
What if there were a pill that could help prevent HIV?
THERE IS.
Ask your doctor if PrEP is right for you.

PrEP

Mark Bloch
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Sydney Australia

1. PrEP in Sydney
2. Effectiveness of PrEP
3. STIs
4. PrEP toxicity
5. Future of PrEP

Figure 1: Number of NSW residents notified with newly diagnosed HIV infection from 2009 to 2015

Current status of PrEP in Australia

TGA approval – licensed for use in Australia

PBAC reimbursement – rejected on first application

EPIC PrEP study

Study Aim: Reduction in new HIV infections in NSW

(Estimated 50% on modelling)

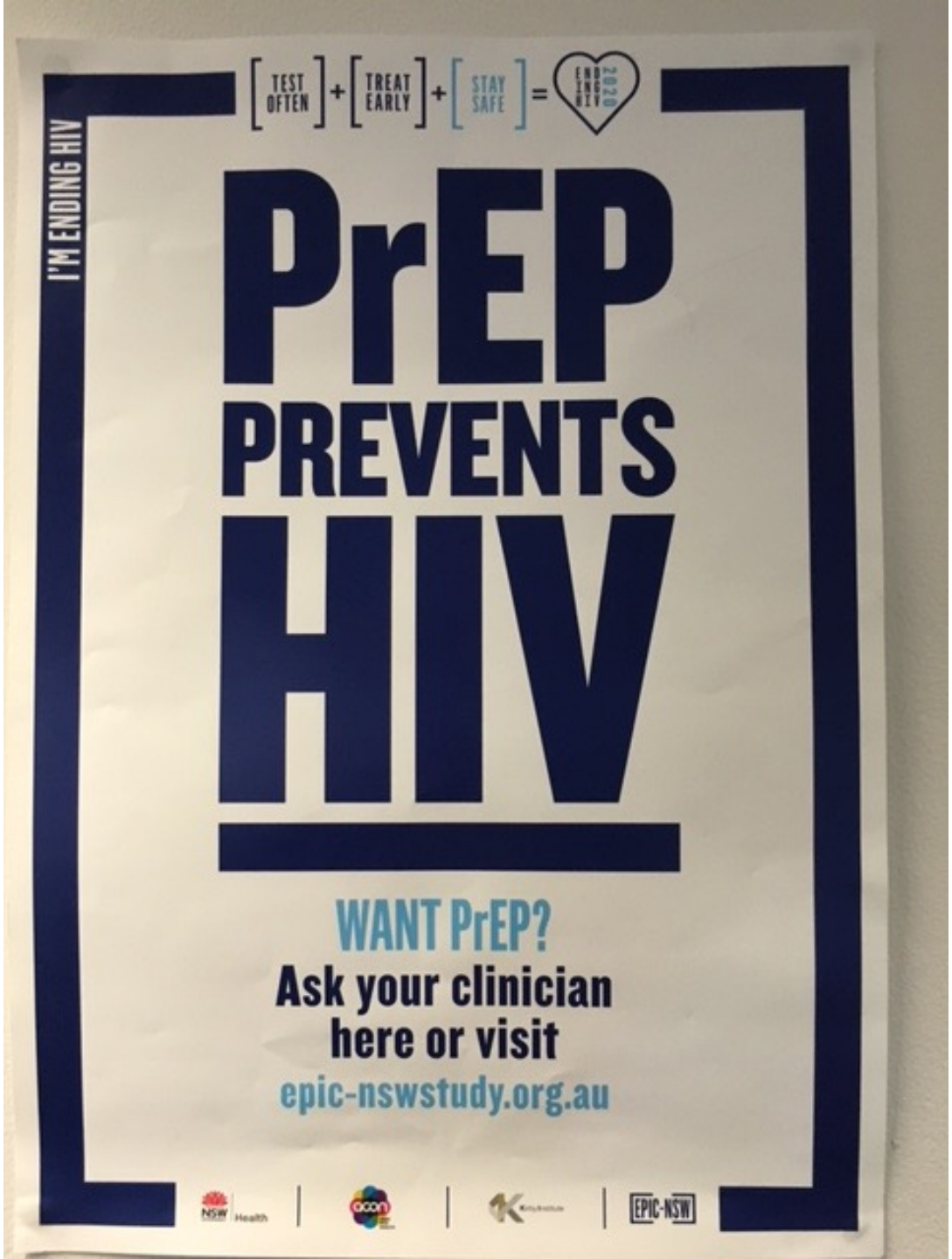
EPIC PrEP study

- 3700 (+300) individuals at high risk of HIV acquisition
- Enrolment from March 2016 3300
- 2 year access to tenofovir 300/emtricitabine 200
- Taken 1/day
- Study visits: screen/baseline, month 1,3, then 3 monthly

EPIC PrEP study

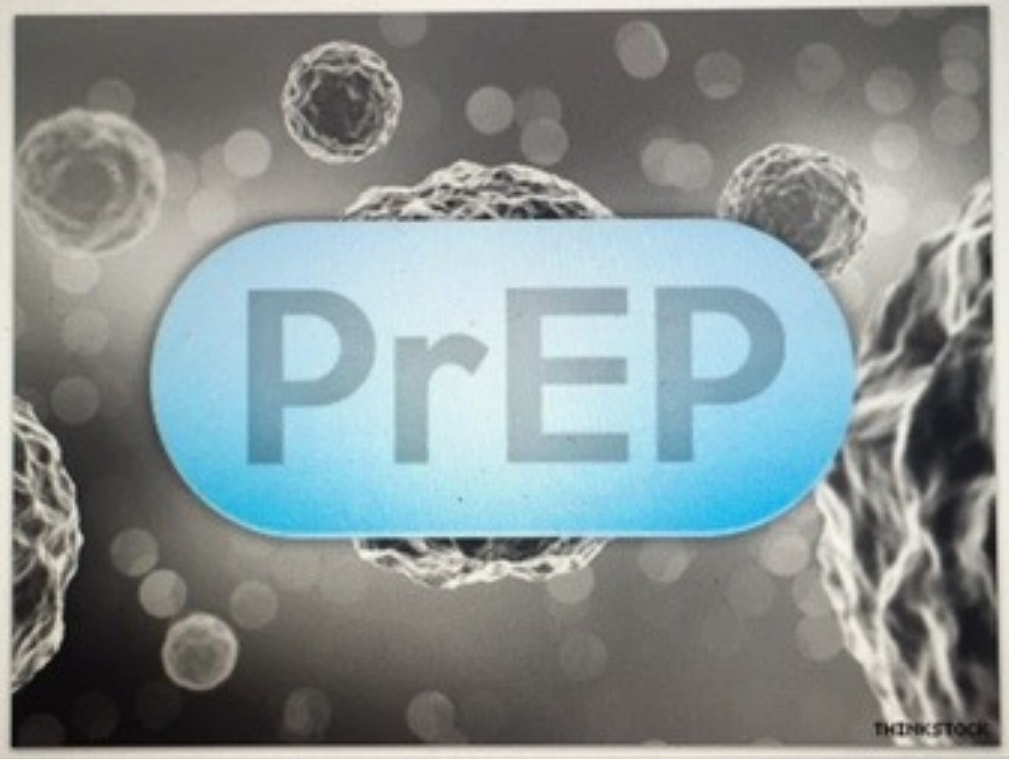
Entry Criteria

- Likely to have unprotected anal intercourse in next 3 months
- Regular sexual partner HIV+ and not undetectable viral load
- Unprotected anal intercourse in previous 3 months
- STIs in previous 3 months: syphilis, rectal chlamydia or gonorrhoea
- Use of crystal methaphetamine in previous 3 months


[TEST OFTEN] + [TREAT EARLY] + [STAY SAFE] = ENDING HIV 2020
I'M ENDING HIV
PrEP PREVENTS HIV
WANT PrEP?
Ask your clinician here or visit
epic-nswstudy.org.au
NSW Health
EPIC-NSW

TREATMENT ▶ PREVENTION

Exactly Zero Men on PrEP Contract HIV in 2.5-Year Study



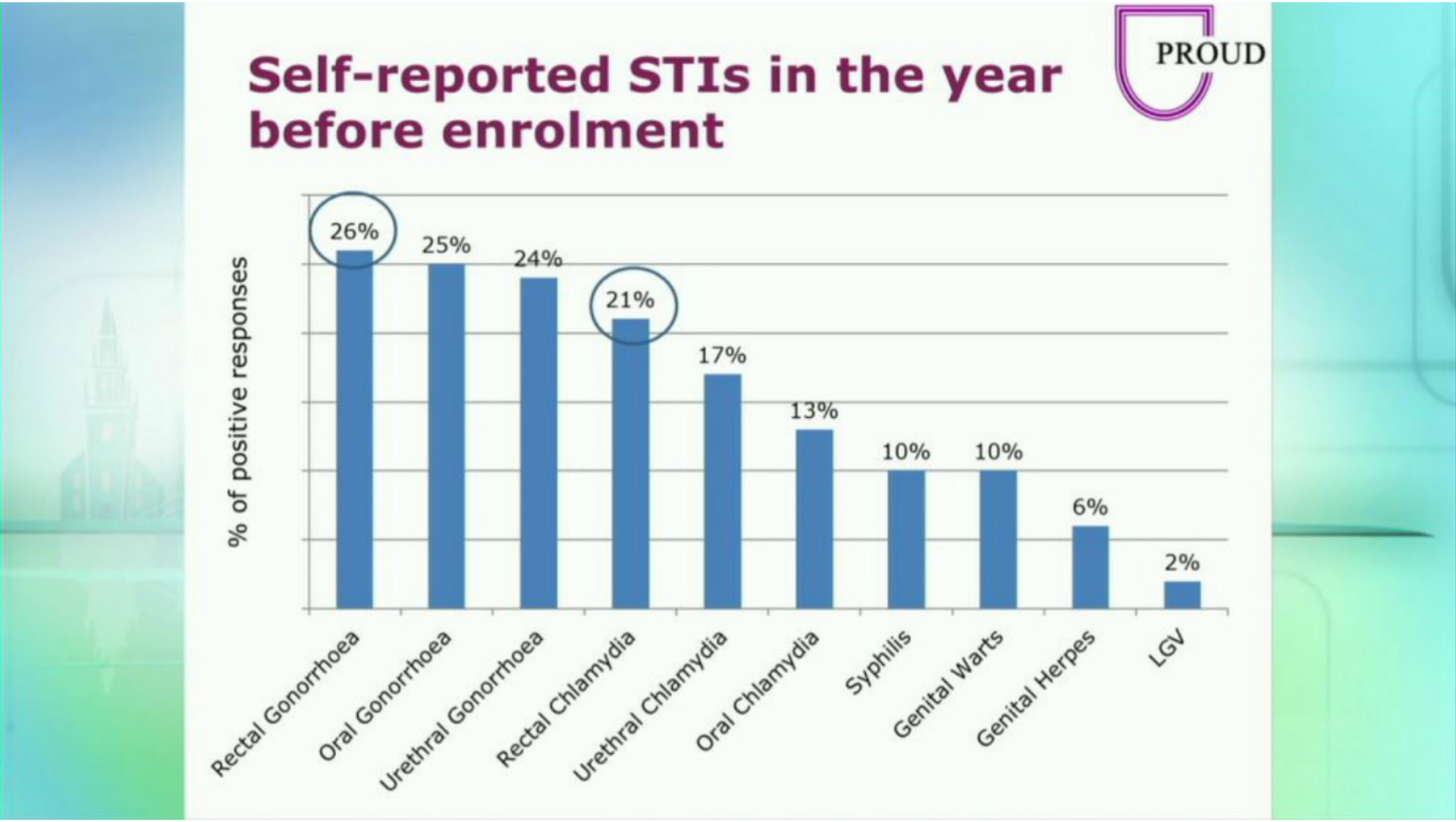
The findings confirm PrEP to be a powerful tool against contracting the virus.

HIV-1 Infection With Multi-class Resistance Despite Pre-Exposure Prophylaxis (PrEP)

DC Knox[1], PL Anderson[2], PR Harrigan[3], DHS Tan[4].

1 Maple Leaf Medical Clinic, Toronto, ON, Canada; 2 University of Colorado Anschutz Medical Campus, Aurora, CO, USA; 3 BC Centre for Excellence in HIV/AIDS, Vancouver, BC, Canada; 4 Division of Infectious Diseases, St. Michael's Hospital, Toronto, ON, Canada

STIs


Self-reported STIs in the year before enrolment
PROUD
% of positive responses
26%
25%
24%
21%
17%
13%
10%
10%
6%
2%
Rectal Gonorrhoea
Oral Gonorrhoea
Urethral Gonorrhoea
Rectal Chlamydia
Urethral Chlamydia
Oral Chlamydia
Syphilis
Genital Warts
Genital Herpes
LGV


Chlamydia
Chlamydia
Gonorrhoea
Gonorrhoea

STIs during both phases of PROUD

Infection	Prior year # ppts	IMM # ppts 256-263	DEF # ppts 233-240	DEF post DEF # ppts 198-203	IMM post DEF # ppts 232-234
Rectal GC	26	23	23	26	27
Rectal CT	21	22	14	28	28
Syphilis	10	11	9	17	22

Gonorrhoea

- 1940s – resistant to sulphonamides
- 1980s – resistant to penicillin
- 1990s - resistant to tetracylclines
- 2000s – resistant to quinolones
- 2015 – recommendation = ceftriaxone 500mg IM + azithromycin 1g oral
- 201? - Multidrug-Resistant *Neisseria gonorrhoeae*

Quarterly Screening Optimizes STI Detection Among PrEP Users in the Demo Project

Stephanie Cohen[1,2]; Eric Vittinghoff, PhD[2]; Susan S. Philip, MD, MPH[1,2]; Susanne Doblecki-Lewis, MD[3]; Oliver Bacon, MD, MPH[1,2]; Wairimu Chege, MD, MPH[4]; Richard Elion, MD[5]; Susan Buchbinder, MD[1,2]; Michael A. Kolber, PhD, MD[3]; Albert Liu, MD, MPH[1,2]

[1]San Francisco Department of Public Health; [2]University of California, San Francisco; [3]University of Miami, Miller School of Medicine; [4]National Institutes of Health, Division of AIDS; [5]Washington DC Department of Health, Center for Sexual Health

Background

STIs are common among PrEP users; optimal STI screening frequency unclear

Objectives

1) Determine % of gonorrhea, chlamydia, and syphilis infections for which treatment would have been delayed without q3mo screening
2) Determine the mean and median # of sex partners potentially exposed by participants with STIs during the 3 month inter-visit interval

Results

Fig.1. Percent infections for which treatment would have been delayed with q6 month, as opposed to q3 month, screening

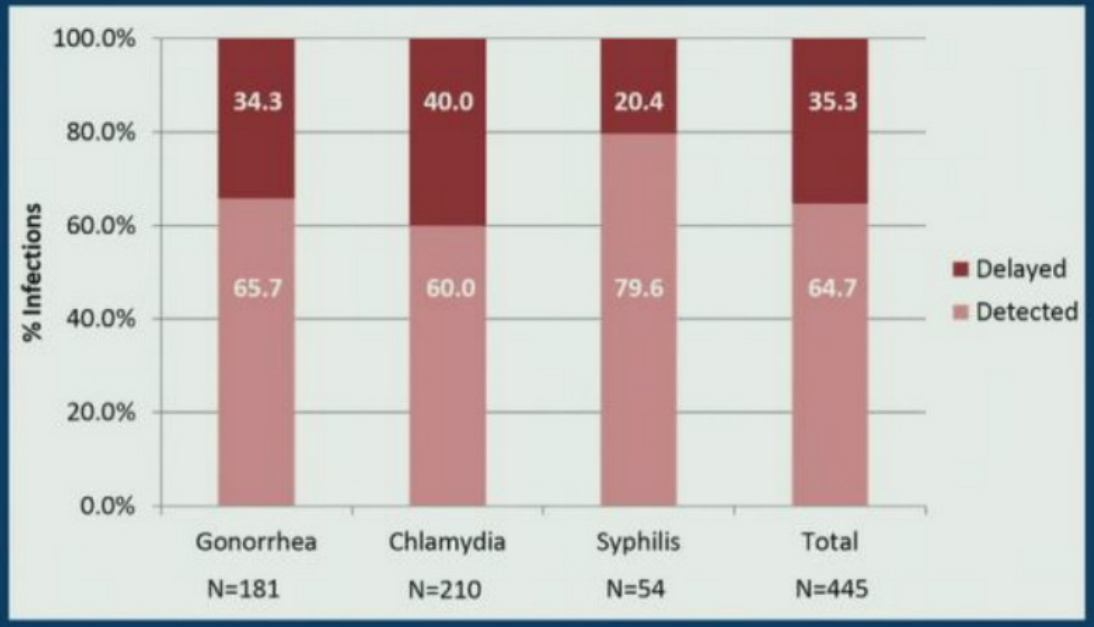


Table 1. STI transmission potential during inter-visit interval from participants with an asymptomatic STI

Asymptomatic STI[1]	N (%) reporting any condomless *receptive* anal intercourse (CRAI) at subsequent quarterly visit	Mean (median) # of *condomless* anal sex partners in inter-visit interval[2]
Rectal GC (N=38)	28 (73.7%)	6.5 (2.5)
Rectal CT (N=98)	78 (79.6%)	8.7 (4)
	N (%) reporting any condomless *insertive* anal intercourse (CIAI) at subsequent quarterly visit	
Urethral GC (N=4)	4 (100%)	28 (5.5)
Urethral CT (N=24)	21 (87.5%)	15.2 (4.5)
	N (%) reporting any CRAI or CIAI at subsequent quarterly visit	
Early latent syphilis (N=16)	14 (87.5)	8.1 (4)
At least one asx STI (N=139)	124 (89.2)	8.1 (3)

[1]Total N restricted to ppts who had an asymptomatic STI at week 12, 24 or 36 *and* attended the subsequent quarterly visit
[2]Did not collect # of partners by position in sex act

Conclusions

- Treatment would have been delayed for 35% of STIs if screening had been conducted q6 months
- q3 month STI screening prevented a median of 3 sex partners/STI case from being exposed
- Additional modeling work needed to estimate # STIs averted and cost-effectiveness of q3 mo STI screening for MSM on PrEP

PrEP Toxicity

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

Adverse Events

Nb of Participants (%)	TDF/FTC n=199	Placebo n=201	P value
Any AE	184 (92)	178 (89)	0.18
Any Serious AE	18 (9)	16 (8)	0.70
Any Grade 3 or 4 AE	17 (9)	14 (7)	0.56
Treatment D/C due to AE	1*	0	
Drug-Related GI AEs	25 (13)	11 (6)	0.013
Nausea/vomiting	15	2	
Abdominal pain	11	4	
Diarrhea	7	5	

* deep veinous thrombosis with suspected DDI with dabigatran

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Agence autonome de l'Inserm

Is TDF-based PrEP associated with proximal tubular injury?

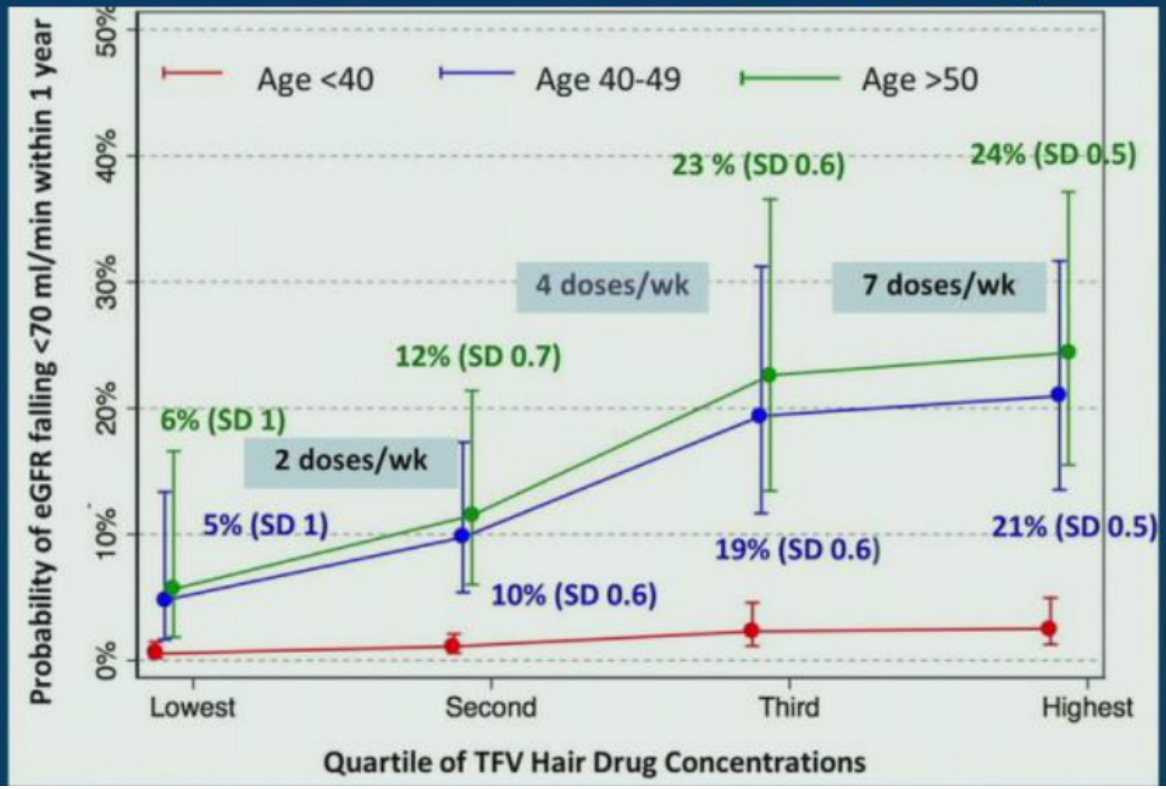
- Proximal tubular injury (tubulopathy), the primary TDF-related toxicity on the kidneys, can occur without severe decline in glomerular filtration rate (GFR).
- From the Partners PrEP Study data we conducted:
  1. A cohort analysis to assess the frequency of tubulopathy.
  2. A nested case-control of persons on TDF or FTC-TDF PrEP to determine whether tubular injury is associated with ≥25% eGFR decline.

Primary aim: To determine whether FTC-TDF PrEP compared to placebo causes proximal tubular injury.

Variable	FTC-TDF (n=776)	Placebo (n=773)	P-value
Tubulopathy*	**13 (1.7%)**	**10 (1.3%)**	0.68
Phosphaturia	20 (2.6%)	21 (2.7%)	0.85
Normoglycemic glycosuria	10 (1.3%)	7 (0.9%)	0.63
Tubular proteinuria	**57 (7.3%)**	**31 (4.0%)**	<0.01

*Proximal tubulopathy: ≥ 2 of tubular proteinuria, normoglycemic glycosuria, increased urinary phosphate or uric acid excretion

Higher exposure, baseline eGFR <90, older age associated with clinically significant eGFR decreases to <70 ml/min



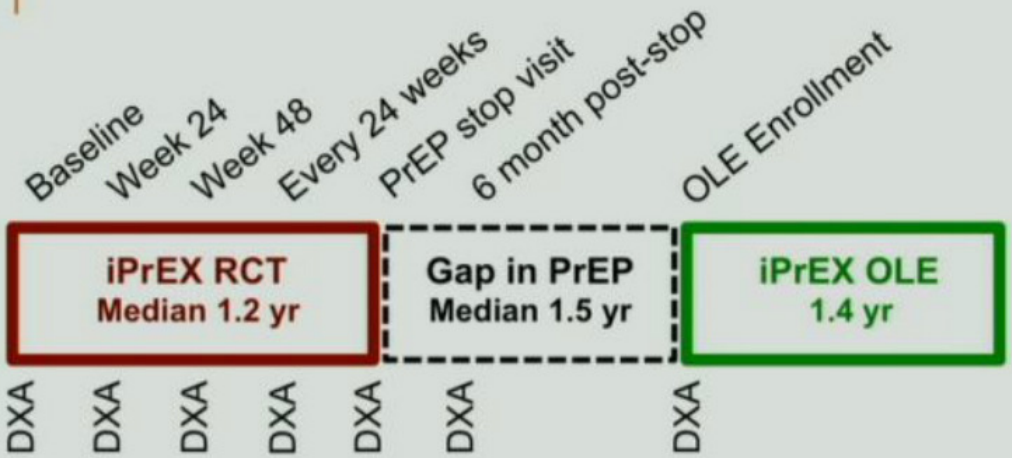
- If baseline CrCl <90 ml/min (n=942), 27% probability of CrCl falling to <70 in a year
- In subset with hair levels, age and exposure matter:
  - In those 40-50 years and >50 years, 19-24% probability of CrCl falling to < 70ml/min within 1 year with *higher exposure* (4-7 doses/wk)

Recovery of bone mineral density after stopping oral HIV pre-exposure prophylaxis.

Robert M Grant, Kathleen Mulligan, Vanessa McMahan,
Juan Guanira, Albert Liu, Suwat Chariyalertsak,
Linda-Gail Bekker, Mauro Schechter,
Validilea G Veloso, David V Glidden
for the iPrEx study team.

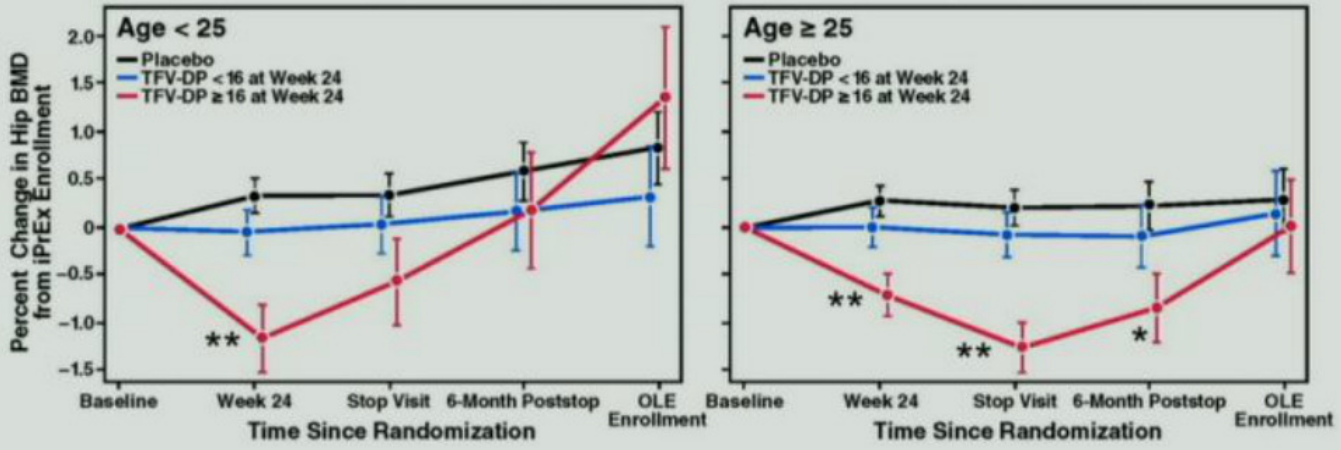
Sponsored by
NIH/NIAID/DAIDS
and drug donated by
Gilead Sciences

DXA Substudy Schema



- DXA scans of hip and spine at…
  - Baseline and every 24 weeks during PrEP/Placebo use,
  - 24 weeks after stopping PrEP/Placebo,
  - At enrollment in Open Label Extension (OLE).
- Drug concentrations in vPBMCs collected in all DXA participants at…
  - Week 24 concentrations used to stratify analysis of BMD,
  - Strong predictor of consistent drug detection at subsequent visits.

Recovery of Hip BMD by Age and PrEP Use



N=						
Placebo	127	84	62	124	88	73
TFVDP @ w24 <16	72	54	24	69	54	40
TFVDP @ w24 ≥16	29	24	17	57	45	35

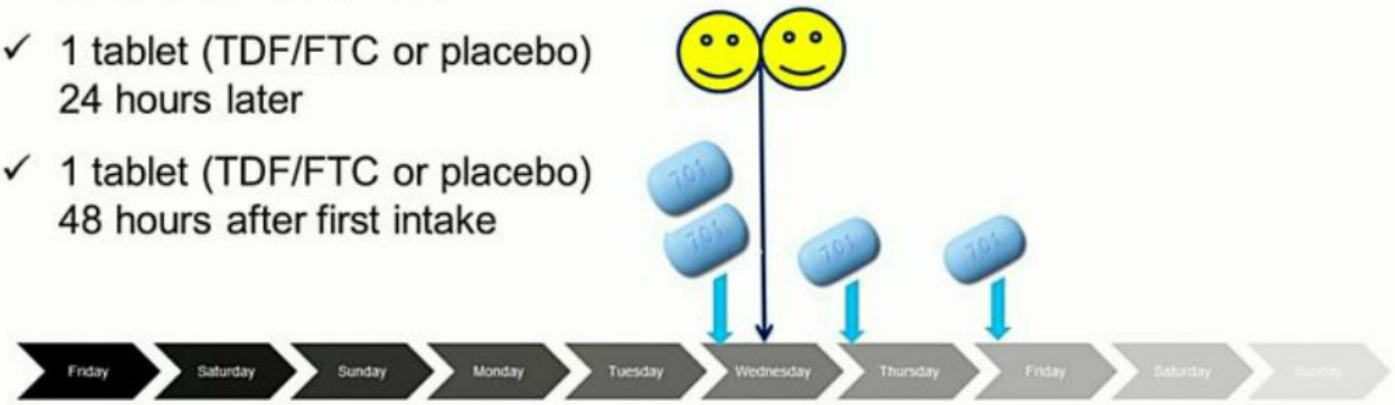
*P<0.05; **P<0.001; Grant CROI Boston 2016

Future of PrEP

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

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



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Modeling PrEP and PrEP cost-effectiveness

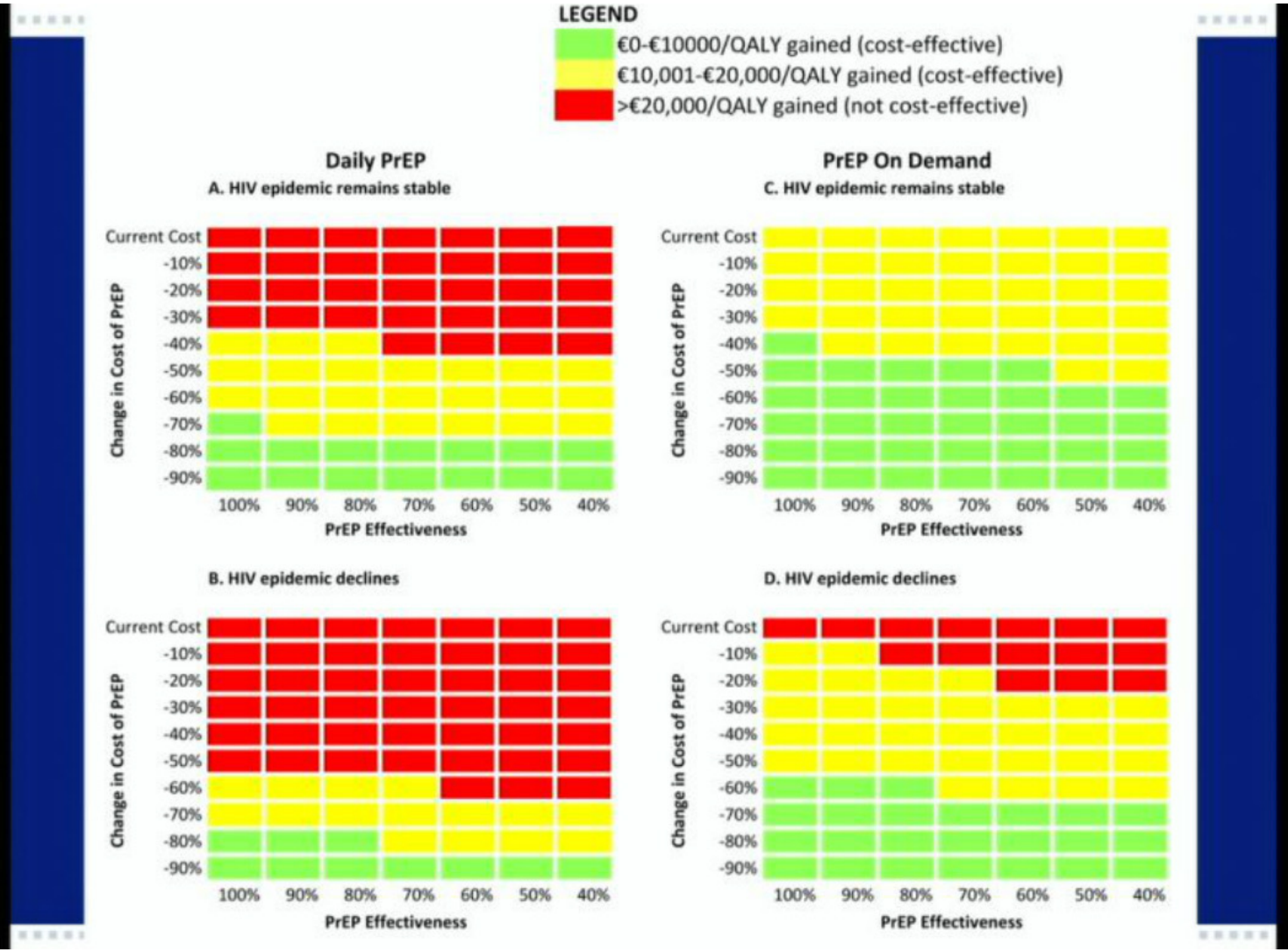
- Deterministic mathematical model of HIV transmission: calibrated to Dutch HIV epidemic among MSM
- PrEP to 4,500 MSM (approximately 2-3% of all MSM in the Netherlands) that have at least 1 new partner per year

PrEP on demand

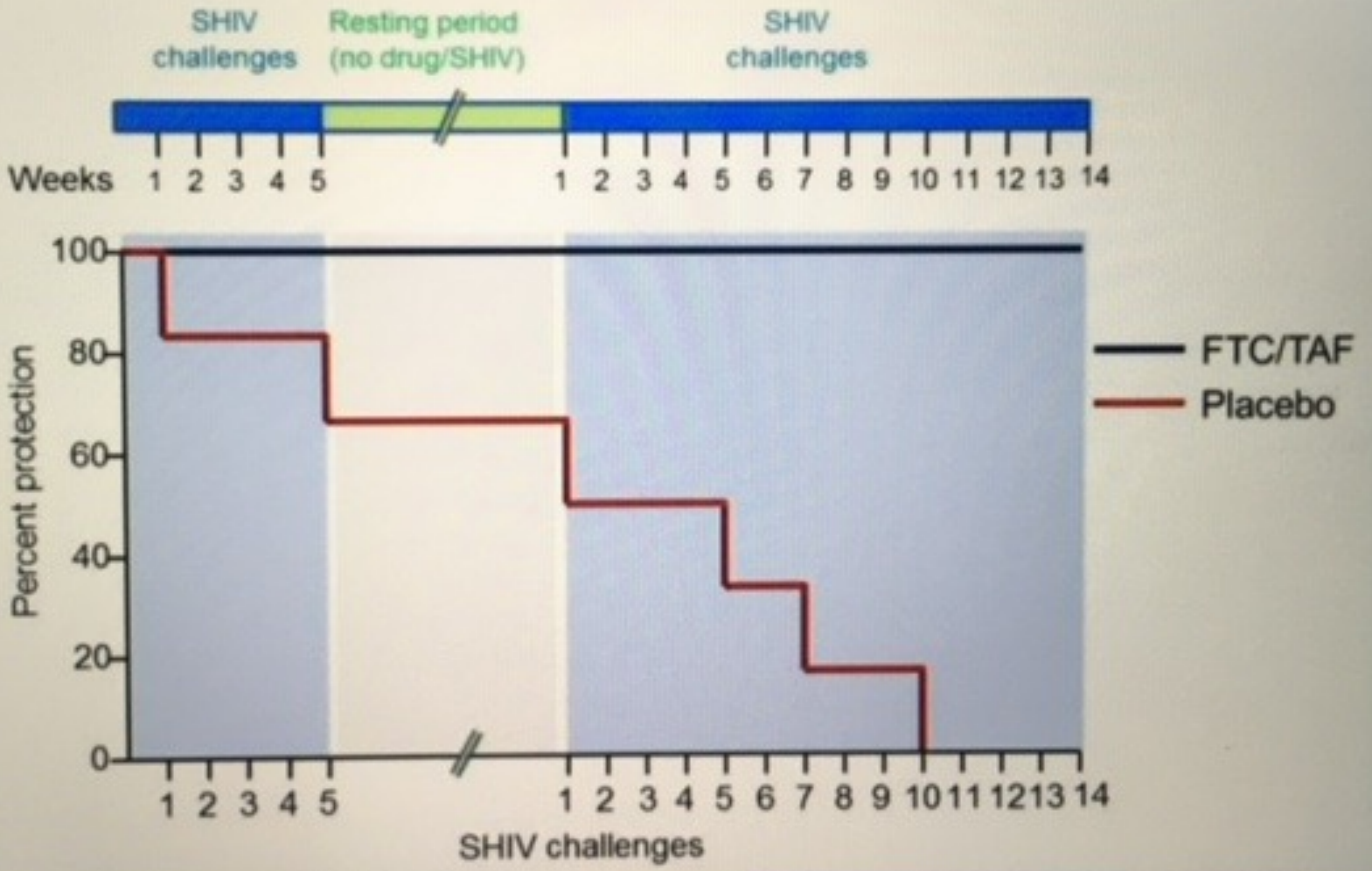
Daily PrEP

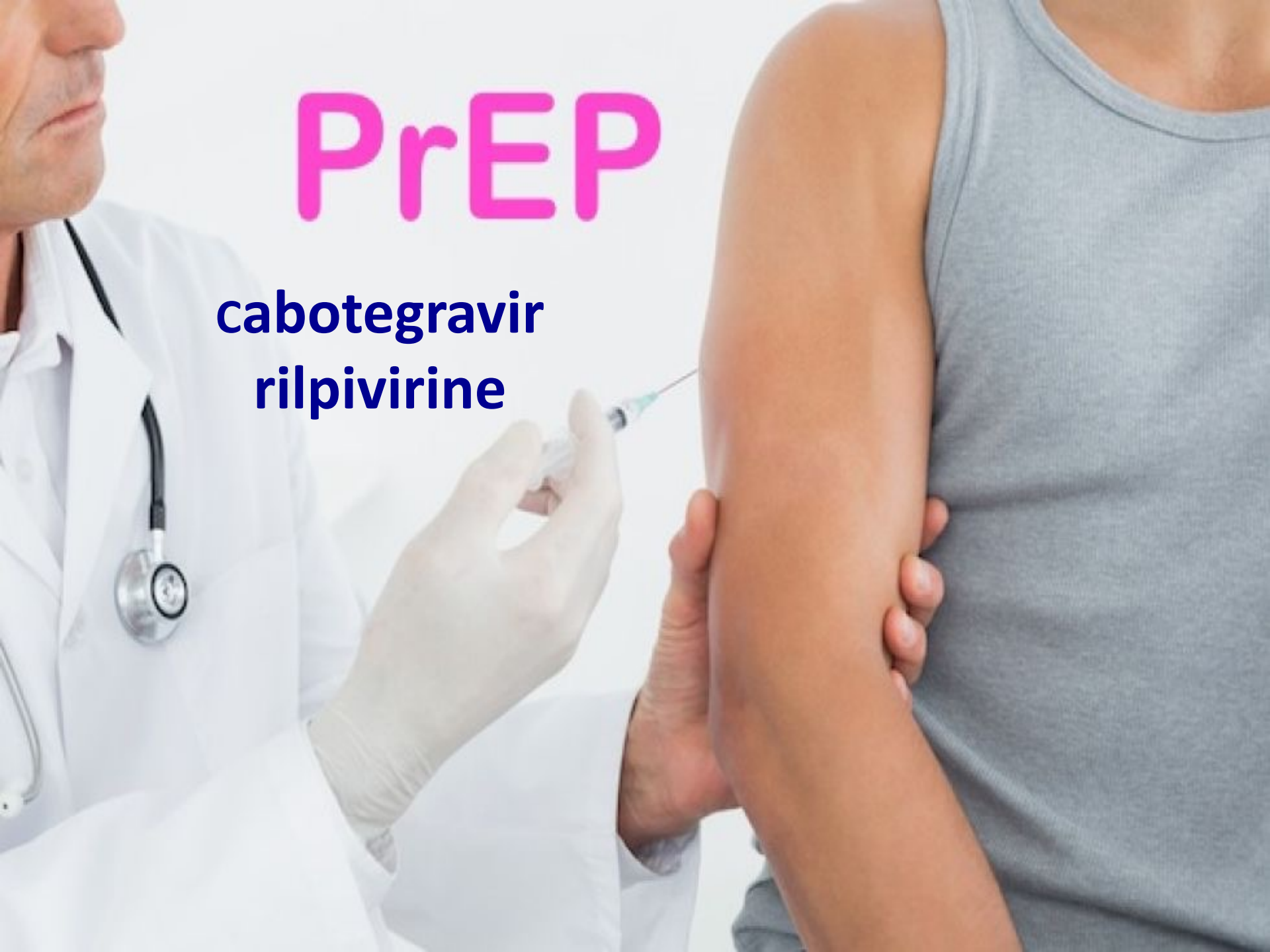
Equally efficacious: 86%
PrEP on demand: ~50% less expensive

Molina et al. 2015 NEJM; McCormack et al. 2016 Lancet


LEGEND
€0-€10000/QALY gained (cost-effective)
€10,001-€20,000/QALY gained (cost-effective)
>€20,000/QALY gained (not cost-effective)
Daily PrEP
A. HIV epidemic remains stable
PrEP On Demand
C. HIV epidemic remains stable
B. HIV epidemic declines
D. HIV epidemic declines
Current Cost
-10%
-20%
-30%
-40%
-50%
-60%
-70%
-80%
-90%
Change in Cost of PrEP
100% 90% 80% 70% 60% 50% 40%
PrEP Effectiveness

Prophylactic efficacy of FTC/TAF against rectal SHIV infection




PrEP
cabotegravir
rilpivirine

PrEP: Patient Perspective

"I've heard of your studies and all the fantastic work you do to fight against several diseases.
I am a gay man living in Sydney and I am looking for more information
about a possible enrollment in your PrEP medical program here in NSW.

I am still HIV negative and some parts of my sexuality may drive me to unsafe situations, that's also the reason why
I want to help medical research go further to help fighting this virus.
Please let me know more about it – Thanks"


GET PrEP TODAY IN SYDNEY 8038 1044
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