EUROPEAN HIV NURSING CONFERENCE

18-19 November 2016 • Barcelona, Spain

PrEP 2016:

Nurses' Role in Scaling Up PrEP Access within a Combination HIV Prevention Approach

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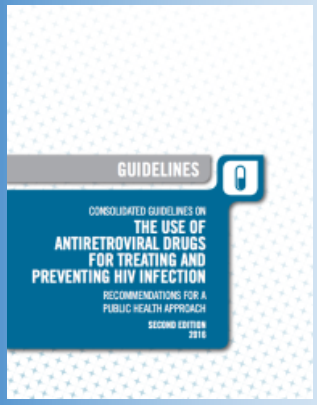
Objectives

- Describe clinical indications for PrEP
- Apply findings from current research to PrEP implementation and adherence
- Appreciate lessons learned from PrEP implementation in US, France and England



NEW

Recommendation

Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (strong recommendation, high-quality evidence).

Source: Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Geneva: World Health Organization; 2015 (http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en).

Defining risk (CDC): Men who have sex with men

BOX B1: RECOMMENDED INDICATIONS FOR PREP USE BY MSM[2]

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following

- Any anal sex without condoms (receptive or insertive) in past 6 months
- Any STI diagnosed or reported in past 6 months
- Is in an ongoing sexual relationship with an HIV-positive male partner

Defining risk (CDC): Heterosexuals

BOX B2: RECOMMENDED INDICATIONS FOR PREP USE BY HETEROSEXUALLY ACTIVE MEN AND WOMEN

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner

Defining risk (CDC): People who inject drugs

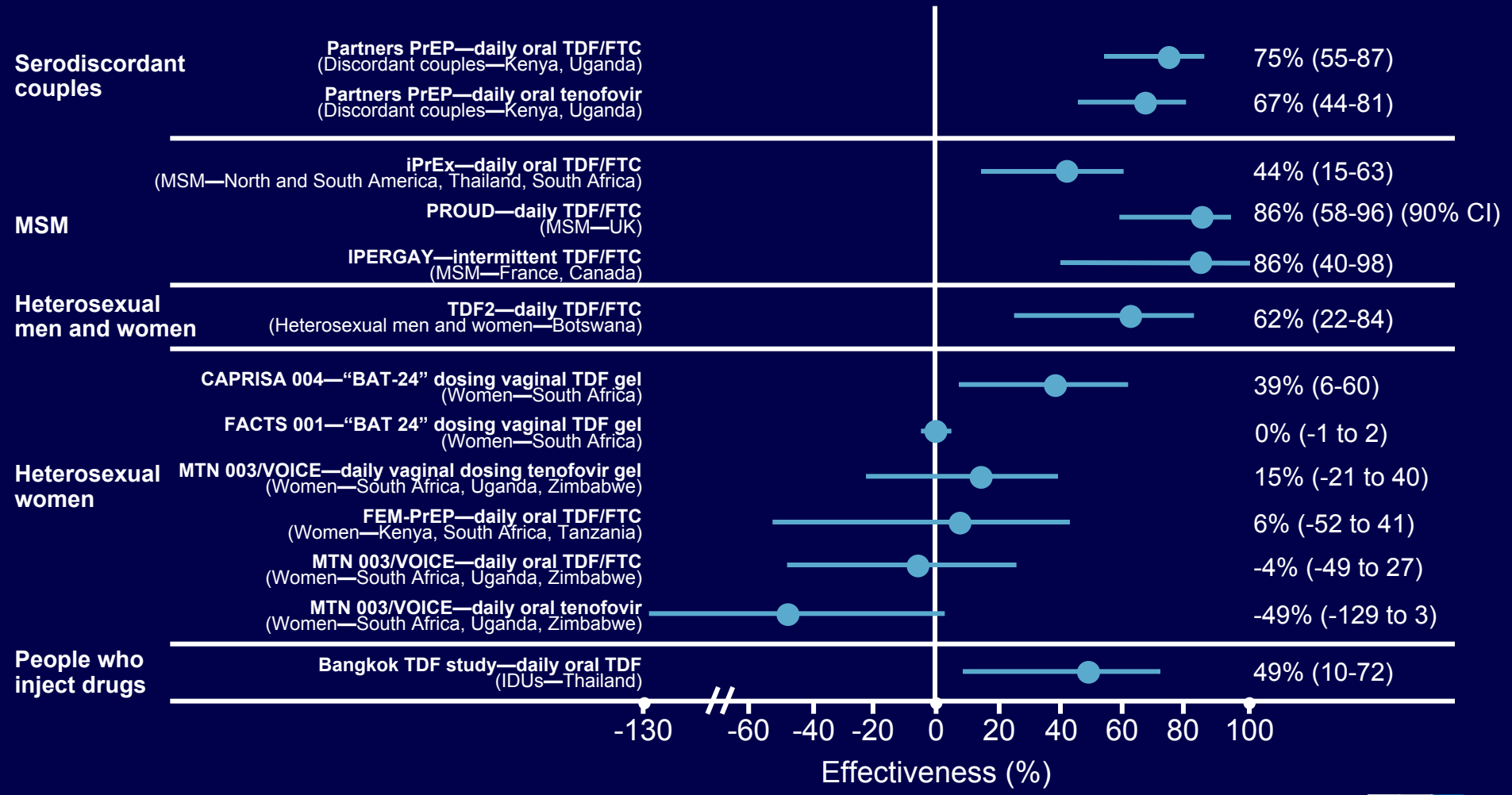
BOX B3: RECOMMENDED INDICATIONS FOR PREP USE BY INJECTION DRUG USERS

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Been in a methadone, buprenorphine, or suboxone treatment program in past 6 months
- Risk of sexual acquisition (also evaluate by criteria in Box B1 or B2)

Clinical Trial Evidence for Oral and Topical TDF-Based Prevention

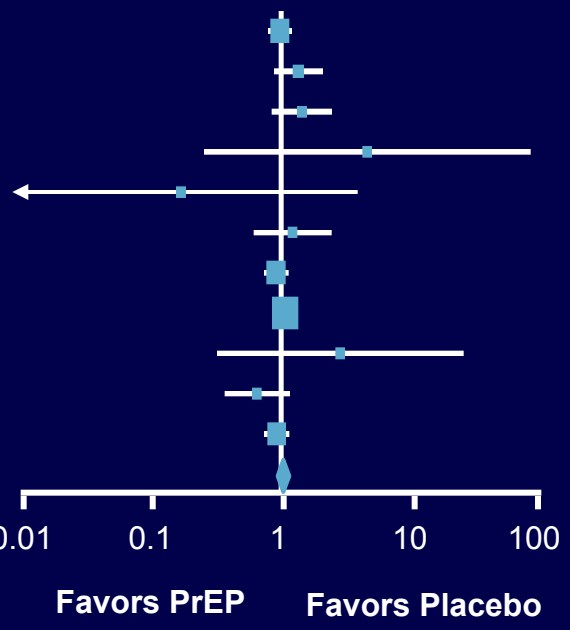


Mayer KH, et al. Curr Opin HIV AIDS. 2015;10:226-232.
Modified from AVAC Report. 2013.

Slide credit: clinicaloptions.com

PrEP Is Well Tolerated; Discontinuations due to Adverse Events Are Rare

Study Name	Subgroup Within Study	Comparison	Risk Ratio	Lower Limit	Upper Limit	Z-Value	*P* Value
BKK TDF Study	Men and women	Daily PrEP vs PBO	0.979	0.797	1.203	-0.202	.840
CDC Safety Study	MSM	Daily PrEP vs PBO	1.357	0.890	2.069	1.420	.155
FEM-PrEP	Women	Daily PrEP vs PBO	1.446	0.855	2.445	1.376	.169
IAVI Kenya Study	MSM and FSW	Multiple PrEP dosing	4.592	0.257	81.944	1.037	.300
IAVI Uganda Study	Men and women	Multiple PrEP	0.170	0.007	4.025	-1.097	.272
Ipergay	MSM	Intermittent PrEP	1.226	0.622	2.420	0.589	.556
iPrEx	MSM and TG	Daily PrEP vs PBO	0.919	0.747	1.129	-0.806	.420
Partners PrEP-Main	Men and women	Daily PrEP vs PBO	1.077	0.954	1.215	1.194	.233
Project PrEPare	MSM	Daily PrEP vs PBO	2.850	0.324	25.069	0.944	.345
TDF2	Men and women	Daily PrEP vs PBO	0.652	0.370	1.150	-1.477	.140
VOICE	Women-all PrEP	Daily PrEP vs PBO	0.925	0.746	1.147	-0.713	.476
			1.016	0.916	1.127	0.305	.760



- No difference in proportion of participants reporting any AE (RR: 1.01; 95% CI: 0.99-1.03, P = .27) or any grade 3/4 AE in PrEP vs placebo arms
- Several studies noted subclinical declines in renal functioning and BMD among PrEP users

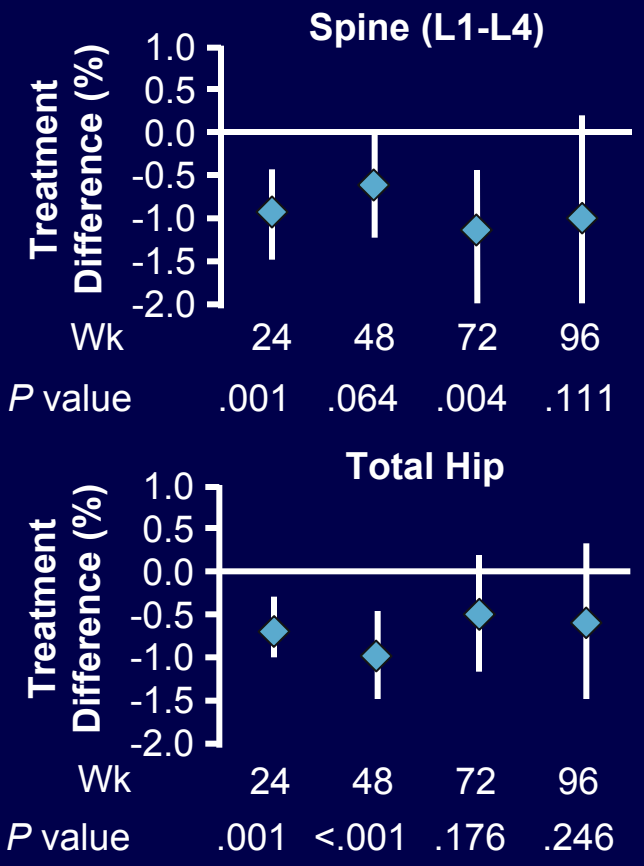
WHO. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV.

Slide credit: clinicaloptions.com

iPrEX: Bone Mineral Density Substudy

- iPrEX substudy: dual-energy x-ray absorptiometry assessment (N = 498)
- Small net decrease in spine and total hip BMD with TDF/FTC vs PBO at Wk 24 (-0.91% and -0.61%, respectively; *P* = .001 for both)
- No difference in fracture rate between groups (*P* = .62)

Mean Net Treatment Difference in BMD Change, Placebo – TDF/FTC (95% CI)

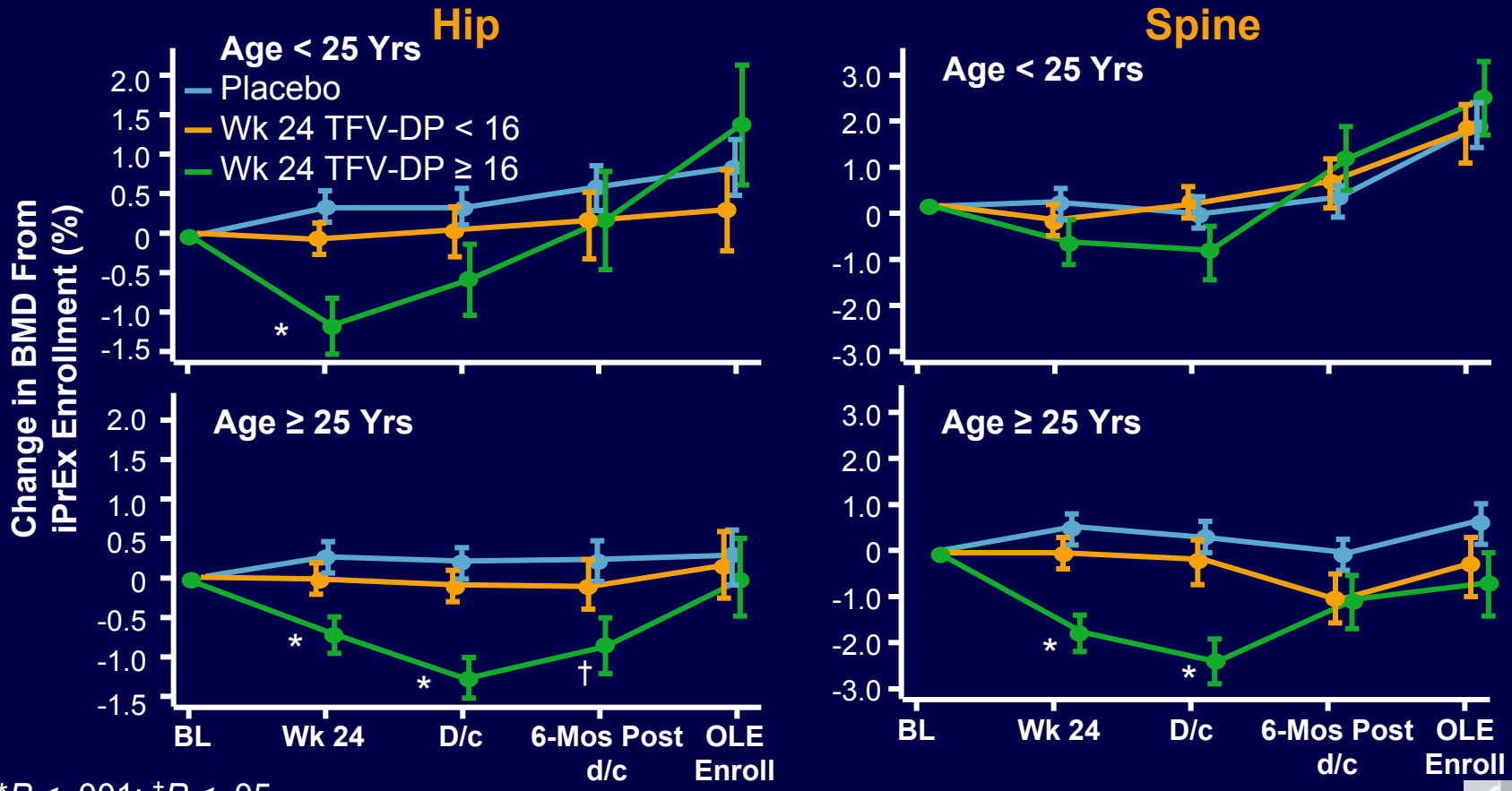


Mulligan K, et al. Clin Infect Dis. 2015;61:572-580.

Slide credit: clinicaloptions.com

iPrEx BMD Substudy: BMD Recovery After Discontinuation of TDF/FTC PrEP

- Data compared for TFV-DP < or ≥ 16 fmol/M viable PBMC, concentration associated with 90% reduction in HIV infection risk in MSM/TGW



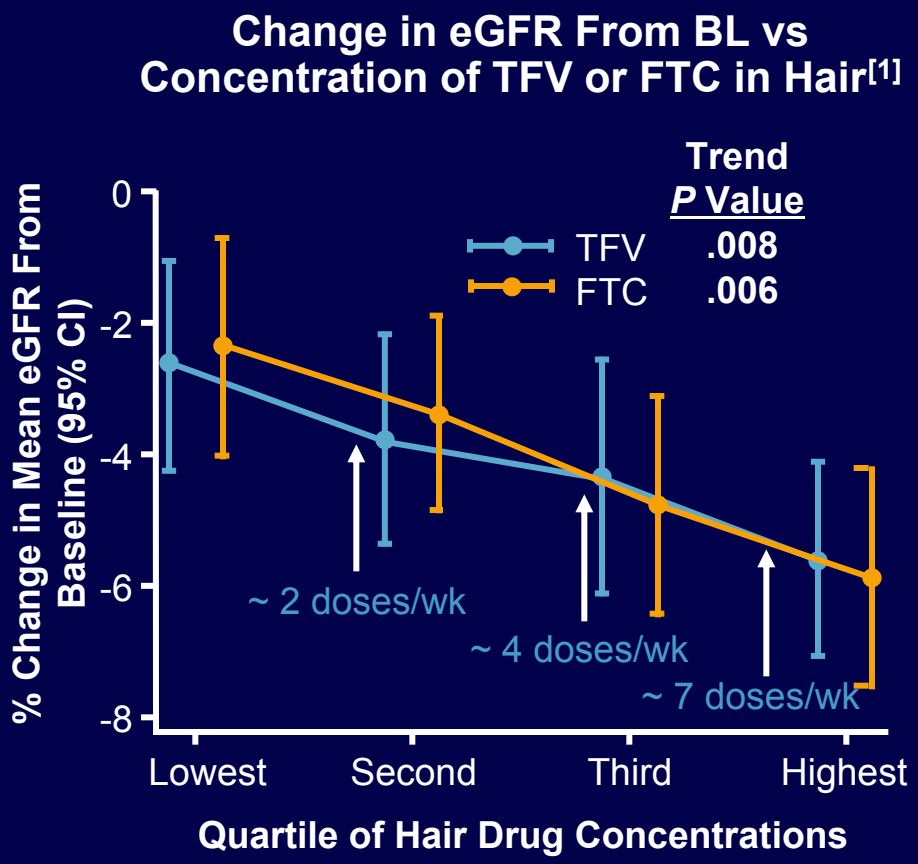
*P < .001; †P < .05

Grant R, et al. CROI 2016. Abstract 48LB.

Slide credit: clinicaloptions.com

Cumulative TFV/FTC Exposure During PrEP Assoc. With Decline in Renal Fxn

- Higher TFV exposure associated with greater eGFR decreases in 2 studies
  - iPrEx OLE[1] (n = 220): hair sampling for exposure
  - US Demo Project[2] (n = 557): dried blood spot sampling for exposure
- In both studies, eGFR decrease to < 70 mL/min more frequent among those with BL eGFR < 90 mL/min and older persons (older than 40-45 yrs)

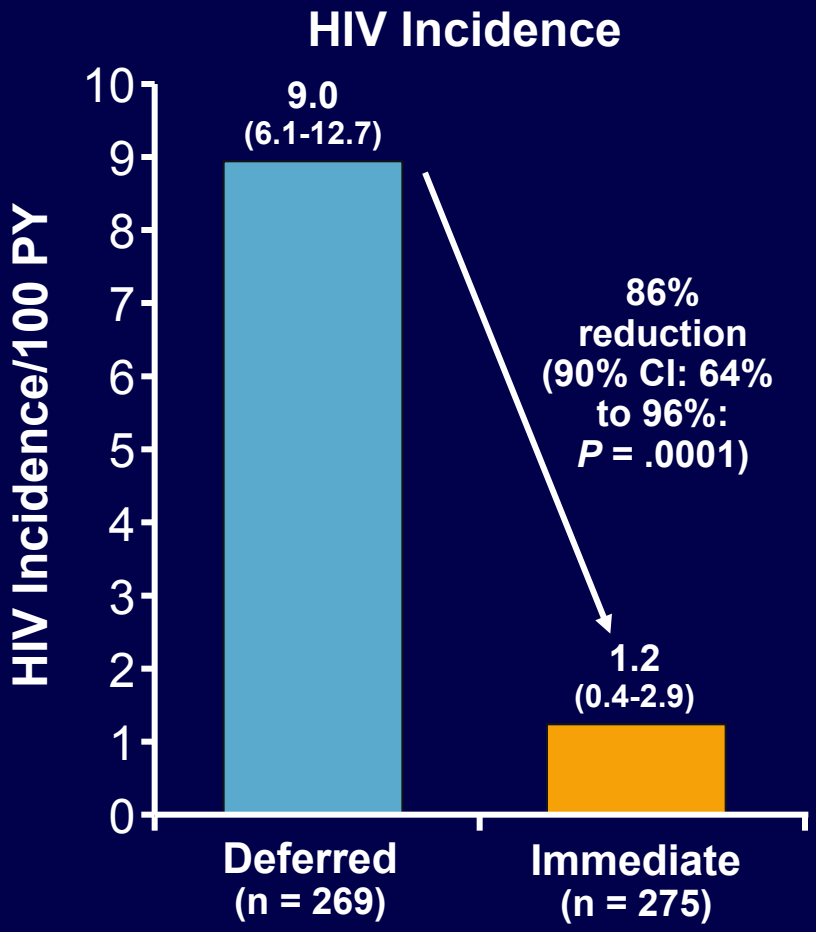


1. Gandhi M, et al. CROI 2016. Abstract 866.
2. Liu AY, et al. CROI 2016. Abstract 867.

Slide credit: clinicaloptions.com

PROUD: Immediate vs Deferred PrEP in High-Risk MSM in "Real World" Trial

- Randomized, open-label trial of daily oral TDF/FTC PrEP in uninfected MSM at high risk for HIV infection in England
  - PrEP: immediate vs deferred for 12 mos
- Fewer new HIV infections with immediate vs deferred PrEP (3 vs 20)
  - Number needed to treat to prevent 1 infection: 13
- PEP used by 32% in deferred arm
- Risk behaviors similar between arms

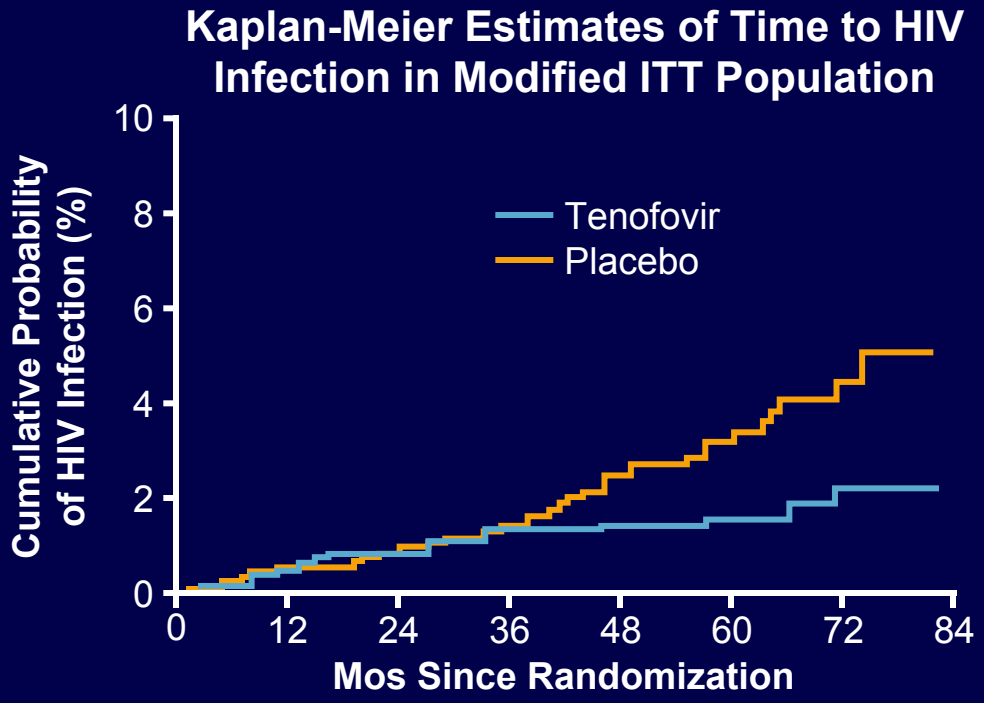


McCormack S, et al. Lancet. 2016;387:53-60.

Slide credit: clinicaloptions.com

Bangkok Tenofovir Study: PrEP Efficacy in IDUs

- HIV-negative adults aged 20-60 yrs reporting IDU in previous yr randomized to PrEP with TDF QD (n = 1204) or PBO (n = 1209); pts could choose DOT or monthly visits

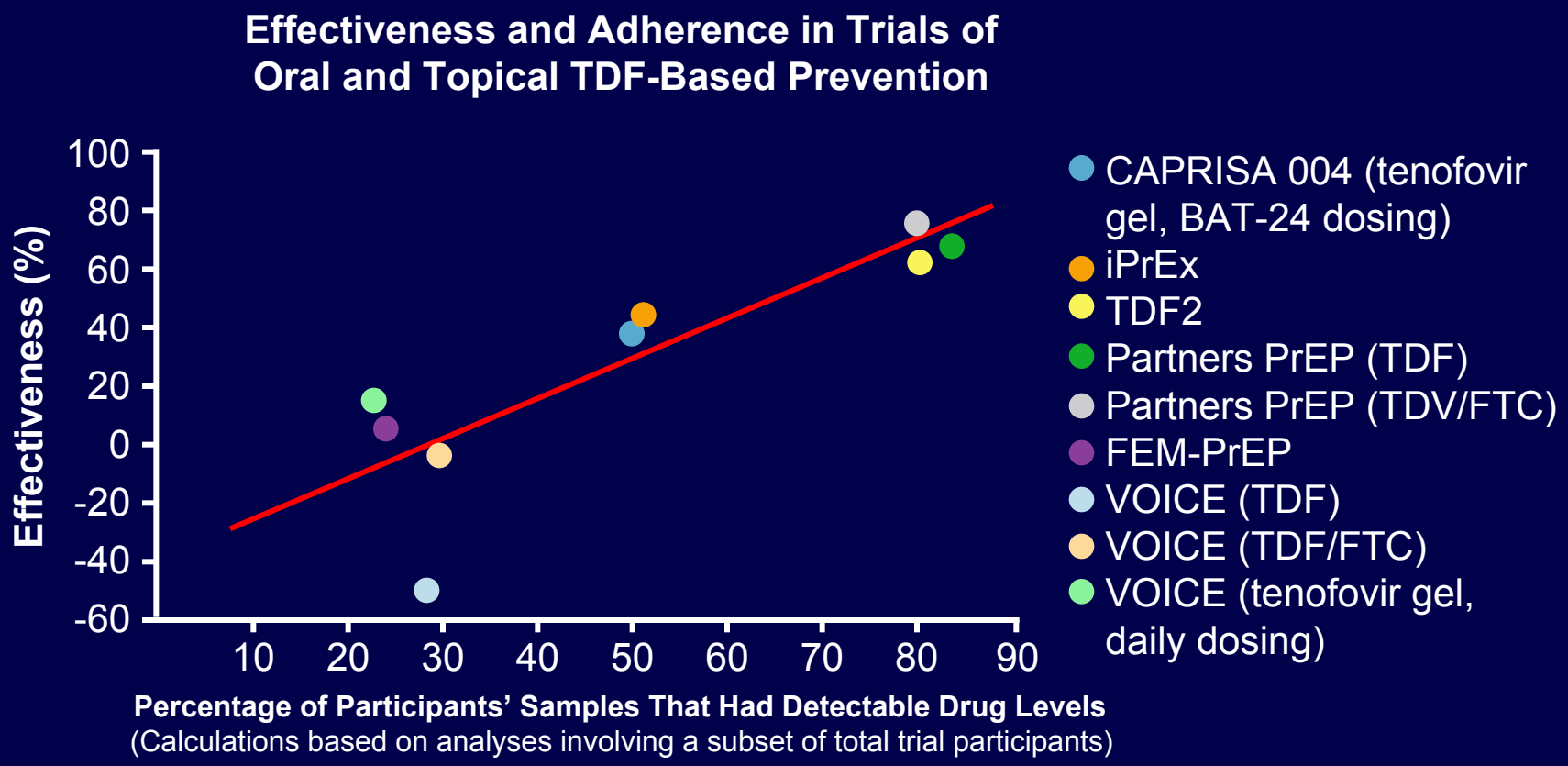


- Risk of infection significantly decreased with TDF PrEP (48.9%; *P* = .01)
- For pts who became infected and met adherence criteria (took study drug > 71% of days with < 2 consecutive days off study drug, n = 17), TDF PrEP reduced risk of infection 55.9% (-18.8% to 86.0%; *P* = 0.11)
  - In pts with detectable TDF: 73.5% (16.6% to 94.0%; *P* = .03)

Choopanya K, et al. Lancet. 2013;381:2083-2090.

Slide credit: clinicaloptions.com

Effectiveness and Adherence in Trials of Oral and Topical TDF-Based Prevention



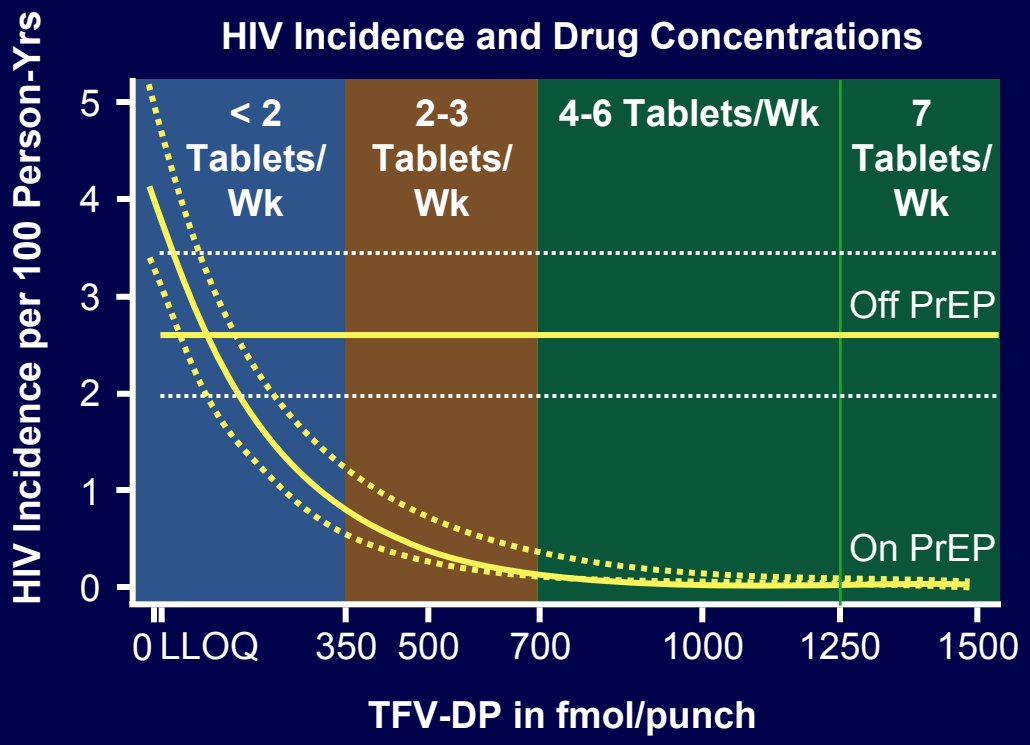
- Higher adherence associated with greater protection

AVAC Report. 2013.

Slide credit: clinicaloptions.com

iPrEX OLE: PrEP Reduces Incidence of HIV Even With Incomplete Adherence

- Open-label extension of iPrEX trial; N = 1603 (75% receiving PrEP)
- 100% adherence was not required to attain full benefit from PrEP
  - Benefit of 4-6 tablets/wk similar to 7 tablets/wk
  - 2-3 tablets/wk also associated with significant risk reduction
- Higher levels of sexual risk taking at baseline associated with greater adherence to PrEP

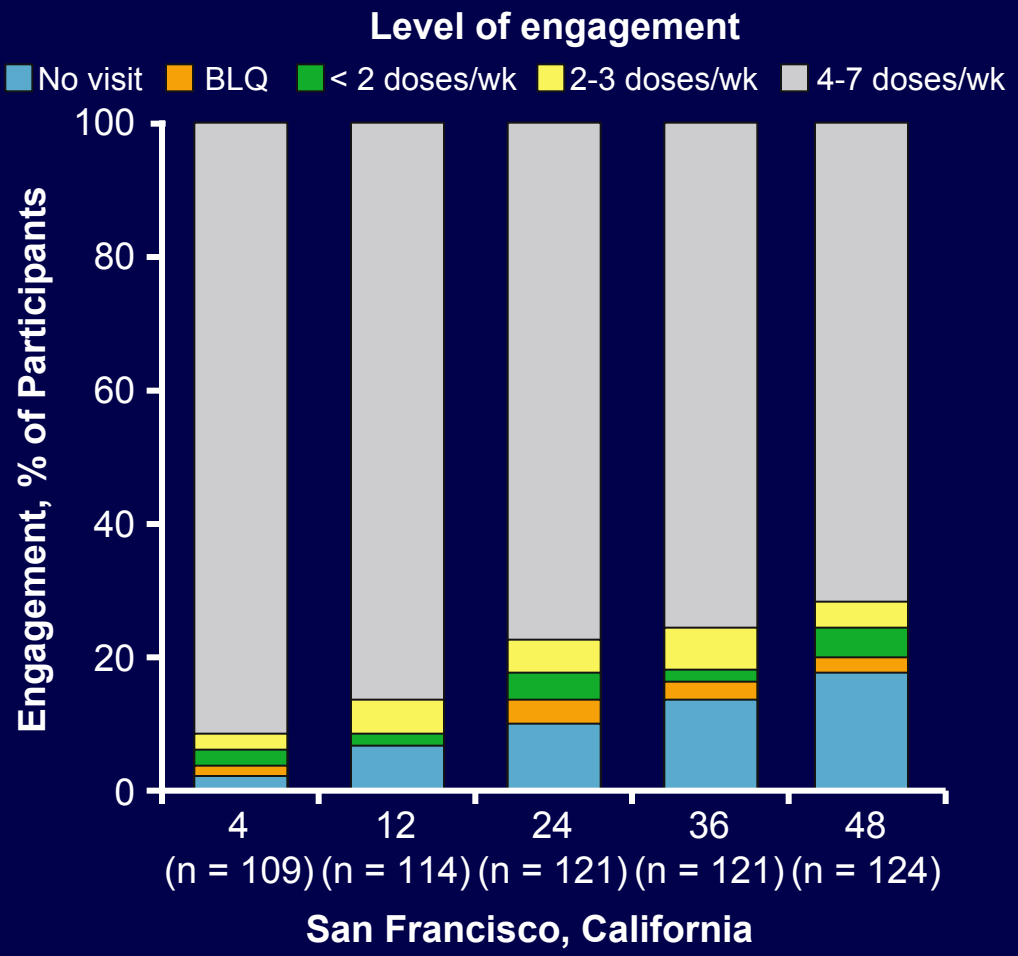


Grant R, et al. IAC 2014. Abstract TUAC0105LB.
Grant R, et al. Lancet Infect Dis. 2014;14:820-829.

Slide credit: clinicaloptions.com

PrEP Demonstration: High Adherence in STD/Community-Based Clinics

- Prospective, open-label study of 48 wks of daily oral TDF/FTC PrEP for MSM/TGW (N = 557)
  - 3 US STD or community-based clinics in San Francisco, Miami, and Washington, DC
- Of pts with at least 2 DBS tested (n = 272), 62.5% had protective TFV levels (consistent with ≥ 4 doses/wk) at all visits
  - 3% had TFV levels consistent with < 2 doses/wk
- PrEP dispensation interrupted in 15%: most commonly due to AE concerns or low perceived risk
- Overall STI incidence remained stable during follow-up (90/100 PY)



Liu AY, et al. JAMA Intern Med. 2016;176:75-84.

Slide credit: clinicaloptions.com

Practical Considerations for PrEP

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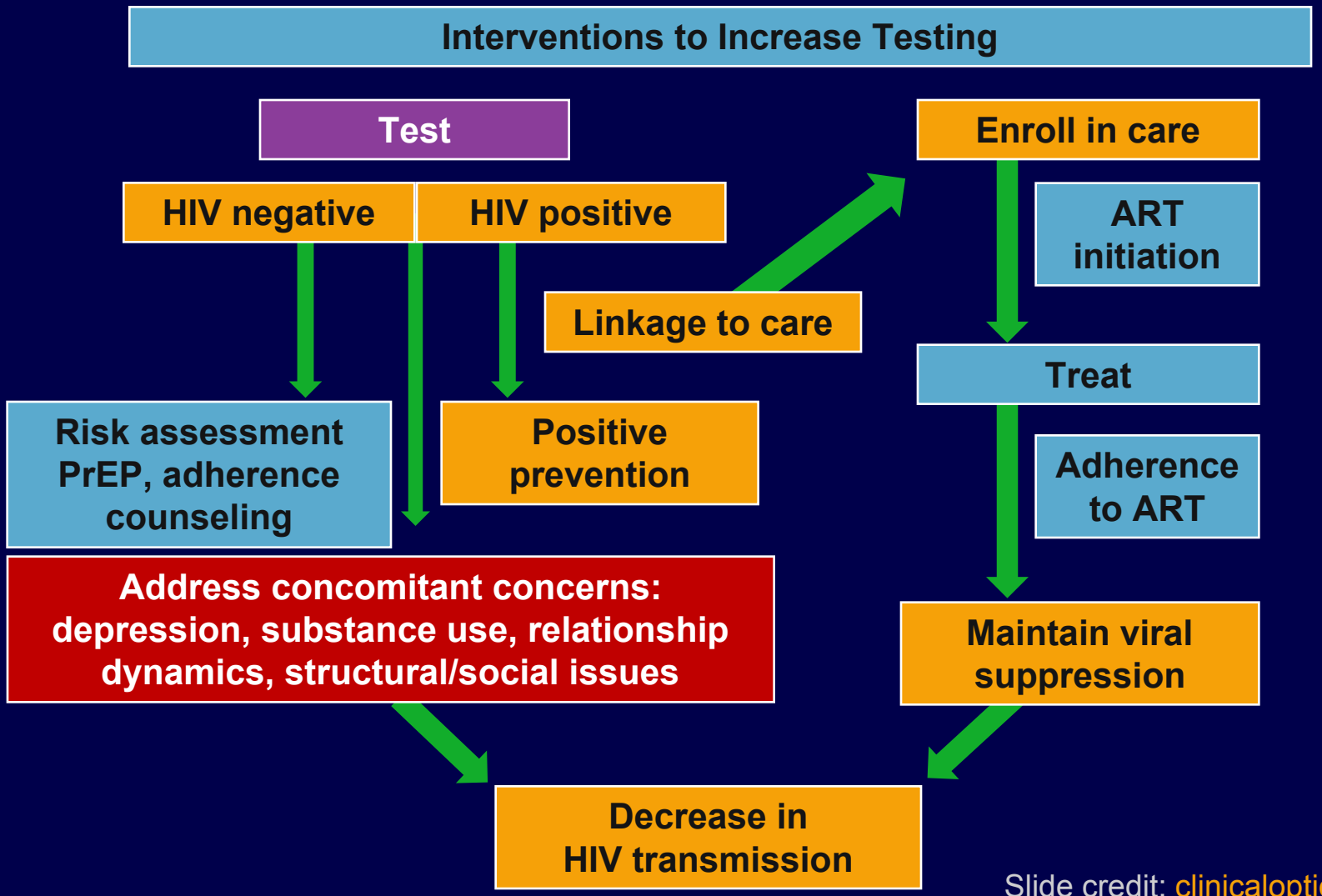
PrEP Alone Is Not Sufficient



Slide credit: clinicaloptions.com

STI Screening and Incidence During PrEP

- Analysis of STI occurrence in pts in SPARK, a PrEP demonstration project at a NY health care center[1]
  - Pts screened for STIs every 3 mos while receiving PrEP; also visited clinic if experienced symptoms
  - CDC PrEP guidelines suggest STI screening every 6 mos[2]

Time Point	N	STI Diagnosis, n (%)	Diagnosed by Routine Screening, n (% STIs)	Repeat STIs, n (% STIs)
6 mos before PrEP	280	35 (13)	NA	NA
PrEP prescription	280	31 (11)	31 (100)	8 (26)
3-mo follow-up	225	30 (13)	23 (77)	10 (33)
6-mo follow-up	196	41 (21)	34 (83)	20 (48)
9-mo follow-up	169	25 (15)	17 (68)	21 (84)
12-mo follow-up	128	17 (13)	13 (77)	13 (77)

- At all time points, majority of pts (> 71%) had rectal STIs

1. Golub S, et al. CROI 2016. Abstract 869.
2. CDC. PrEP Guidelines. 2014.

PrEP is not foolproof, even with optimal adherence.

POZ

Thinkstock

TREATMENT NEWS

PrEP Fails in Gay Man Adhering to Daily Truvada, He Contracts Drug-Resistant HIV

February 25, 2016 • By Benjamin Ryan

POZ

Istock

TREATMENT NEWS

Second Man Contracts Rare HIV Strain While Adhering to PrEP

But such cases are likely to remain very uncommon.

October 19, 2016 • By Benjamin Ryan

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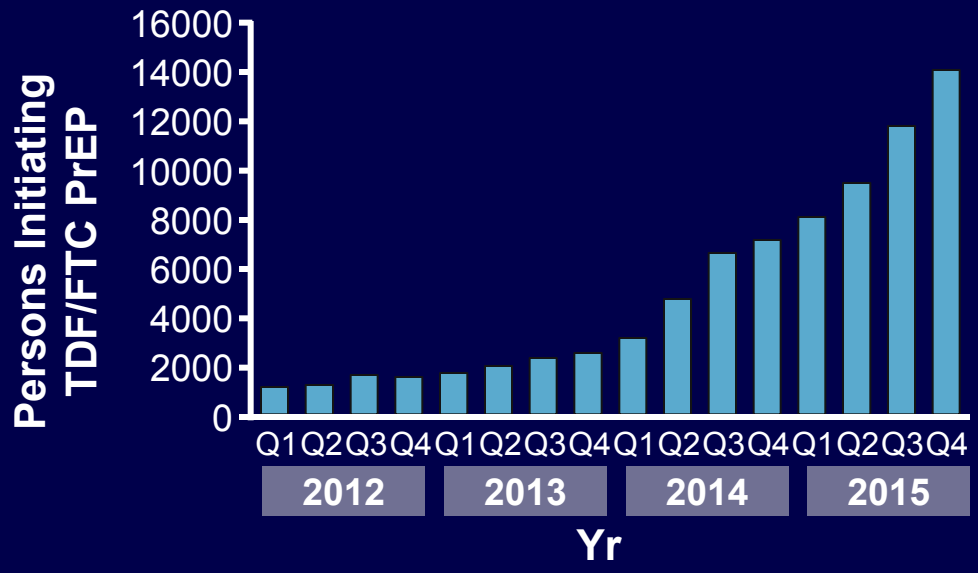
PrEPWatch.org

US TDF/FTC PrEP Use From 2012-2015

- Analysis of TDF/FTC PrEP prescription data from 2012-2015 in US retail pharmacies
- PrEP initiation increased 738% from 2012-2015

Persons Initiating TDF/FTC PrEP, 2012-2015 (N = 79,684)



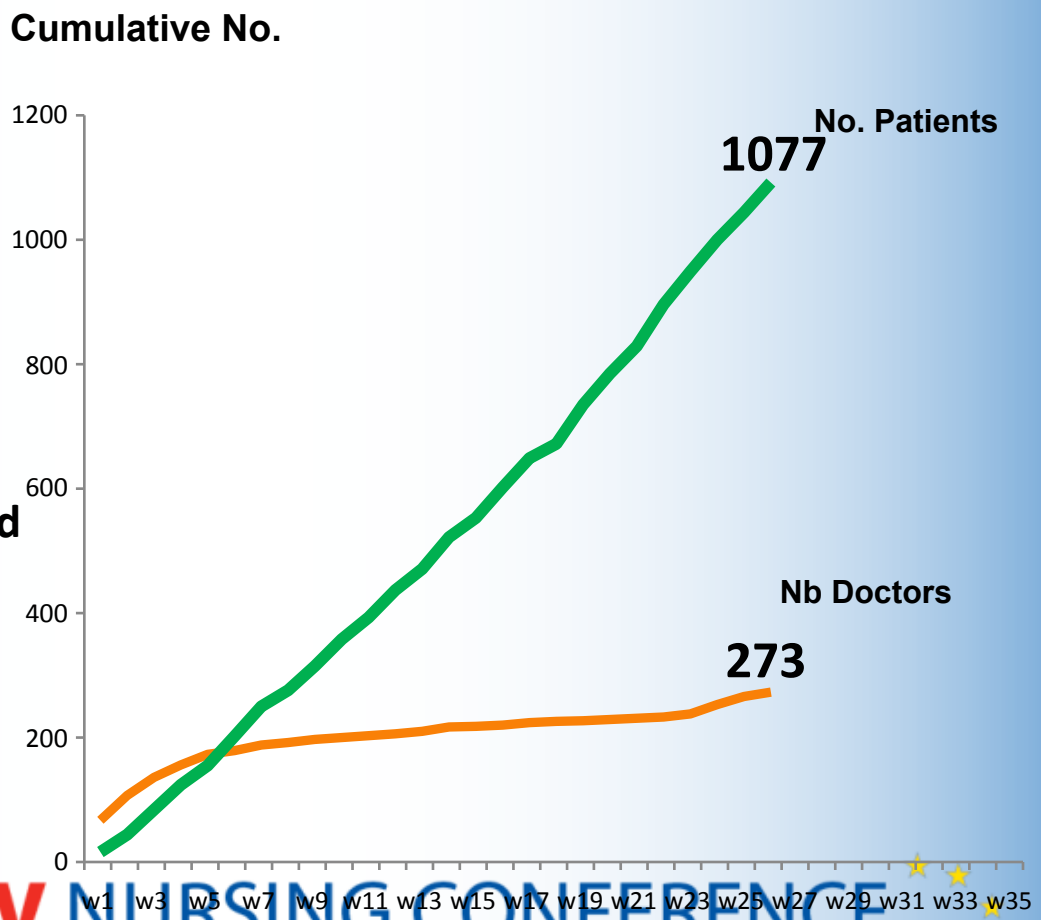
- Women comprised 44% of individuals starting PrEP in 2012 vs 17% in 2015
- Mean age of those initiating PrEP in 2015: 36.2 yrs

Mera R, et al. IAC 2016. Abstract TUAX0105LB.

Slide credit: clinicaloptions.com

PrEP Implementation in France in 2016

- > 90 PrEP clinics have opened, initially in ANRS Ipergay sites (Paris, Lyon, Nice, Lille, Nantes)
- AIDES Website: http://www.aides.org/info-sante/prep
- TDF/FTC can be prescribed by hospital-based HIV specialists and STI clinics since June 2016
- TDF/FTC can be obtained at private and hospital pharmacies



PrEP Use and HIV/STI Incidence Clinical Practice (San Francisco)

- **Analysis of PrEP use and HIV/STI incidence in PrEP users in large healthcare system (Kaiser Permanente San Francisco) from 2012 to 2015**
  - 1045 referrals for PrEP; 801 individuals with ≥ 1 intake visit
  - 657 initiated PrEP (82%*); mean duration of use 7.2 mos
- **Key results (PrEP initators):**
  - No HIV diagnoses (388 PY follow-up)
  - After 12 months, 50% diagnosed with any STI
    - 33% rectal STI; 33% chlamydia; 28% gonorrhea
  - After 6 mos PrEP, self-reported condom use was decreased in 41% of individuals

Volk JE, et al. Clin Infect Dis. 2015;61:1601-1603.

PrEP Implementation: Denver

- **APEX Family Medicine**
  - Largest private HIV treatment and PrEP provider in region
  - General/Family Practice providers
    - 3 physicians
    - 4 nurse practitioner/physician assistant
  - 1000 HIV+ patients, 500 on PrEP
  - No HIV seroconversion among PrEP patients in 2 years

Online PrEP Purchase: London

- 56 Dean Street Clinic, London
- 191/208 patients purchased PrEP online
  - Most was Cipla *Tenvir-EM*
  - *£1.68/pill (vs £11.86 in BNF)*
- *Drug testing found adequate levels*
- *No cases of HIV seroconversion*
- *Kidney function normal*

Nwokolo, HIV Glasgow 2016

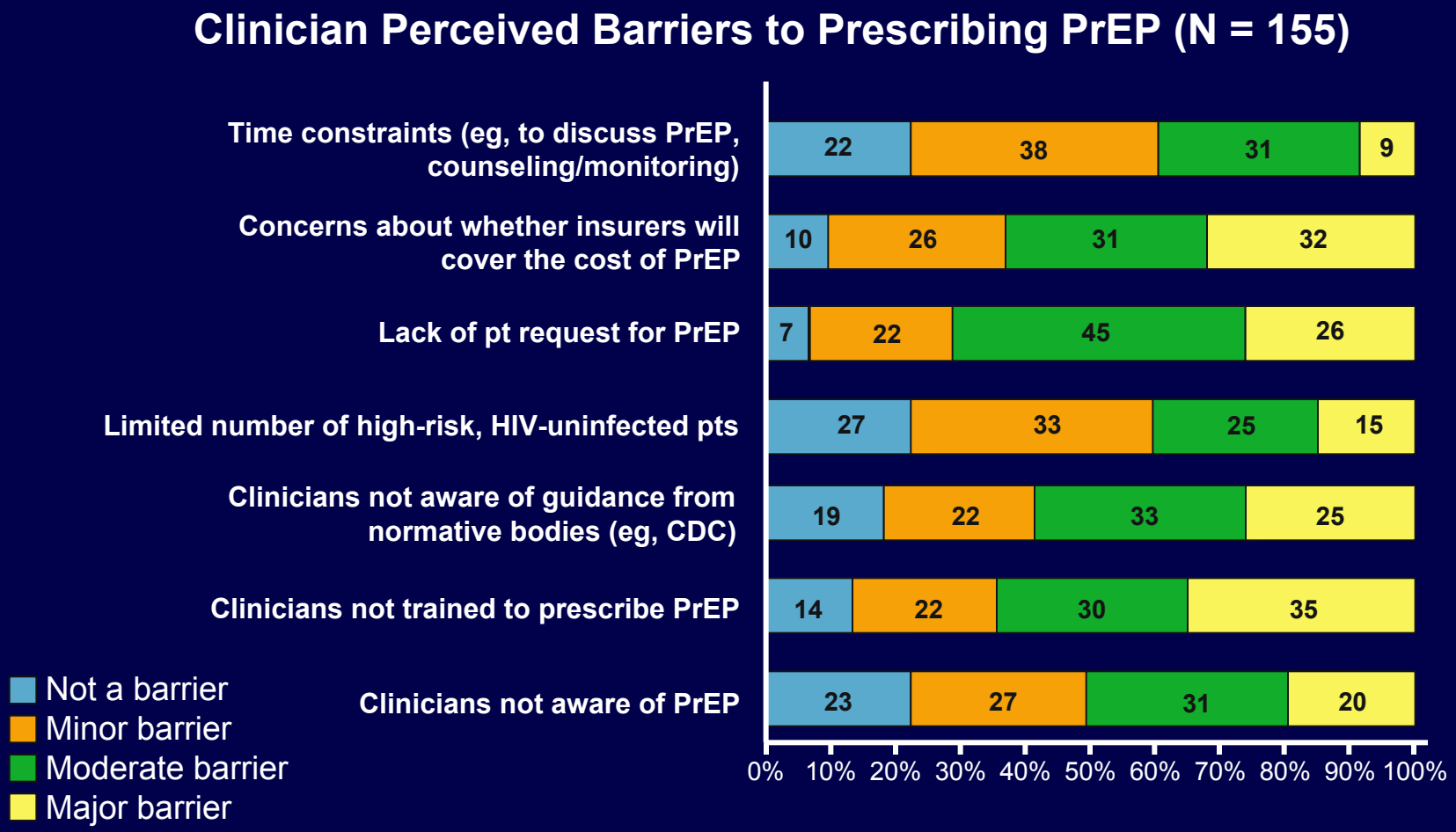
Lessons Learned: France

- Close partnership with the community and strong political support have led to PrEP approval
- Increase PrEP awareness among doctors and people at risk (MSM, transgender, and heterosexual migrants)
- Adapt available resources to provide comprehensive sexual health care and meet the demand
- Define best models of care and access points (hospitals, sexual health clinics, GP)
- High risk people self-select for PrEP: HIV-infection detected at screening or soon after PrEP initiation

Challenges with PrEP Roll-Out:France

- Dedicated nurses to provide information/appointment by email and tel
- Organize outpatient clinic to meet the demand
  - Inform nurses and administrative personnel
  - Identify doctors willing to provide PrEP (> 10 doctors)
  - Increase offer: 10 consultations per week (2 to 3 from 6-10 pm)
- PrEP can be started at first visit and patients seen at Month 1 and every 3 months
- Adapt outpatient clinic for STI treatment (injections)
- Peer-counseling (PrEP adherence, risk reduction)

New England Prescribers Perceived Numerous Barriers to Prescribing PrEP



Numbers within bars represent the percentage of participants selecting each response category.

Krakower DS, et al. PLoS One. 2015;10:e0132398.

Slide credit: clinicaloptions.com

Successful Implementation of HIV Preexposure Prophylaxis: Lessons Learned From Three Clinical Settings

Julia L. Marcus[1] · Jonathan E. Volk[2] · Jess Pinder[3] · Albert Y. Liu[4] · Oliver Bacon[4] · C. Bradley Hare[2] · Stephanie E. Cohen[4]

- **PrEP programs in health maintenance organization, STD clinic and primary care practice**.
- PrEP reaching high-risk populations, but gaps exist (minority/adolescent MSM, PWID, TG)
- Building capacity among primary care providers to take sexual history needed.
- Self-collection for STI screening may reduce burden healthcare system
- Train non-physician providers to administer aspects of PrEP care.
- More frequent STI testing in some settings.
- Cost continues to be a barrier for some.
- Engagement of public health departments can support PrEP implementation

Curr HIV/AIDS Rep (2016) 13:116-124

Take-home points

- PrEP works, and access is improving (if slowly) in Europe
  - Where not available, people are accessing PrEP privately or via internet
- Clinic/laboratory monitoring critical (HIV, HBV, renal, bone)
- PrEP is an important component of comprehensive sexual healthcare
- Nurses can aid in PrEP advocacy, access and service delivery
- Addressing barriers to care and appropriate task shifting are key to effective PrEP implementation

Thank you!
Gracies!

APEX Family Medicine, Denver

Mia Scott, DO; Michael Mohr DO; Lorraine Van Slyke NP;

Allison Russell PA; Derek Miller PA; Barb Widick, RN; Amy Thomas; Billie Thomas

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