

# PrEP for HIV Prevention: what you need to know

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Disclosures:

Spouse is stockholder in Gilead Sciences, Inc.

# Objectives

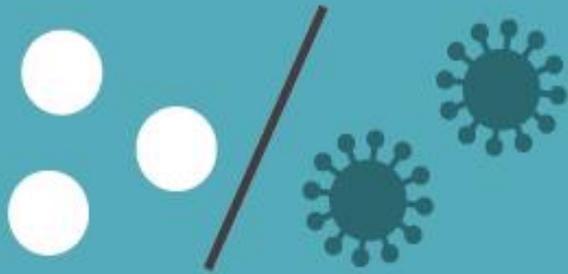
1. Describe the evidence supporting PrEP to prevent HIV infection
2. Summarize the CDC clinical guidelines for PrEP
3. Identify strategies for integrating PrEP into clinical care

# PrEP 101: What is PrEP?

# PrEP Basics

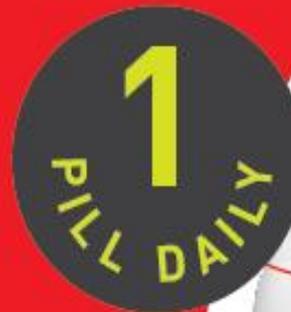
PrEP stands for  
**Pre-Exposure Prophylaxis**

The word “prophylaxis” means to prevent or control the spread of an infection or disease



PrEP can help prevent you from getting HIV if you are exposed to the virus

PrEP is an HIV prevention option that works by taking  
**one pill every day**



**P**

**E**

**P**



PEP involves taking anti-HIV drugs as soon as possible after having been exposed.



To be effective, PEP must begin within 72 hours of exposure, before the virus has time to rapidly replicate in your body.



PEP consists of 2-3 antiretroviral medications taken for 28 days.

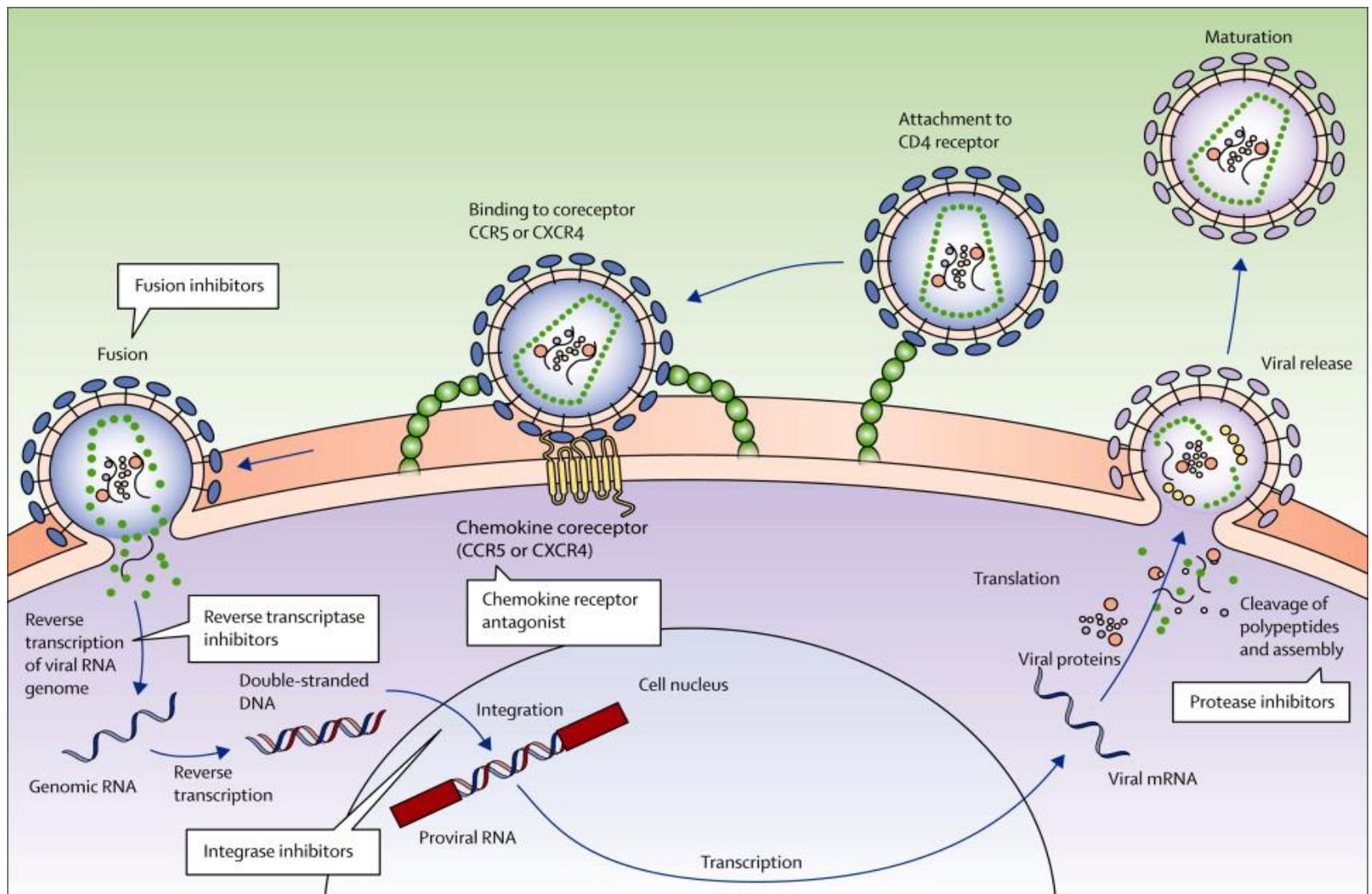


Figure 2. HIV life cycle showing the sites of action of different classes of antiretroviral drugs  
Adapted from Walker and colleagues,36 by permission of Elsevier.

Maartens, et al., *Lancet* 2014.

Why we need PrEP

## Estimated Incidence of HIV Infection, Overall, and by Sex, 2007-2010 — United States

	2007	2008	2009	2010
	No. (95% CI) <sup>a</sup>	No. (95% CI)	No. (95% CI)	No. (95% CI)
<b>Male</b>	<b>39,600</b> (34,900–44,300)	<b>35,500</b> (31,300–39,700)	<b>34,400</b> (30,300–38,400)	<b>38,000</b> (33,400–42,600)
<b>Female</b>	<b>13,600</b> (11,500–15,600)	<b>12,000</b> (10,100–13,900)	<b>10,600</b> 9,000–12,300	<b>9,500*</b> (8,100–10,900)
<b>Total</b>	<b>53,200</b> (47,000–59,400)	<b>47,500</b> (42,000–53,000)	<b>45,000</b> (39,900–50,100)	<b>47,500</b> (42,000–53,000)

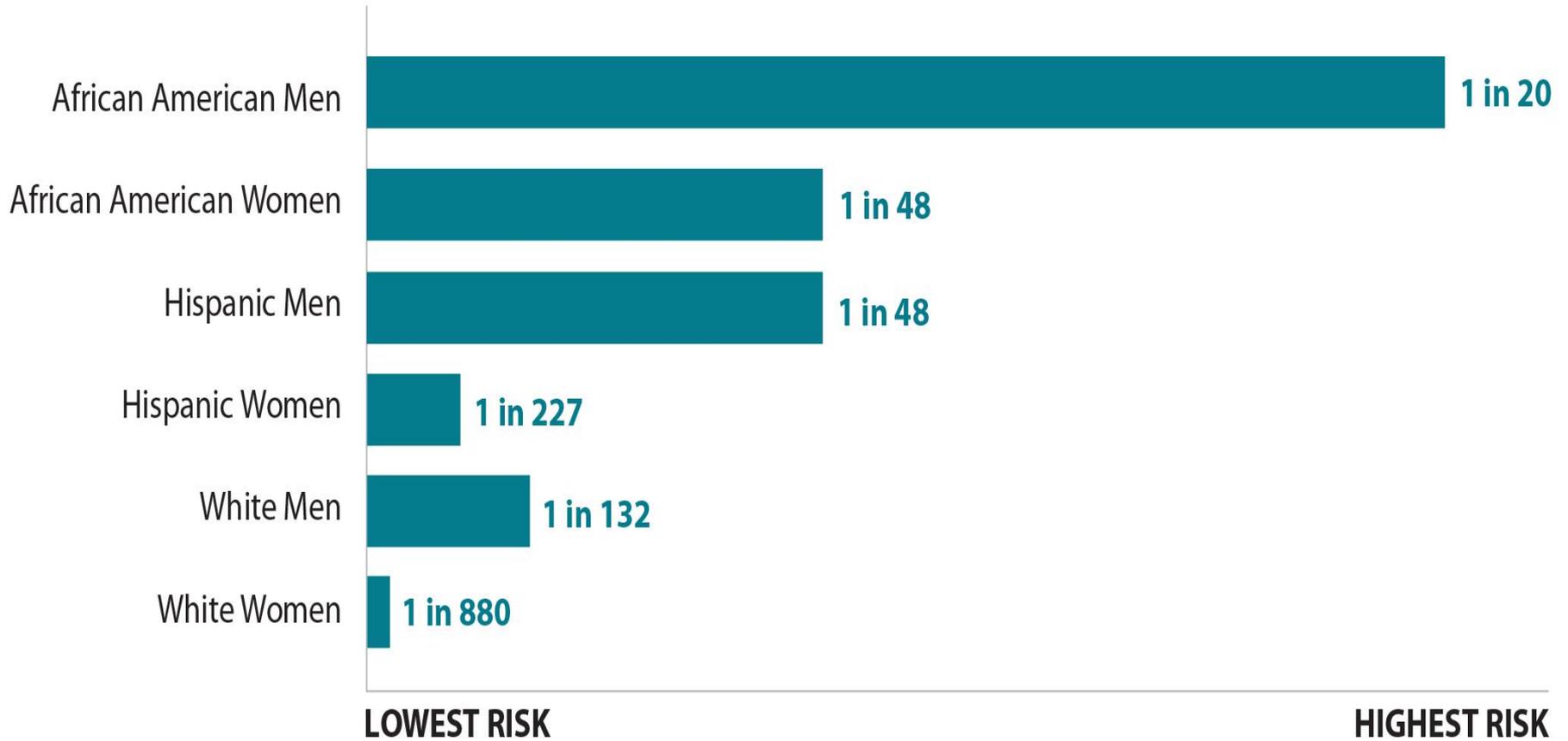
Note: Because column totals for estimated numbers were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total.

<sup>a</sup>CI = Confidence Interval. Confidence intervals reflect random variability affecting model uncertainty but may not reflect model-assumption uncertainty; thus, they should be interpreted with caution.

\* Indicates significantly different ( $p < 0.05$ ) from the 2008 estimate for the same group.



## Lifetime Risk of HIV Diagnosis by Race/Ethnicity

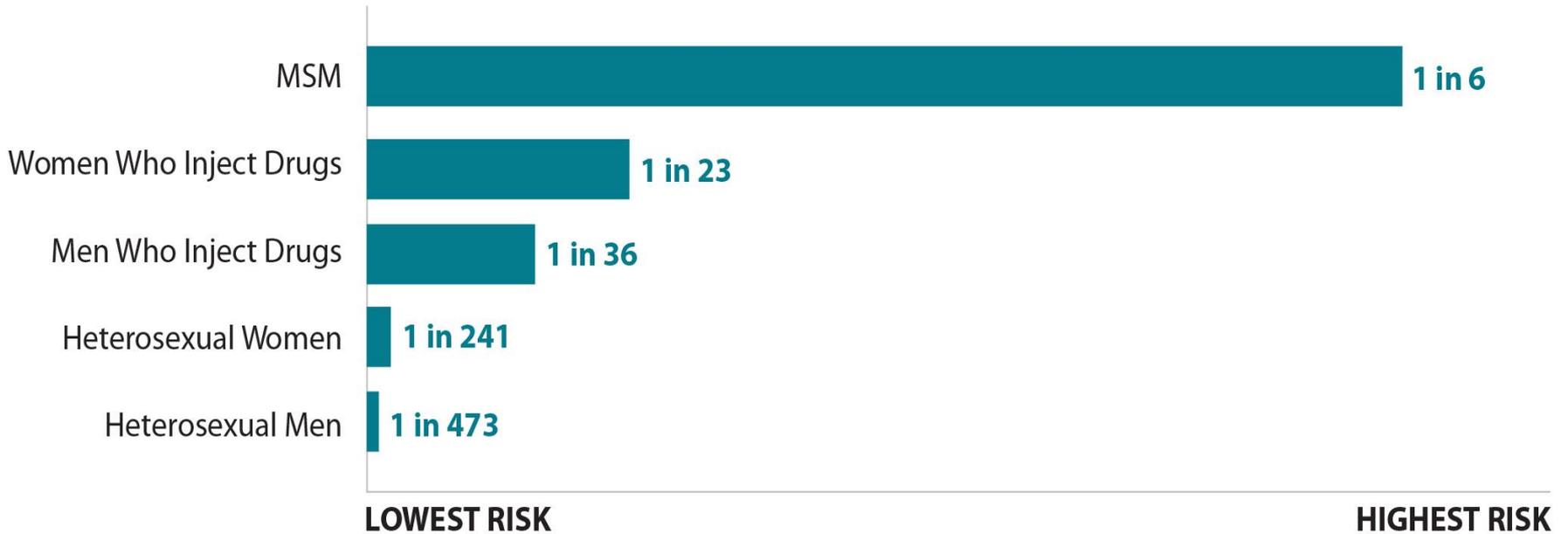


Source: Centers for Disease Control and Prevention

Hess K et al., CROI 2016.

From <http://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics>, accessed 02/29/2016.

## Lifetime Risk of HIV Diagnosis by Transmission Group



Source: Centers for Disease Control and Prevention

Hess K et al., CROI 2016.

From <http://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics>, accessed 02/29/2016.

## Lifetime Risk of HIV Diagnosis among MSM by Race/Ethnicity

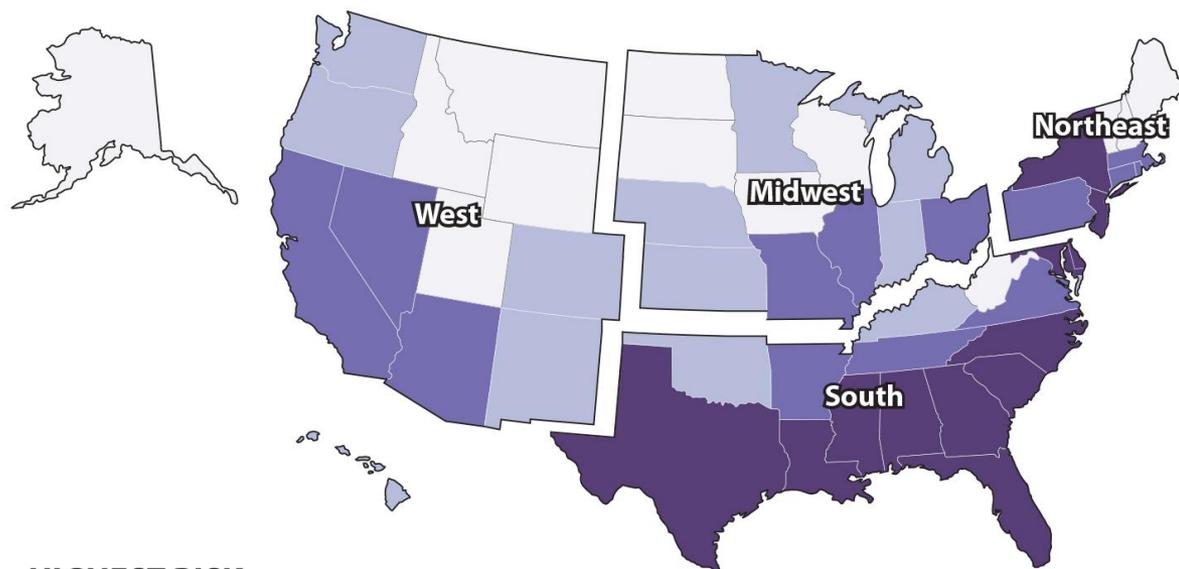


Source: Centers for Disease Control and Prevention

Hess K et al., CROI 2016.

From <http://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics>, accessed 02/29/2016.

## Lifetime Risk of HIV Diagnosis by State



### HIGHEST RISK

### LOWEST RISK

State	One in "n"	State	One in "n"	State	One in "n"	State	One in "n"
District of Columbia	13	Nevada	98	Michigan	167	West Virginia	302
Maryland	49	Illinois	101	Oklahoma	168	Wisconsin	307
Georgia	51	California	102	Kentucky	173	Iowa	342
Florida	54	Tennessee	103	Indiana	183	Utah	366
Louisiana	56	Pennsylvania	115	Washington	185	Maine	373
New York	69	Virginia	115	Colorado	191	Alaska	384
Texas	81	Massachusetts	121	New Mexico	196	South Dakota	402
New Jersey	84	Arizona	138	Hawaii	202	New Hampshire	411
Mississippi	85	Connecticut	139	Oregon	214	Wyoming	481
South Carolina	86	Rhode Island	143	Minnesota	216	Vermont	527
North Carolina	93	Ohio	150	Kansas	262	Idaho	547
Delaware	96	Missouri	155	Nebraska	264	Montana	578
Alabama	97	Arkansas	159			North Dakota	670

Source: Centers for Disease Control and Prevention

Hess K et al., CROI 2016.

From <http://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics>, accessed 02/29/2016.



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# Evidence for PrEP

# Efficacy of PrEP

Study	Population	Number of participants	Modified Intent-to-treat Efficacy	Efficacy by blood detection of drug measures (CI)
iPrEX	MSM, TG women	TDF/FTC = 1251 Placebo = 1248	44% (15-63%)	92% (40-99%)
US MSM Safety Trial	MSM	TDF = 201 Placebo = 199	No infections in men who received TDF	
Partners PrEP	Heterosexual men and women	TDF = 1589 TDF/FTC = 1583 Placebo = 1586	TDF 67% (44-81%) TDF/FTC 75% (55-87%)	TDF 86% (67-94%) TDF/FTC 90% (58-98%)
TDF2	Heterosexual men and women	TDF/FTC = 611 Placebo = 608	62% (22-83%)	85%
BTS	Injection drug users	TDF = 1204 Placebo = 1207	49% (10-72%)	74% (17-94%)

Modified from: CDC. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline.

**Table 2: Evidence Summary—Overall Evidence Quality (per GRADE Criteria<sup>28</sup>)**

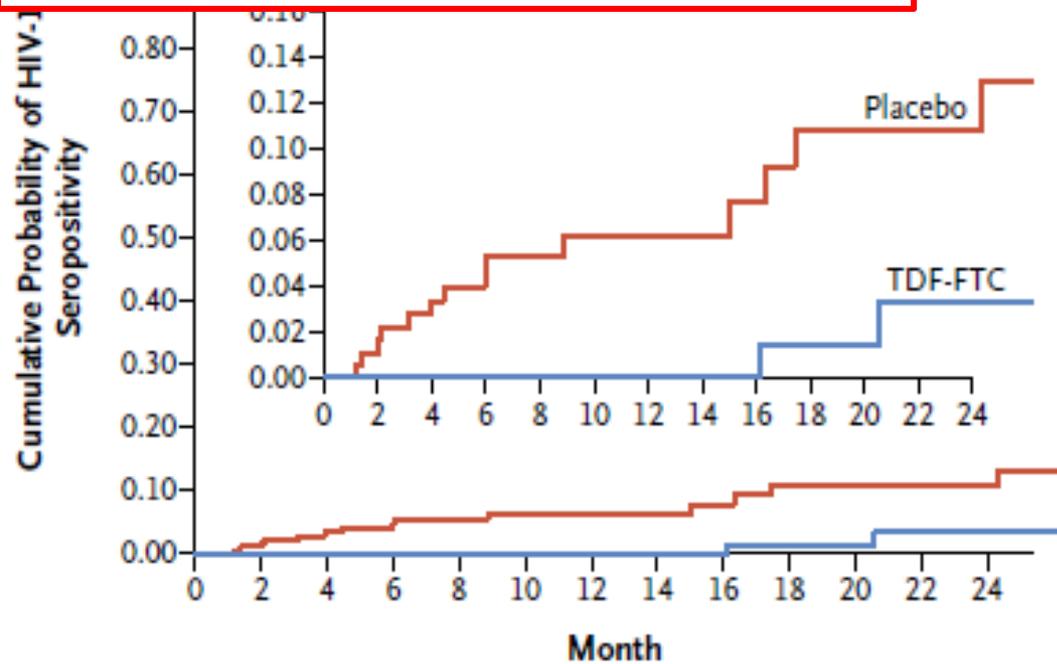
Study	Design <sup>a</sup>	Participants		Limitations	Quality of Evidence (See Table 14, Appendix 2)
		Agent	Control		
Among Heterosexual Women					
FEM-PrEP	Phase 3	TDF/FTC (n = 1062)	Placebo (n = 1058)	Stopped at interim analysis, limited follow-up time; very low adherence to drug regimen	Low
West African Trial	Phase 2	TDF (n = 469)	Placebo (n = 467)	Stopped early for operational concerns; small sample size; limited follow-up time on assigned drug	Low
VOICE	Phase 2B	TDF (n = 1007) TDF/FTC (n = 1003)	Placebo (n = 1009)	TDF arm stopped at interim analysis (futility); very low adherence to drug regimen in both TDF and TDF/FTC arms	Low

ORIGINAL ARTICLE

## On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

J.-M. Molina, C. Capitant, B. Spire, G. Pialoux, L. Cotte, I. Charreau, C. Tremblay, J.-M. Le Gall, E. Cua, A. Pasquet, F. Raffi, C. Pintado, C. Chidiac, J. Chas, P. Charbonneau, C. Delaugerre, M. Suzan-Monti, B. Loze, J. Fonsart, G. Peytavin, A. Cheret, J. Timsit, G. Girard, N. Lorente, M. Préau, J.F. Rooney, M.A. Wainberg, D. Thompson, W. Rozenbaum, V. Doré, L. Marchand, M.-C. Simon, N. Etien, J.-P. Aboulker, L. Meyer, and J.-F. Delfraissy, for the ANRS IPERGAY Study Group\*

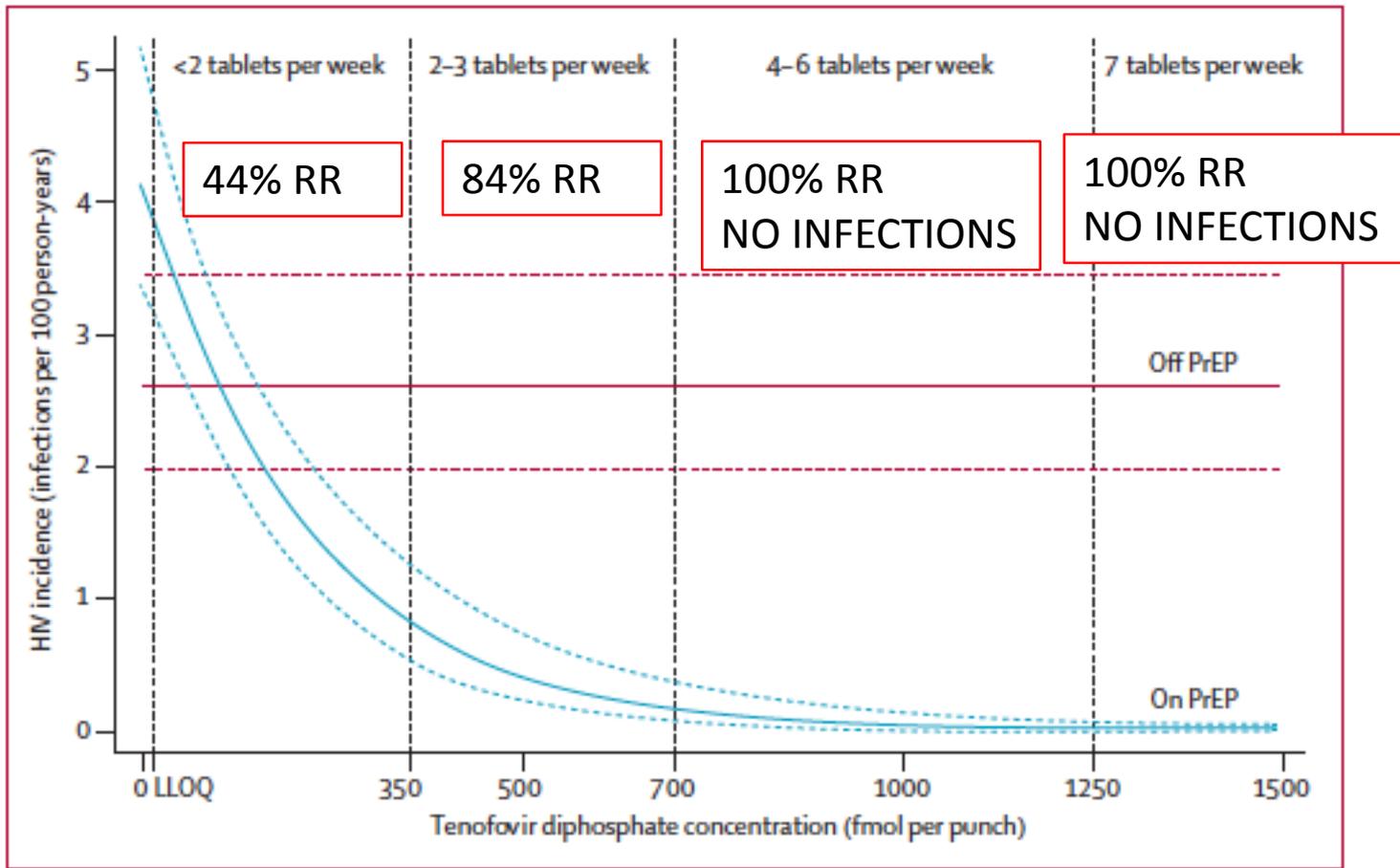
86% relative risk reduction



No. at Risk					
Placebo	201	141	74	55	42
TDF-FTC	199	141	82	58	43

**Figure 3. Kaplan–Meier Estimates of the Probability of HIV-1 Infection.**

The cumulative probability of HIV-1 acquisition is shown for the two study groups in the modified intention-to-treat analysis. The inset shows the same data on an enlarged y axis.



**Figure 2: Pre-exposure prophylaxis and HIV incidence**

For those visits on PrEP, the incidence of HIV is estimated by exponential regression by tenofovir diphosphate in dried blood spots. The incidence for the concomitant off-PrEP group is depicted as a constant for reference. The dotted lines represent the estimate bounded by 1 SE. Dosing for each interval is estimated by pharmacokinetic modelling. LLOQ=lower limit of quantitation.

# Open enrollment studies and demonstration projects

Study	Study population	Study type	n	Outcome
iPrEX OLE	MSM, transgender women	open-label extension	1225	no infections >/= 4 tablets per week
UK PROUD	MSM transgender women	open-label randomised (immediate vs. deferred)	533 (stopped early)	86% RR 3 infections immediate group, no breakthrough
Partners PrEP	Serodifferent heterosexual couples	prospective open-label cohort	1,013 couples	96% RR 2 infections immediate group, no detectable TDF
US Demo Project	MSM, transgender women	prospective open-label cohort	557	2 infections, low/no detectable TDF
IPERGAY update	MSM, transgender women	open-label extension	362	95% RR 1 infection, d/c'd TDF-FTC

Grant, et al. *Lancet Infect Dis* 2014; McCormack, et al. *Lancet* 2016; Baeten, et al. CROI 2016; Liu, et al. *JAMA* 2015; Molina, et al. CROI 2016.

# “Real world” (open-label and demonstration project) results

- High enrollment among those at highest risk
- Greater adherence among those at greatest risk
- High rates of STI diagnoses
- High effectiveness to prevent HIV infection (no infections  $\geq$  4 doses per week)
- One case report of breakthrough infection with multidrug resistant virus

Grant, et al. *Lancet Infect Dis* 2014; McCormack, et al. *Lancet* 2016;  
Baeten, et al. CROI 2016; Liu, et al. *JAMA* 2015;  
Molina, et al. CROI 2016; Knox, et al. CROI 2016.

# Concerns about PrEP

Resistance

Low rates of resistance (most at time of PrEP initiation)

Renal toxicity

Rare renal toxicity in clinical trials; mild-moderate effects in recent studies

Bone toxicity

Decreased bone mineral density; reversible; no increased fracture risk

Risk compensation

None in randomized trials; mixed in subsequent studies; high rates of STI in recent studies

CDC, 2014 PrEP Guidelines; Grant et al., *Lancet Infect Dis* 2014; Marcus et al., *PLoS ONE* 2013; Volk et al., *CID* 2015; Liu et al., *JAMA Int Med* 2015; Sagaon et al., *CROI* 2016; McCormack, et al. *Lancet* 2016; Aurbach et al., *JAIS* 2015; Molina et al. *NEJM* 2015; Golub S et al, *CROI* 2016; Cohen S et al. *CROI* 2016; Gandi M. et al., *CROI* 2016; Liu AY et al., *CROI* 2016; Mugwanya KK, et al., *CROI* 2016; Grant, et al., *CROI* 2016; Baeten, et al. *CROI* 2016; Liu, et al. *JAMA* 2015; Molina, et al. *CROI* 2016; Grant, et al. *CROI* 2016.

Guidelines for PrEP - Preexposure  
Prophylaxis for the Prevention of HIV  
Infection in the United States – 2014  
Clinical Practice Guideline

**Table 1: Summary of Guidance for PrEP Use**

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	<p>HIV-positive sexual partner</p> <p>Recent bacterial STI</p> <p>High number of sex partners</p> <p>History of inconsistent or no condom use</p> <p>Commercial sex work</p>	<p>HIV-positive sexual partner</p> <p>Recent bacterial STI</p> <p>High number of sex partners</p> <p>History of inconsistent or no condom use</p> <p>Commercial sex work</p> <p>In high-prevalence area or network</p>	<p>HIV-positive injecting partner</p> <p>Sharing injection equipment</p> <p>Recent drug treatment (but currently injecting)</p>
Clinically eligible	<p>Documented negative HIV test result before prescribing PrEP</p> <p>No signs/symptoms of acute HIV infection</p> <p>Normal renal function; no contraindicated medications</p> <p>Documented hepatitis B virus infection and vaccination status</p>		
Prescription	<p>Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply</p>		
Other services	<p>Follow-up visits at least every 3 months to provide the following:                      HIV test, medication adherence counseling, behavioral risk reduction support,                      side effect assessment, STI symptom assessment</p> <p>At 3 months and every 6 months thereafter, assess renal function</p> <p>Every 6 months, test for bacterial STIs</p>		
	<p>Do oral/rectal STI testing</p>	<p>Assess pregnancy intent</p> <p>Pregnancy test every 3 months</p>	<p>Access to clean needles/syringes and drug treatment services</p>

STI: sexually transmitted infection

# Patient assessment

- Sexual health history:
  - Gender identity
  - Sexual behaviors
  - Condom use
  - Number of sexual partners
  - Characteristics of sexual partners
    - HIV status known/unknown
    - If HIV+ on ART/HIV VL
    - Identity known/unknown
    - Gender identity
    - Sexual behaviors
  - History of STI
  - Engagement in transactional sex
  - Last HIV test and result
  - Desire for pregnancy and contraception use
  - Use of hormones
    - Inject/share needles

# Patient assessment

- Drug and alcohol use history
  - Sex while intoxicated
  - Frequency of use
  - Injection drug use
  - Type of drug/alcohol
  - Sharing equipment
  - Enrollment in a methadone or other medication-based drug treatment program
- Assessment of intimate partner violence
- Housing status
- Prevalence of HIV in area or network

PrEP should not be offered as a sole intervention for HIV prevention. PrEP should only be prescribed as part of a comprehensive prevention plan.

PrEP should be offered in supportive,  
non-judgmental, LGBTQ-friendly  
environments

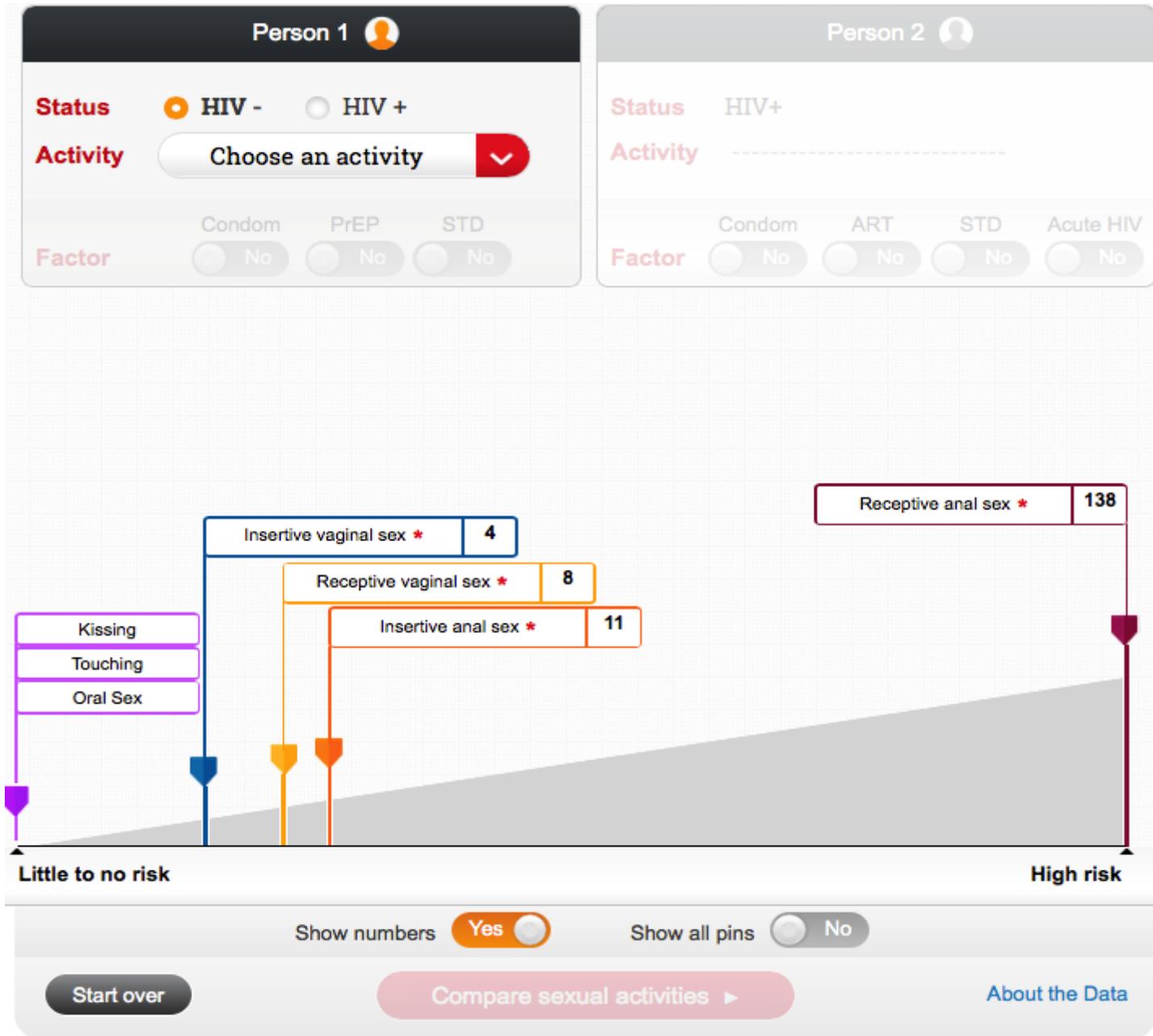
# IA

<b>Men Who Have Sex with Men</b>	<b>Heterosexual Women and Men</b>	<b>Injection Drug Users</b>
HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work  In high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)

CDC. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline.

# CDC HIV Risk Tool

<http://wwwnc.cdc.gov/hivrisk/index.html>,  
accessed 3/27/16



\* This flag represents sexual activity without protective factors, such as condoms, PrEP, or ART, and without risk factors, such as STDs or acute HIV infection.

# IIB

Discuss PrEP with heterosexually-active HIV-discordant couples wishing to conceive and during pregnancy

## IIIB

Currently the data on the efficacy and safety of PrEP for adolescents are insufficient. Therefore, the risks and benefits of PrEP for adolescents should be weighed carefully in the context of local laws and regulations about autonomy in health care decision-making by minors.

### Pre-Prescription Visit:

- Discuss PrEP use; clarify misconceptions
- Perform following laboratory tests:
  - HIV test (see Table 6 for guidance on what type of test to use)
  - Metabolic panel
  - Urinalysis
  - Hepatitis A, B, and C serology
  - STI screening
  - Pregnancy test

After confirmation of negative HIV test:  
**Prescribe 30-day supply of PrEP**  
Follow up in 2 weeks to assess side effects  
(in person or by phone)

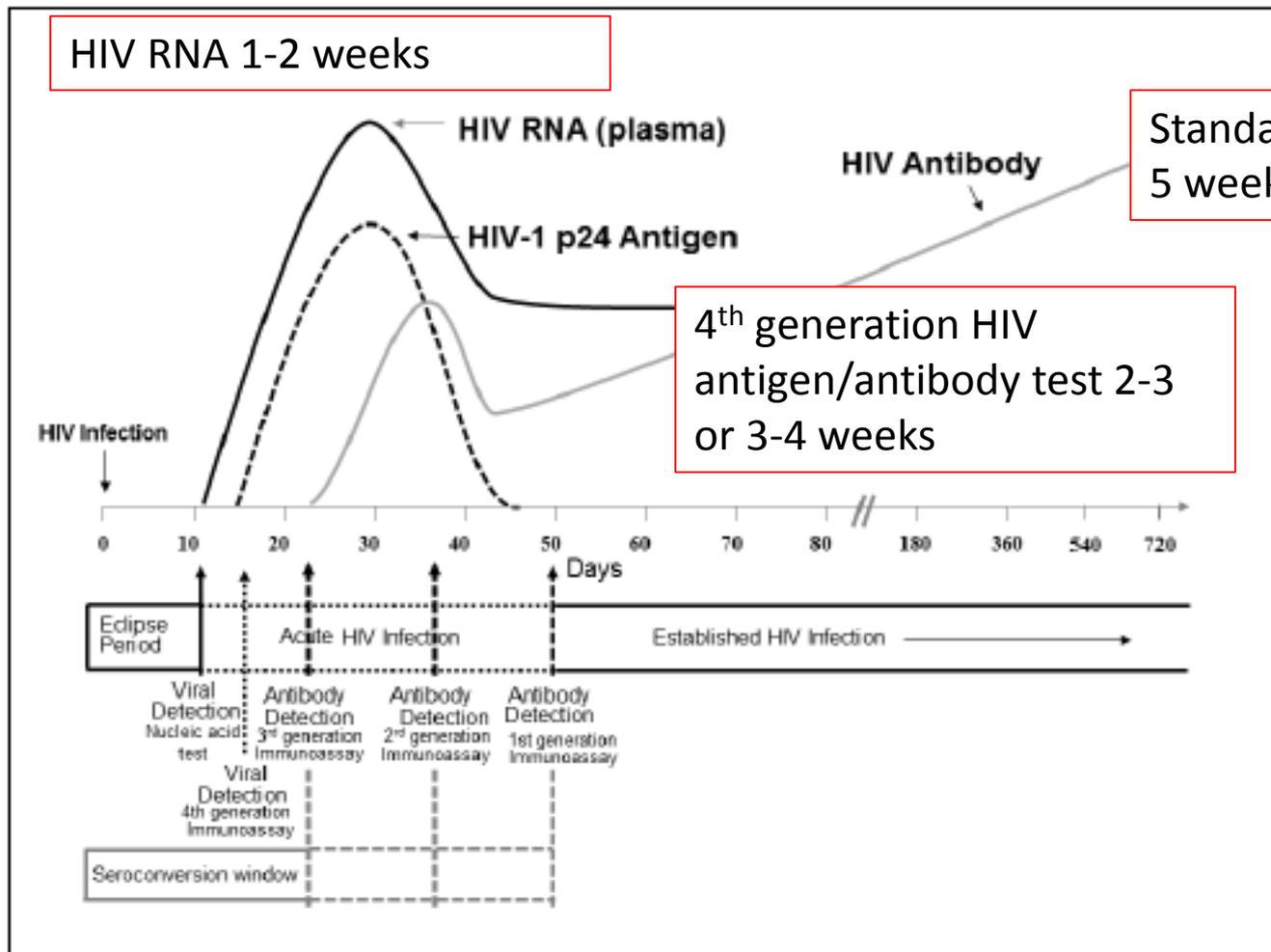
Adherence and commitment should be assessed at each visit. Schedule visits every 30 days for patients who report poor adherence or intermittent use.

# Exclude HIV infection (IA)

- Assess for signs/symptoms of acute HIV infection
- Document a negative antibody\* test result within the week before initiating (or reinitiating) PrEP medications.

**\*I recommend 4<sup>th</sup> generation HIV antigen/antibody test and consider HIV RNA testing and/or nPEP depending on risk**

**Figure 1. Sequence of appearance of laboratory markers for HIV-1 infection**



*Note.* Units for vertical axis are not noted because their magnitude differs for RNA, p24 antigen, and antibody. Modified from MP Busch, GA Satten (1997)<sup>50</sup> with updated data from Fiebig (2003),<sup>48</sup> Owen (2008),<sup>49</sup> and Masciotra (2011, 2013).<sup>46,66</sup>

Slide courtesy of Anne Monroe, MD

### 3-month visit

- HIV test
- Ask about STI symptoms
- Discuss risk reduction and provide condoms
- Serum creatinine and calculated creatinine clearance
- Pregnancy test

### 6-month visit

- HIV test
- Obtain STI screening tests (see Table 8)
- Discuss risk reduction and provide condoms
- Pregnancy test

### 9-month visit

- HIV test
- Ask about STI symptoms
- Discuss risk reduction and provide condoms
- Serum creatinine and calculated creatinine clearance
- Pregnancy test

### 12-month visit

- HIV test
- Obtain STI screening tests (see Table 8)
- HCV serology for MSM, IDUs, and those with multiple sexual partners
- Discuss risk reduction and provide condoms
- Pregnancy test
- Urinalysis

# **At least every 12 months**

- Evaluate the need to continue PrEP as a component of HIV prevention

# Integrating PrEP into clinical practice

- Provide PrEP patient education materials
- Educate clinical and non-clinical staff
- Update clinic protocols and procedures
  - Routinely assess sexual history\*
  - Recommend PrEP evaluation for high-risk individuals (HIV testing, STI testing, STI diagnoses, partners of HIV+ individuals, IDU, commercial sex work, high-prevalence network)\*
  - Develop PrEP protocols and procedures

Conniff, *JABFM* 2016

\*my recommendations

# Integrating PrEP into clinical practice

- Understand billing codes and PrEP patient assistant programs
- Use check lists
- Identify clinic champions\*
- Utilize technical assistance from other clinics/organizations\*

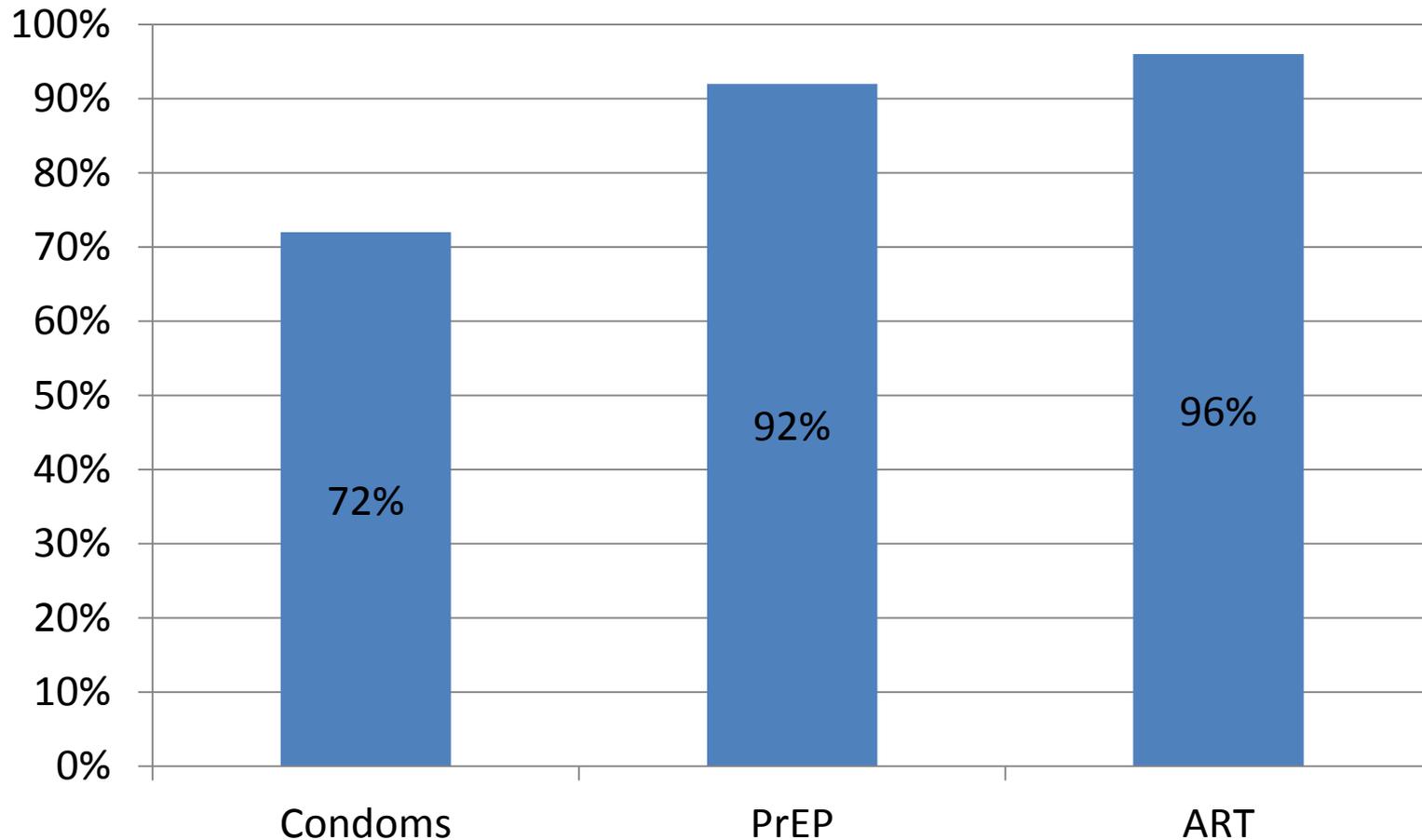
Conniff, *JABFM* 2016

\*=my recommendations

# Integrating PrEP into clinical practice: know your tools for HIV prevention

- Decrease behavioral risk
  - Sexual activity
  - Needle exchange
  - Barrier methods
- Treatment as prevention
- Male circumcision
- nPEP
- PrEP

# Risk reduction for receptive anal intercourse (1 in 72 risk with HIV+ partner)



Smith, et al. *JAIDS* 2015 Grant, et al. *NEJM* 2010  
Cohen, et al. *NEJM* 2011  
Patel, et al. *AIDS* 2014

# Future directions

- Alternate dosing intervals (i.e. on-demand PrEP)
- Alternate antiretrovirals
- Long-acting injectable antiretrovirals
- Broadly neutralizing antibodies
- Vaginal rings
- Vaginal and rectal gels
- Vaginal films

# DO NOT use tenofovir-alafenamide (TAF) for PrEP

Sample site	Tenofovir level (TAF vs. TDF)
Plasma	19X lower
Cervical and vaginal tissue	2X lower
Cervical and vaginal fluid	11X lower
Rectal tissue	10X lower
PBMC (TFV-DP)	9X higher (TFV-DP)

**TDF = tenofovir disoproxil fumarate**

**TFV-DP = tenofovir diphosphate (active agent)**

**Less duration of detectable levels over time (TAF vs. TDF)**

**More research is needed to determine efficacy for PrEP**

# PrEP: what you need to know

- PrEP works!
- CDC guidelines provide a useful template for evaluation, prescription and follow up of PrEP
- PrEP as a tool for HIV prevention can and should be integrated into routine clinical care

Questions?

Thank you!

Joyce Jones

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# PrEP resources

US Public Health Service Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline

<http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf>

US Public Health Service Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Providers' Supplement

<http://www.cdc.gov/hiv/pdf/PrEPProviderSupplement2014.pdf>

Gilead Pharmacy Assistance Program

Patients can access assistance with copays and medication coverage through the Gilead Pharmacy Assistance Program (PAP) by calling 1-855-330-5479, Monday through Friday between 9:00 a.m. and 8:00 p.m to see if they are eligible for the PAP program through Gilead.

# PrEP resources

## **PrEP Support Hotline for Clinicians**

**PrEPline, 1-855-448-7737 (1-855 HIV-PREP).**

The CCC Pre-Exposure Prophylaxis Service

11 a.m. – 6 p.m. ET

For more information on the services offered through the PrEPline, visit the National Clinicians Consultation Center. <http://nccc.ucsf.edu>

## **Maryland PrEP website**

<http://prepmaryland.org>

## **Johns Hopkins REACH Institute and AIDS Education Training Center**

PrEP Skills Building Course

Technical Assistance

<https://www.facebook.com/JohnsHopkinsAETC/info/>

# PrEP resources

CDC

<http://www.cdc.gov/hiv/risk/prep/index.html>

San Francisco City Clinic:

<http://www.sfcityclinic.org/services/prep.asp>

The Fenway Institute:

<http://thefenwayinstitute.org/prepareforlife/>

New York City Department of Health and Mental Hygiene

<http://www.nyc.gov/html/doh/html/hcp/csi-prep-pep.shtml>

National Minority AIDS Council

[www.nmac.org/prepareforlife](http://www.nmac.org/prepareforlife)

# PrEP resources

simple video explaining PrEP may be found  
at: <http://www.whatisprep.org/>

# PrEP resources

CDC HIV Risk Reduction Tool

<http://wwwn.cdc.gov/hivrisk/>

Development of a clinical effectiveness and cost effectiveness of PrEP including a PrEP risk calculator (kind of like the Framingham risk calculator for cardiovascular disease)

link to article:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4186823/>

link to calculators:

Individual risk

calculator: <https://ictrweb.johnshopkins.edu/ictr/utility/prep.cfm>

Population cost-effectiveness

calculator: <https://ictrweb.johnshopkins.edu/ictr/utility/prep2.cfm>