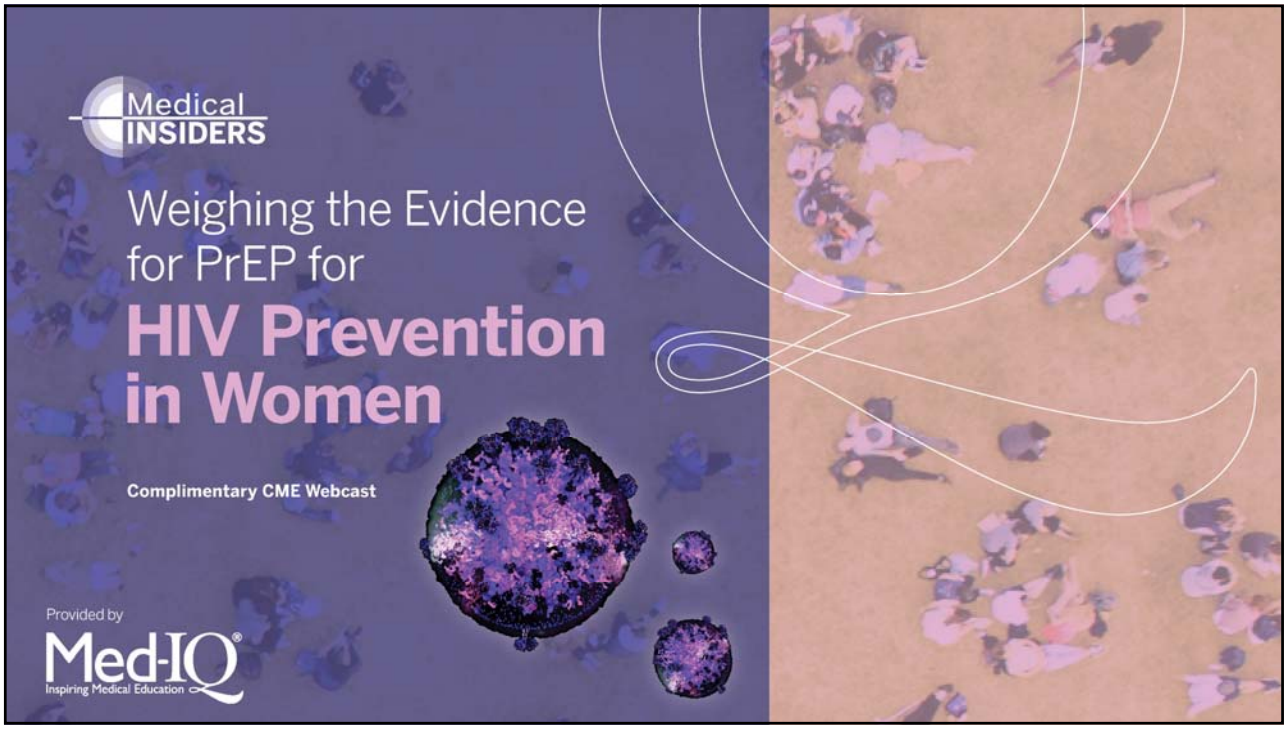
Medical INSIDERS
Weighing the Evidence for PrEP for
HIV Prevention in Women
Complimentary CME Webcast
Provided by
Med-IQ
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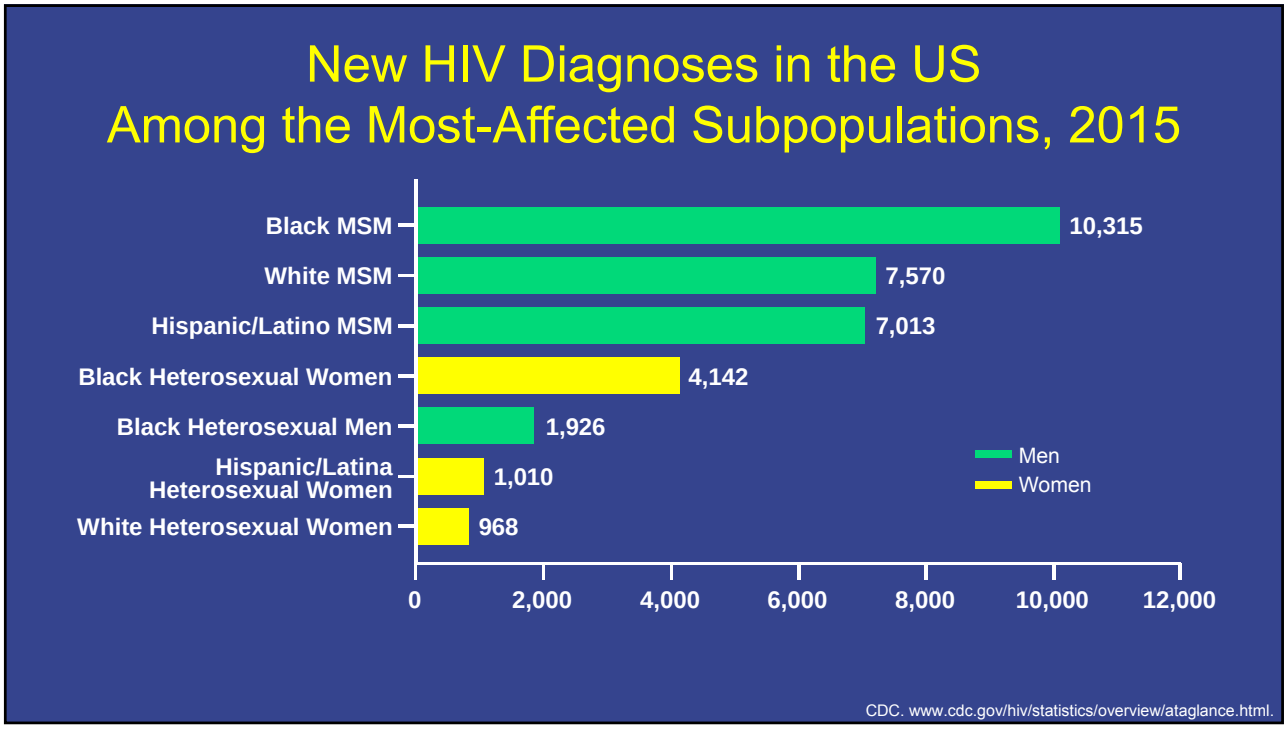

New HIV Diagnoses in the US
Among the Most-Affected Subpopulations, 2015
Black MSM
White MSM
Hispanic/Latino MSM
Black Heterosexual Women
Black Heterosexual Men
Hispanic/Latina Heterosexual Women
White Heterosexual Women
10,315
7,570
7,013
4,142
1,926
1,010
968
Men
Women
0
2,000
4,000
6,000
8,000
10,000
12,000
CDC. www.cdc.gov/hiv/statistics/overview/ataglance.html.

Guidelines for PrEP in Heterosexual Women

- Has had any sex with opposite-sex partner(s) in the last 6 months

AND

- Is not in a monogamous relationship with a recently tested HIV-negative partner

AND

- Is in an ongoing relationship with an HIV-positive partner OR inconsistently uses condoms with partner(s) at risk of HIV acquisition

- Additional consideration: transactional sex and high community and/or sexual network HIV prevalence

USPHS/CDC. www.cdc.gov/hiv/pdf/prepguidelines2014.pdf; CDC. www.cdc.gov/hiv/risk/estimates/index.html.

Eligibility Screening for PrEP

- Before PrEP is initiated:
  - HIV
    - HIV negative[a]
  - Renal function
    - CrCl ≥ 60 mL/min
  - HBV
    - TDF is an approved treatment for HBV, but TDF/FTC is not[a]
    - Refer patients to a provider experienced in HBV treatment
  - Pregnancy
    - Positive pregnancy test result does not preclude women from PrEP, but potential risks and benefits of PrEP should be discussed

[a]Boxed warning.

USPHS/CDC. www.cdc.gov/hiv/pdf/prepguidelines2014.pdf.

On-Treatment Monitoring

At Least Every 3 Months	At Least Every 6 Months	At Least Every 12 Months
Repeat HIV test	Monitor eCrCl	Evaluate the need to continue PrEP as part of HIV prevention
Repeat pregnancy test (for women)	Perform recommended STI testing for sexually active adults (eg, syphilis, gonorrhea, chlamydia)	
Authorize PrEP refill for no more than 90 days		
Assess side effects,[a,b] adherence, HIV acquisition risk		
Provide support for adherence and risk-reduction behavior		

[a]The most common side effects associated with PrEP medication are nausea, cramping, and weight loss. These symptoms are mild and usually temporary. Losses in BMD associated with TDF/FTC as PrEP use are recovered after stopping TDF/FTC.
[b]Boxed warning: Lactic acidosis and severe hepatomegaly with steatosis have been reported with the use of nucleoside inhibitors, including TDF.

USPHS/CDC. www.cdc.gov/hiv/pdf/prepguidelines2014.pdf; Truvada [package insert]. Foster City, CA: Gilead Sciences, Inc.; 2016.

Clinical Trials of PrEP in Heterosexual Women

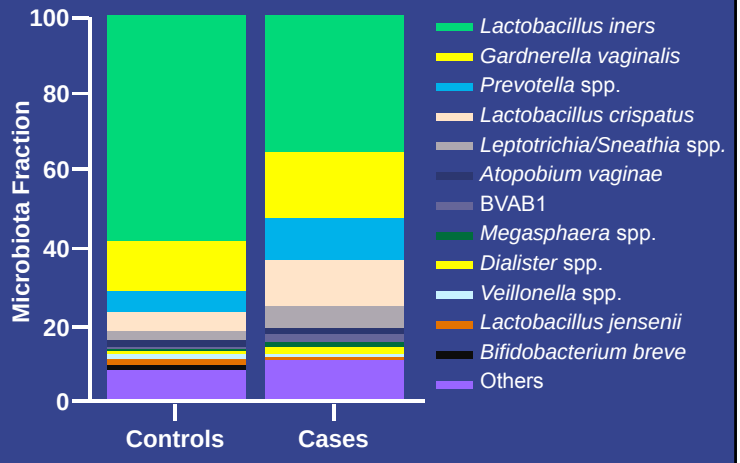
Study	Location	Population	Overall HIV Risk Reduction	*P* Value
Partners PrEP	Kenya, Uganda	Men	84%	< .001
		Women	66%	.005
TDF2	Botswana	Men and women	62%	.03
FEM-PrEP	3 African countries	Women	6%	.81
VOICE	3 African countries	Women	-4%	-

- Partners PrEP and TDF2: Significant reduction in HIV risk
  - Serodiscordant, heterosexual couples
- FEM-PrEP and VOICE: No effect on HIV risk
  - Young, predominantly unmarried women

Baeten JM, et al. *N Engl J Med*. 2012;367:399-410; Thigpen MC, et al. *N Engl J Med*. 2012;367:423-34; Van Damme L, et al. *N Engl J Med*. 2012;367:411-22; Marrazzo JM, et al. *N Engl J Med*. 2015;372:509-18.

Vaginal Bacteria Associated With Increased Risk of HIV Acquisition in African Women

- Disruption of the vaginal microbiota associated with risk of HIV
- Shannon diversity index higher in cases (median, 0.9; IQR, 0.4-2.3) vs controls (median, 0.7; IQR, 0.1-1.4), *P* = .03
  - Lower relative abundance of *Lactobacillus* spp. associated with reduced vaginal health
  - *Gemella* genus significantly associated with HIV



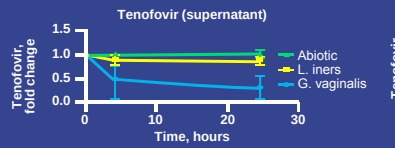
McClelland RS, et al. AIDS. Durban, South Africa. July 18-22, 2016. Abstract WEPDC0201.

Can Vaginal Bacteria Interfere With Efficacy of Tenofovir Gel[a] as PrEP?

- Tenofovir gel[a] highly protective against HIV with *Lactobacillus* dominance
- Tenofovir rapidly depleted by *Gardnerella* but not *Lactobacillus*
- Levels of tenofovir diphosphate in genital tissues and tenofovir in plasma are correlated to markers of bacterial vaginosis
- Vaginal microbiota may affect tenofovir uptake when applied intravaginally

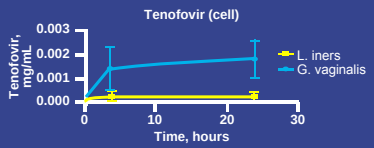
60% of *Lactobacillus*-Dominant Woman vs 61.4% of non-*Lactobacillus* –Dominant Woman Had > 50% Gel Adherence (Monthly Empty Applicator Returns)

	All Participants		> 50% Gel Adherence			
			Lactobacillus Dominant		Non-*Lactobacillus* Dominant	
	Tenofovir	Placebo	Tenofovir	Placebo	Tenofovir	Placebo
Number of HIV-1 Infections	13	26	4	15	9	11
HIV-1 Incidence per 100 Person-Years	3.7	8.6	1.9	8.5	6.4	8.6
HIV-1 Protection Effectiveness (95% CI); *P* Value	56% (12 to 79); *P* = .013		78% (29 to 95); *P* = .003		526% (-98 to 73); *P* = .558	



4 hours:
G. vab vs L. iners: *P* = .002
G. vag vs abiotic: *P* = .005

24 hours:
G. vab vs L. iners: *P* < .001
G. vag vs abiotic: *P* < .001



4 hours:
G. vab vs L. iners: *P* < .001

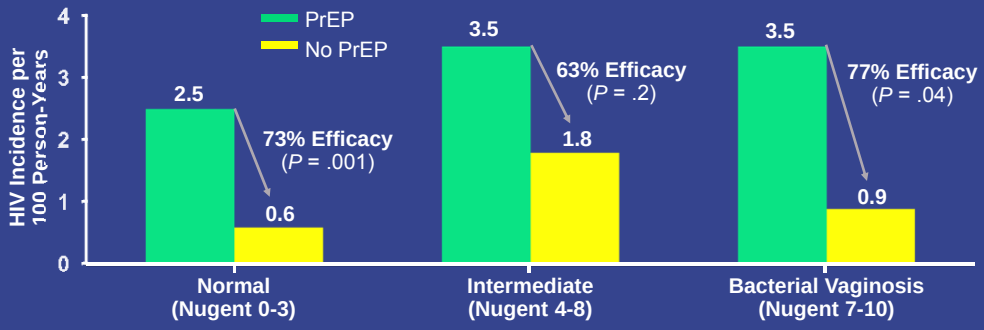
24 hours:
G. vab vs L. iners: *P* < .001

[a]Investigational drug.

Burgener A, et al. AIDS. Durban, South Africa. July 18-22, 2016. Abstract TUSS0605; Hillier SL, et al. CROI. Seattle, WA. February 13-16, 2017. Abstract 86LB.

Can Vaginal Bacteria Interfere With Efficacy of Oral PrEP?

- Oral PrEP is protective against HIV acquisition regardless of degree of bacterial vaginosis



Differences in levels of HIV prevention efficacy were not statistically significant (*P* = .9).

Heffron R, et al. CROI. Seattle, WA. February 13-16, 2017. Abstract 85.

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Abbreviations/Acronyms

BMD = bone mineral density
BVAB1 = bacterial vaginosis–associated bacteria 1
CDC = Centers for Disease Control and Prevention
CrCl = creatinine clearance
eCrCl = estimated creatinine clearance
FTC = emtricitabine
HBV = hepatitis B virus
HIV = human immunodeficiency virus
IQR = interquartile range
MSM = men who have sex with men
PHS = Public Health Service
PrEP = pre-exposure prophylaxis
STI = sexually transmitted infection
TDF = tenofovir disoproxil fumarate