A Pill for HIV Prevention

An Overview of Pre-Exposure Prophylaxis for New Providers

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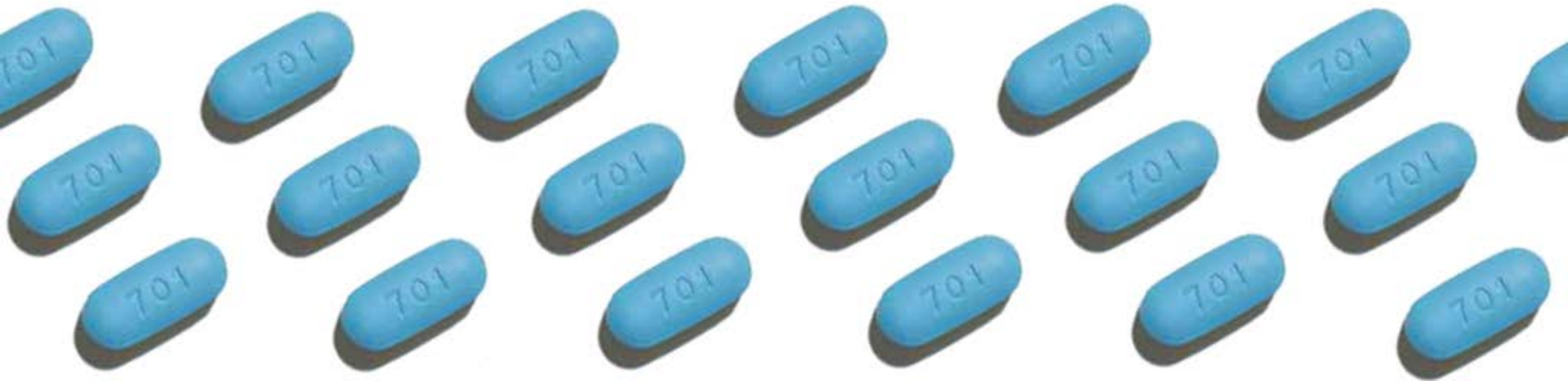

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The views expressed are not necessarily those of the NIH.

What is pre-exposure prophylaxis?

Use of antiretroviral medications **before** an exposure, to reduce the risk of becoming infected

Tenofovir disoproxil fumarate (TDF)
is the most studied agent for PrEP

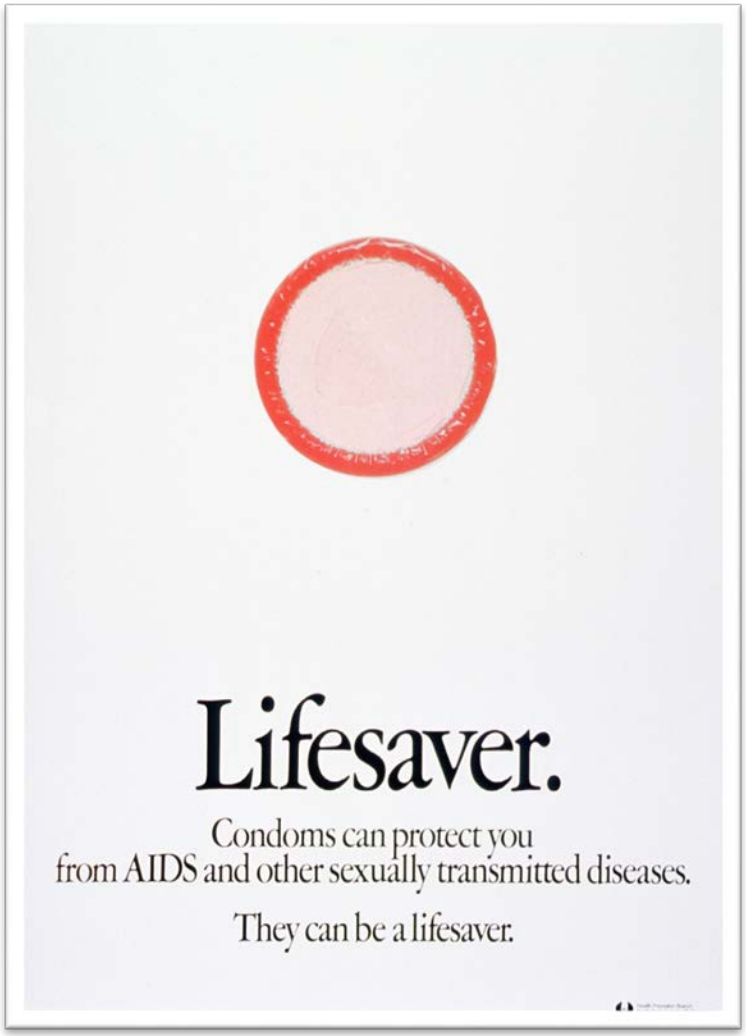
- Properties of drug allow infrequent dosing
- Few drug-drug interactions
- Safe and well tolerated

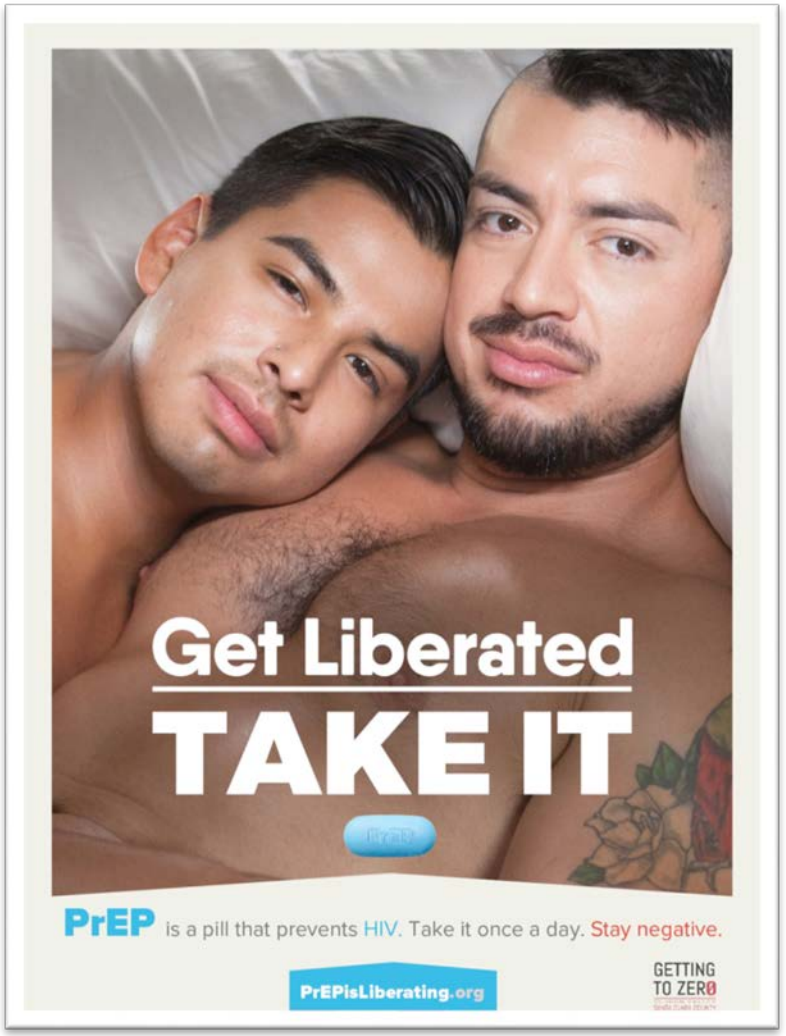
FDA approved in 2012

USPHS guideline in 2014

(emtricitabine / TDF = **Truvada**)

Change may be difficult for many of us





Pregnancy P	Pregnancy Prevention	ention
Education & behavior m	Education & behavior modification	havior modification
Condoms	Condoms 	Condoms
Rings	Rings 	Rings
Birth control pill & injec	Birth control pill & injection 	PrEP (oral & injectable)
“Morning-after pill”	“Morning-after pill” 	posure prophylaxis
Spermicide	Spermicide 	opical microbicides
Implantable birth contro	Implantable birth control 	dly neutralizing Abs Implantables
Vasectomy/Tubal Ligatic	Vasectomy/Tubal Ligation	Vaccination

Adapted from HPTN

You’re seeing Demetrius in clinic

- 19 year-old freshman at UT
- Presenting for new discharge from penis
  - Dysuria preceded discharge
  - Symptoms for about 36 hours
- No constitutional symptoms
- Anxious – first-ever episode

Demetrius, cont'd

- Has sex with men
- Not in a relationship currently
- Meets partners at clubs and online
- Uses condoms "most of the time"
  - (in response to "How often do you…?" question)
- Finished PEP regimen 2 months ago

Pop quiz

Consistent use of condoms reduces the risk of HIV acquisition by how much?

50-60% 70-80% 90-100%

Pop quiz

Consistent use of condoms reduces the risk of HIV acquisition by how much?

MSM Hetero

50-60% **70-80%** 90-100%

Heterosexuals (“always” vs “never” users): Weller S, Davis K. Cochrane Database Syst Rev. 2002;(1):CD003255
MSM (EXPLORE & VAX 004 trials): Smith DK et al. JAIDS 2015;68(3):337-44

Condoms only work if you use them

~90%

of heterosexuals had some condomless sex in the prior year

55%

of MSM didn't use condom with most recent anal sex

30%

of heterosexuals didn't use condom with most recent anal sex

Rosenberger JG, et al. *J Sex Med*. 2012;9(4):1037-47
Sionean C, et al. *MMWR Surveil Summ.* 2014;63(14):1-15

Demetrius, cont’d

- Has tried to be consistent with condoms
- Sex is less enjoyable with them
- Doesn’t always have one handy
- “They just get in the way of the moment”

Pop quiz, part 2

Consistent use of PrEP* reduces the risk of HIV acquisition by how much?

50-60% 70-80% 90-100%

*added to existing prevention methods

Pop quiz, part 2

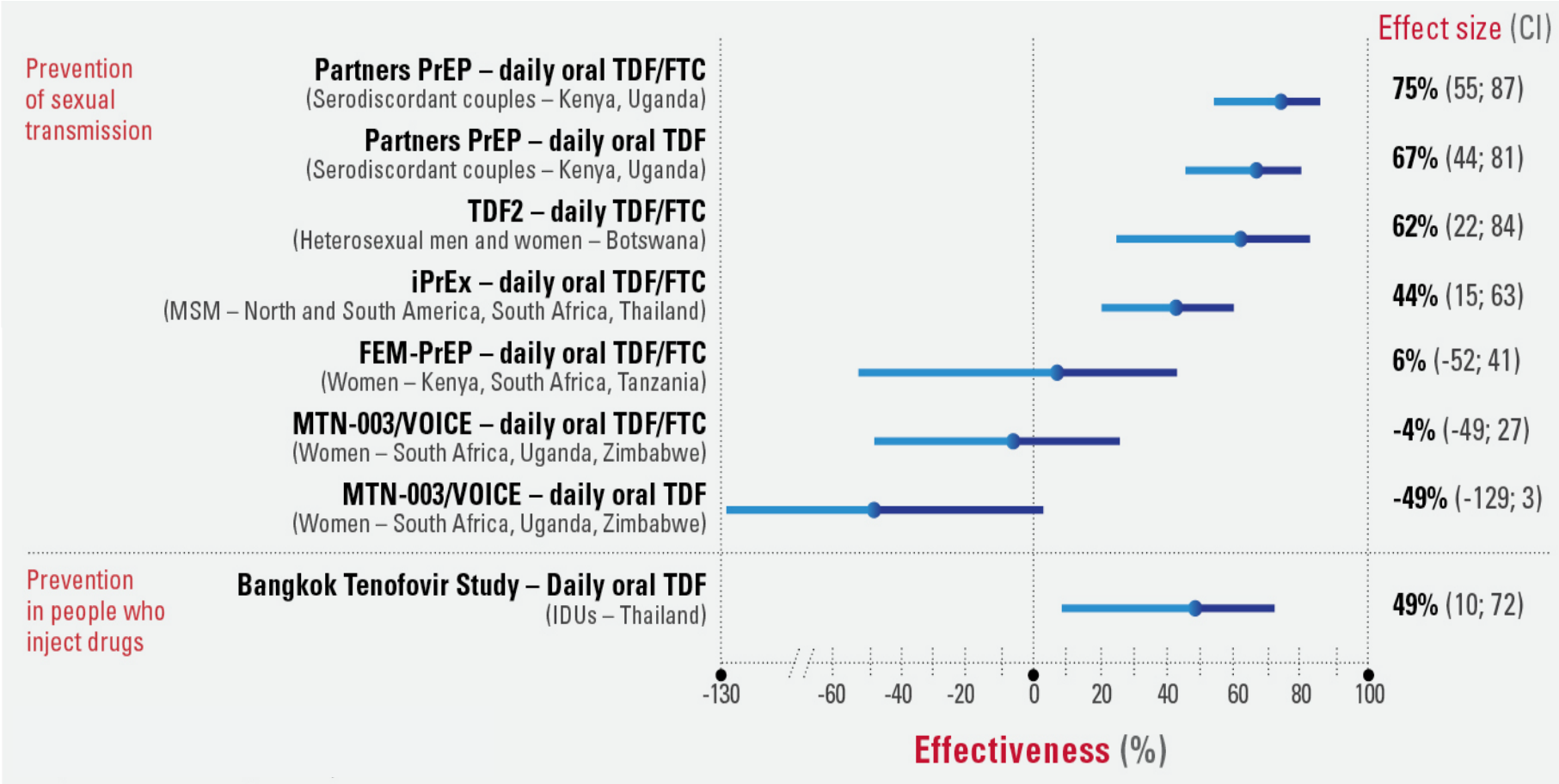
Consistent use of PrEP* reduces the risk of HIV acquisition by how much?

50-60% 70-80% **90-100%**

*added to existing prevention methods

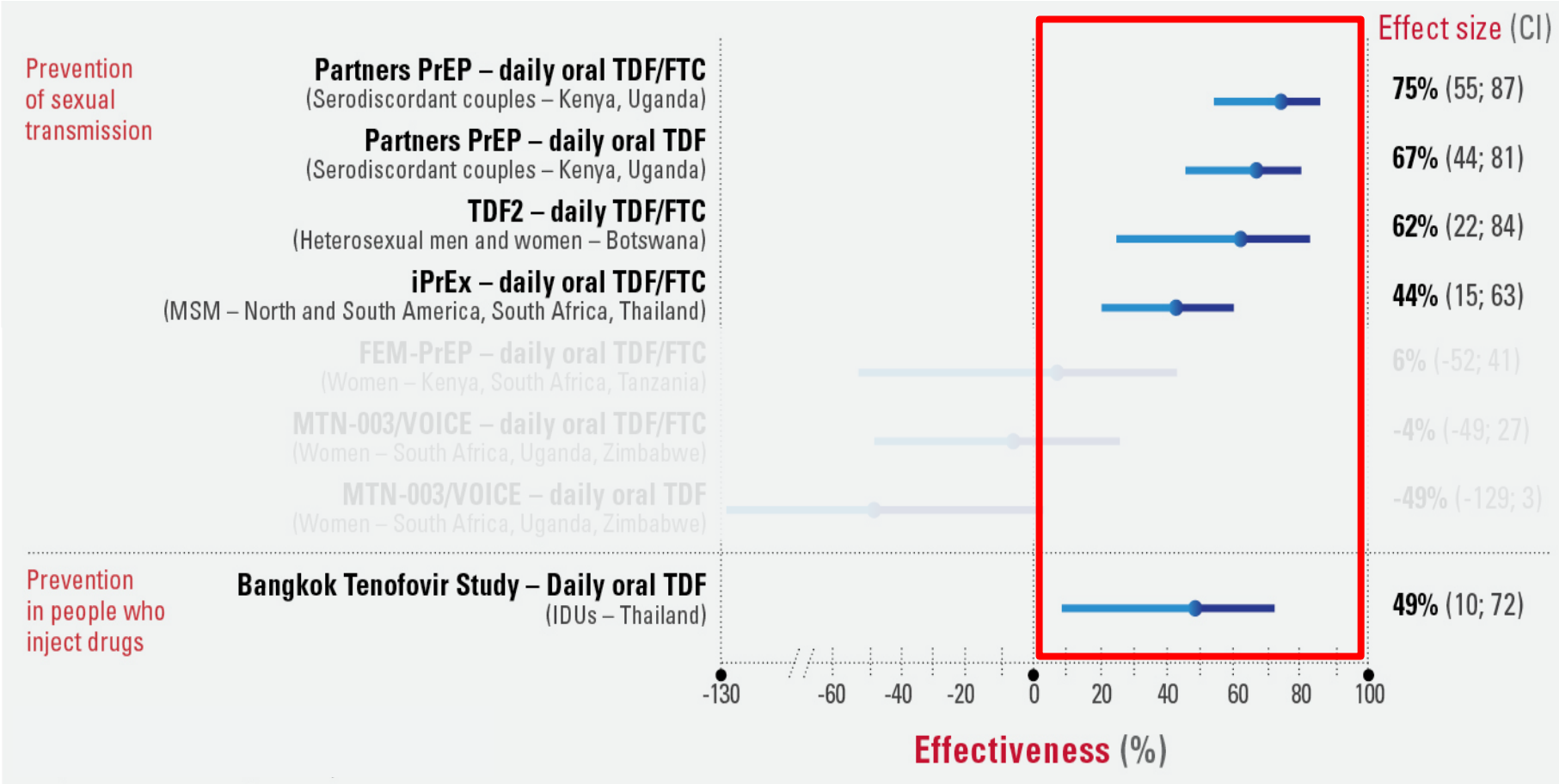
Grant RM, et al. *NEJM*. Dec 2010;363(27):2587-99
Baeten JM, et al. *NEJM.* Aug 2012;367(5):399-410
Grant RM, et al. *Lancet Inf Dis*. Sep 2014;14(9):820-9

Clinical trials leading to PrEP approval



http://www.avac.org/report2013

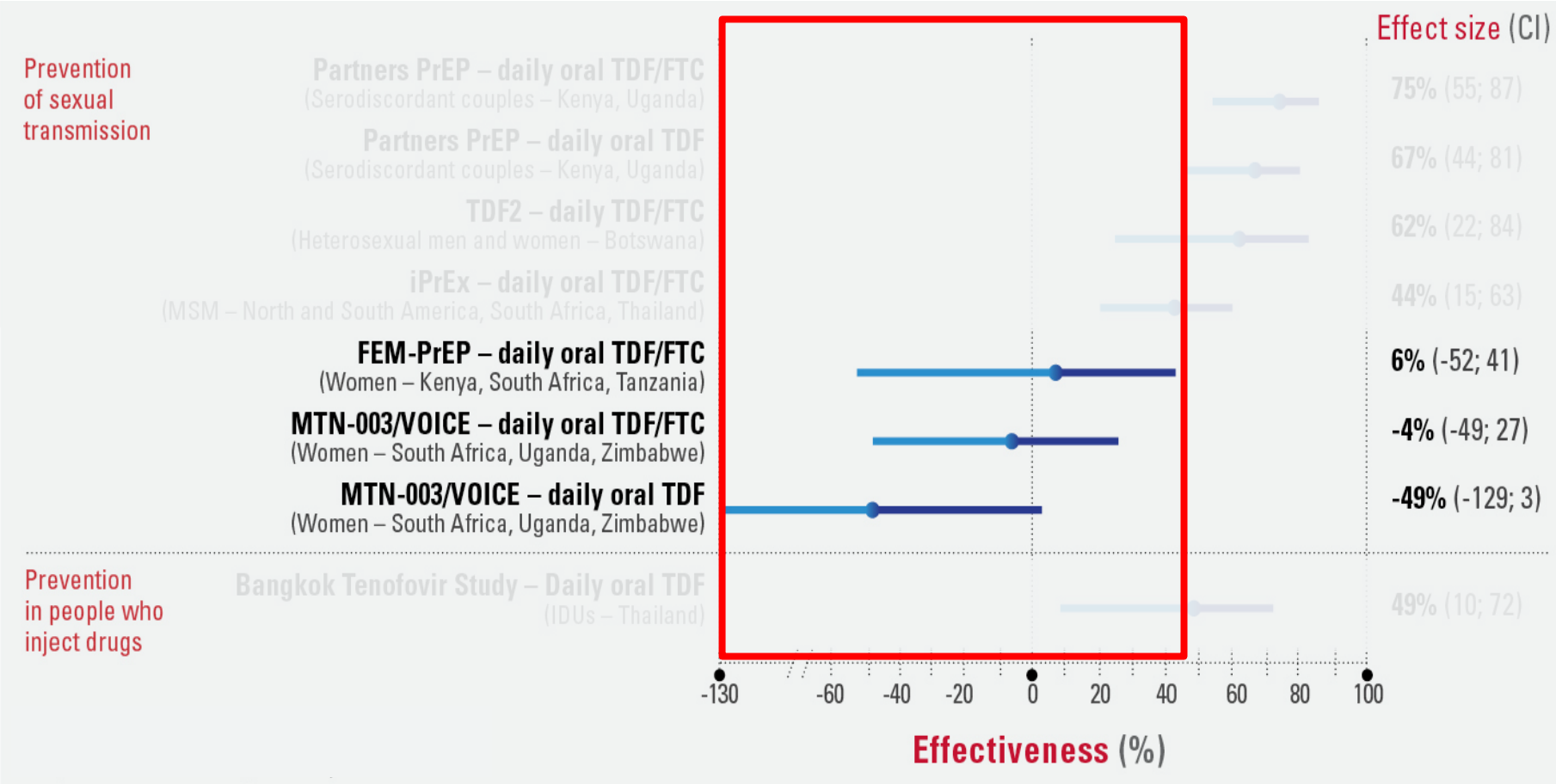
Clinical trials leading to PrEP approval



5 studies showed protective benefit of daily TDF-based PrEP

http://www.avac.org/report2013

Clinical trials leading to PrEP approval



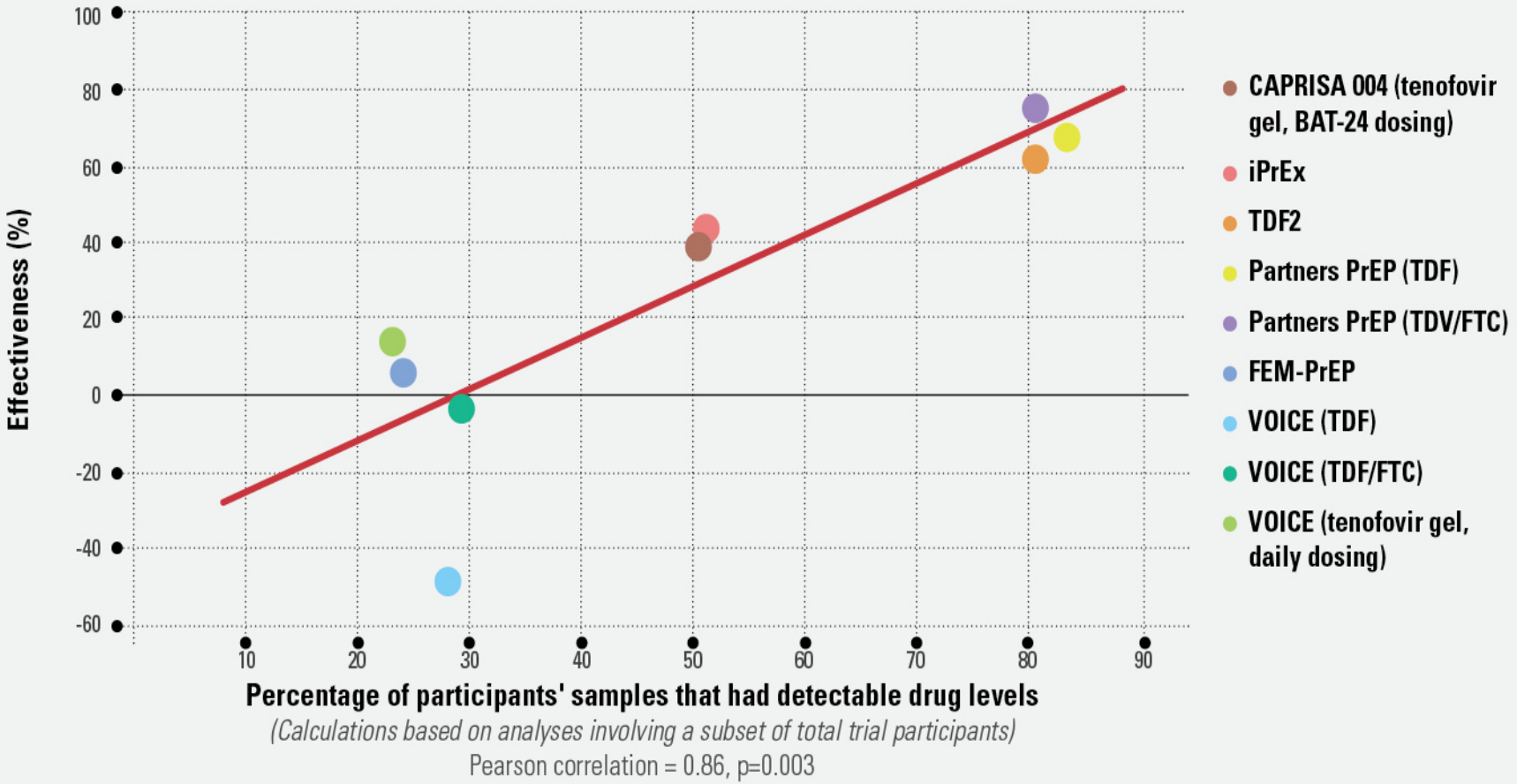
3 studies showed no protective benefit from TDF-based PrEP

http://www.avac.org/report2013

But didn’t you just say the efficacy was 90-100%?

It’s all about adherence

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

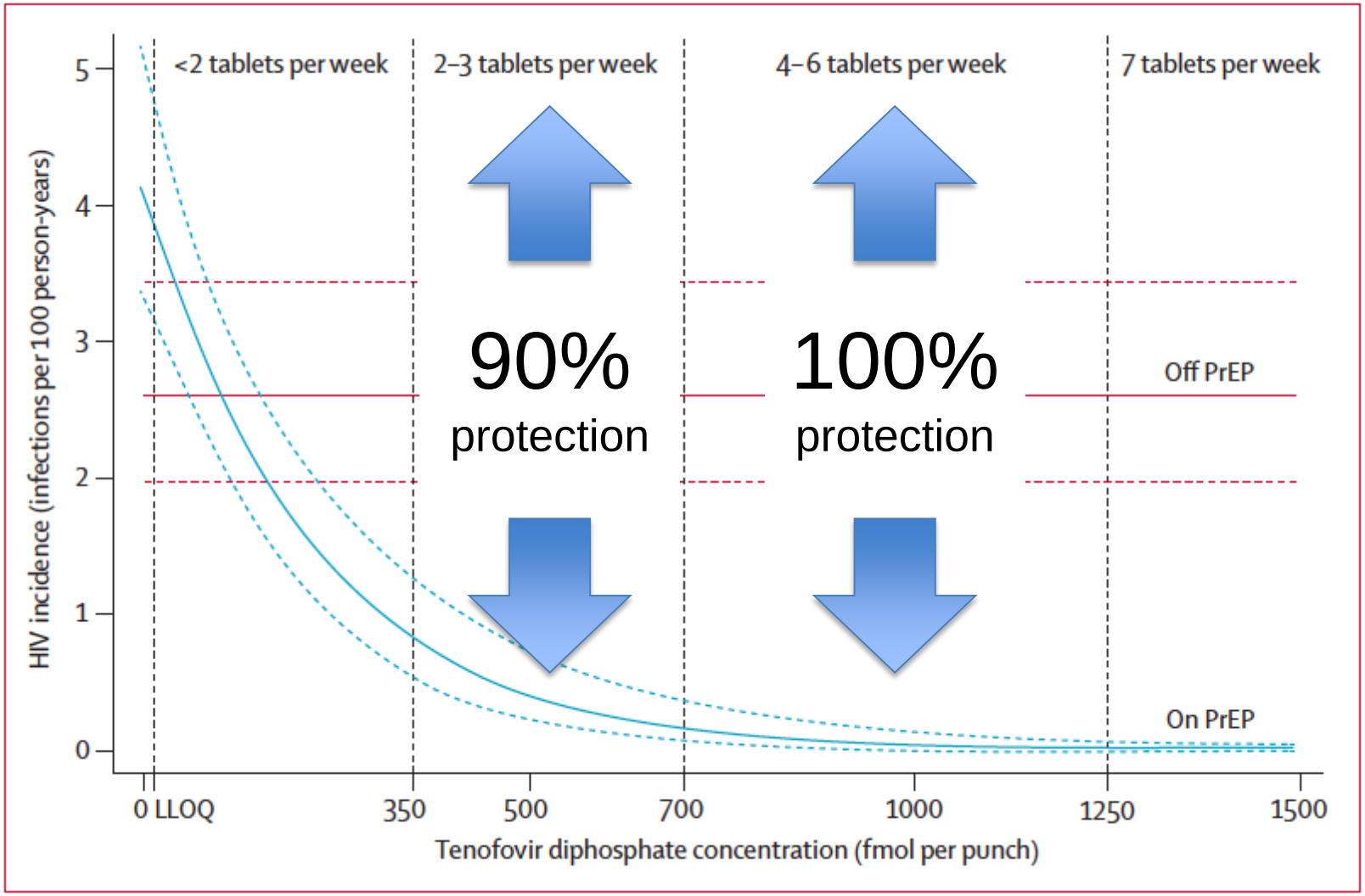


Trials of oral and topical tenofovir-based PrEP show that these strategies reduce risk of HIV infection if they are used correctly and consistently. Higher adherence is directly linked to greater levels of protection.

Source: Salim S. Abdool Karim, CAPRISA

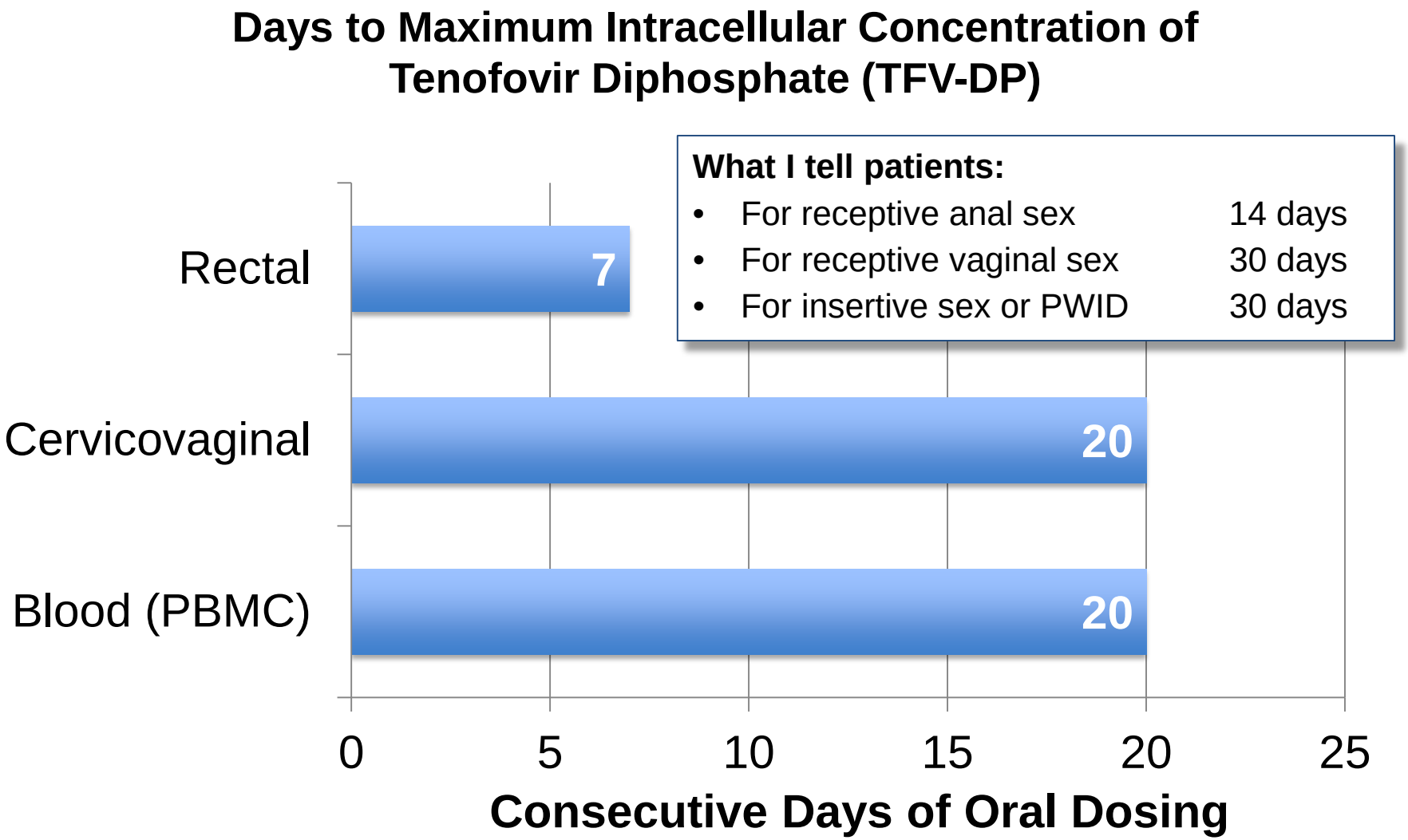
What's "consistent" PrEP use?

Data depicted reflect protective efficacy among MSM and TGW (i.e., principally anal sex)



Grant RM, et al. *Lancet Inf Dis*. Sep 2014;14(9):820-9

Time to optimal protection varies…



US Public Health Service. PrEP Guideline – 2014.

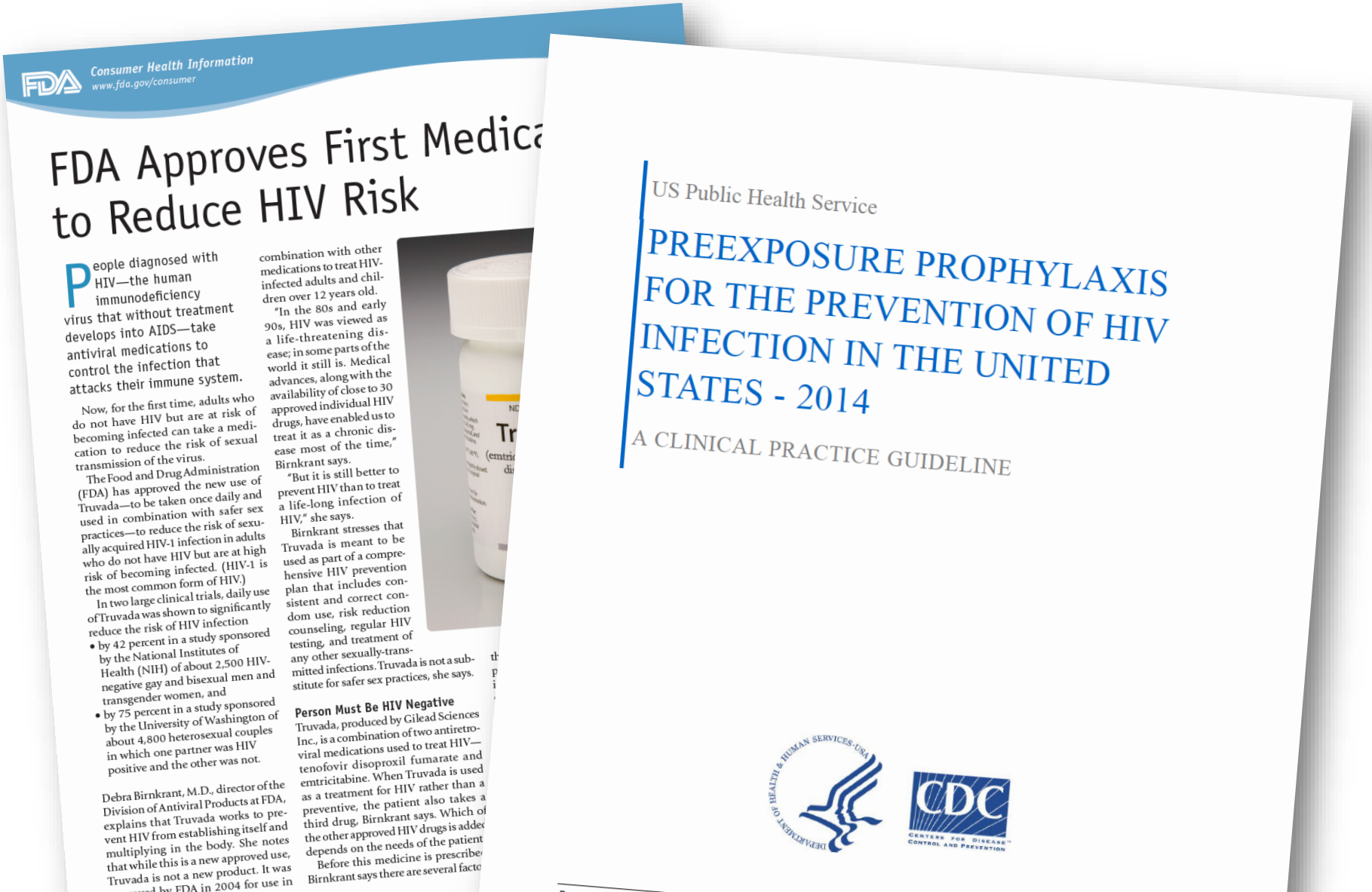
Key points

Daily dosing affords greatest protection

Occasional missed dose probably OK
(less OK for cisgender women…)

Nonadherence creates opportunities for infection

Moving PrEP into practice



Consumer Health Information
www.fda.gov/consumer

FDA Approves First Medica to Reduce HIV Risk

People diagnosed with HIV—the human immunodeficiency virus that without treatment develops into AIDS—take antiviral medications to control the infection that attacks their immune system.

Now, for the first time, adults who do not have HIV but are at risk of becoming infected can take a medication to reduce the risk of sexual transmission of the virus.

The Food and Drug Administration (FDA) has approved the new use of Truvada—to be taken once daily and used in combination with safer sex practices—to reduce the risk of sexually acquired HIV-1 infection in adults who do not have HIV but are at high risk of becoming infected. (HIV-1 is the most common form of HIV.)

In two large clinical trials, daily use of Truvada was shown to significantly reduce the risk of HIV infection

- by 42 percent in a study sponsored by the National Institutes of Health (NIH) of about 2,500 HIV-negative gay and bisexual men and transgender women, and
- by 75 percent in a study sponsored by the University of Washington of about 4,800 heterosexual couples in which one partner was HIV positive and the other was not.

Debra Birnkrant, M.D., director of the Division of Antiviral Products at FDA, explains that Truvada works to prevent HIV from establishing itself and multiplying in the body. She notes that while this is a new approved use, Truvada is not a new product. It was

combination with other medications to treat HIV-infected adults and children over 12 years old.

"In the 80s and early 90s, HIV was viewed as a life-threatening disease; in some parts of the world it still is. Medical advances, along with the availability of close to 30 approved individual HIV drugs, have enabled us to treat it as a chronic disease most of the time," Birnkrant says.

"But it is still better to prevent HIV than to treat a life-long infection of HIV," she says.

Birnkrant stresses that Truvada is meant to be used as part of a comprehensive HIV prevention plan that includes consistent and correct condom use, risk reduction counseling, regular HIV testing, and treatment of any other sexually-transmitted infections. Truvada is not a substitute for safer sex practices, she says.

Person Must Be HIV Negative

Truvada, produced by Gilead Sciences Inc., is a combination of two antiretroviral medications used to treat HIV—tenofovir disoproxil fumarate and emtricitabine. When Truvada is used as a treatment for HIV rather than a preventive, the patient also takes a third drug, Birnkrant says. Which of the other approved HIV drugs is added depends on the needs of the patient.

Before this medicine is prescribed Birnkrant says there are several facto

US Public Health Service

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CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Demetrius, cont'd

- Aware of the term "PrEP"
- Remembers reading something about a study in San Francisco?
- Overall pretty skeptical
- "I've heard these medications are toxic…"

Kaiser Permanente

SF Bay area, July 2012 - Feb 2015

1045 referrals for PrEP

80% evaluated in person

82% started PrEP (62% of those referred)

388 person-years of follow-up

187 new STIs among PrEP users

0 new HIV infections among PrEP users

Volk JE, et al. *Clin Inf Dis*. 2015 Nov 15.61(10):1601-3

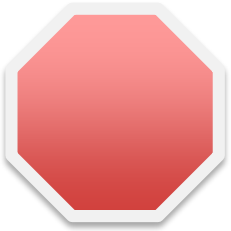
PROUD Study

London, Nov 2012 - Apr 2014

544
MSM &
trans women

½
started
immediately

½
delayed
initiation



DSMB halt
(Oct 2014)

McCormack S, et al. *Lancet*. 2015;387(10013):53-60.

PROUD Study

London, Nov 2012 - Apr 2014

544
MSM & trans women

½
started immediately

½
delayed initiation

86%
protective effectiveness
(95%CI: 58, 96)

13
at-risk MSM need to be treated for 1 year to prevent 1 infection
(95% CI: 9, 23)

For primary prevention: **aspirin** 1667 x 1Y **statin** 104 x 5Y

McCormack S, et al. *Lancet*. 2015;387(10013):53-60. http://www.thennt.com

What are the side effects of PrEP?

“Startup syndrome”

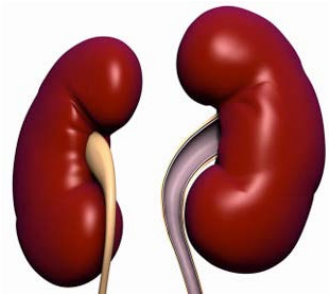
- Flatulence (3-4%)*
- Nausea (8-20%)*
- Mild headache (6-22%)*

- Symptoms resolve within first 30d, for most

* post-marketing reported frequencies (Lexi-Comp)

US Public Health Service. PrEP Guideline – 2014.

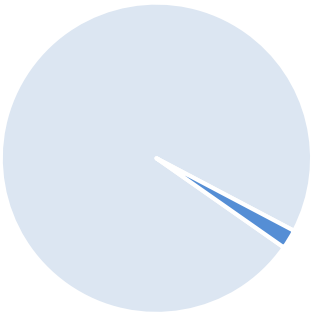
What are the side effects of PrEP?



Proximal tubular toxicity

Fanconi syndome
Hypophosphatemia
Phosphaturia (FE Phos)
Glucosuria (plasma normal)
Proteinuria
Proximal RTA

Of 10,343 HIV+ starting tenofovir



2%
had **any** renal function abnormality

Of 183 starting with normal function

59%
Normalized
(after median 17m)
n=108

9%
Improved
n=18

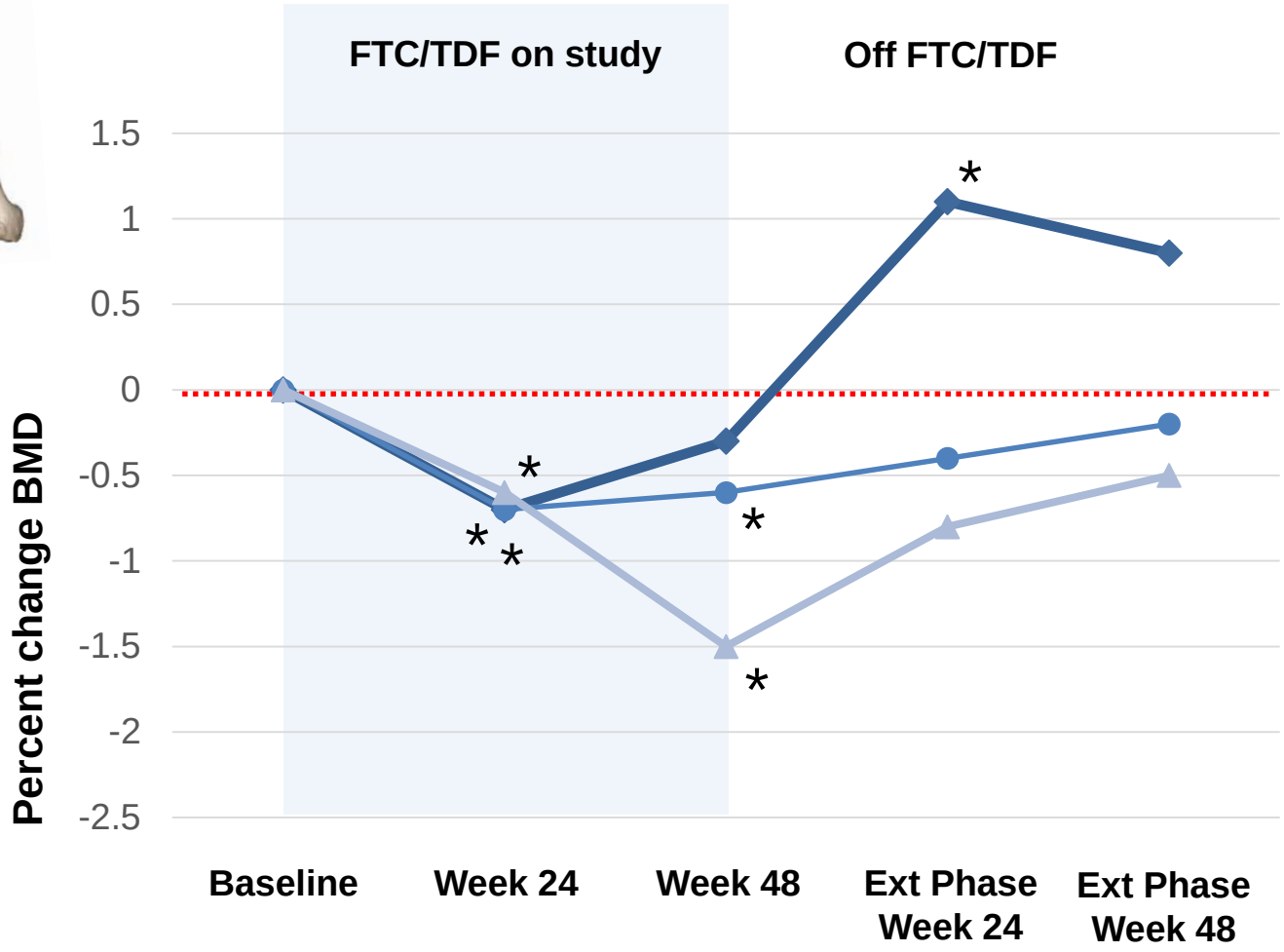
31%
No change
n=57

Nelson MR, et al. *AIDS*. 2007;21(10):1273-81

Bonjoch A, et al. *Antiviral Res*. 2012;96(1):65-9

What are the side effects of PrEP?

Loss of bone mineral density



18-22
years old
(n=72)

Spine
P=0.03 vs W48
P=0.04 vs BL

Whole Body
P=0.01 vs W48
P=0.7 vs BL

Hip
P=0.04 vs W48
P=0.5 vs BL

* *P* < 0.05 vs BL

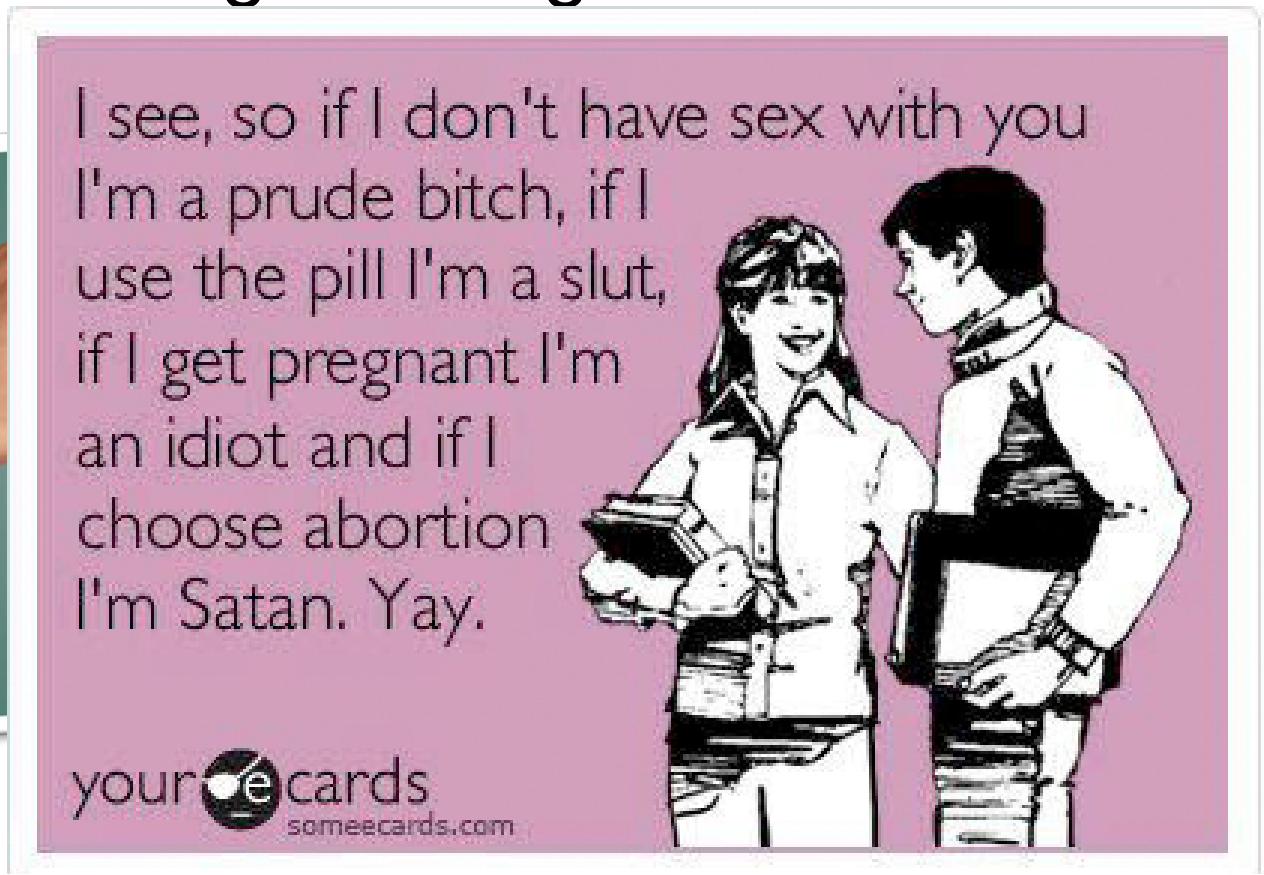
Mulligan K, et al. 18th Int'l Workshop on Comorbidities and Adverse Drug Reactions in HIV. 12-13 Sept 2016. New York City, NY. Abstract 001.

Demetrius, cont’d

- Doesn’t think side effects sound bad
- “People say PrEP is for sluts… and I don’t hook up that much…”
- “Is this still something you’d recommend?”

Won’t PrEP encourage riskier sex?

Slut shaming and stigma are all too real



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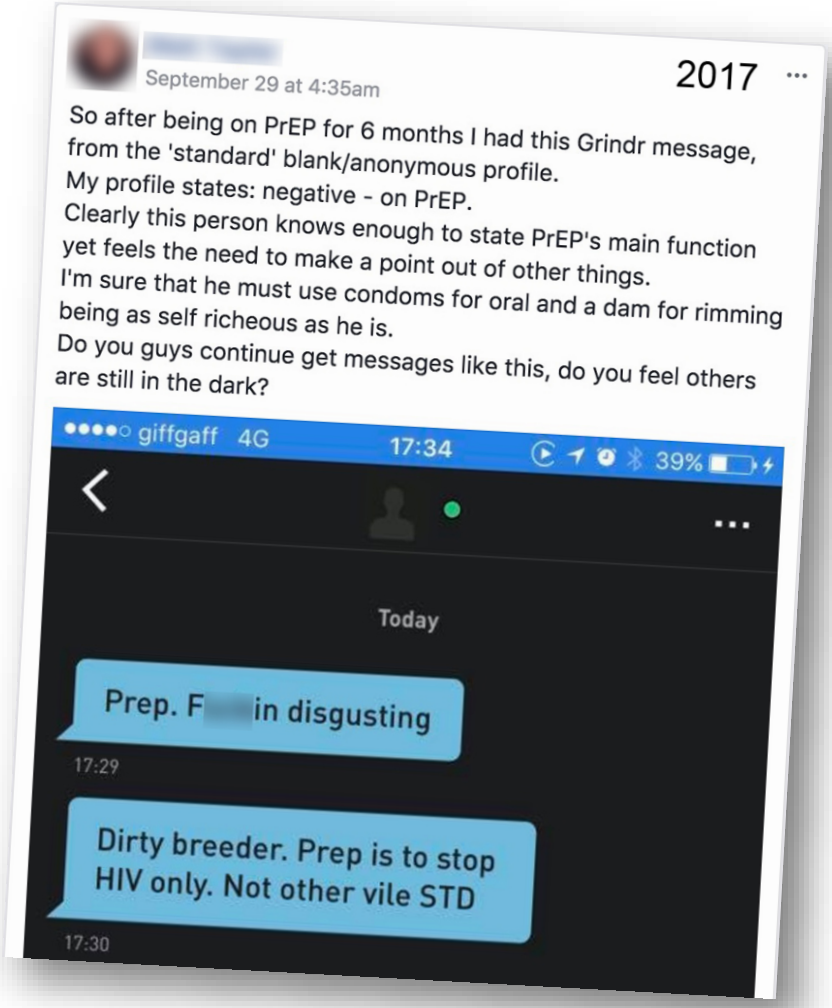
US News and World Report, 1966

Won’t PrEP encourage riskier sex?

Shaming of PrEP users is also real



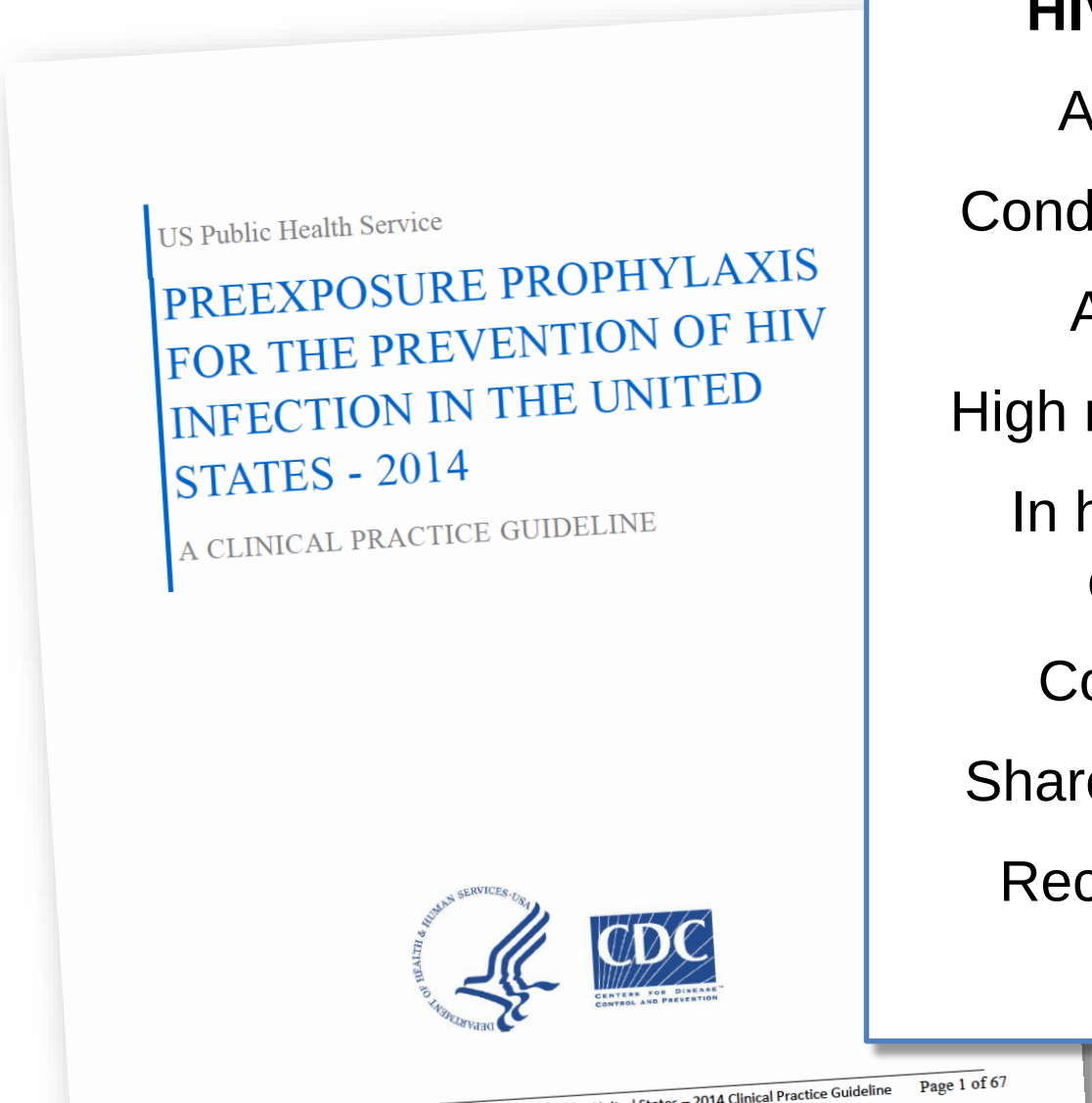
Won’t PrEP encourage riskier sex?

Risk compensation

- Repeatedly examined in multiple trials
  - Indices of risk **stable or reduced**
    - Condomless sex
    - Number of partners
    - Bacterial STIs

Liu AY, et al. *JAIDS*. 2013;64:87-94. Marcus JL, et al. *PLoS ONE*. 2013;8(12):e81997. Guest G, et al. *Sex Transm Dis*. 2008;35(12):1002-8. Baeten JM, et al. *NEJM*. 2012; 367:399-410. Thigpen MC, et al. *NEJM*. 2012;367:423-34. Van Damme L, et al. *NEJM*. 2012;367:411-22.

Who should get PrEP?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States – 2014 Clinical Practice Guideline Page 1 of 67

HIV uninfected, plus:

Any HIV+ partner(s)

Condomless sex in past 6m

Any STI in past 6m

High number of sex partners

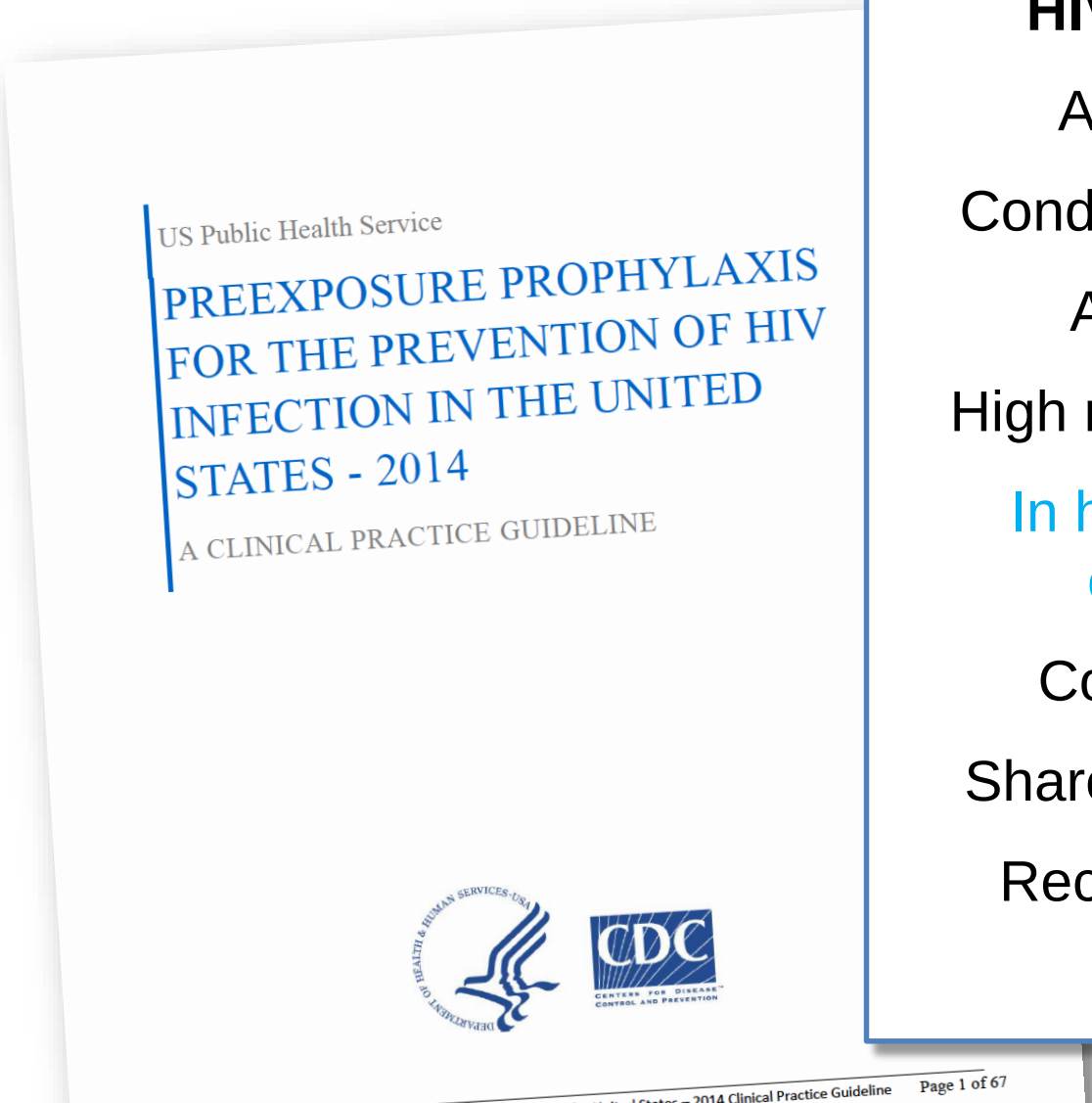
In high-prevalence area or sexual network

Commercial sex work

Shared injection equipment

Recent drug treatment & current relapse

Who should get PrEP?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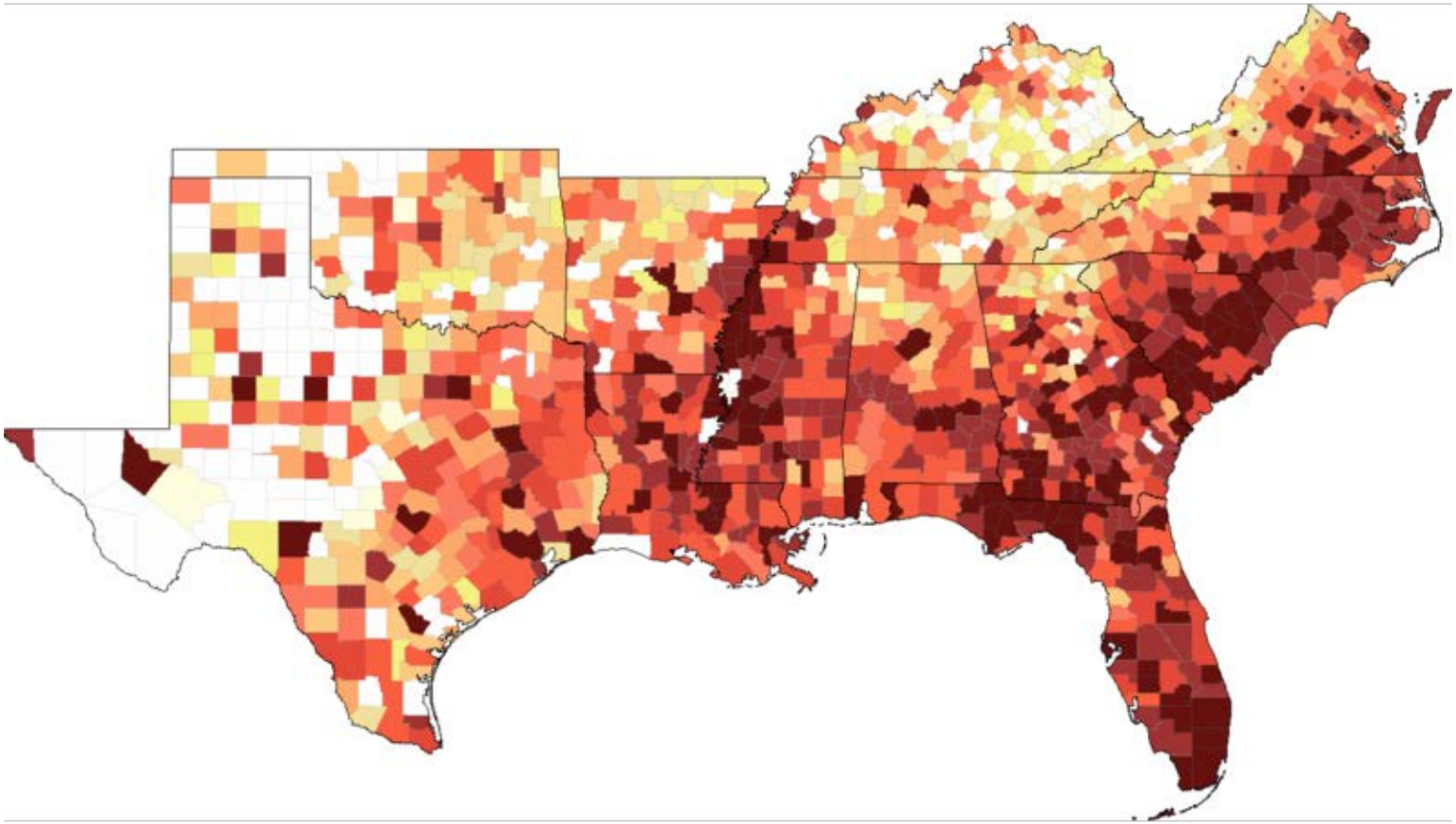
HIV prevalence in the Southeast, 2012

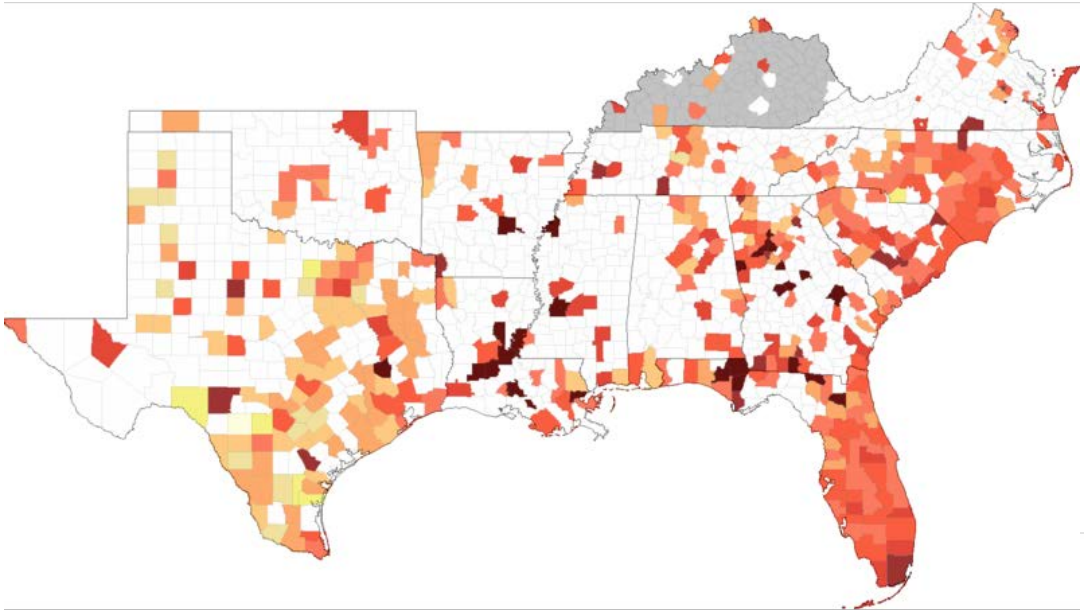


AIDSVu
www.AIDSVu.org

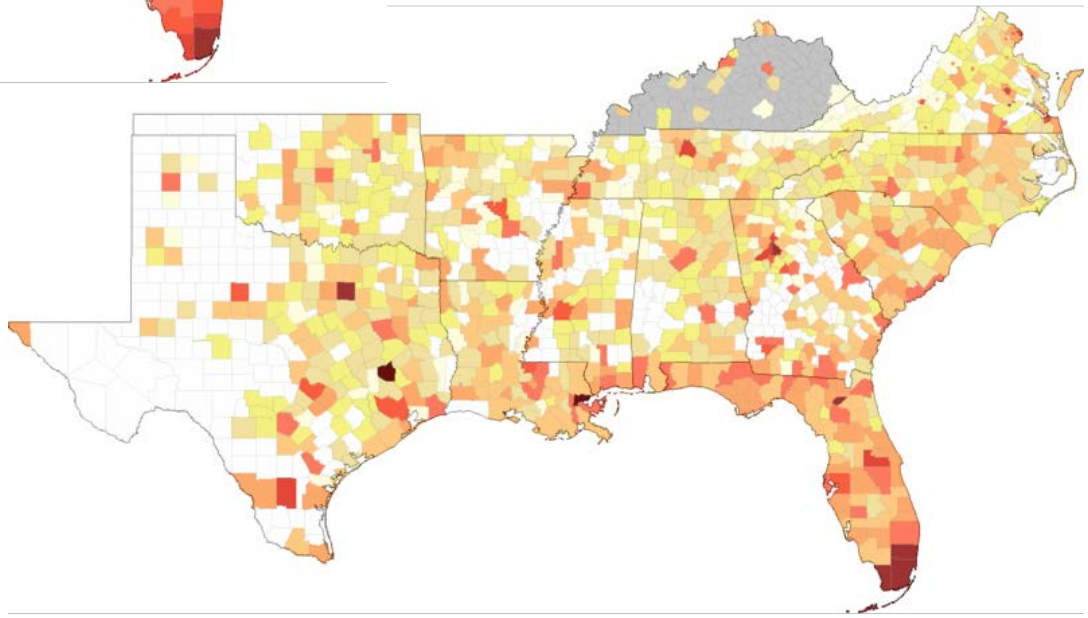
0 - 41	42 - 56	57 - 70	71 - 86	87 - 108	109 - 139	140 - 186	187 - 259	260 - 406	407+

Data not shown *
Data not released to AIDSVu **

Prevalence by race/ethnicity, 2012

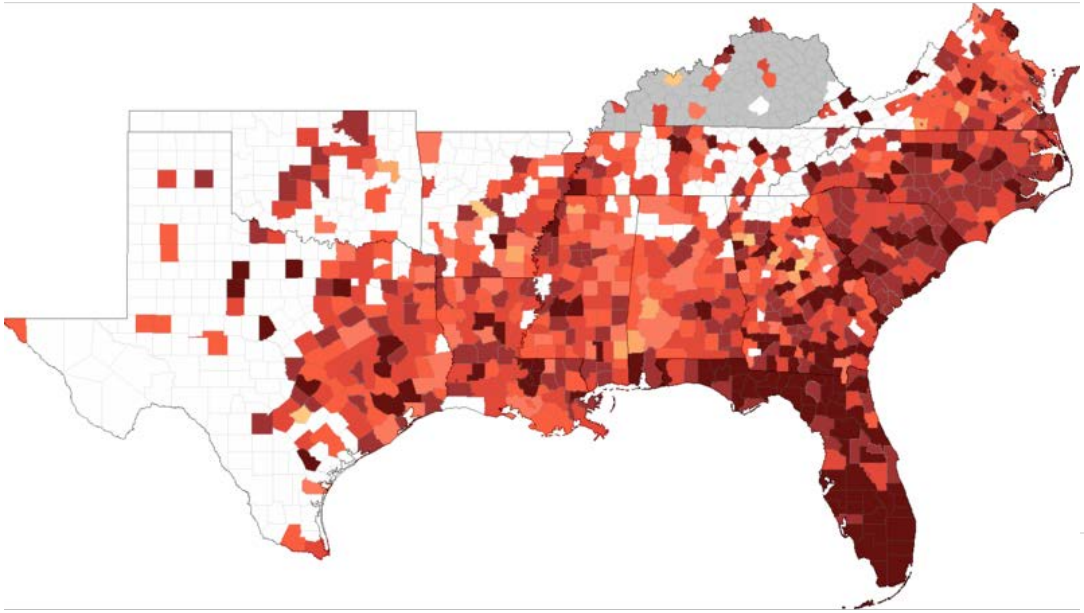


Hispanic/Latino

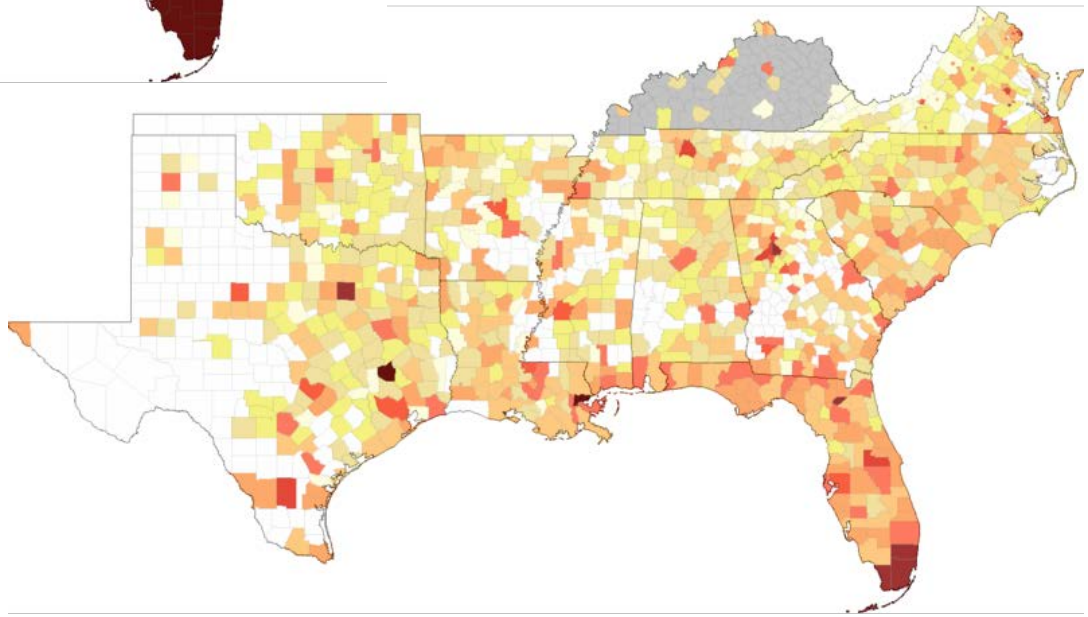


White

Prevalence by race/ethnicity, 2012



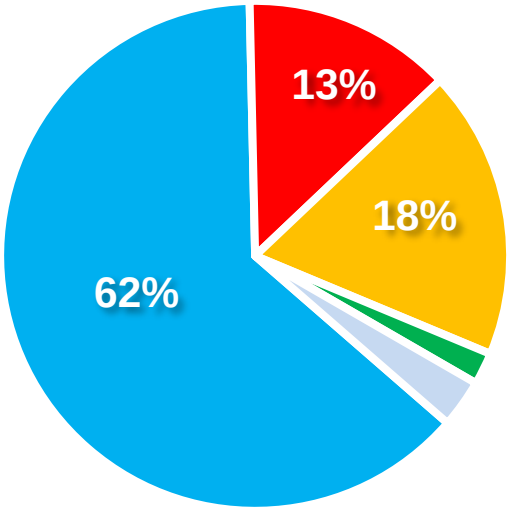
Black



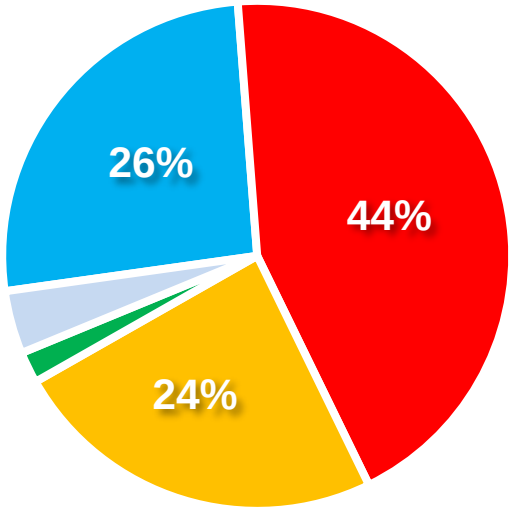
White

PrEP is not reaching those at greatest risk

US Population
2015



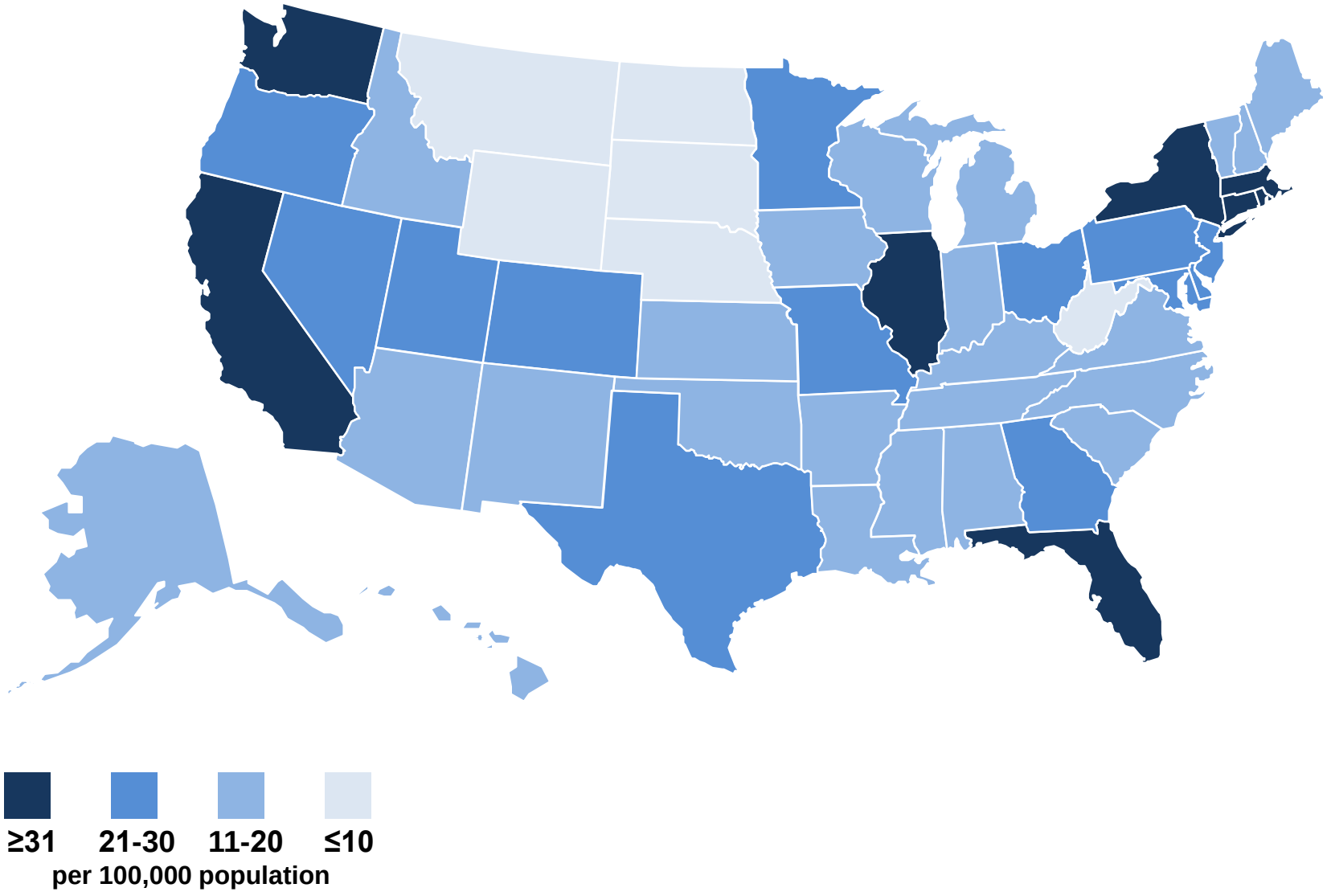
New Infections
2015 (estimated)



Black Hispanic Asian Multi/Other White

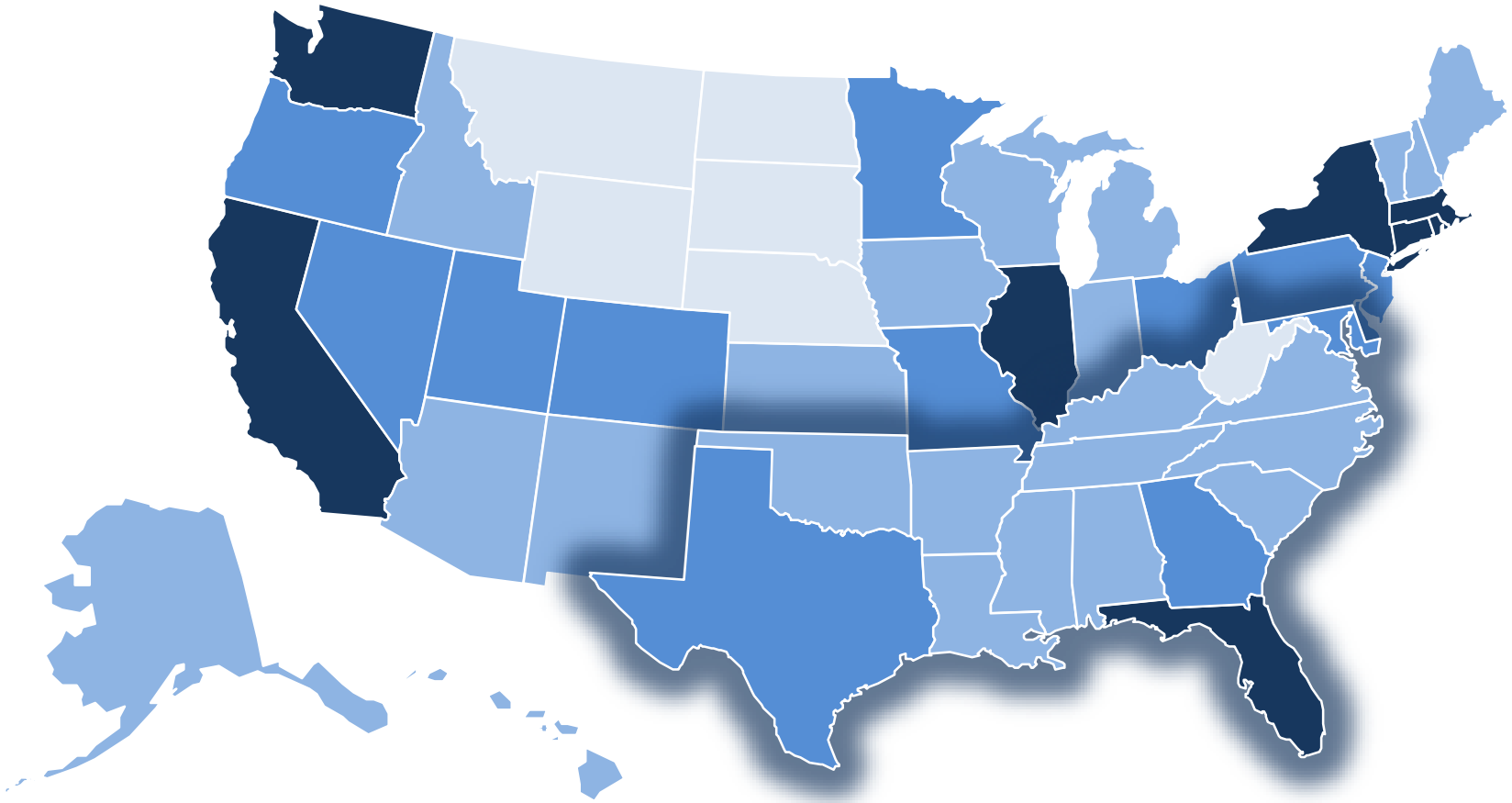
Mera Giler R. et al. IAS Paris 2017, abstract #WEPEC0919
https://www.poz.com/article/estimated-136000-people-prep-us

PrEP users per 100,000 population, 2016



Data from AIDSVu: http://map.aidsvu.org/map?prep=1

PrEP users per 100,000 population, 2016



≥31 21-30 11-20 ≤10

per 100,000 population

More than half of new HIV diagnoses in US in 2016, but only 30% of all PrEP users

Data from AIDSVu: http://map.aidsvu.org/map?prep=1

PrEP is really a matter of social justice

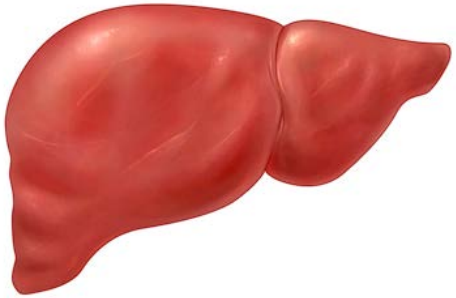


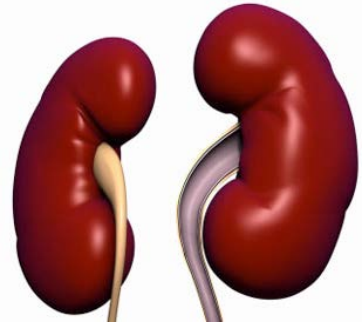


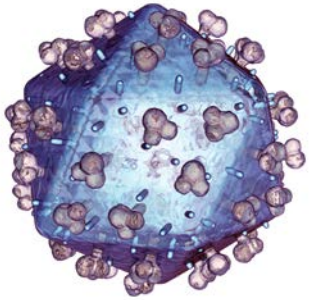

Demetrius, cont’d

- Won over by the compelling evidence
- “What do I have to do to get started?”

Step 1: Determine clinical eligibility







Viral hepatitis

- ❑ **HBsAg**
- ❑ HBsAb
- ❑ HCV Ab

Caution if active HBV

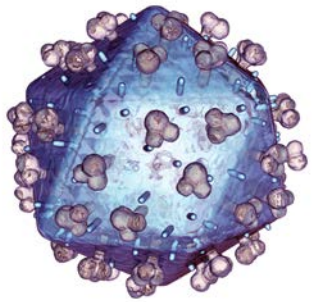
Renal function

- ❑ **Creatinine**
- ❑ eCrCl

eCrCl must be ≥ 60 mL/min

US Public Health Service. PrEP Guideline, 2014

Step 1: Determine clinical eligibility



HIV status **PICK ONE**

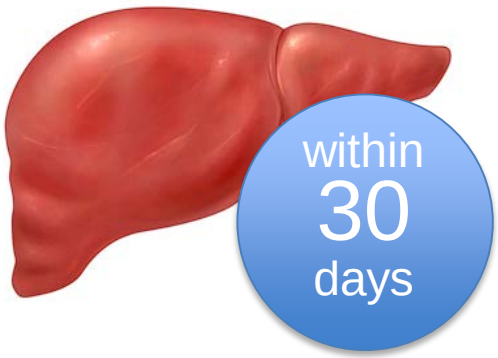
- ❑ **Ag/Ab** **Automated** (over rapid)
- ❑ POC **(on blood)**
- ❑ ELISA / EIA

Must be HIV(–)

→ Maybe RNA, too?

US Public Health Service. PrEP Guideline, 2014

Step 1: Determine clinical eligibility



Viral hepatitis

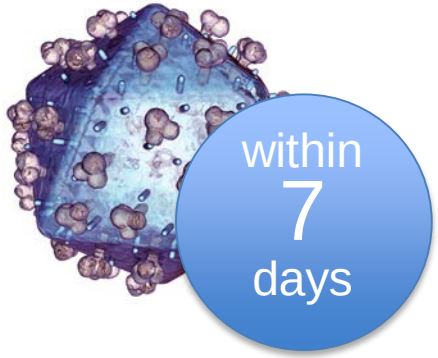
- ❑ **HBsAg**
- ❑ HBsAb
- ❑ HCV Ab

Caution if active HBV

Renal function

- ❑ **Creatinine**
- ❑ eCrCl

eCrCl must be ≥ 60 mL/min



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- ❑ ELISA / EIA

Must be HIV(–)

→ Maybe RNA, too?

US Public Health Service. PrEP Guideline, 2014

Step 1: Determine clinical eligibility

Screen for symptoms of acute HIV

- Must be free of these, within prior **4 weeks**:
  - Fever (75%)
  - Fatigue (68%)
  - Skin rash (48%)
  - Pharyngitis (40%)
  - Cervical adenopathy (39%)
- Suspect acute HIV? **Send HIV RNA (viral load)**

US Public Health Service. PrEP Guideline – 2014.

Step 2: Screen for STIs

If not already done in prior 3-6 months:

- ❑ RPR for syphilis
- ❑ Gonorrhea and chlamydia
  - NAA testing preferred
  - **Extragenital sites too!**

Step 3: Counsel the patient

Adherence strategies

- Pair pill-taking with daily task (even weekends!)
  - Plugging cell phone in before bedtime
- Set an alarm (clock, watch, or phone)
- Use a pill box
- Keep a dose on / near you

US Public Health Service. PrEP Guideline – 2014.

Step 4: Prescribe & follow-up

First Rx: 30-90 days, NO refills

Return to clinic in 30-90 days

- ❑ Adherence?
- ❑ Side effects?
- ❑ Behavior changes?

2nd Rx: 90 days' worth

Step 5: Maintenance & reassessment

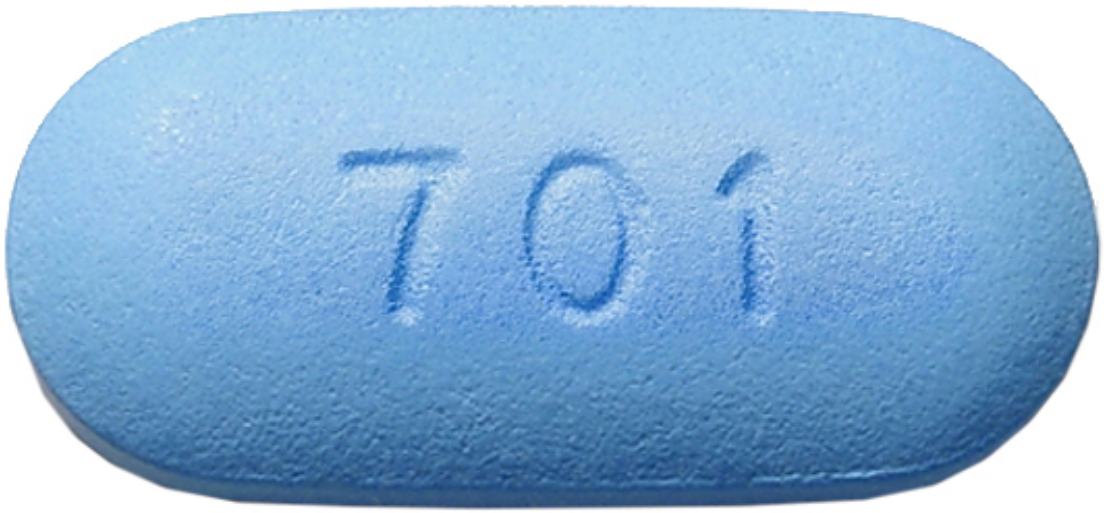
At least every 3 months (i.e., each visit)

- ❑ Assess adherence, side effects, behaviors
- ❑ **Repeat HIV testing ← !!!**
- ❑ Prescription renewal

At least every 6 months, also…

- ❑ Check creatinine and eCrCl
- ❑ Screen for STIs, if not already done
- ❑ Determine need – "**seasons of risk"**

The big picture



PrEP is a **proven**, **well-tolerated**, **highly effective** tool for HIV prevention **when taken every day**.

The New York Times

https://nyti.ms/2jOrEDi

SundayReview | OPINION

My Struggle to Take Anti-H.I.V. Medicine

Xia Gordon

I am a 30-something African-American gay man in New York. H.I.V. is constantly on my mind. Not so much my H.I.V.-negative status. Rather, even though I watched my parents die of AIDS when I was young, I still struggle with whether I should take the drug Truvada, a pre-exposure prophylaxis (PrEP) that can protect almost completely against H.I.V.

Questions?

Please email me!

Christopher Hurt, MD

churt@med.unc.edu

PrEP for Special Populations

Persons Who Inject Drugs, Transgender Persons, and Cisgender Women Trying to Conceive

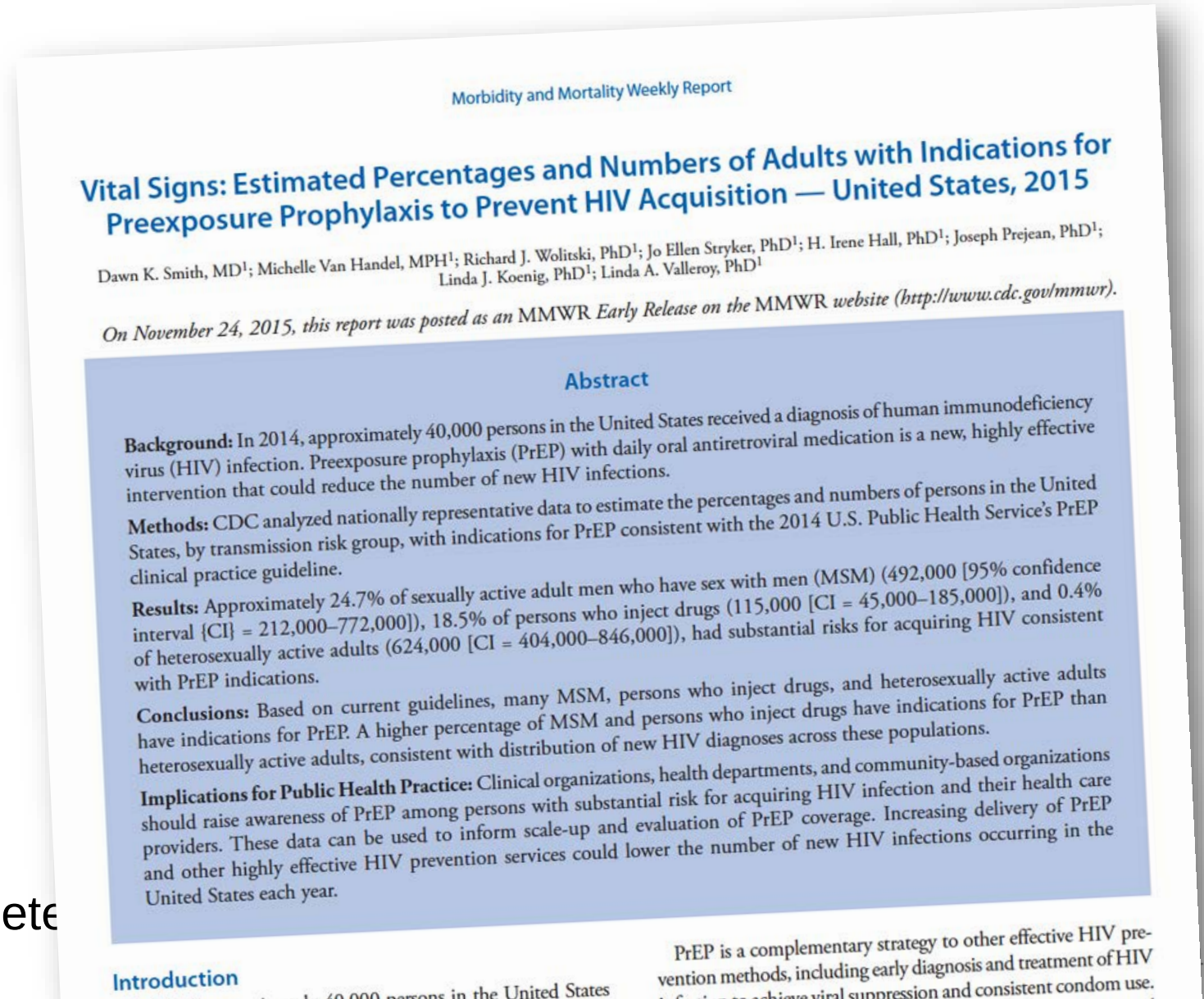
Christopher Hurt, MD

Assistant Professor of Medicine

Division of Infectious Diseases

UNC INSTITUTE FOR GLOBAL HEALTH & INFECTIOUS DISEASES

PrEP is not just for MSM



Morbidity and Mortality Weekly Report

Vital Signs: Estimated Percentages and Numbers of Adults with Indications for Preexposure Prophylaxis to Prevent HIV Acquisition — United States, 2015

Dawn K. Smith, MD[1]; Michelle Van Handel, MPH[1]; Richard J. Wolitski, PhD[1]; Jo Ellen Stryker, PhD[1]; H. Irene Hall, PhD[1]; Joseph Prejean, PhD[1]; Linda J. Koenig, PhD[1]; Linda A. Valleroy, PhD[1]

On November 24, 2015, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

Abstract

Background: In 2014, approximately 40,000 persons in the United States received a diagnosis of human immunodeficiency virus (HIV) infection. Preexposure prophylaxis (PrEP) with daily oral antiretroviral medication is a new, highly effective intervention that could reduce the number of new HIV infections.

Methods: CDC analyzed nationally representative data to estimate the percentages and numbers of persons in the United States, by transmission risk group, with indications for PrEP consistent with the 2014 U.S. Public Health Service's PrEP clinical practice guideline.

Results: Approximately 24.7% of sexually active adult men who have sex with men (MSM) (492,000 [95% confidence interval {CI} = 212,000–772,000]), 18.5% of persons who inject drugs (115,000 [CI = 45,000–185,000]), and 0.4% of heterosexually active adults (624,000 [CI = 404,000–846,000]), had substantial risks for acquiring HIV consistent with PrEP indications.

Conclusions: Based on current guidelines, many MSM, persons who inject drugs, and heterosexually active adults have indications for PrEP. A higher percentage of MSM and persons who inject drugs have indications for PrEP than heterosexually active adults, consistent with distribution of new HIV diagnoses across these populations.

Implications for Public Health Practice: Clinical organizations, health departments, and community-based organizations should raise awareness of PrEP among persons with substantial risk for acquiring HIV infection and their health care providers. These data can be used to inform scale-up and evaluation of PrEP coverage. Increasing delivery of PrEP and other highly effective HIV prevention services could lower the number of new HIV infections occurring in the United States each year.

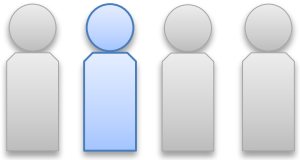
Introduction

PrEP is a complementary strategy to other effective HIV prevention methods, including early diagnosis and treatment of HIV

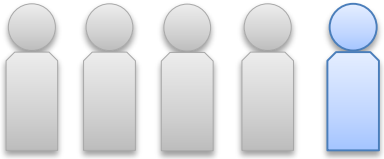
hete

6):1291-1295

PrEP is not just for MSM

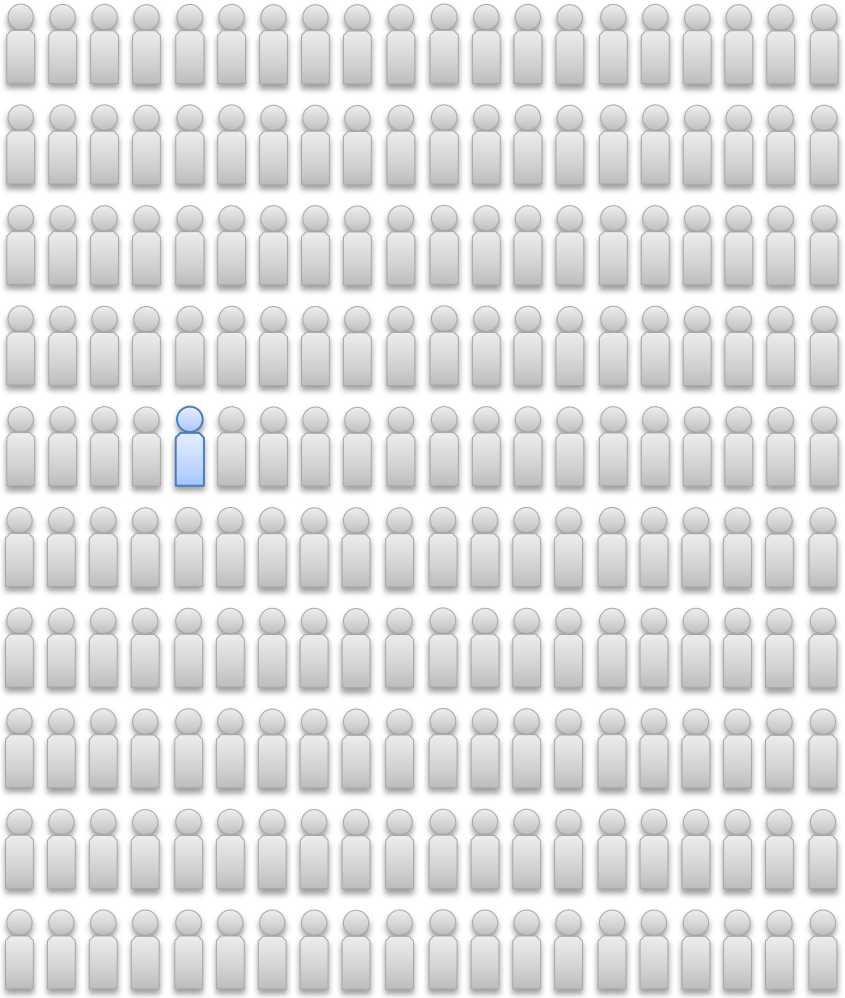


492,000
sexually active MSM



115,000
persons who inject

624,000
heterosexually active adults



Smith DK et al. MMWR 2015 64(46):1291-1295

Bangkok Tenofovir Study

Persons who inject drugs

June 2005 - June 2012 (endpoint reached Nov 2011)

2413
injectors randomized
(9665 P-Y of f/u)

17
infections on TDF
(among 1204)

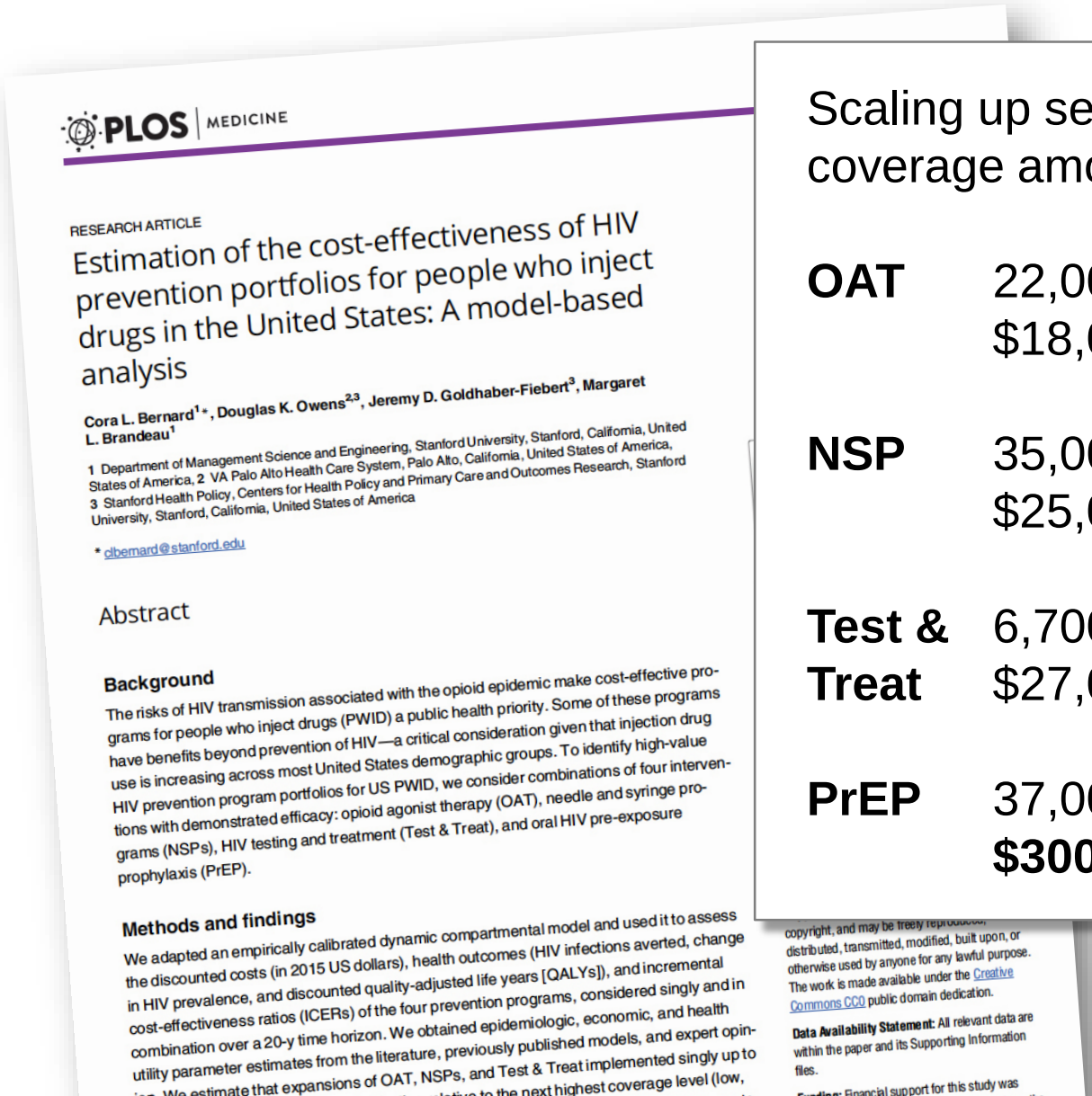
33
infections on placebo
(among 1207)

49%
efficacy mITT
(95% CI: 9.6, 72.2)

83.5%
preventive efficacy among 849 participants with ≥97.5% adherence

Martin M, et al. *AIDS*. 2015 Apr 24; 29(7):819-24

Efficacious, but may be too expensive...



PLOS | MEDICINE

RESEARCH ARTICLE

Estimation of the cost-effectiveness of HIV prevention portfolios for people who inject drugs in the United States: A model-based analysis

Cora L. Bernard[1]*, Douglas K. Owens[2,3], Jeremy D. Goldhaber-Fiebert[3], Margaret L. Brandeau[1]

1 Department of Management Science and Engineering, Stanford University, Stanford, California, United States of America, 2 VA Palo Alto Health Care System, Palo Alto, California, United States of America, 3 Stanford Health Policy, Centers for Health Policy and Primary Care and Outcomes Research, Stanford University, Stanford, California, United States of America

* clbernard@stanford.edu

Abstract

Background

The risks of HIV transmission associated with the opioid epidemic make cost-effective programs for people who inject drugs (PWID) a public health priority. Some of these programs have benefits beyond prevention of HIV—a critical consideration given that injection drug use is increasing across most United States demographic groups. To identify high-value HIV prevention program portfolios for US PWID, we consider combinations of four interventions with demonstrated efficacy: opioid agonist therapy (OAT), needle and syringe programs (NSPs), HIV testing and treatment (Test & Treat), and oral HIV pre-exposure prophylaxis (PrEP).

Methods and findings

We adapted an empirically calibrated dynamic compartmental model and used it to assess the discounted costs (in 2015 US dollars), health outcomes (HIV infections averted, change in HIV prevalence, and discounted quality-adjusted life years [QALYs]), and incremental cost-effectiveness ratios (ICERs) of the four prevention programs, considered singly and in combination over a 20-y time horizon. We obtained epidemiologic, economic, and health utility parameter estimates from the literature, previously published models, and expert opinion. We estimate that expansions of OAT, NSPs, and Test & Treat implemented singly up to

Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: Financial support for this study was

Scaling up services to 50% coverage among US PWID…

OAT	22,000 infections averted $18,000 / QALY
NSP	35,000 infections averted $25,000 / QALY
Test & Treat	6,700 infections averted $27,000 / QALY
PrEP	37,000 infections averted **$300,000 / QALY**

Bernard CL, et al. *PLoS Med*. 2017 May 27;14(5):e1002312

FTC/TDF among transgender persons

No interactions[1] with:

- Estradiol
- Progestins
- Spironolactone

No predicted interaction with testosterone[2]

Effectively <u>no data</u> on TGM[3]

- HIV risk for TGM affected by:
  - Vaginal thinning/atrophy
  - Loss of self-lubrication

1 Anderson PL, et al. *JAIDS*. 2016 Aug 15; 72 Suppl 3:S230-4.
2 https://hiv-druginteractions.org/interactions/77395
3 http://www.aidsmap.com/Trans-men-and-PrEP/page/3016709/

CDC acknowledges PrEP in conception planning

Morbidity and Mortality Weekly Report

Strategies for Preventing HIV Infection Among HIV-Uninfected Women Attempting Conception with HIV-Infected Men — United States

Jennifer F. Kawwass, MD[1,2]; Dawn K. Smith, MD[3]; Dmitry M. Kissin, MD[1,2]; Lisa B. Haddad, MD[1,2]; Sheree L. Boulet, DrPH[1]; Saswati Sunderam, PhD[1]; Denise J. Jamieson, MD[1,2]

By the end of 2014, a total of 955,081 persons in the United States (299.5 per 100,000 population) had received a diagnosis of human immunodeficiency virus type 1 (HIV-1) infection (*1*). The annual estimated number of HIV infections and incidence rate in the United States decreased from 2010 to 2014, and the survival rate has increased over time (*1*). Effective highly active antiretroviral therapy (HAART) is helping persons with HIV to live longer, healthier lives. Many of these persons, including an unknown percentage in discordant relationships (i.e., one partner is HIV-infected, and the other is HIV-uninfected), might wish to have their own biologic children. When the female partner is HIV-infected and the male partner is not, a discordant couple can undergo autologous sperm intrauterine inseminations to achieve conception without placing the man at risk for infection. However, for HIV-discordant couples in which the man is HIV-infected and the woman is not, strategies to minimize the risk for sexual transmission are needed. In 1988, CDC recommended against insemination with semen from HIV-infected men (*2*). Since 1988, new information has emerged regarding prevention of HIV transmission in HIV-discordant couples. This report reviews laboratory and epidemiologic information regarding the prevention of HIV transmission for HIV-discordant couples, in which the male is HIV-infected and the female is HIV-uninfected, who would like to attempt conception.

Insemination with sperm from an HIV-negative donor is the safest option for an HIV-uninfected woman to conceive with an HIV-infected male partner. However, risk-reducing approaches using sperm from an HIV-infected male partner do exist. One strategy is the use of viral suppression with HAART for the male partner, with intercourse without condom protection limited to the time around ovulation, while the female partner is taking daily oral antiretroviral preexposure prophylaxis (PrEP) (*3*). Another strategy that can be used in conjunction with HAART and PrEP is collection and washing of the male partner's sperm to remove cells infected with HIV, [illegible] to confirm the absence of HIV prior to

provider who can relay the risks and benefits of each t
modality as it applies to the couple's specific situatio

Background

The American College of Obstetricians and Gyn
the American Society of Reproductive Medicine,
ers have published guidance documents that emp
importance of considering HIV a chronic disease o
which should not result in discrimination and for w
ity treatment should be offered if it is desired (*5,6*
treatments that require the assistance of a physicia
limited by financial and legal barriers. These barr
state laws that preclude the use of HIV-positiv
fear of liability if seroconversion occurs, physicia
to treat discordant couples, and concerns based
publications, including those from CDC, that wa
use of sperm from HIV-infected men for insemina
Whereas HIV-infected men who are currently u
of a physician are likely already receiving HAAR
partners might or might not be using PrEP.

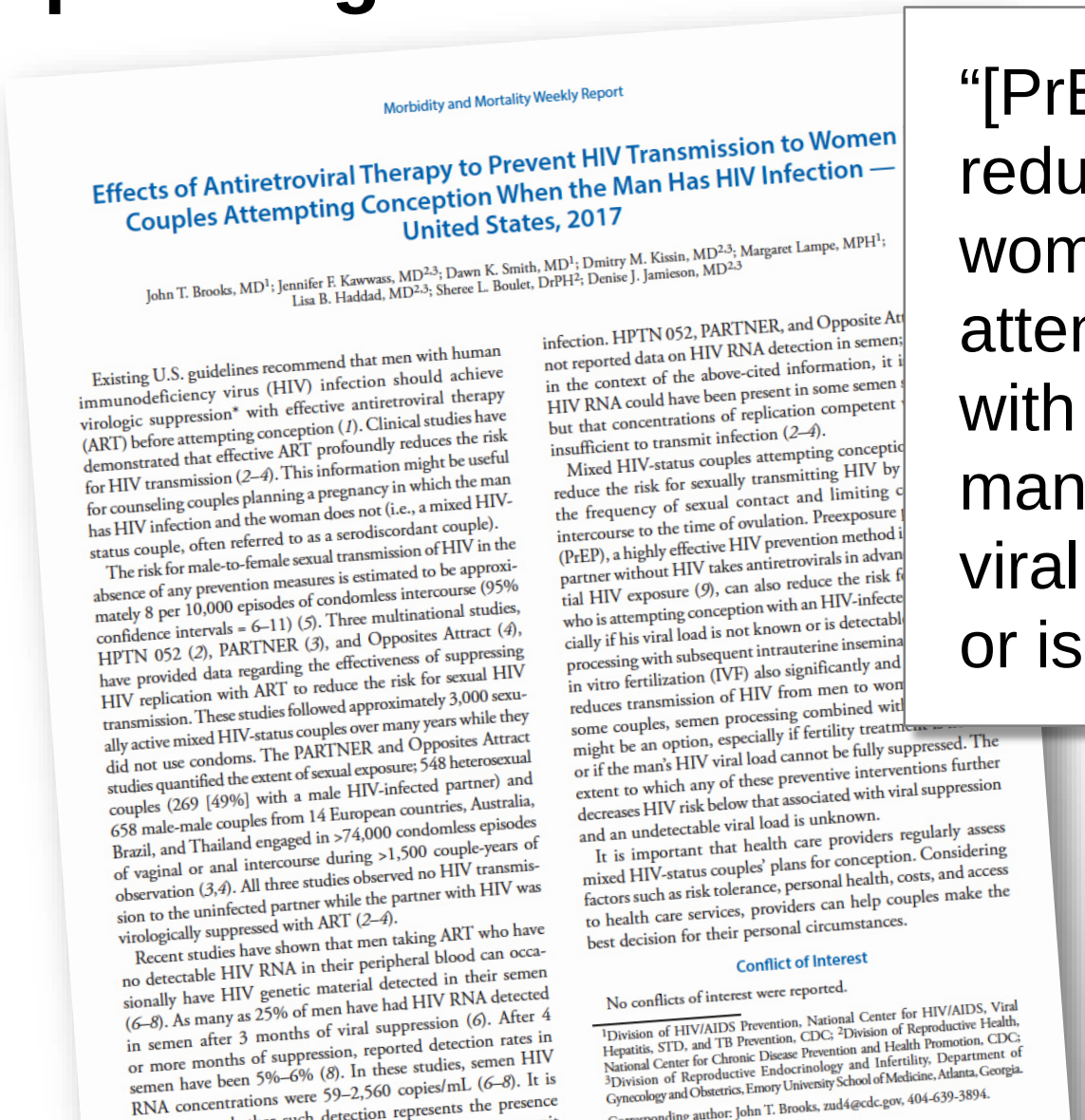
Rationale and Evidence

For HIV-discordant couples (HIV-infected male and HIV-uninfected female) who want to conceive, considerations in choosing the optimal method to achieve pregnancy include transmission risk, treatment efficacy, and affordability. Use of HIV-negative donor sperm that meets Food and Drug Administration donor eligibility criteria remains the safest option for avoiding HIV infection of the female partner (*2,8*). Recent evidence suggests that discordant couples who wish to have their own biologic children might consider using condomless intercourse timed to coincide with ovulation, or IUI or IVF in combination with sperm washing (*4*). Avoidance of HIV transmission is optimized when the male partner is virologically suppressed on HAART and the female partner is on PrEP (*3*). Further considerations apply when the couple has infertility issues. Many men with HIV infection have altered semen parameters that make insemination or IVF the optimal form [illegible] infertility factors

"One strategy is… viral suppression… for the male partner, with intercourse… around ovulation, while the female partner is taking… PrEP."

Kawwass JF, et al. *MMWR*. 2 June 2017;66(21):554-7

CDC acknowledges PrEP in conception planning



Morbidity and Mortality Weekly Report

Effects of Antiretroviral Therapy to Prevent HIV Transmission to Women Couples Attempting Conception When the Man Has HIV Infection — United States, 2017

John T. Brooks, MD[1]; Jennifer F. Kawwass, MD[2,3]; Dawn K. Smith, MD[1]; Dmitry M. Kissin, MD[2,3]; Margaret Lampe, MPH[1]; Lisa B. Haddad, MD[2,3]; Sheree L. Boulet, DrPH[2]; Denise J. Jamieson, MD[2,3]

Existing U.S. guidelines recommend that men with human immunodeficiency virus (HIV) infection should achieve virologic suppression* with effective antiretroviral therapy (ART) before attempting conception (*1*). Clinical studies have demonstrated that effective ART profoundly reduces the risk for HIV transmission (*2–4*). This information might be useful for counseling couples planning a pregnancy in which the man has HIV infection and the woman does not (i.e., a mixed HIV-status couple, often referred to as a serodiscordant couple).

The risk for male-to-female sexual transmission of HIV in the absence of any prevention measures is estimated to be approximately 8 per 10,000 episodes of condomless intercourse (95% confidence intervals = 6–11) (*5*). Three multinational studies, HPTN 052 (*2*), PARTNER (*3*), and Opposites Attract (*4*), have provided data regarding the effectiveness of suppressing HIV replication with ART to reduce the risk for sexual HIV transmission. These studies followed approximately 3,000 sexually active mixed HIV-status couples over many years while they did not use condoms. The PARTNER and Opposites Attract studies quantified the extent of sexual exposure; 548 heterosexual couples (269 [49%] with a male HIV-infected partner) and 658 male-male couples from 14 European countries, Australia, Brazil, and Thailand engaged in >74,000 condomless episodes of vaginal or anal intercourse during >1,500 couple-years of observation (*3,4*). All three studies observed no HIV transmission to the uninfected partner while the partner with HIV was virologically suppressed with ART (*2–4*).

Recent studies have shown that men taking ART who have no detectable HIV RNA in their peripheral blood can occasionally have HIV genetic material detected in their semen (*6–8*). As many as 25% of men have had HIV RNA detected in semen after 3 months of viral suppression (*6*). After 4 or more months of suppression, reported detection rates in semen have been 5%–6% (*8*). In these studies, semen HIV RNA concentrations were 59–2,560 copies/mL (*6–8*). It is

infection. HPTN 052, PARTNER, and Opposite At
not reported data on HIV RNA detection in semen;
in the context of the above-cited information, it i
HIV RNA could have been present in some semen
but that concentrations of replication competent
insufficient to transmit infection (*2–4*).

Mixed HIV-status couples attempting conceptio
reduce the risk for sexually transmitting HIV by
the frequency of sexual contact and limiting c
intercourse to the time of ovulation. Preexposure
(PrEP), a highly effective HIV prevention method i
partner without HIV takes antiretrovirals in advan
tial HIV exposure (*9*), can also reduce the risk f
who is attempting conception with an HIV-infecte
cially if his viral load is not known or is detectabl
processing with subsequent intrauterine insemina
in vitro fertilization (IVF) also significantly and
reduces transmission of HIV from men to won
some couples, semen processing combined wit
might be an option, especially if fertility treatm
or if the man's HIV viral load cannot be fully suppressed. The extent to which any of these preventive interventions further decreases HIV risk below that associated with viral suppression and an undetectable viral load is unknown.

It is important that health care providers regularly assess mixed HIV-status couples' plans for conception. Considering factors such as risk tolerance, personal health, costs, and access to health care services, providers can help couples make the best decision for their personal circumstances.

Conflict of Interest

No conflicts of interest were reported.

[1]Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; [2]Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; [3]Division of Reproductive Endocrinology and Infertility, Department of Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, Georgia.
Corresponding author: John T. Brooks, zud4@cdc.gov, 404-639-3894.

"[PrEP]… can also reduce the risk for a woman who is attempting conception with an HIV-infected man, especially if his viral load is not known or is detectable."

Brooks JT, et al. *MMWR*. 18 Aug 2017;66(32):859-60

Safety of FTC/TDF in pregnancy is clear

FTC/TDF is category B[1]

No evidence of birth defects among babies born to mothers taking TDF for HIV[1]

No data suggesting PrEP is unsafe in pregnancy or lactation[2]

1 Wang L, et al. *Clin Infect Dis*. 2013 Dec;57(12):1773-81
2 Mofenson LM, et al. *AIDS*. 2017 Jan 14;31(2):213-232

Efficacy of PrEP in pregnancy is unknown

Risk of HIV acquisition higher during pregnancy & post-partum[1]

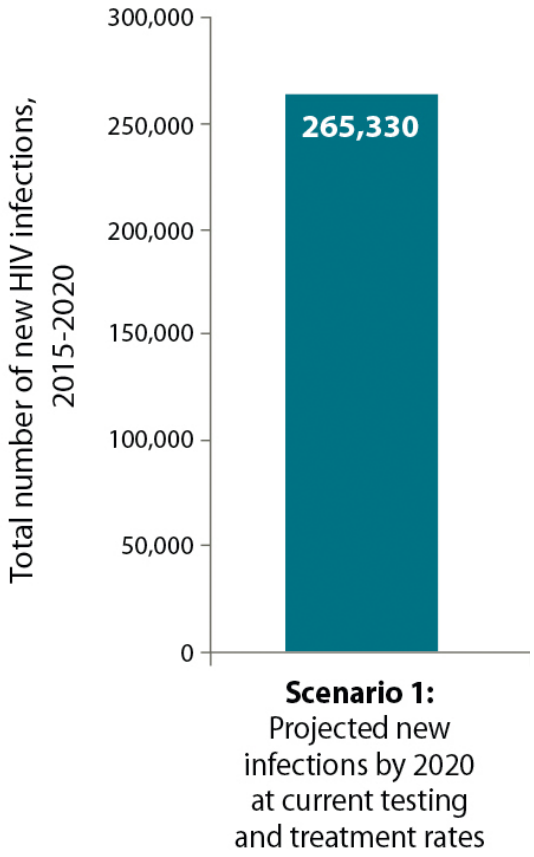
Women who became pregnant in PrEP trials stopped FTC/TDF[2]

CDC/USPHS 2014 [3]

- Ensure male partner undetectable
- Begin PrEP 1 month before, continue for 1 month after conception attempt

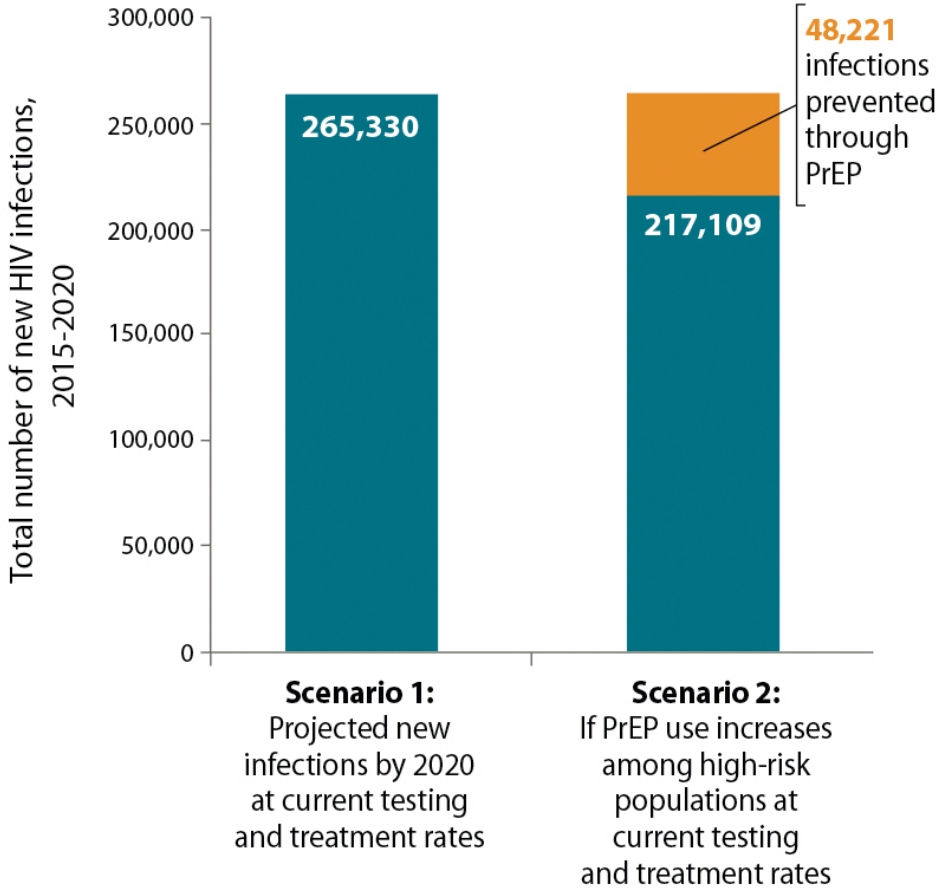
1 Thomson KA, et al. *J Infect Dis*. 2018 Mar 5. [ePub ahead of print]
2 Mofenson LM. *PLoS Med*. Sep 2016;13(9):e1002133
3 CDC/USPHS 2014 PrEP Guideline – **Clinical Providers' Supplement**

Potential impact of interventions, 2015-2020



Yaylali E et al. CROI 2016, abstract #1051
Graphic from CDC

Potential impact of interventions, 2015-2020



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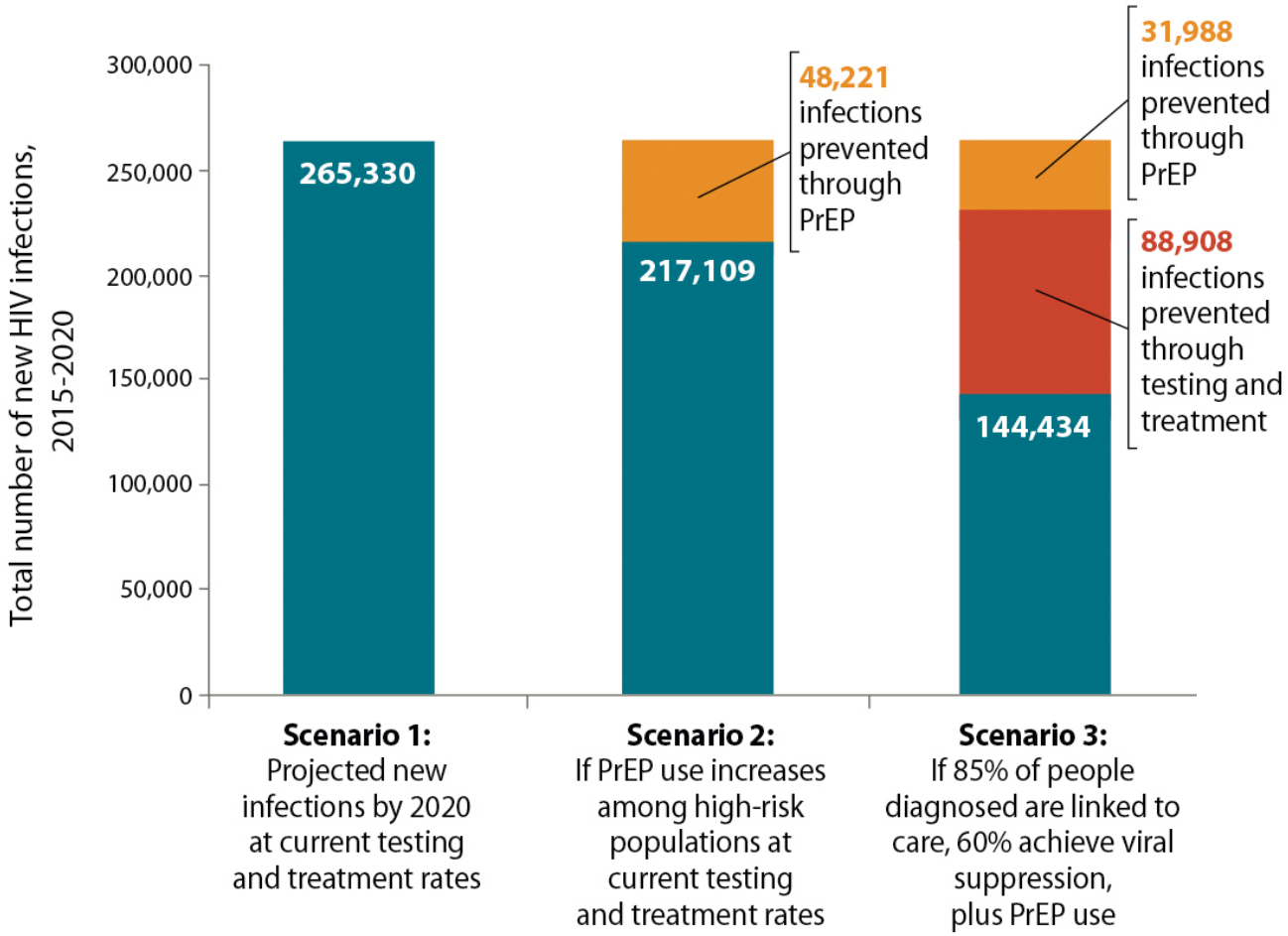
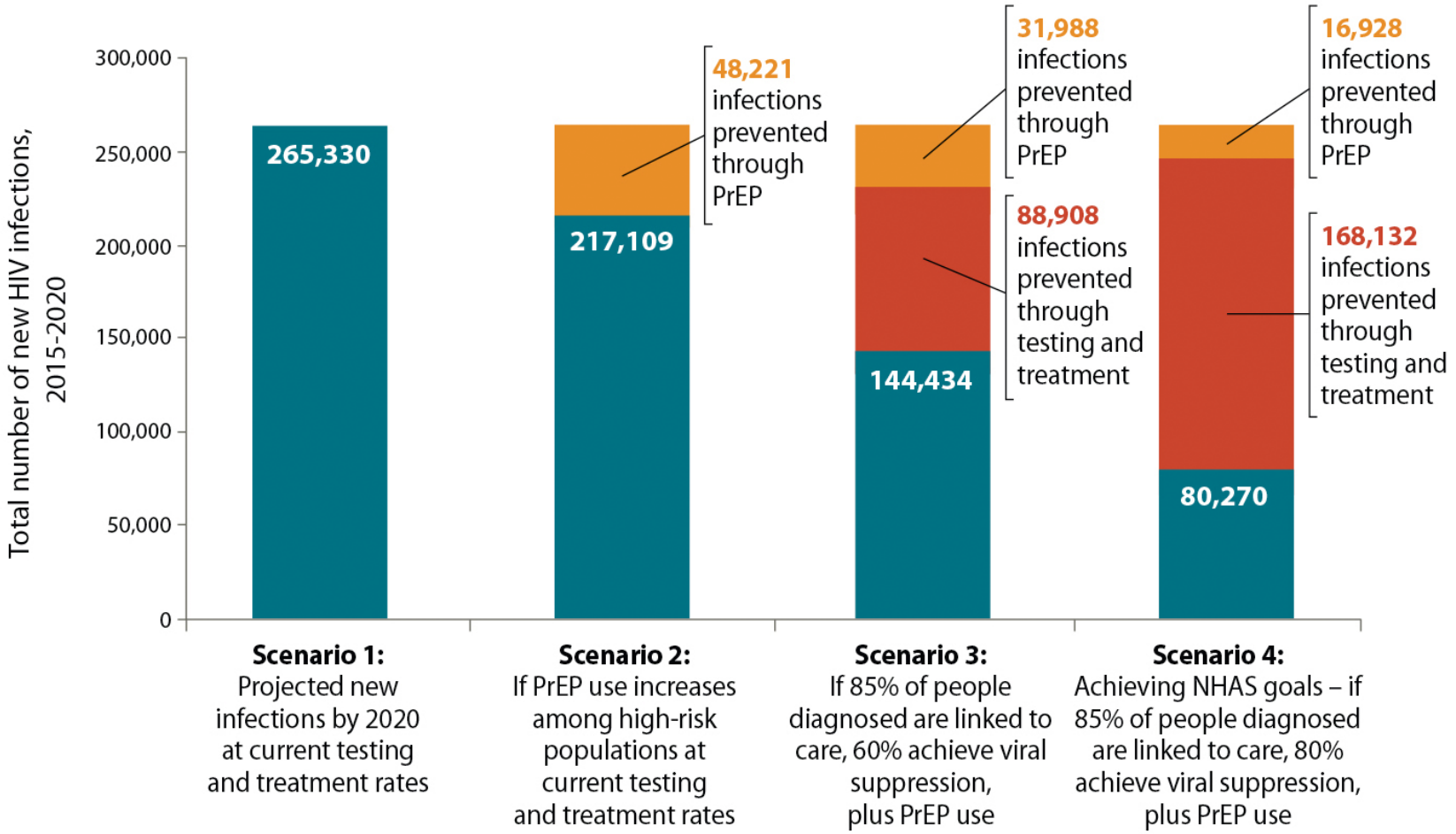
Graphic from CDC

Potential impact of interventions, 2015-2020

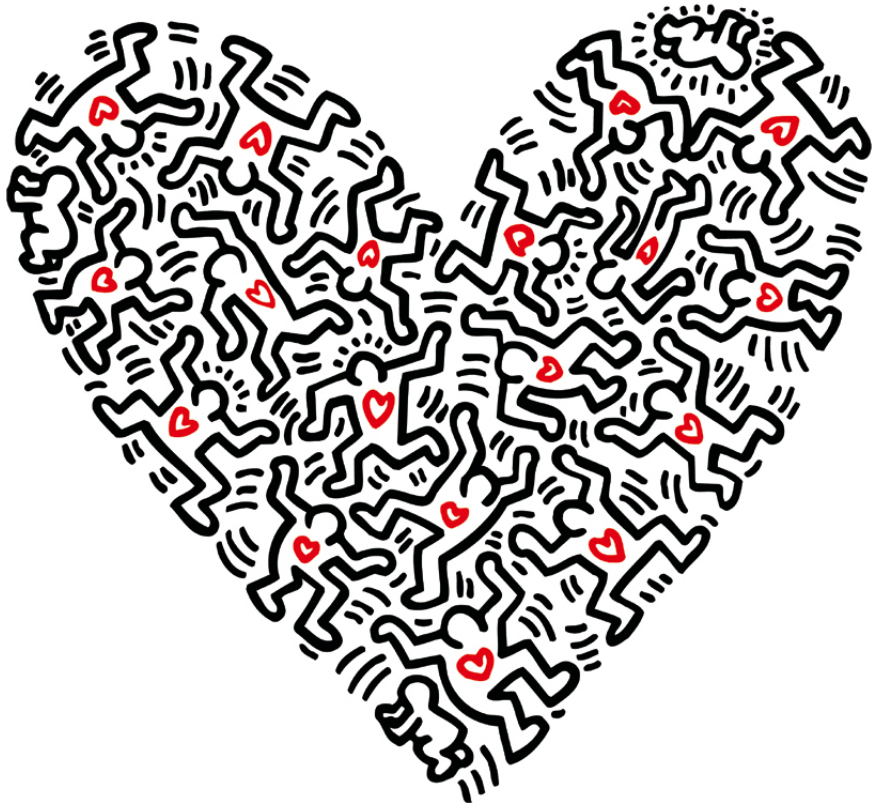


Yaylali E et al. CROI 2016, abstract #1051
Graphic from CDC

Potential impact of interventions, 2015-2020



Yaylali E et al. CROI 2016, abstract #1051
Graphic from CDC



Questions?

Please email me!

Christopher Hurt, MD

churt@med.unc.edu

EXTRA SLIDES

Post-exposure prophylaxis (PEP)

Key points

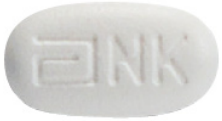
- Two classifications:
  - Occupational (sometimes “oPEP”)
  - Nonoccupational (“nPEP”)
- Effective if given within 72h (**earlier = better**)
- Historically, 28d of: Combivir **2 NRTIs** + Kaletra **PI**
  - Suboptimal completion rates due to side effects
- 2013 – CDC oPEP guidelines updated

Post-exposure prophylaxis (nPEP)

As of 2016, recommended regimen is **28 days** of:

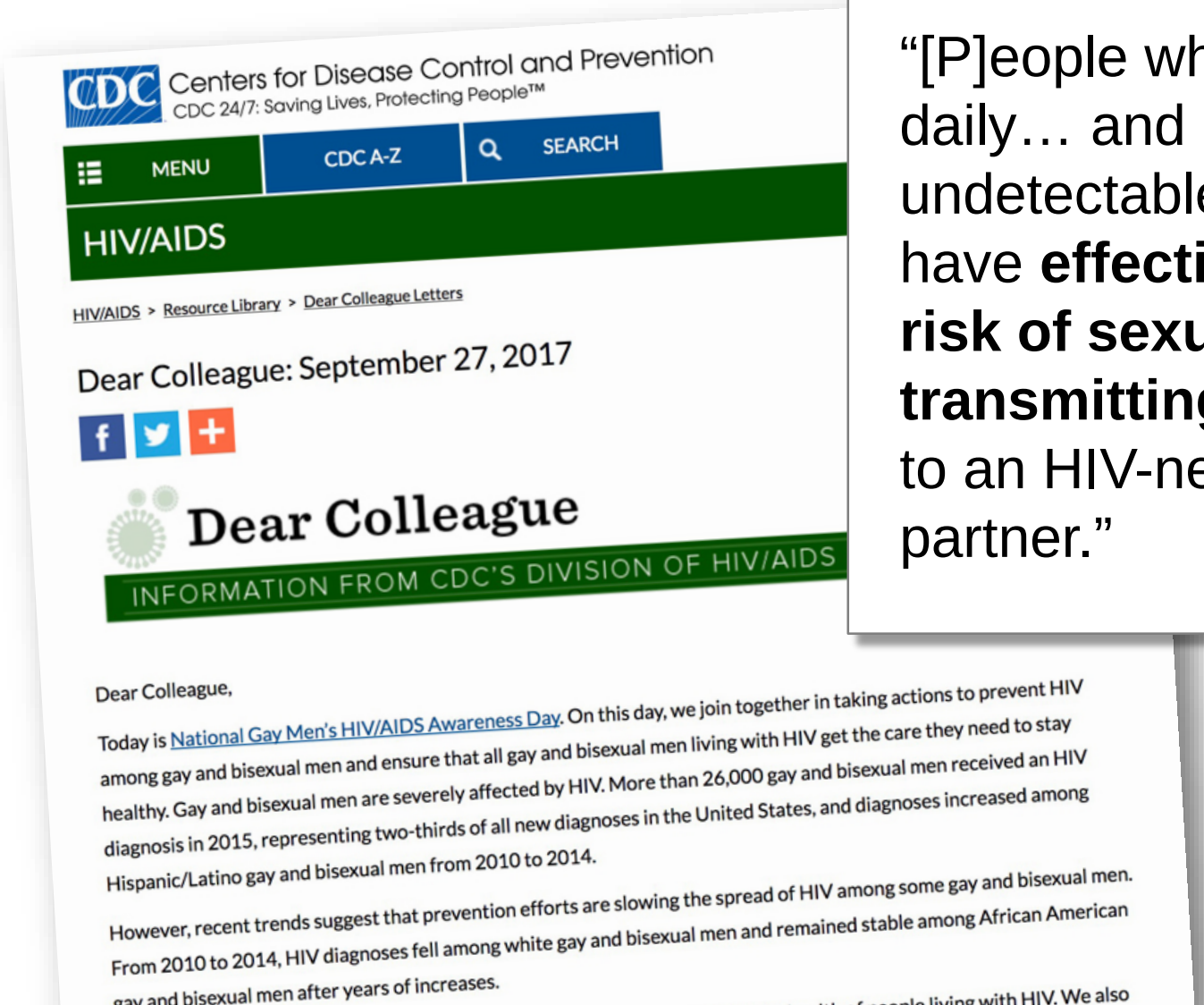
emtricitabine/tenofovir DF [2 NRTIs] QD
Truvada (Gilead)

plus ONE from either column

Preferred	Alternative
 **raltegravir** [INI] BID Isentress (Merck)	 **darunavir** [PI] QD Prezista (Janssen) **BOOSTED WITH**
 **dolutegravir** [INI] QD Tivicay (ViiV)	 **ritonavir** [PKE] QD Norvir (AbbVie)

Dominguez KL, et al. CDC nPEP Guidelines 2016. https://stacks.cdc.gov/view/cdc/38856

CDC is on board with “U=U”



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

MENU | CDC A-Z | SEARCH

HIV/AIDS

HIV/AIDS > Resource Library > Dear Colleague Letters

Dear Colleague: September 27, 2017

Dear Colleague

INFORMATION FROM CDC'S DIVISION OF HIV/AIDS

Dear Colleague,

Today is National Gay Men's HIV/AIDS Awareness Day. On this day, we join together in taking actions to prevent HIV among gay and bisexual men and ensure that all gay and bisexual men living with HIV get the care they need to stay healthy. Gay and bisexual men are severely affected by HIV. More than 26,000 gay and bisexual men received an HIV diagnosis in 2015, representing two-thirds of all new diagnoses in the United States, and diagnoses increased among Hispanic/Latino gay and bisexual men from 2010 to 2014.

However, recent trends suggest that prevention efforts are slowing the spread of HIV among some gay and bisexual men. From 2010 to 2014, HIV diagnoses fell among white gay and bisexual men and remained stable among African American gay and bisexual men after years of increases.

“[P]eople who take ART daily… and maintain an undetectable viral load have **effectively no risk of sexually transmitting the virus** to an HIV-negative partner.”

https://www.cdc.gov/hiv/library/dcl/dcl/092717.html