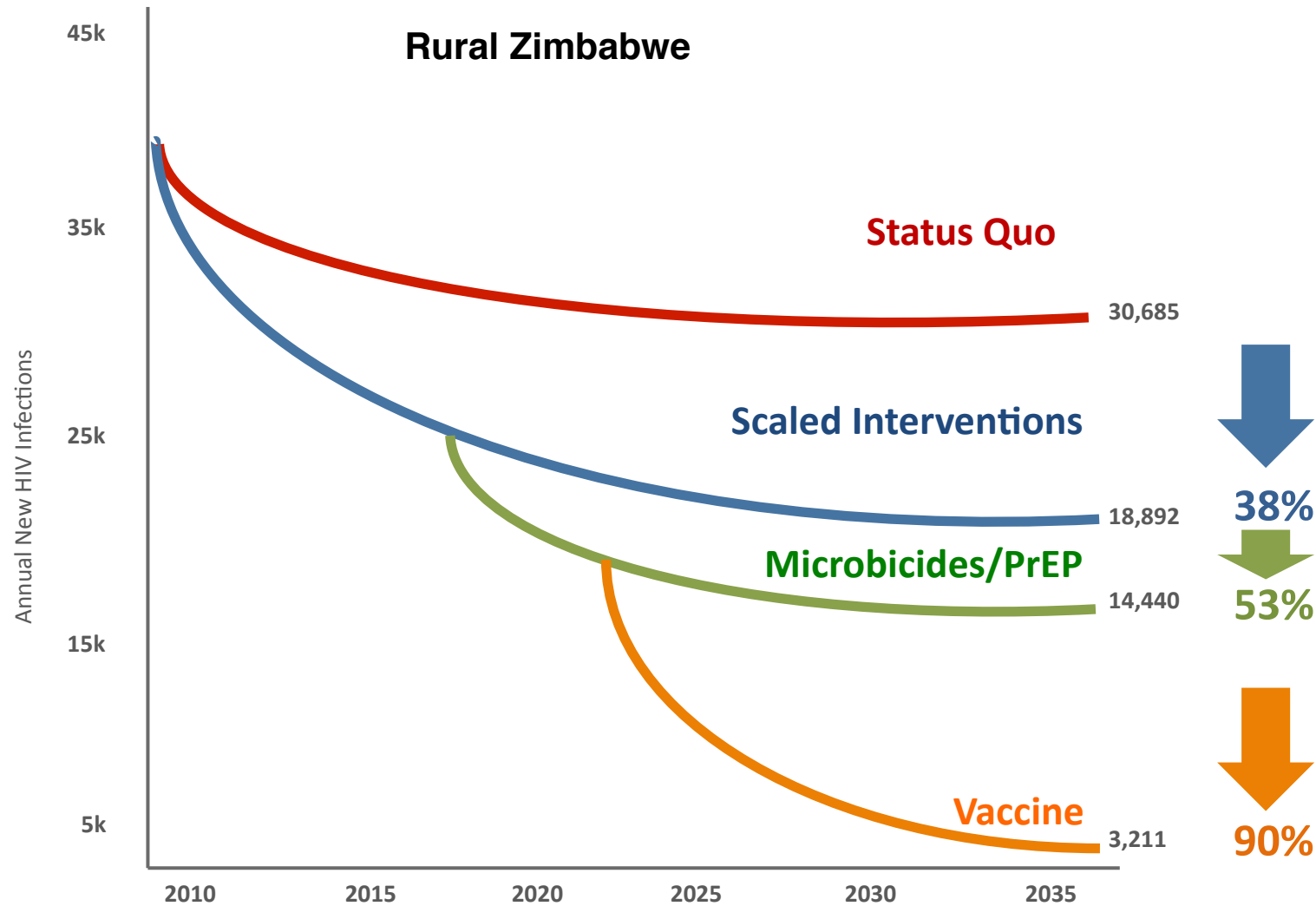
Vienna - The world Aids forum
cheered South African scientists
on from the

Antibody Kills 91% of HIV Strains

Thursday, July 8, 2010
By Ivan Garcia, Assistant Editor

The Wall Street Journal today reported a new
development in the fight against HIV/AIDS - In a
significant step toward an AIDS vaccine, U.S. government
scientists have discovered three powerful antibodies, the
strongest of which neutralizes 91% of HIV strains, more
than any AIDS antibody yet discovered.

New prevention technologies will reduce HIV incidence...
but only a vaccine will end the epidemic







I'm negative. What about you?

Talk to your partner. Use condoms. Get tested...together.



For free, confidential HIV testing and counseling,
contact the Baltimore City Health Department at
www.baltimorecity.gov/health

Thank you

For further information please contact :

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