

HIV Preexposure Prophylaxis and Treatment as Prevention

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Division of Disease Control
Annual Infectious Disease Conference
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DEPARTMENT OF POPULATION MEDICINE



Disclosures

Gilead Sciences - unrestricted research project support

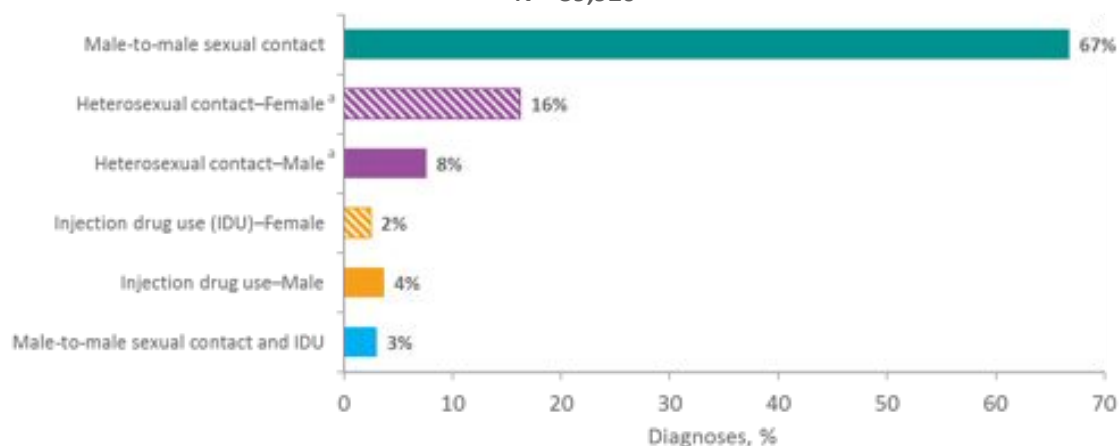
Learning Objectives

- 1.) Describe the epidemiology of HIV in the US, including notable disparities.
- 2.) Define the evidence base for HIV PrEP.
- 3.) Identify patients for PrEP during routine primary care and apply CDC guidelines for prescribing PrEP using case-based scenarios.

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Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2015—United States and 6 Dependent Areas

N = 39,920



Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. Data for the year 2015 are preliminary and based on 6 months reporting delay. Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises less than 1% of cases.

^a Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

Disparities in new HIV diagnoses exist in Massachusetts (and the U.S.)

Annual rate of HIV diagnosis among...

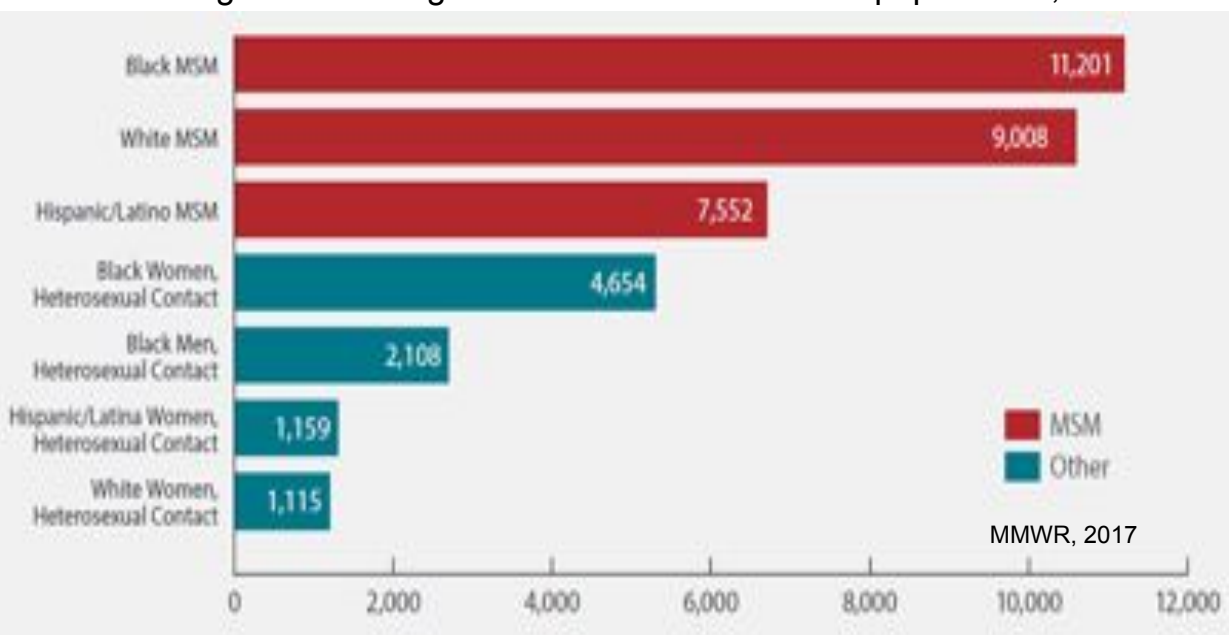
MSM = 28x that of non-MSM men

Black women = 33x that of white women

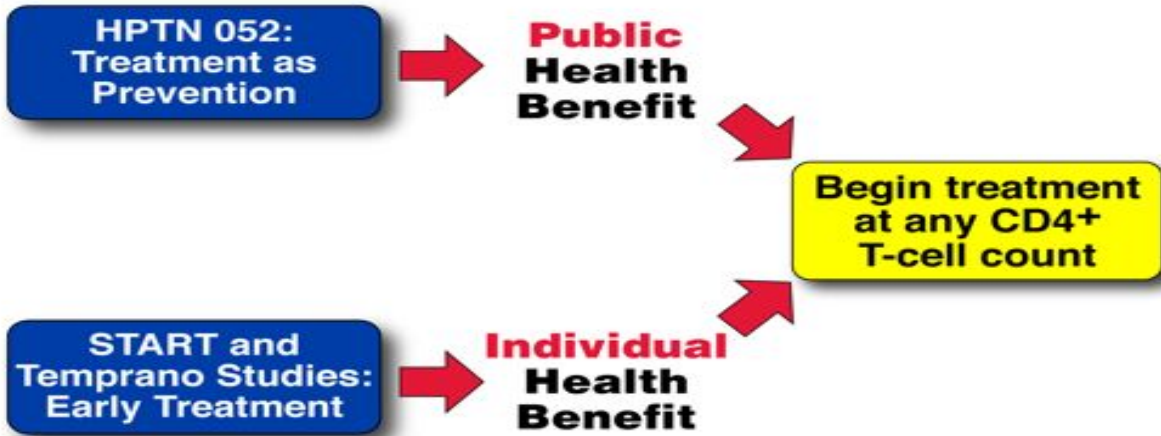
Hispanic/Latina women = 12x that of white women

Non-US born individuals = 2x that of those born in US or Puerto Rico

New HIV Diagnoses Among the Most-Affected U.S. Subpopulations, 2014



The New Paradigm: Treatment as Prevention



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Study	Efficacy overall	Drug detected overall	Estimated Risk reduction with drug detection
MSM and Transgender Women (iPrEx)	42%	~50%	92%
Heterosexual Serodiscordant Couples (Partners PrEP)	67-75%	82%	90% (FTC/TDF) 86% (TDF)
Heterosexual Men and Women (TDF2)	62%	80%	78%
Persons who Inject Drugs (Bangkok Tenofovir Study)	49%	N/A	74%
Young Women (Fem-PrEP)	No efficacy	26%	“adherence too low to assess efficacy”
Young Women (VOICE)	No efficacy	29%	“ ”

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Bacterial STIs in PROUD Study			
	Immediate	Deferred	P
Any	57%	50%	0.74
Gonorrhea	39%	37%	0.46
Chlamydia	30%	22%	0.27
Syphilis	11%	9%	0.39
Rectal gonorrhea or Chlamydia	36%	32%	0.99



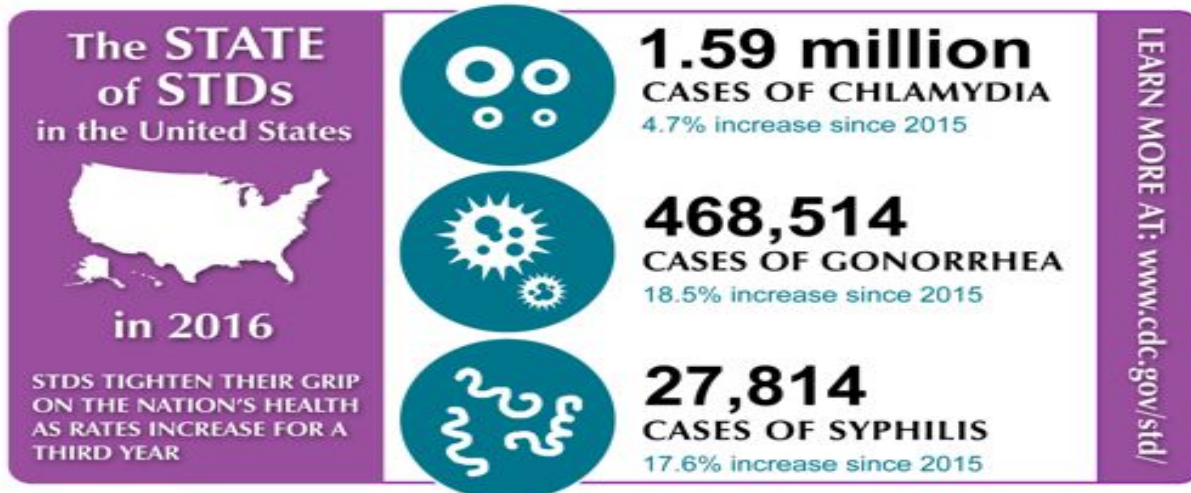
Beth Israel Deaconess Medical Center

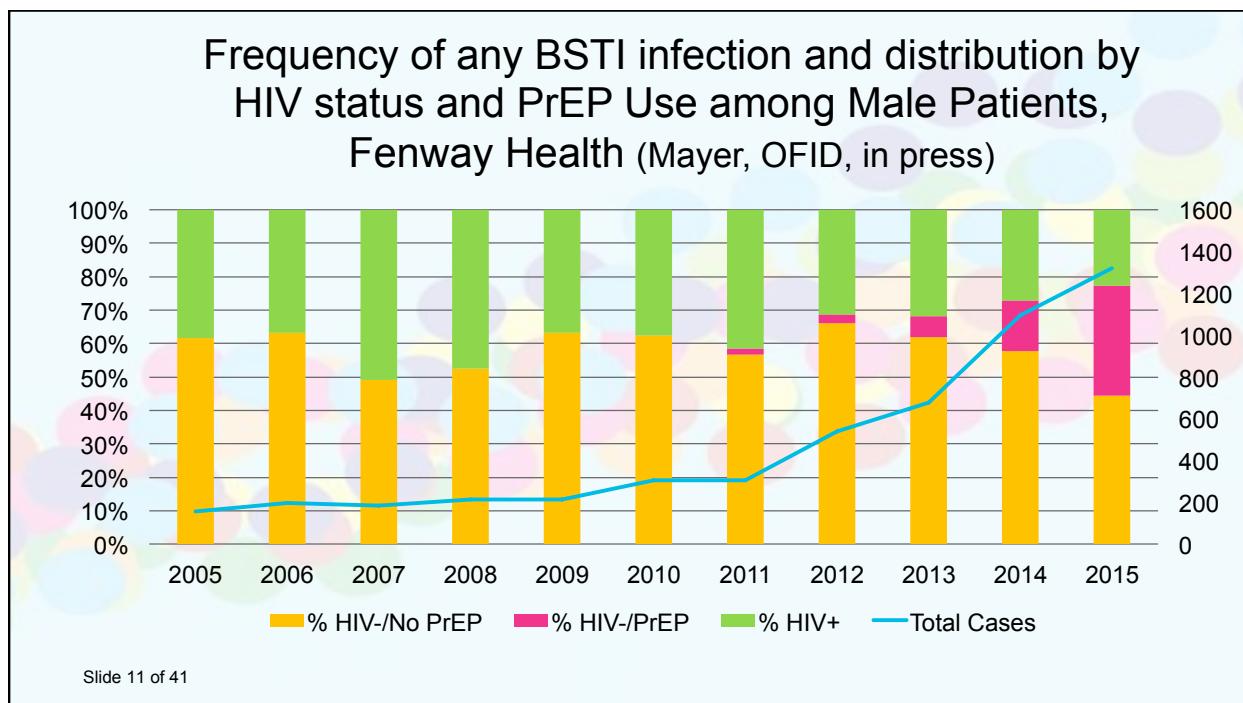


A teaching hospital of Harvard Medical School



McCormack Lancet 2015





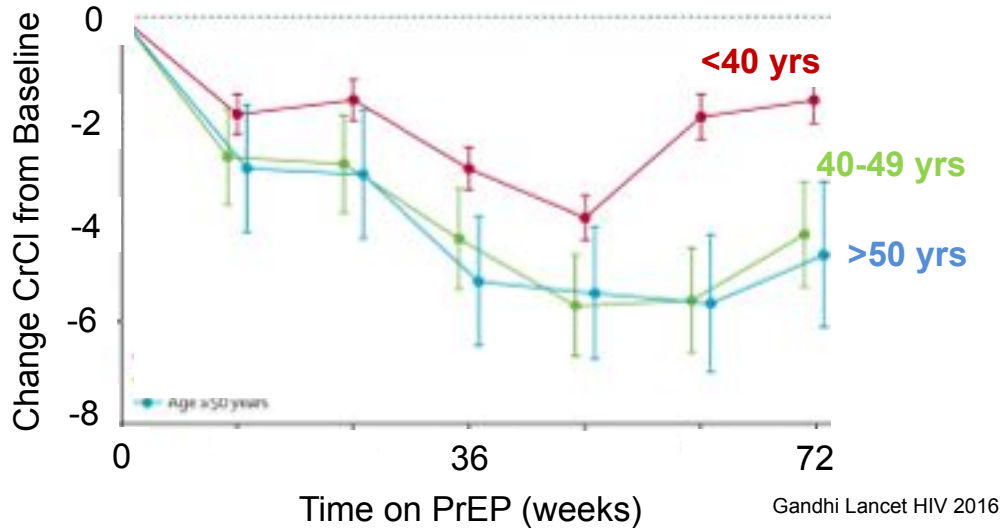
Preexposure Prophylaxis for HIV Prevention in a Large Integrated Health Care System

(J Marcus, JAIDS, 2017, CID 2017)

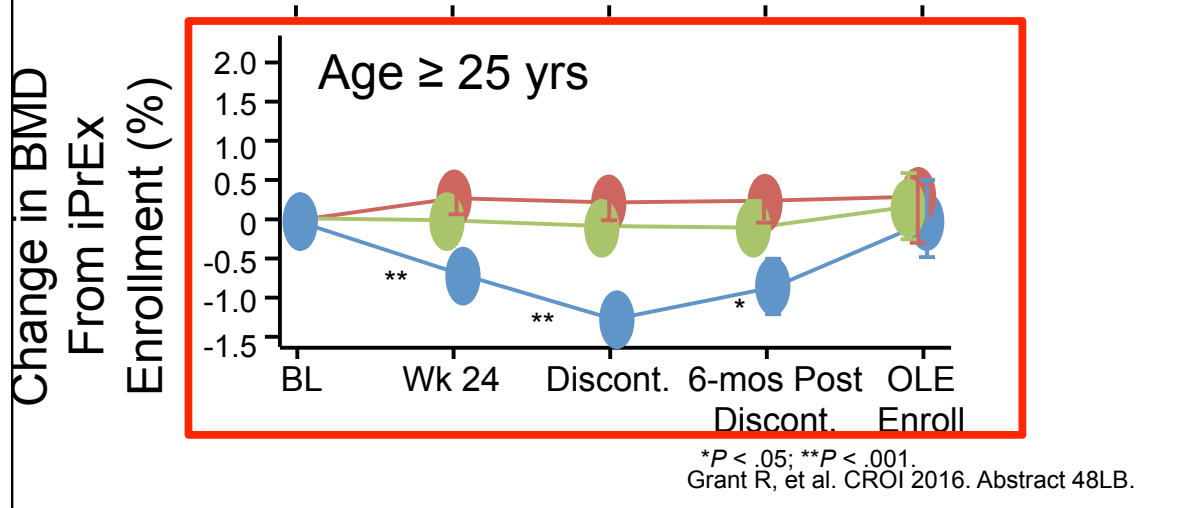
- 972 Kaiser pts, 850 py f/u
- Mean adherence 92%, no seroconversions on PrEP, 2 among those who discontinued
- Less adherence among pts who were Black, smokers, and/or had higher co-pays
- 22.5% discontinued
- Women, those with substance use disorders more likely to stop
- Only 5 discontinued b/c renal function
- STD rates continued to rise
- Update: ~5000 and no infections among adherent pts

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Mild changes in renal function may occur with TDF/FTC as PrEP



PrEP associated with small decreases in bone mineral density that reverse after stopping PrEP



Case Reports: HIV Infection with High Adherence to PrEP			
Pt	PrEP Adherence	Seroconversion	Likely Cause of PrEP Failure
43-yr-old MSM ^[1]	24 mos, supported by pharmacy records, blood, and clinical history	Acquired MDR HIV infection	Exposure to PrEP-resistant, multiclass-resistant HIV strain
MSM in his 20s ^[2]	Excellent by self report, supported by blood and hair concentration analyses	Acquired MDR HIV condomless anal intercourse with 2 different partners within 11 weeks before diagnosis	Exposure to PrEP-resistant, multiclass-resistant HIV strain
50-yr-old MSM ^[3]	Excellent by self report, supported by blood analyses	Acquired wild-type HIV infection after 2-5 median condomless anal sex partners per day in each month following PrEP initiation	Chronic rectal inflammation +/- trauma

USPHS/CDC Guidelines on Prescribing PrEP



- Determine Eligibility (negative HIV test, at high-risk for HIV acquisition, renal function, screen/treat for STIs, screen/vaccinate for Hep B, HCV Ab; pregnancy test)
- Prescribe tenofovir-emtricitabine 1 tablet by mouth daily
- Provide condoms and risk-reduction counseling
- Monitor closely (q 2-3 mo: HIV test, risk assessment/ counseling; q 6 mo: renal function, STI screen **(q 3 months for some populations?)**)

18 www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf

Persons likely to benefit from using PrEP

MSM and Transgender Women	Heterosexual Men and Women	Persons who Inject Drugs
Not in monogamous relationship with recently tested, HIV-neg partner AND...		Any use of injection drugs AND...
<input type="checkbox"/> Ongoing relationship with HIV+ partner	<input type="checkbox"/> Ongoing relationship with HIV+ partner	<input type="checkbox"/> Any sharing of injection equipment (past 6 months)
<input type="checkbox"/> Condomless anal sex (past 6 months)	<input type="checkbox"/> Man who is behaviorally bisexual	<input type="checkbox"/> Been in methadone, suboxone, buprenorphine treatment program (past 6 months)
<input type="checkbox"/> STI (past 6 months)	<input type="checkbox"/> Infrequent condom use with partner(s) at risk for HIV acquisition	<input type="checkbox"/> Risk of sexual acquisition

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34F with HIV-infected male partner, stable relationship. He declines ART, VL 9,000. Vaginal sex 2-3x/week, do not use/wish to use condoms.

- 1. PrEP
- 2. No PrEP
- 3. Other

34F with HIV-infected male partner, stable relationship. He uses ART, VL < 20. Vaginal sex 2-3x/week, do not use/wish to use condoms.

- 1. PrEP
- 2. No PrEP
- 3. Other



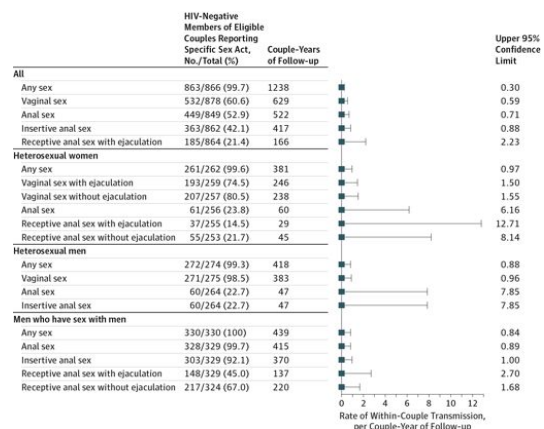
PrEP if serodiscordant partner has a suppressed viral load?

PARTNER study

- 888 HIV discordant couples
- HIV+ partner VL < 200
- 39% MSM couples
- ~36,000 condomless sex acts
- No transmissions when HIV+ pts' PVL BLD

Opposites Attract

- 358 HIV discordant MSM couples
- >12,000 condomless anal acts
- No HIV transmissions when HIV+ pt. PVL BLD
- 3 pts infected by outside partner



Rodger JAMA 2016; Bavington IAS 2017

Same couple, would like to have children.

- 1. Sperm washing
- 2. ART for him
- 3. Periconception PrEP for her
- 4. ART plus periconception PrEP
- 5. Timed condomless sex to peak fertility
- 6. Screen and treat for STIs
- 7. Other



1.2 million Americans are likely to benefit from using HIV pre-exposure prophylaxis (PrEP)



- 1 in 4 sexually active MSM.....492,000
- 1 in 5 persons who inject drugs...115,000
- 1 in 200 heterosexual adults.....624,000

~100,000 have been prescribed PrEP so far



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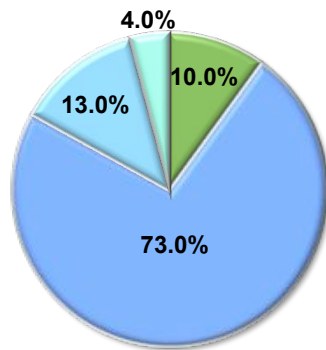
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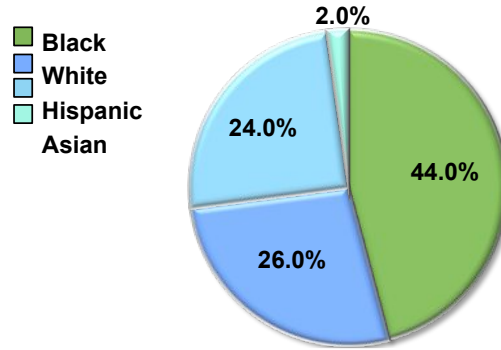
Smith MMWR 2015; McCallister IAS 2016

PrEP Utilization in the US

PrEP Use (2016)



New HIV Infections (2015)



PrEP Use Among Blacks and Hispanics Was Low Relative to Rate of New HIV Infections

Mera Giler R, et al. *J Int AIDS Soc.* 2017;20(suppl 4). Abstract WEPEC0919.

16y adolescent male has sex with men. Receptive anal sex without condoms with multiple partners. Heard about PrEP and would like to try it.

- 1. Prescribe
- 2. Decline
- 3. Other

ATN 110/113

- Young MSM 15 to 22 y.o.
- PrEP plus individual versus group intervention to ↑ risk reduction in YMSM
- HIV incidence: 3.3% in 18-22; 6.4% in 15-17 y.o. (better than < 30 y.o. in HPTN 061)
- Black MSM least adherent
- Youth were more adherent during first 3 months of the study, with monthly visits → whether more frequent contact would enhance adherence?



Answers to FAQ

V01	Contact with or exposure to communicable diseases
V01.7	Exposure to other viral diseases
V01.8	Exposure to other communicable diseases
V07.8	Other specified prophylactic measure

Financial issues

- Gilead patient assistance program: <https://start.truvada.com/hcp/prep-cost>
- Patient assistance network: <http://www.panfoundation.org/hiv-treatment-and-prevention>

- Time to protection: 7-21 days?
- Duration after last exposure: 28 days?

28y MSM presents for PEP. Syphilis 6 months ago, condomless anal sex with 4 partners since then.

- 1. No PrEP
- 2. PEP, wait for negative HIV Ab/Ag, then PrEP
- 3. PEP to PrEP, no break
- 4. Other



How to improve chemoprophylaxis effectiveness?

New oral PrEP drugs and dosing strategies



Novel adherence strategies



Alternative delivery systems and formulations



Vaginal & Rectal Microbicides
(Tenofovir, other ARVs)



Intravaginal rings
(Dapivirine, Tenofovir)
+/- Contraception)



Injectables:
ARVs and mAbs
(Cabotegravir, VRC01)

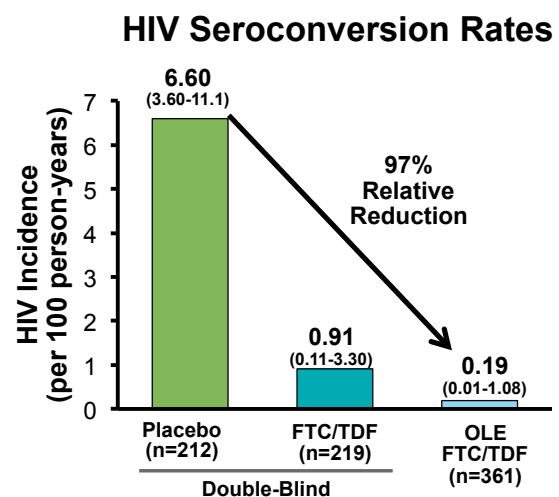
**23y MSM has sex every few months with anonymous partners in NYC.
Would like on demand PrEP.**

- 1. Prescribe on demand PrEP
- 2. Recommend daily PrEP, but prescribe on demand if he insists
- 3. Recommend daily PrEP, do not prescribe on demand
- 4. Recommend daily PrEP or PEP as needed
- 5. Other

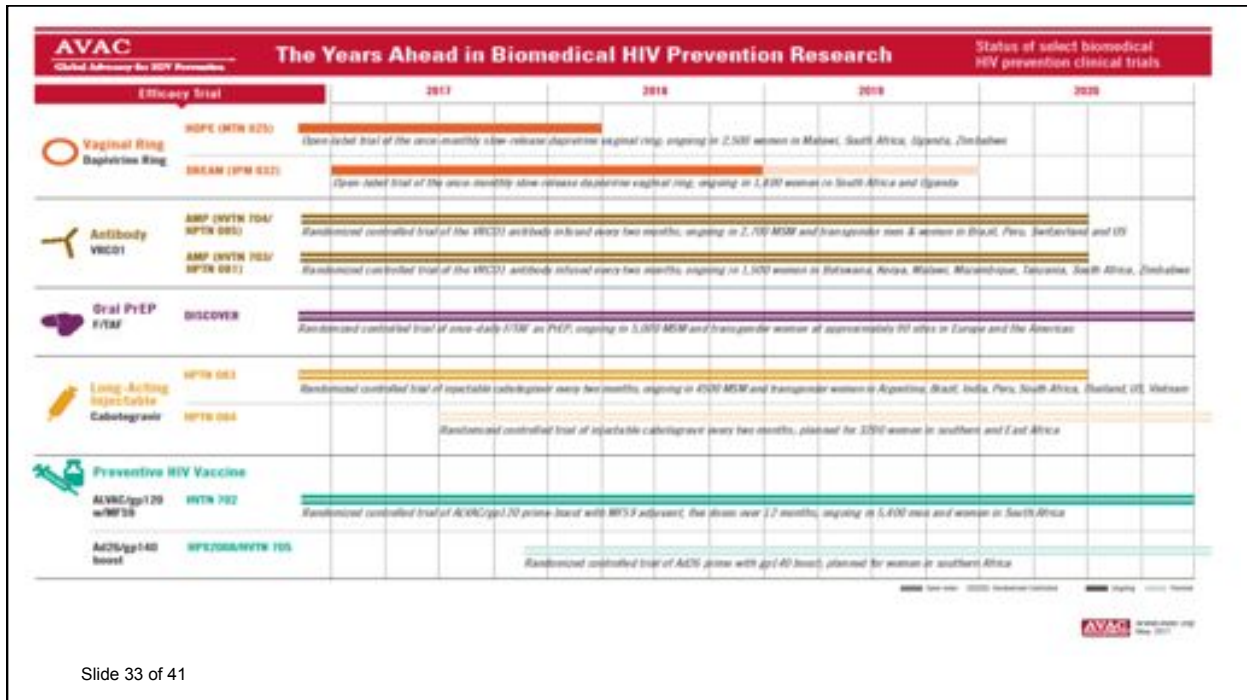



Ipergay Trial Open-Label Extension Study

- Median follow-up: 18.4 months
- Single incident HIV infection
 - Subject had not used PrEP in 40 months
 - Neither emtricitabine nor tenofovir were detectable at time of HIV diagnosis
- Estimated efficacy
 - 97% relative reduction in HIV transmission versus placebo



Molina J-M, et al. *Lancet HIV*. 2017;Jul 21. [Epub ahead of print].

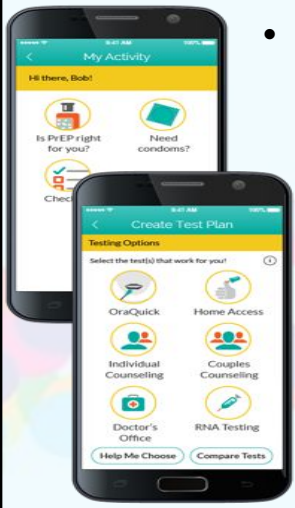
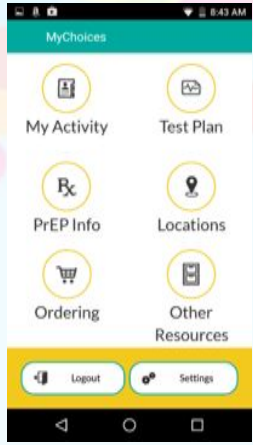




MyChoices (Biello/Mayer), also Lynx (Liu/Scott)

- Create an HIV testing plan with built-in reminders
 - Find testing locations
 - Order home test kits & condoms
- Assess if PrEP might be appropriate
 - Info about local PrEP providers
 - FAQs, PEP, STIs, Insurance

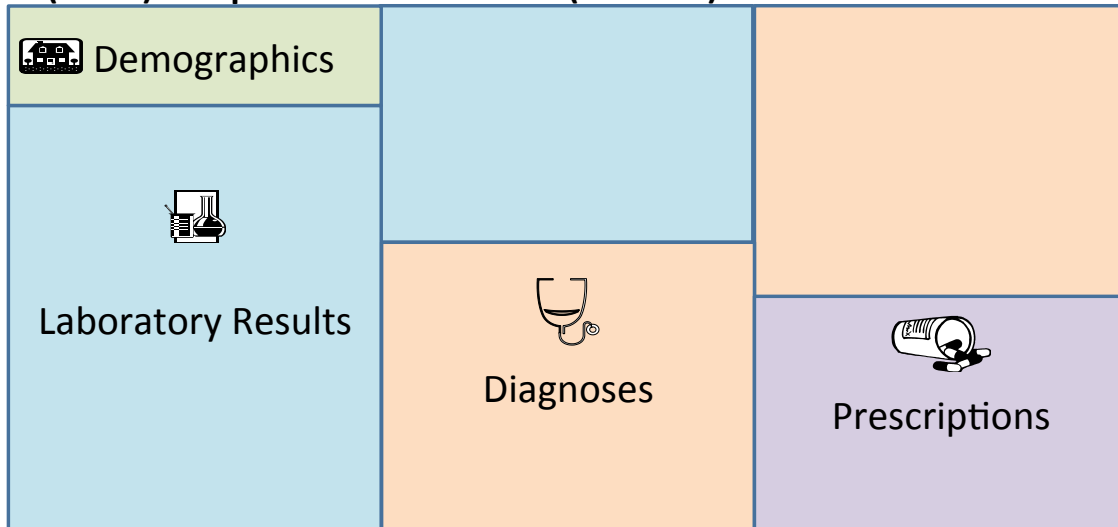
Other approach PrEP@home

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Using EHR data to identify PrEP candidates: patients with incident HIV (cases) and patients without HIV (controls)



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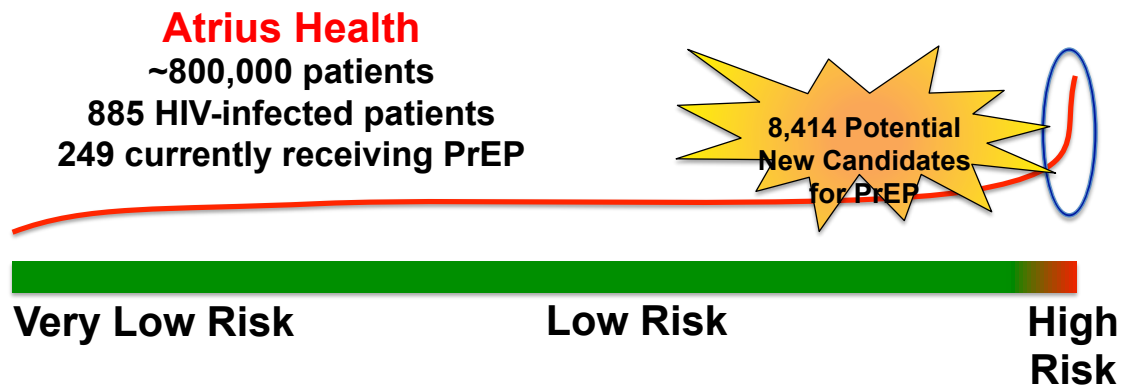
Using EHR data to identify PrEP candidates: patients with incident HIV (cases) and patients without HIV (controls)

- Age
- Race
- Sex
- Home language
- No. of Encounters per Year
- No. of Gonorrhea tests per year
- Positive Gonorrhea tests per year
- Rectal Gonorrhea tests per year
- Positive rectal Gonorrhea tests per year
- Pharyngeal Gonorrhea tests per year
- Positive pharyngeal Gonorrhea tests per year
- No. of Chlamydia tests per year
- Positive Chlamydia tests per year
- Rectal Chlamydia tests per year
- Positive rectal Chlamydia tests per year
- Pharyngeal Chlamydia tests per year
- Positive pharyngeal Chlamydia tests per year
- No. of syphilis tests per year
- Syphilis diagnosis per ESP
- LGV testing
- Anal cytology testing
- No. of HCV antibody tests
- No. of HCV RNA tests
- HCV antibody or RNA tests positive
- Acute Hepatitis C per ESP
- No. of HBV DNA tests per year
- HBSAg or HBV DNA positive
- Acute Hepatitis B per ESP
- No. of HIV ELISA tests per year
- No. of HIV Western Blots per year
- No. of HIV RNA tests per year
- HIV status per ESP
- HIV new diagnosis
- History of HIV meds
- HIV negative with HIV RNA tests
- Abnormal anal cytology
- Dx for Syphilis
- Dx for Anal syphilis
- Dx for Gonococcal infection of anus
- Dx for Gonococcal pharyngitis
- Dx for Chlamydia infection of anus
- Dx for Chlamydia pharyngitis
- Dx for LGV
- Dx for Chancroid
- Dx for Granuloma inguinale
- Dx for non-gonococcal urethritis
- Dx for HSV with complications
- Dx for Genital Herpes
- Dx for Anogenital warts
- Dx for Anorectal ulcers
- Dx for PID
- Dx for Contact / exposure to STD
- Dx for High risk sexual behavior
- Dx for HIV counseling
- Dx for HIV counseling
- Dx for Anorexia nervosa
- Dx for Bulimia nervosa
- Dx for Eating disorders
- Dx for Counseling for childhood sex abuse
- Dx for Alcohol dependence
- Dx for Opioid dependence
- Dx for Sedative, hypnotic, or anxiolytic dependence
- Dx for Cocaine dependence
- Dx for Amphetamine dependence
- Rx for bicillin
- Rx for azithromycin 1g
- Rx ceftriaxone 125mg or 250mg
- Rx for methadone
- Rx for Suboxone
- Rx for sildenafil or tadalafil or vardenafil

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8,414 (1.1%) of patients in the HMO population had HIV prediction scores above an inflection point in the distribution of scores

(D Krakower, ID Week, 2016)



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“Getting (close) to **zero**” new infections is a realistic goal

- PrEP works if taken, and is generally safe
- Uptake is increasing in some centers, but disparities exist
- STIs are at an all time high in the US; screen and counsel
- New PrEP modalities under development
- Combination of prevention strategies most effective way to control epidemic

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Thank You

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