HIV Pre-Exposure Prophylaxis: Beyond the Basics

Joey Shemuel, BA
PrEP Coordinator
UCSF 360 Wellness Center
Saturday, February 20, 2016

Disclosures and Acknowledgments

The views expressed here are not necessarily the views of UCSF Medical Center.

Thanks to:

- Shannon Weber, MPH / Director, HIVE
- Robert Grant, MD MPH / Senior Investigator, Gladstone Institutes
- Lisa Dazols, LCSW / Clinical Social Worker, UCSF 360
- Allan Paschke, RN / Nurse Manager, UCSF 360
- Malcolm John, MD MPH / Director, UCSF 360

Agenda

1. Background
2. New Data and Guidance
3. Scaling Up
4. PrEP and Women, Transpeople, and Young People
5. PrEP Access
6. The Future of PrEP

PrEP: Pre-Exposure Prophylaxis

- 16 July 2012: Truvada (tenofovir disproxil fumarate 200mg / emtricitabine 300mg [aka TDF/FTC]) receives FDA approval for prevention of HIV in HIV-negative adults ≥18yo
- Approval largely based on two international RCTs:
  - iPrEX (MSM and TW, n=2,441), QD dosing, **44% efficacy***
  - Partners PrEP (het couples, n=9,516), TDF/FTC vs. FTC alone vs. placebo; QD dosing; **75% efficacy**

Sources: Food and Drug Admin. *FDA approves first drug for reducing the risk of sexually acquired HIV infection.* 16 July 2012.

Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010;363(27):2587-2599.

Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012;367(5):399-410.

***Efficacy**: 44% by Intent-to-treat analysis, 73% in those who self-reported adherence, 92% in those with measurable TDF/FTC blood levels

Efficacy: PrEP Works!

"The argument is over about PrEP. If you take the drug, it works, not only in a clinical trial, but in the field." -Anthony Fauci, MD, Director, NIAID, 15 Dec 2015

Since 2012, several major studies have established efficacy of TDF/FTC PrEP:

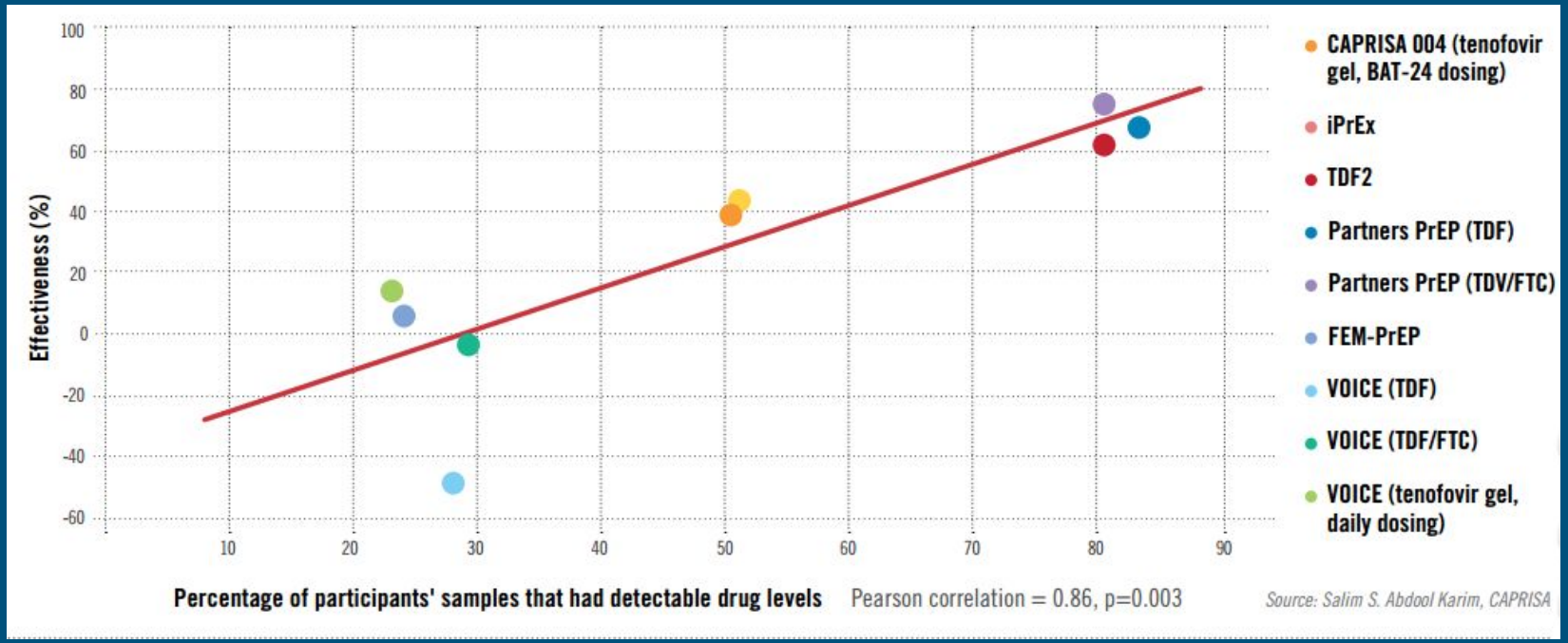
- iPrEX Open-Label Extension: n=1,603 MSM and TGW in US, Thailand, and Latin America; QD dosing; **50% efficacy overall, *100% in those taking ≥4 doses/wk***
- IPERGAY: n=400, MSM and TW in Quebec and France; RCT, intermittent "event-driven" dosing vs. placebo; **86% efficacy**
- PROUD: n=544, MSM and TW in UK; open-label; QD dosing; immediate start vs. delayed arm; **86% efficacy**

Sources: Grant, R et al. *Preexposure chemoprophylaxis for HIV prevention in men who have sex with men*. N Engl J Med, 363 (2010), pp. 2587–2599.

Molina J-M et al. *On Demand PrEP With Oral TDF-FTC in MSM: Results of the ANRS Ipergay Trial*. 2015 Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, USA, abstract 23LB, 2015.

McCormack S et al. *Pragmatic Open-Label Randomised Trial of Preexposure Prophylaxis: The PROUD Study.* 2015 Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, USA,abstract 22LB, 2015.

Adherence and Efficacy



Source: AVAC. *PrEP By the Numbers*. January 2016.

New Guidance

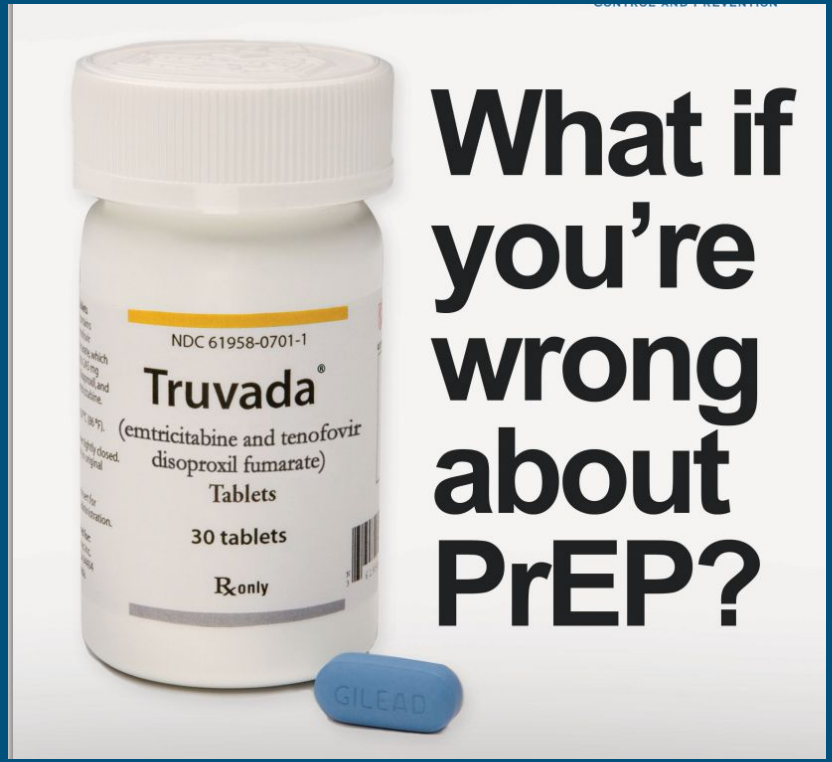
National and international medical regulatory and advisory bodies have overwhelmingly approved PrEP as a prevention intervention and published guidelines for its use in May and June, 2014:

Centers for Disease Control and Prevention
American College of Obstetricians and Gynecologists
World Health Organization
International AIDS Society, US Panel

But not everyone approved...

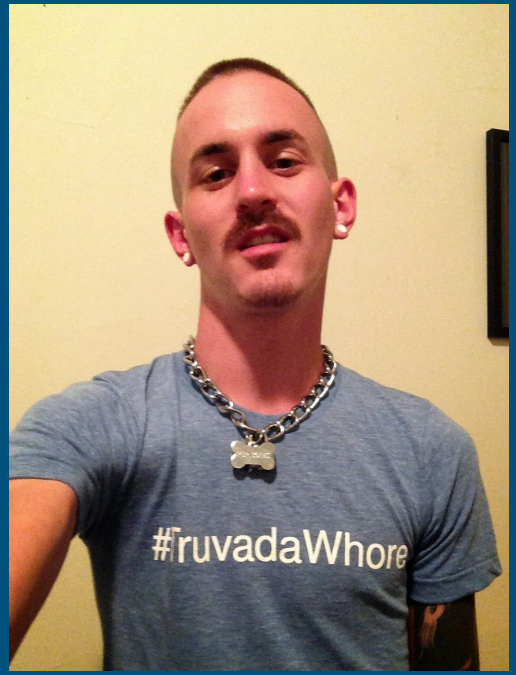
AIDS Healthcare Foundation (AHF) has been a vocal critic of PrEP as a prevention intervention, due to three concerns:

- poor adherence
- low condom use
- STI incidence



AHF. *What if you're wrong about PrEP?*. Various Publications. 17 Nov 2014

Truvada Whores and Truvotters: Buy-In



Adam Zebowski

T-shirt designs by Sean-Franc Strang

Supervisor Scott Wiener

“In the end I thought it was very important to be public given the district I represent and the community I represent precisely because we need to remove the stigma from PrEP.” Sept. 17 2014, NYT

Where the Rubbers Hit (or Don’t) the Road

Concerns about low adherence and “risk compensation” *may* be unwarranted:

- In iPrEX OLE:
  - **92%** of ppts in San Francisco took ≥4 tablets per week
  - **better** adherence associated with **more** sexual risk behavior
- In IPERGAY and PROUD:
  - **no change** in mean number of partners
  - **no change** in mean number of condomless anal sex partners

Sources: Source: Grant R. *Scale Up of Pre-Exposure Prophylaxis in San Francisco to Impact HIV Incidence.* CROI 2015.

Molina J-M et al. *On Demand PrEP With Oral TDF-FTC in MSM: Results of the ANRS Ipergay Trial*. 2015 Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, USA, abstract 23LB, 2015.

McCormack S et al. *Pragmatic Open-Label Randomised Trial of Preexposure Prophylaxis: The PROUD Study.* 2015 Conference on Retroviruses and Opportunistic Infections (CROI), Seattle, USA,abstract 22LB, 2015.

Local Successes: Cohort Studies

- Magnet (clinic in Castro, SF): n=~600, 99% cis-MSM; **not a single seroconversion** over mean observation time of ~1 year
- Connecting Resources for Urban Sexual Health (CRUSH) (Oakland): n=252, 95% cis-MSM; **not a single seroconversion** over mean observation time of 10 months

- Kaiser: n=657, 99% cis-MSM; **not a single seroconversion** over mean observation time of 7 months

Sources: Highleyman, L.. *Evidence for PrEP efficacy grows, but implementation presents challenges*. AIDSMAP. 18 Dec 2015.

Volk J et al. *No New HIV Infections with Increasing Use of HIV PrEP in Clinical Practice*. Clin Infectious Dis. 2015; 61(10) 1601-3.

Scaling Up: Multi-Site Demo Project

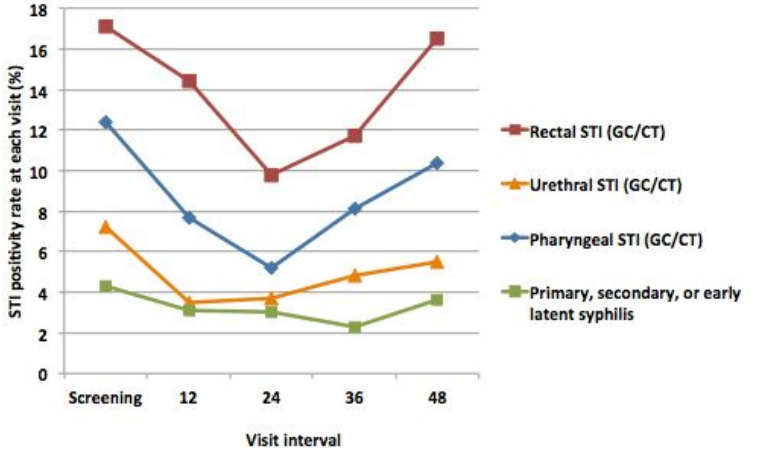
557 HIV-negative MSM and TGW enrolled between Nov 2012 and Jan 2014.

- San Francisco (n=300), Miami (n=157), Washington, D.C.(n=100)
- Good adherence: 63% of participants w/ protective blood levels of TDF/FTC at all visits.
  - ≥2 condomless anal intercourse partners at enrollment was independently associated with higher adherence (OR 1.82, p=.01)!
- Highly effective: Only **2** infections during follow-up, both in individuals w/ low adherence -- lower than placebo arm of IPERGAY and deferred arm of PROUD

Source: Liu A et al. *Adherence, Sexual Behavior, and HIV/STI Incidence among MSM and Transgender Women in the Us PrEP Demo Project*. IAS 2015.

No Overall Increase in STIs or Risk Bx

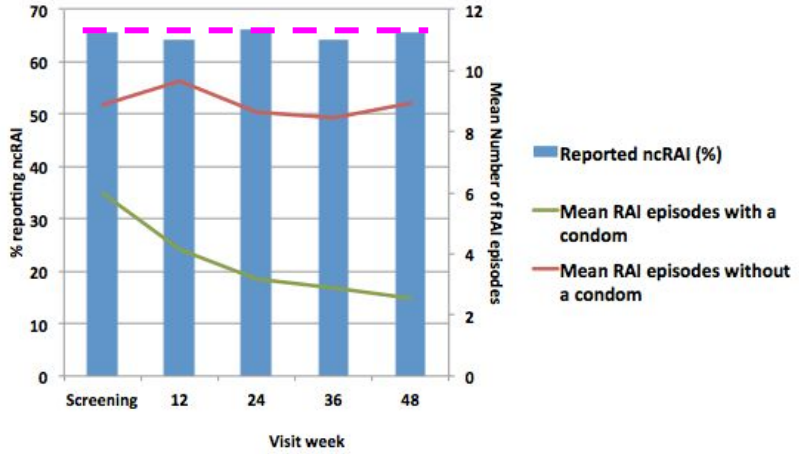
Results: STI positivity



Overall STI incidence (90/100 person years) remained stable during follow-up (P>0.1)

Results: Sexual behaviors

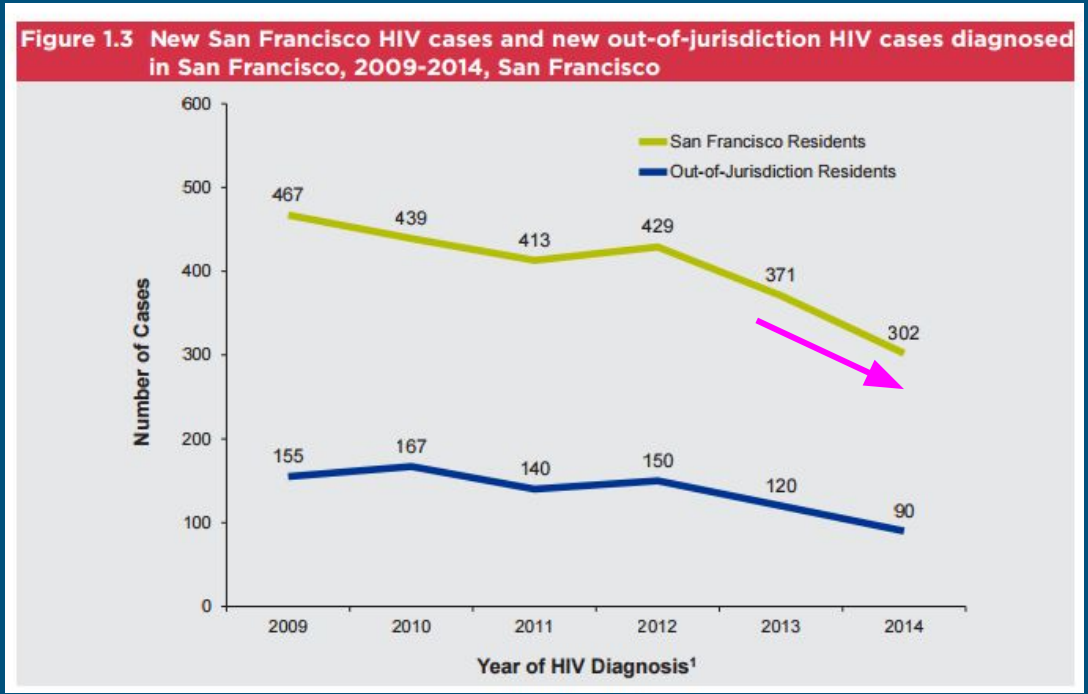
Mean number of anal sex partners declined from 10.9 to 9.3 (p=0.04)



Source: Liu A et al. *Adherence, Sexual Behavior, and HIV/STI Incidence among MSM and Transgender Women in the Us PrEP Demo Project*. IAS 2015.

The Bigger Picture

New HIV infections fell 18% 2013-2014, from 371 to 302, partly due to an uptick in PrEP use starting in 2013.



Source: SFDPH HIV Epidemiology Annual Report 2014

The Bigger Picture

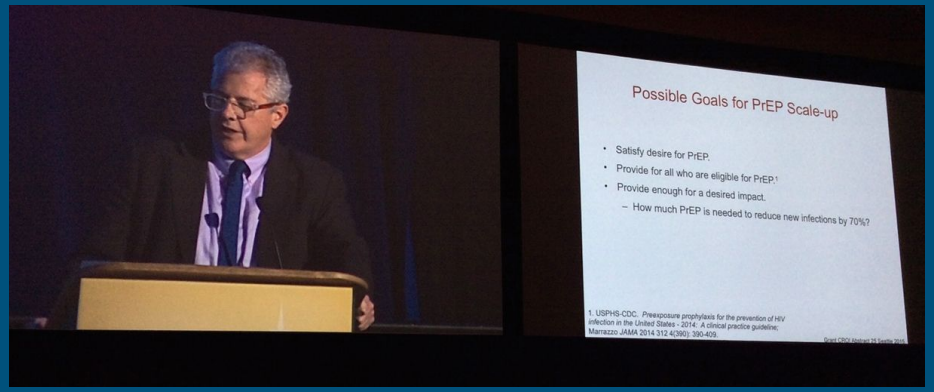
Other factors driving this reduction are:

- Wider availability of pooled RNA testing (shorter window period than 3rd Gen Antibody or “4th generation” Ab/p24 antigen) detecting infection sooner
- Rapid access to ART → faster viral suppression*
- Increased, systematized efforts to retain patients in care*

Source: Buchbinder, S. *Getting To Zero Report to the SF Health Commission*. 01 December 2015.

Scaling Up Further

- SFAF survey Nov 2014 (n=126): 16% of participants taking PrEP, 60% want to start.



- As of early 2015, ~5,000 people in San Francisco had started PrEP in the past year, mostly white MSM, equal to 10-15% of MSM.

Source: Grant R. *Scale Up of Pre-Exposure Prophylaxis in San Francisco to Impact HIV Incidence.* CROI 2015.

Scaling Up Further for Impact

- High-risk HIV-negative men + MSM w/ (+) GC/CT/syphilis test in past year + cis-women w/ HIV+ cis-male/TGW partner + all TGW = ~16,000 eligible for PrEP use in San Francisco.
  - ~5,000 (~30%) currently using
  - If ~14,200 of this group took PrEP, assuming constant rate of viral suppression among PLWH (62%), new infections could fall **70%** from 2011 levels, to **125/year**.

Source: Grant R. *Scale Up of Pre-Exposure Prophylaxis in San Francisco to Impact HIV Incidence.* CROI 2015.

New CDC Guidance

November 27, 2015 MMWR:

TABLE 2. Estimated percentages and numbers of adults with indications for preexposure prophylaxis (PrEP), by transmission risk group — United States, 2015

Transmission risk group	% with PrEP indications*	Estimated no.	(95% CI)
Men who have sex with men, aged 18–59 yrs†	24.7	492,000	(212,000–772,000)
Adults who inject drugs, aged ≥18 yrs§	18.5	115,000	(45,000–185,000)
Heterosexually active adults, aged 18–59 yrs¶	0.4	624,000	(404,000–846,000)
Men**	0.2	157,000	(62,000–252,000)
Women	0.6	468,000	(274,000–662,000)
Total	—	**1,232,000**	**(661,000–1,803,000)**

No mention of transgender people!

Source: Smith D et al. *Estimated Percentages and Numbers of Adults with Indications for Pre-Exposure Prophylaxis*. MMWR 2015: 64(46); 1291-5

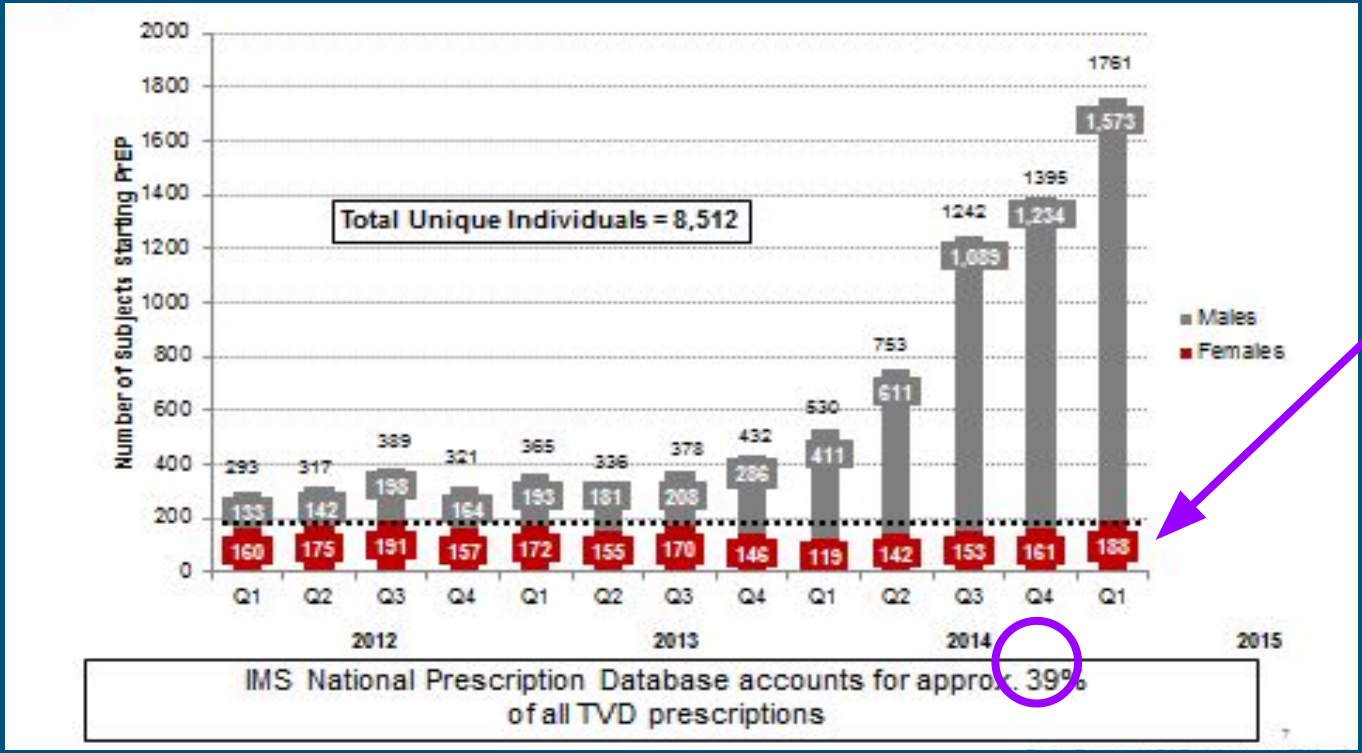
Cis-Women and PrEP

Shannon Weber, MPH; Director, HIVE

- Data are scant.
- San Francisco's HIV epidemic is MSM-driven: just 14 new infections in cis-women in SF in 2014.
- Vaginal/cervical PK + low adherence = low PrEP efficacy in this population in several trials (VOICE, Fem-PrEP).
    - ***Higher adherence required to reach efficacy vaginally (6-7 tablets/wk).***

Source: Cottrell ML et al. *Predicting Effective Truvada PrEP Dosing Strategies With a Novel PK-PD Model Incorporating Tissue Active Metabolites and Endogenous Nucleotides (EN)*. HIV Research for Prevention (HIV R4P). Cape Town, South Africa, October 28-31, 2014. Abstract OA22.06 LB

New PrEP Starts by [Cis]Gender



New PrEP starts in women lag far behind men.

Source: Bush, S et al. *Significant Uptake of Truvada for PrEP Utilization in Late 2014-Q12015 in US.* IAPAC 2015.

Transwomen, HIV, and PrEP

Transwomen are disproportionately affected by HIV. Prevalence as high as **28%**.

Transwomen have never been included in adequate numbers in PrEP studies to date.

Still no CDC guidelines on PrEP use in TGW.

Transwomen were originally ignored in iPrEX results, but a recent analysis has brought to light new data:

- 339 participants (14%) in iPrEX were transwomen.
- TGW in TDF/FTC group had 11 new infections vs. 10 in the placebo arm

Source: Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Charihalertsak S, Grant R (2015, November 5). HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. The Lancet. DOI: http://dx.doi.org/10.1016/S2352-3018(15)00206-4.

Transwomen and PrEP: iPrEX, redux

All seroconverters in drug arm had low adherence.

- On the other hand: “PrEP use in the subgroup of transgender participants with evidence of high [≥4 tablets/wk] medication adherence was protective.”

DDIs not contributory to low efficacy: “as the type of drugs used in [TDF/FTC] PrEP, and estrogens/progestins are metabolized through different pathways, it is unlikely that any interactions could occur...”

Sources: Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Charihalertsak S, Grant R (2015, November 5). HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. The Lancet. DOI: http://dx.doi.org/10.1016/S2352-3018(15)00206-4.

University of California, San Francisco. (2011) Review of literature relating to possible drug interactions between antiretrovirals and estrogen therapy used for MTF gender transition.

Transmen and PrEP

HIV prevalence in transmen ~2%

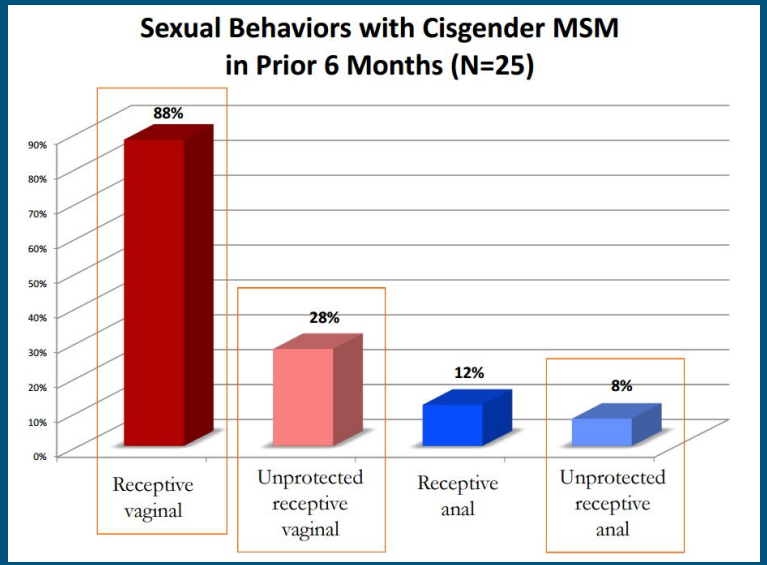
"In urban areas where HIV prevalence rates among non-trans MSM have been estimated to be 17–40%, and STI rates are increasing, *trans MSM who engage in risky receptive anal and/or vaginal intercourse with non-trans MSM may be especially vulnerable to HIV and STI acquisition*."

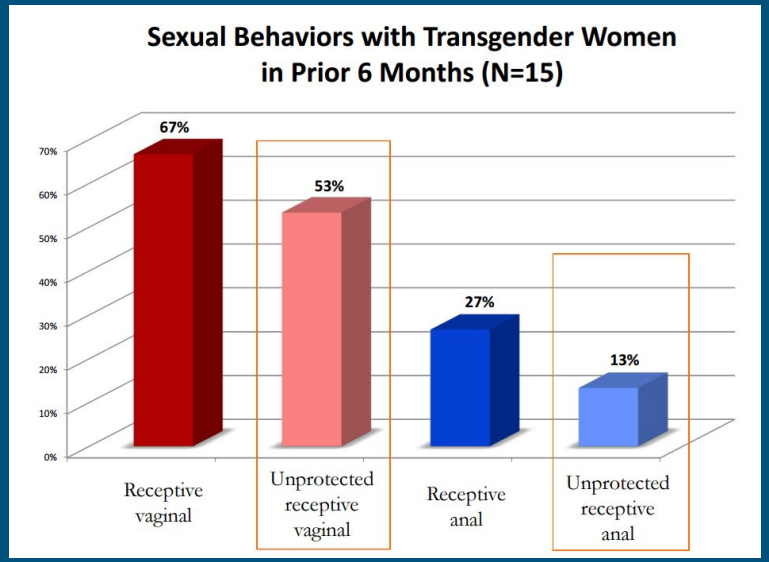
- Transmen not included in ***any*** PrEP trials → STRIPE Study

Sources: Sevelius J. *"There's no pamphlet for the kind of sex I have": HIV-related risk factors and protective behaviors among transgender men who have sex with nontransgender men.* J Assoc Nurses AIDS Care.2009;20(5):398–410.

STRIPE Study

- First-ever NIH-funded HIV surveillance study of TGM (n=20 qual, 80 quant)
  - 38% report sex with cis-MSM; 23% with transwomen





Source: Wilson E, Raymond H. *STRIPE: A Survey of Transmen in San Francisco 2014-15.* SFDPH. Presentation given 2015.

STRIPE Study: Results

- Significant HIV acquisition risk
- Zero new HIV infections in this cohort
- Low STI incidence (relative to cis-MSM) despite risk behaviors
  - 1.6% +GC, 3.3% +CT last 12 months prior to study per self-report

→ **More research needed!**

Source: Wilson E, Raymond H. *STRIPE: A Survey of Transmen in San Francisco 2014-15.* SFDPH. Presentation given 2015.

LGBT Youth and Survival Sex

- High rates of survival sex
  - Inconsistent barrier use (~37% not using always)
  - High HIV prevalence (6.1% per self-report)
  - Protective factor: high medical provider utilization in this group (**97%** in past six months!)

Sources: Dank M et al. *Access To Safety: Health Outcomes, Substance Use And Abuse, And Service Provision For LGBTQ Youth, YMSM, And YWSW Who Engage In Survival Sex.* Urban Institute. 18 Feb 2016. Published online.

Wilson P et al. *Sexual Risk Behaviors Among Virologically-Detectable HIV-Infected YMSM*. JAMA Peds. 2016;170(2):125-131

Young MSM and HIV

- Disproportionate incidence among YMSM 13-24yo (>25% of new diagnoses), **<u>especially Black YMSM</u>**
  - Isolation, discrimination, coercion
  - Risk trifecta:
    - high rate of *undetected* infection → high community VL
    - poor retention in care → high community VL
    - *higher* VL associated with *lower* condom use for anal intercourse

Source: Wilson P et al. *Sexual Risk Behaviors Among Virologically-Detectable HIV-Infected YMSM*. JAMA Peds. 2016;170(2):125-131

Young MSM and PrEP

- → **Need for PrEP in YMSM**
  - Better adherence associated with risk behavior
- Challenges:
  - Overall concern re: adherence
  - Decreases in BMD correlated with PrEP use in this population
  - Access difficult for those under <18yo or on parents' insurance

Sources: Dank M et al. *Access To Safety: Health Outcomes, Substance Use And Abuse, And Service Provision For LGBTQ Youth, YMSM, And YWSW Who Engage In Survival Sex.* Urban Institute. 18 Feb 2016. Published online.

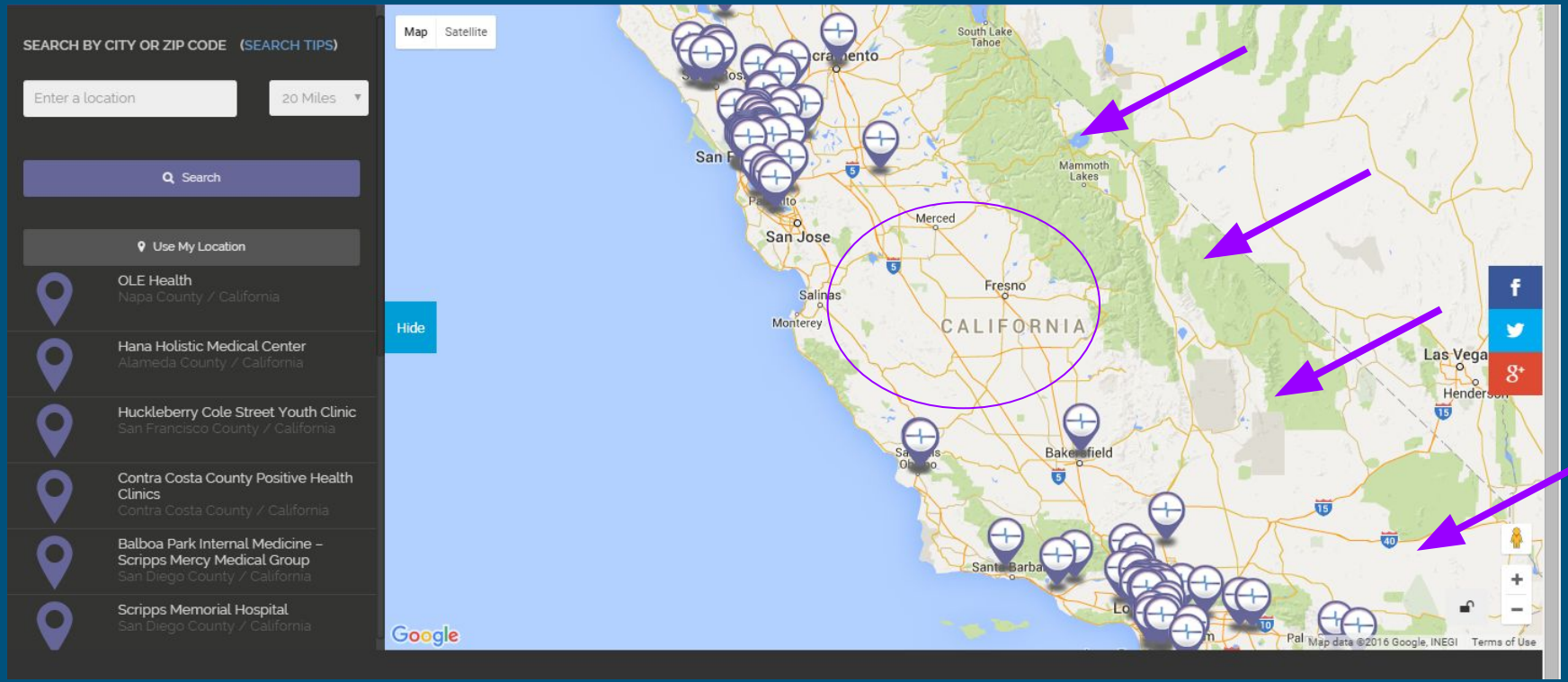
Hosek S et al. *An HIV pre-exposure prophylaxis (PrEP) demonstration project and safety study for young men who have sex with men in the United States (ATN 110).* Eighth International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2015), Vancouver. Abstract no TUAC0204LB. 2015.

Mulligan K et al. *Bone Changes in Young Men Ages 18-22 Enrolled in a Pre-Exposure Prophylaxis Safety and Demonstration Study Using Tenofovir Disoproxil Fumarate/Emtricitabine.* 17th International Workshop on Comorbidities and Adverse Drug Reactions. October 2015.

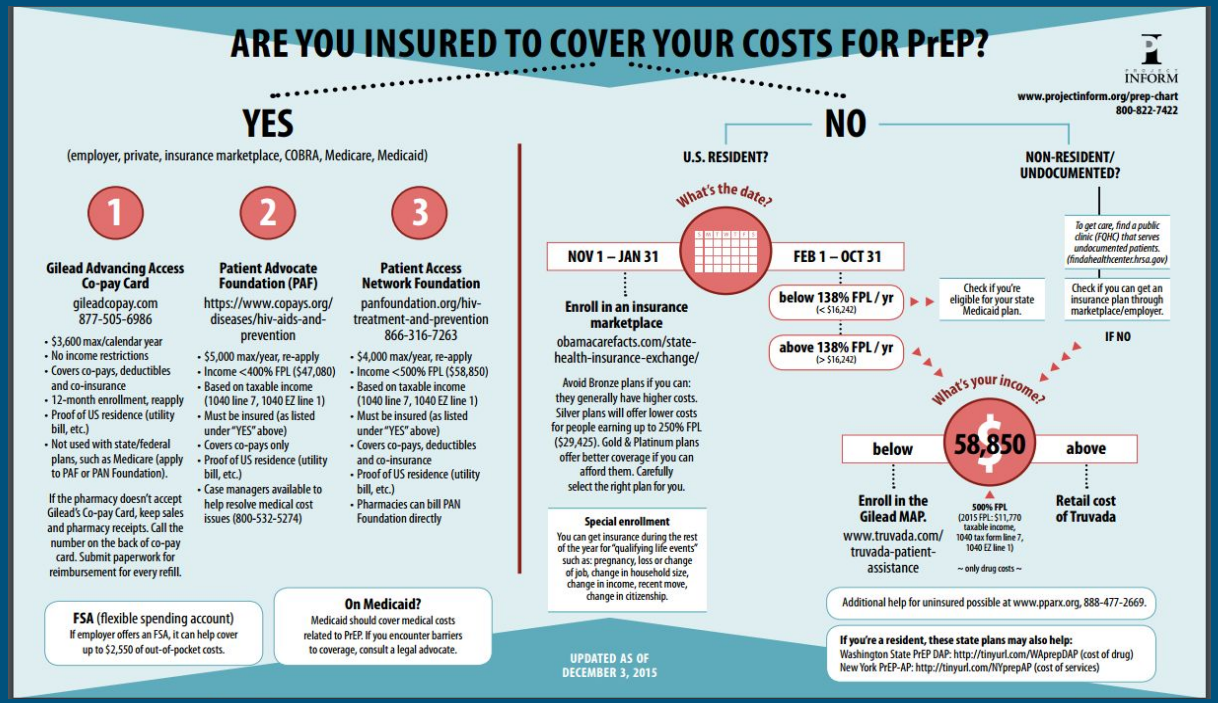
PrEP Access

- PrEP is covered by Medi-Cal!
- Please PrEP Me!
- Navigation is key!
  - Labs
  - Out of pocket costs
  - Adherence
- Financial assistance readily available
  - Gilead
  - PAN
  - PAF
  - 340b

PleasePrEPMe.org - Geogaphic Disparities



Don’t Reinvent the Wheel

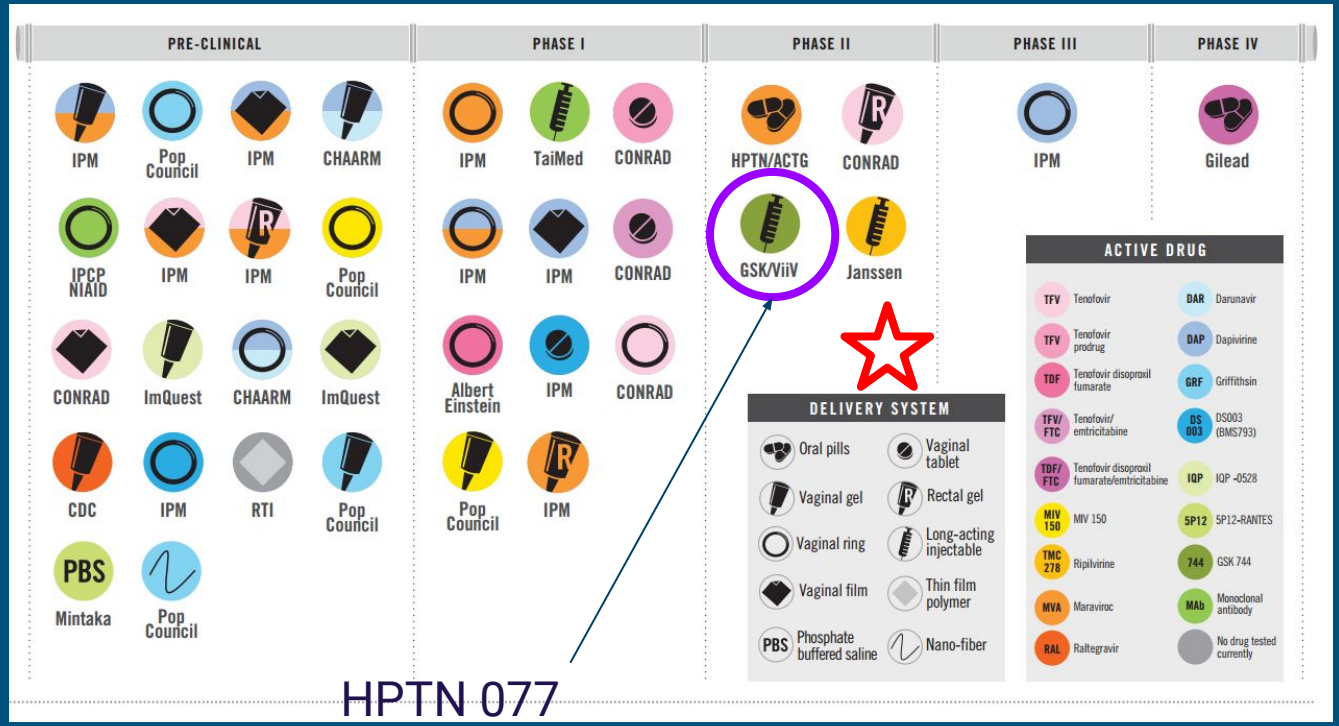


PrEP Access chart from Project Inform

Investigational PrEP Drugs: Beyond TDF/FTC

Not a comprehensive list.

New F/TAF data expected from macaques at CROI next week...



Source: AVAC. PrEP By the Numbers. January 2016.

Take-Home Points

1. PrEP works in MSM and TGW with moderate adherence and cis-women with high adherence
2. More data are needed on cis-women, transmen, and transwomen!
3. Interventions to increase knowledge, uptake, and adherence are needed to impact incidence on a larger scale
4. PrEP is accessible and affordable in SF (navigation services help)
5. Many new forms of PrEP are in the pipeline
6. Research is happening right here in SF

Questions?

joseph.shemuel@ucsf.edu

Public PrEP Criticism

AHF President Michael Weinstein

"All of the scientific studies have shown that it will not work on a community-wide basis because of consistently bad adherence by study subjects – even under ideal circumstances."

AHF. *What if you're wrong about PrEP?*. Various Publications. 17 Nov 2014

Other PrEP Champions

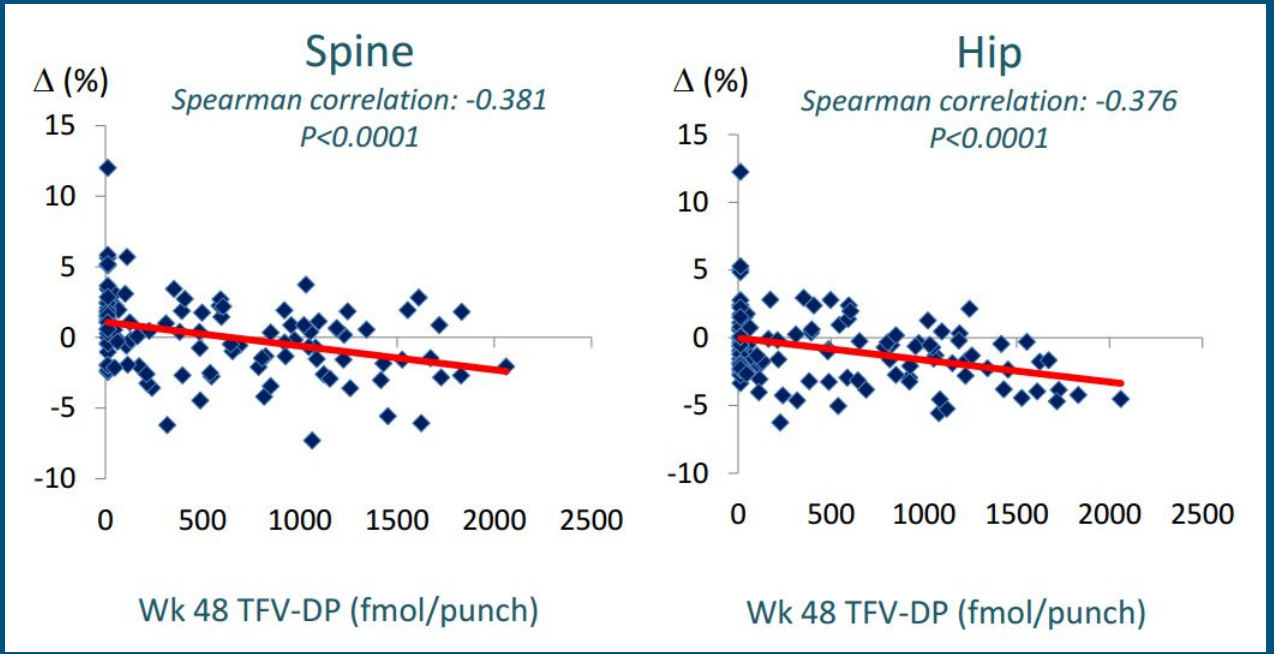
Serodiscordant couples:

“I see my husband’s HIV infection as a medical condition, not who he is. Early in our relationship, we knew we wanted to have a child together. PrEP helped me stay safe as I became pregnant with our daughter. Our little girl is healthy, and I remain HIV negative.”
- Poppy Morgan

Poppy and her family, WHO photo

Young MSM, PrEP, and BMD

BMD changes correlated with TDF adherence in ATN 110



Mulligan K et al. *Bone Changes in Young Men Ages 18-22 Enrolled in a Pre-Exposure Prophylaxis Safety and Demonstration Study Using Tenofovir Disoproxil Fumarate/Emtricitabine.* 17th International Workshop on Comorbidities and Adverse Drug Reactions. October 2015.