PrEP for Cis & Transgender Women

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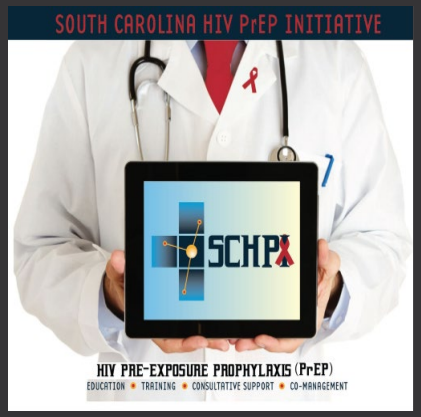

Disclosures

- None

Acknowledgement

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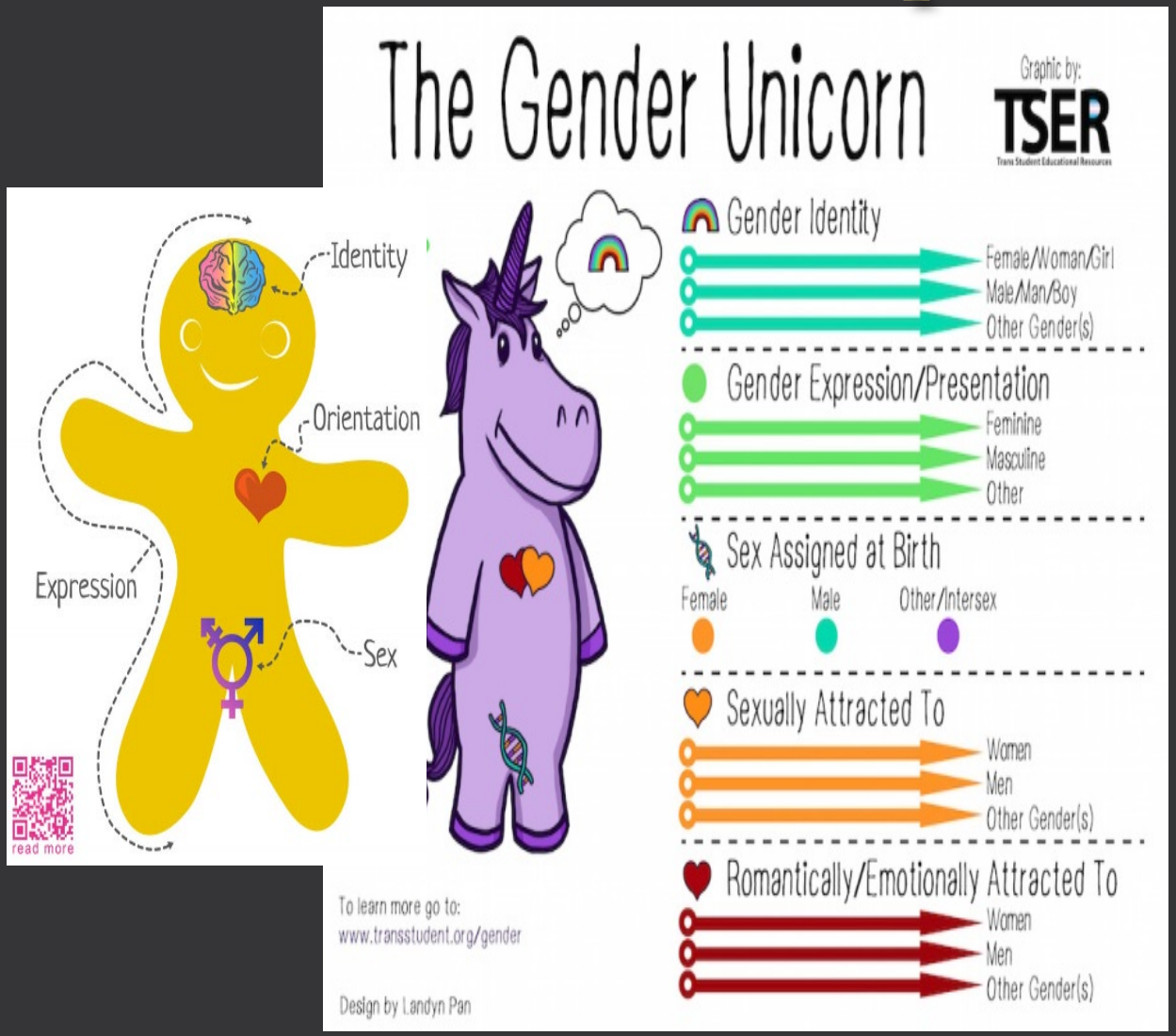
Learning Outcomes

1. Review the epidemiology of HIV in cis and transgender women
    I. What is PrEP ?
2. Discuss data supporting HIV PrEP in cis and transgender women
    I. The PrEP workflow
    II. PrEP for pregnancy
3. Describe the process of overcoming the barriers to providing PrEP for cis and transgender women

Definitions- Title Explained



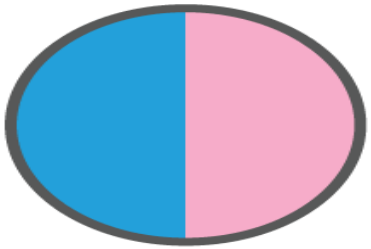
Gender identity(GI) – labels used when socially constructing sexed personas
<u>How you feel, who you are</u>

Gender expression - situational expression of cultural cues which communicate GI
<u>How you dress</u>

Gender orientation- subjective experience of one's body, including it's sexed attributes

Definitions: Gender Identity

GENDER DEFINITIONS

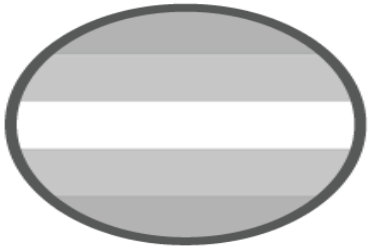


GENDER

The state of being male or female in typically regarding to social constructs rather than physical attributes.

TRANSGENDER

Does not identify with gender assigned at birth



CISGENDER

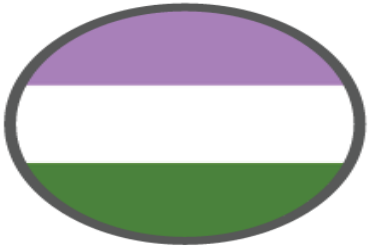
Identifies with gender assigned at birth

NON-BINARY

Refers to someone who does not identify as exclusively male or female.

GENDER FLUID

Refers to someone whose gender identity changes over time from one end of the spectrum to the other.



GENDERQUEER

Refers to someone whose gender identify falls on the spectrum between male and female.

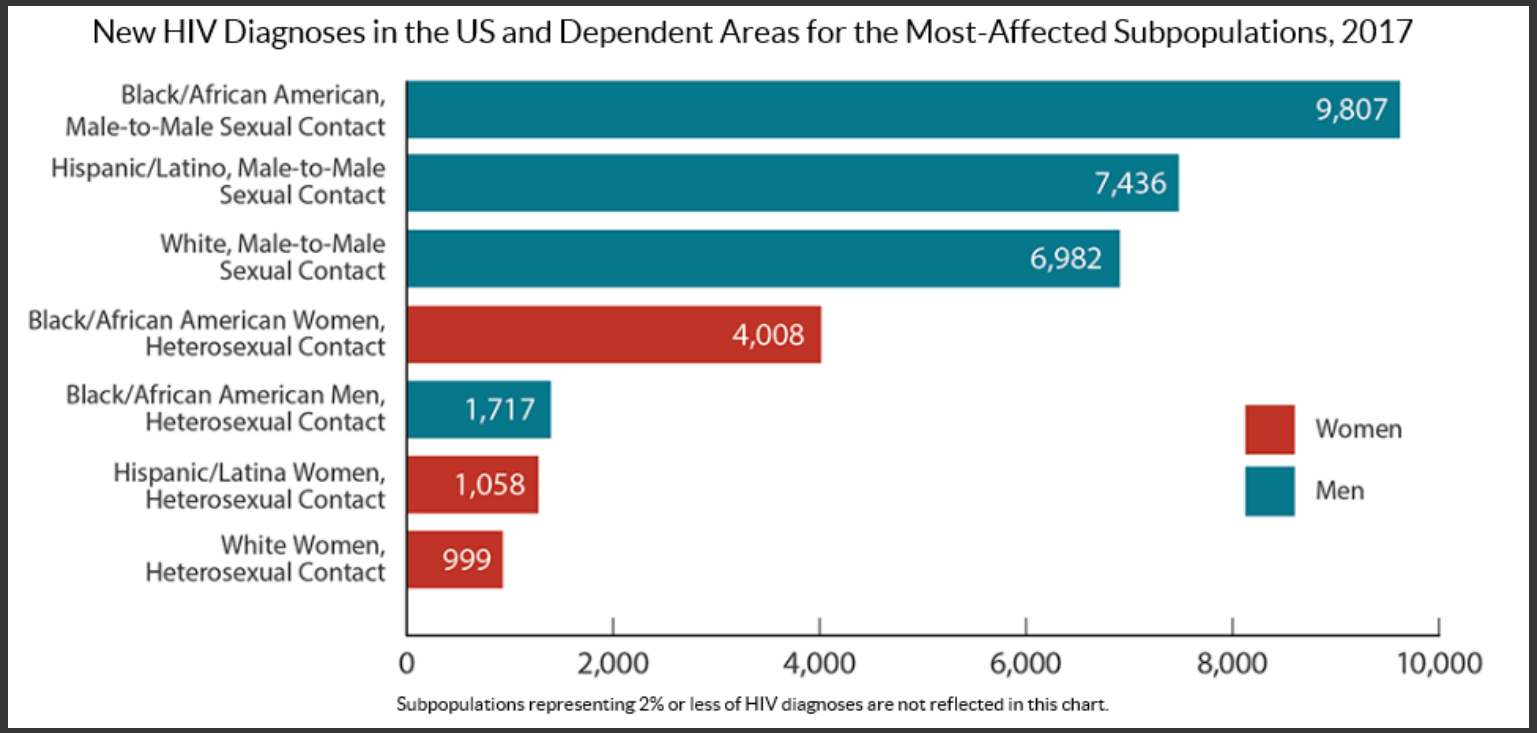
https://www.liveabout.com/what-does-it-mean-to-be-gender-non-conforming-1415327

Learning Outcome 1

1. Review the epidemiology of HIV in cis and transgender women

HIV and Women – US data

- 19% (7,401) of new HIV diagnoses(2017) were in women
- Ethnicity/Race difference



https://www.cdc.gov/hiv/group/gender/women/index.html

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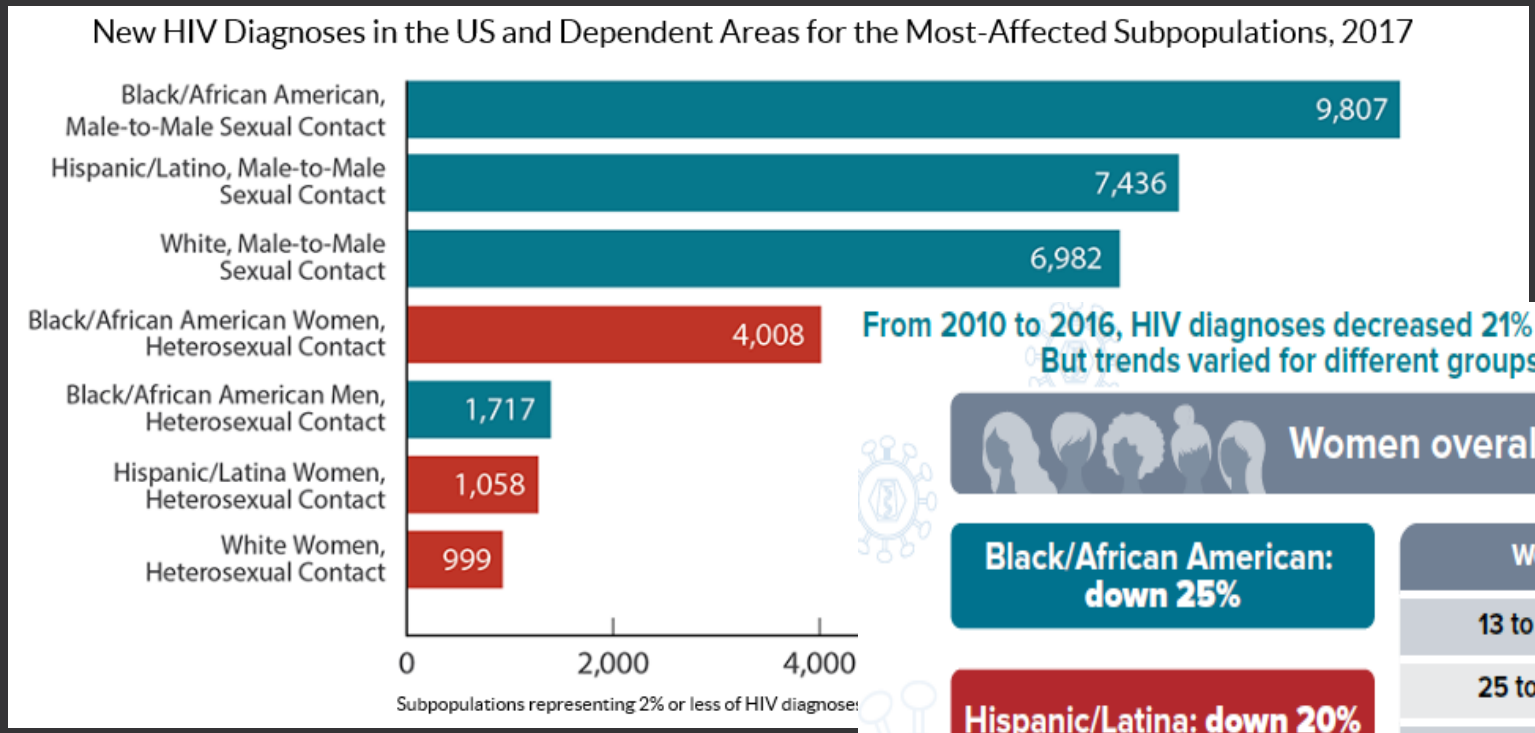
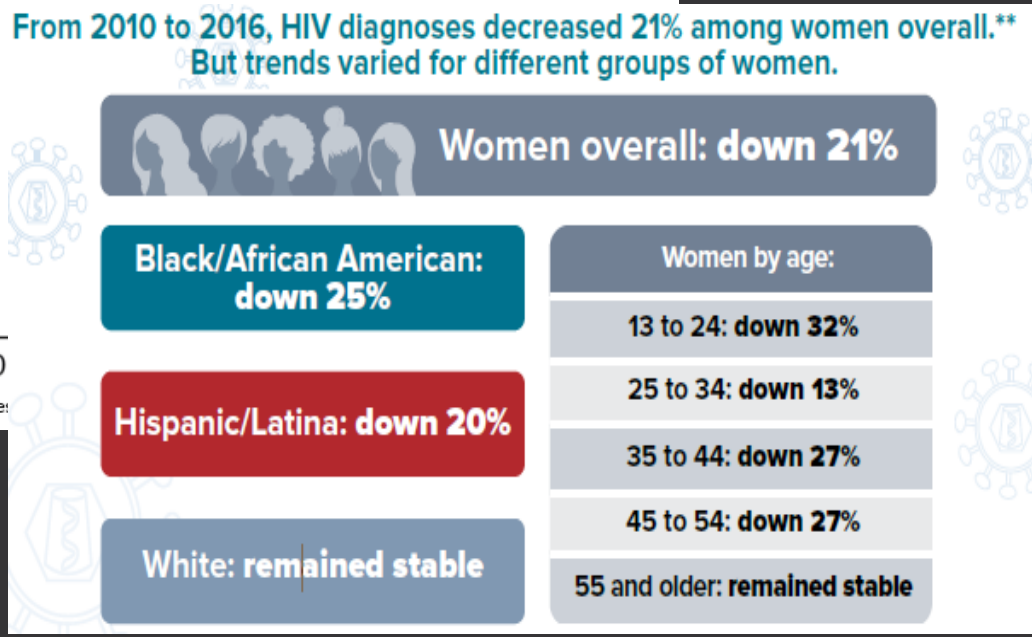
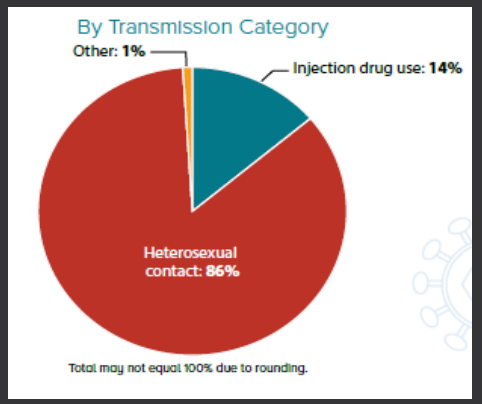




https://www.cdc.gov/hiv/group/gender/women/index.html

Focus Group for PrEP: Cis-Women

- New diagnosis of HIV in women by Transmission



- Why are women at risk for HIV
  - **Unaware of their male partner's risks** (IVDU or having sex with men) → No condoms (93% of HIV-negative high-risk women had vaginal sex without a condom; 26% had anal sex without condom[2])

"Southern women are sometimes too polite to ask" -TC

  - **At higher risk for getting HIV during vaginal/anal sex** than their sex partners
  - HIV **testing rates lower** among women (20% who had anal sex had HIV test[3])
  - **STI** (gonorrhea, syphilis) greatly increase the likelihood of HIV transmission
  - Women s/p sexual abuse more likely to **engage in sexual risk behaviors** - sex for drugs, multiple sex partners, or having sex without a condom

1https://www.cdc.gov/hiv/group/gender/women/index.html
2. behavioral survey(https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-number-19.pdf)
3. Evans et al Am J Obstet Gynecol.2018- Low HIV testing rates among US women who report anal sex and other HIV sexual risk, 2011-2015

Focus Group: Transgender Women - Transgender and HIV Risk

- ~1 million adults in the US are trans (underreported, pooled data)
- Time between identifying as transgender/ gender non confirming and HIV + = 5 years[1]

- Become providers of choice
- Start HIV testing !!!!
- Offer PrEP if -ve
- Safe sex

1. 2011 The National Gay and Lesbian Task Force and the National Center for Transgender Equality
2. Chung, et al. Positively Trans: Initial report of a national needs assessment ... Oakland, California: Transgender Law Center. 2016
3. Herbst, Estimating HIV prevalence and risk behaviors of transgender persons in the US AIDS Behav 2008
4. https://www.cdc.gov/hiv/group/gender/transgender/index.html

Focus Group for PrEP - Transgender

Why is this group high risk?

1. Risky behavior: multiple partners, anal/vaginal sex + no condoms or sharing needles to inject hormones/drugs (or pumping party)

Silicone Injections Given at Party Blamed in Transgender Woman's Death

By Vikki Vargas and Asher Klein

Published at 9:16 AM PST on Jan 30, 2015 | Updated at 12:17 PM PST on Jan 30, 2015

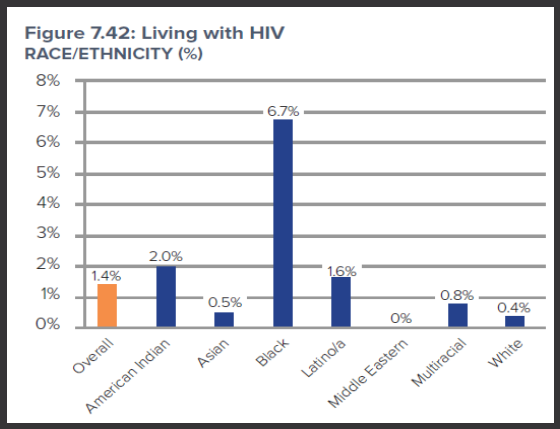
2. Social: stigma, discrimination, rejection/exclusion, commercial sex work
3. Providers not sensitive to trans issues → barrier for trans people living with HIV for treatment and care
4. HIV prevention programs may not address needs of trans people
5. Current HIV testing programs may not be enough to reach trans people

https://www.cdc.gov/hiv/pdf/group/gender/transgender/cdc-hiv-transgender-factsheet.pdf
https://www.cdc.gov/hiv/group/gender/transgender/index.html

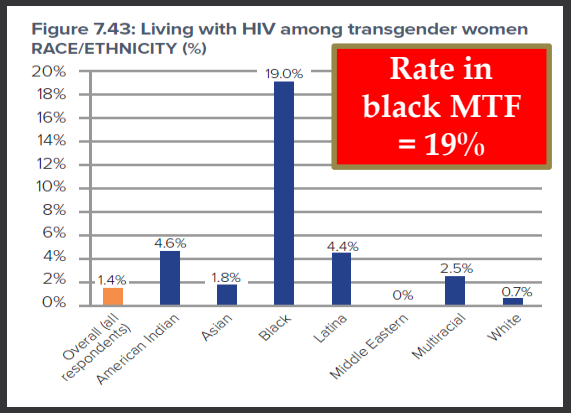
Health Disparities: - Transgender and HIV

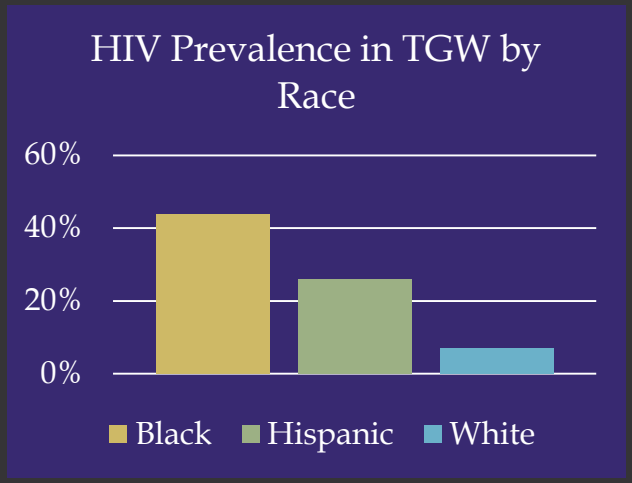
- [1]Overall rate of HIV in trans = 1.4%
  - > 4X higher than US pop. (0.3%)
  - Higher rates in blacks
  - Higher rates in trans women (TGW) 3.4%

- More recently HIV prevalence[2]
  - Transgender women= 18.8%
  - Transgender men= 2.0%
  - Majority of new HIV infections in TG are between 13-29 years old(56%)[3]



2015 US Transgender Survey





1. Center for Transgender Equality- 2015 survey (n=27,715)
2. Becasen J, et al. AJPH 2018,
3. Habarta N, et al. AJPH, 2015

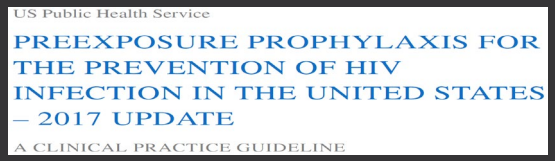
Learning Outcome 1a

1. What is PrEP?
2. Where we are in the South?

PrEP: What is HIV PrEP

- Pre-exposure prophylaxis (PrEP)
  - Method of preventing an uninfected person from acquiring disease

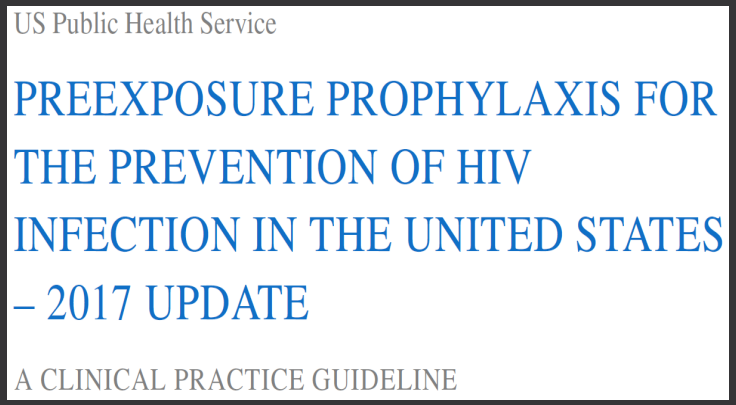
- HIV PrEP

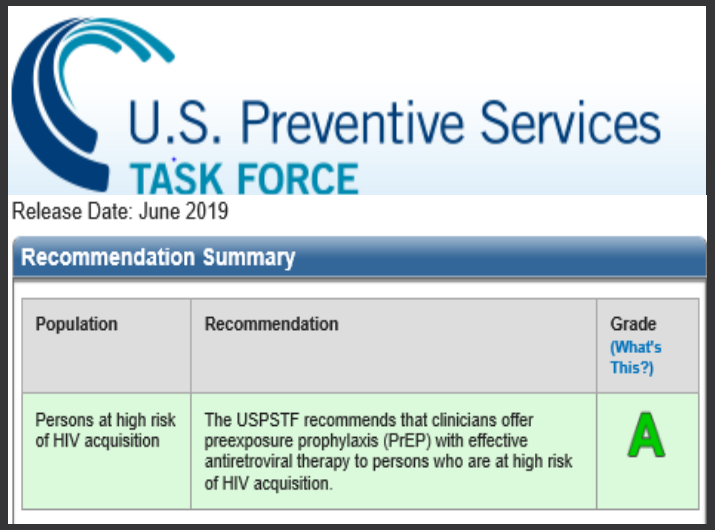


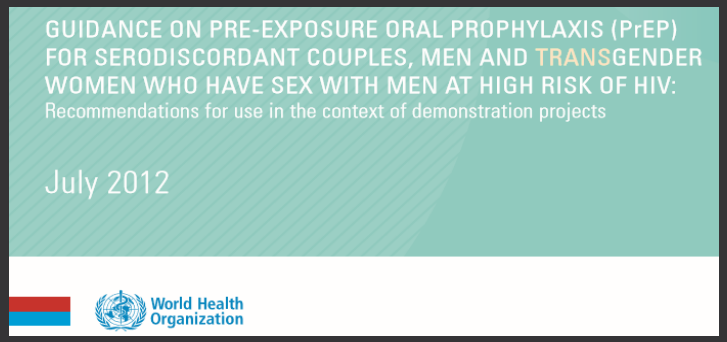
  - Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg + emtricitabine (FTC) 200 mg has been shown to be **safe and effective** in reducing the risk of HIV acquisition in at risk adults(AI)[1]
    - Truvada® (FDA approved) for patients with eGFR >=60
    - FDA approved for adolescents over 35 kgs(2018)

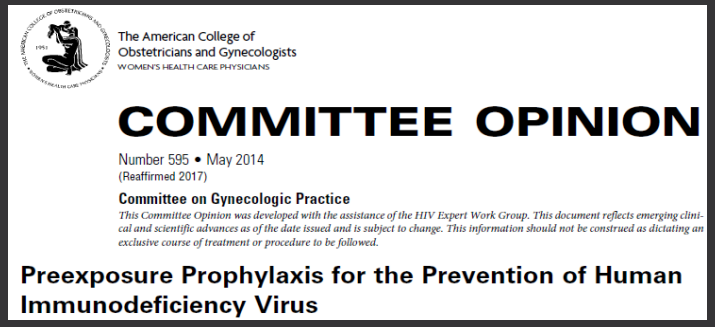
1. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf
2. Centers for Disease Control and Prevention. *HIV surveillance Report, 2016;* vol 28. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2016-vol-28.pdf

PrEP: Who Recommends/Endorses it









1) https://www.cdc.gov/hiv/risk/prep/index.html (CDC- 2017 guidelines)
2) http://apps.who.int/iris/bitstream/handle/10665/75188/9789241503884_eng.pdf;jsessionid=F0C57C0B6ADFA651F46AF51949D6848F?sequence= (WHO 2012 guidelines)
3) https://www.uspreventiveservicestaskforce.org/BrowseRec/Search?s=PREP
4) https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Gynecologic-Practice/Preexposure-Prophylaxis-for-the-Prevention-of-Human-Immunodeficiency-Virus

PrEP: An Alternative to daily TDF/FTC
On-Demand or Event-Driven PrEP ("2-1-1") Peri-coital TDF/FTC

International Antiviral Society–USA Panel
Saag et al JAMA 2018

Approved in France

- **MSM** with infrequent sexual exposures (IPERGAY[1,2])
  - **2** doses with food 2-**24**hrs before sex
  - **1** dose 24 hours after the first (double) dose
  - **1** dose 24 hours later

Lack of data: transgender, heterosexuals and IVDU

- Detectable levels in colorectal tissue in 81% and 98% of the population when administered 2 and 24 hours prior[3]

- For consecutive sexual contacts,
  - Initiate double dose, then 1 pill/day until 2 days after the last encounter

- Not if Hep B+

1. Molina *N Engl J Med*. 2015; 2 Molina 9th International AIDS Society Conference 2017; 3 Cottrell *J Infect Dis*. 2016

PrEP: An Alternative to daily TDF/FTC

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Not an option for Cis/trans Women

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PrEP Case 1

- A 30-year-old cis-gender woman is referred for PrEP
- She is married to cis-gender male and they have sex with 2 other occasional male partners
- Rectal gonorrhea 3 months ago
- PMH IgA nephropathy
  - Serum creatinine is **1.72 (eGFR ~ 40)**
- An HIV antibody/antigen test is negative

PrEP Case 1

- What would you recommend for PrEP for this patient based on current guidelines?
  - Tenofovir disoproxil fumarate -emtricitabine(TDF-FTC)
  - Tenofovir alafenamide-emtricitabine(TAF-FTC)
  - Maraviroc
  - No PrEP

PrEP: An Alternative to daily TDF/FTC
Options for Near Future

1. TAF/FTC –Recommended by the FDA Antimicrobial Drugs Advisory Committee for MSM and transgender women (July 2019)- pending FDA official approval and incorporation into guidelines

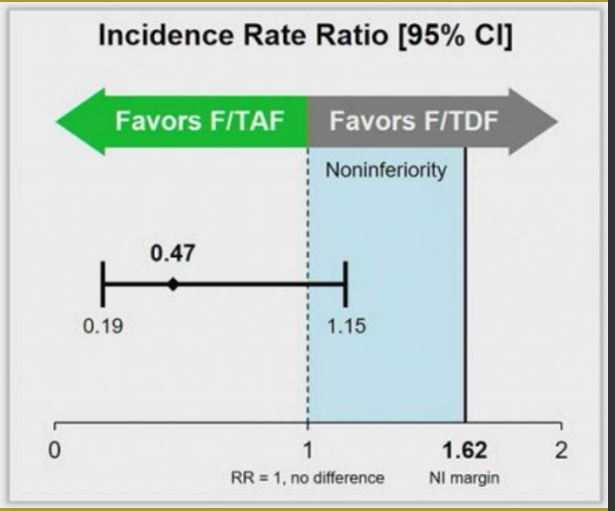
Not an option for Cis Women

PrEP: An Alternative to daily TDF/FTC
Options for Near Future
Discover: Phase III RCT of F-TAF vs. F-TDF for PrEP

- Truvada® (TDF/FTC) only FDA approved drug for PrEP
- In treatment trials TAF less renal toxicity and bone toxicity than TDF
- Can FTC/TAF (Descovy®) be used for PrEP?

- RCT of Truvada® vs Descovy® for PrEP
  - MSM and TGW
  - Enrolled ~6000
  - Followed to 96 wks
  - 74 TGW
  - 9% black race
  - High rates STI and chemsex

- 22 HIV transmission
- 7 TAF and 15 TDF



CROI 2019

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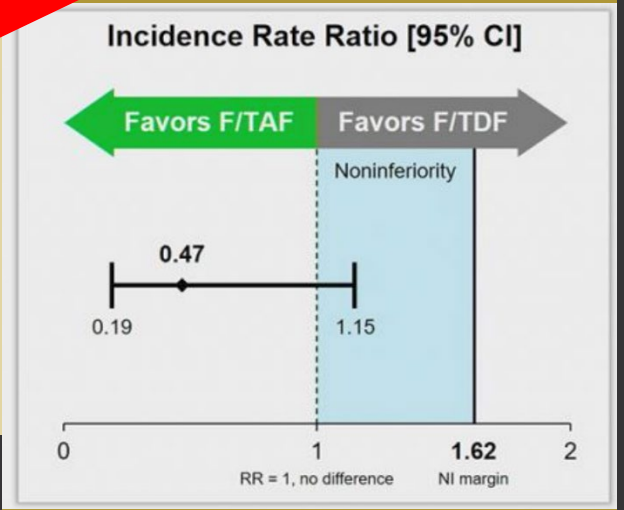
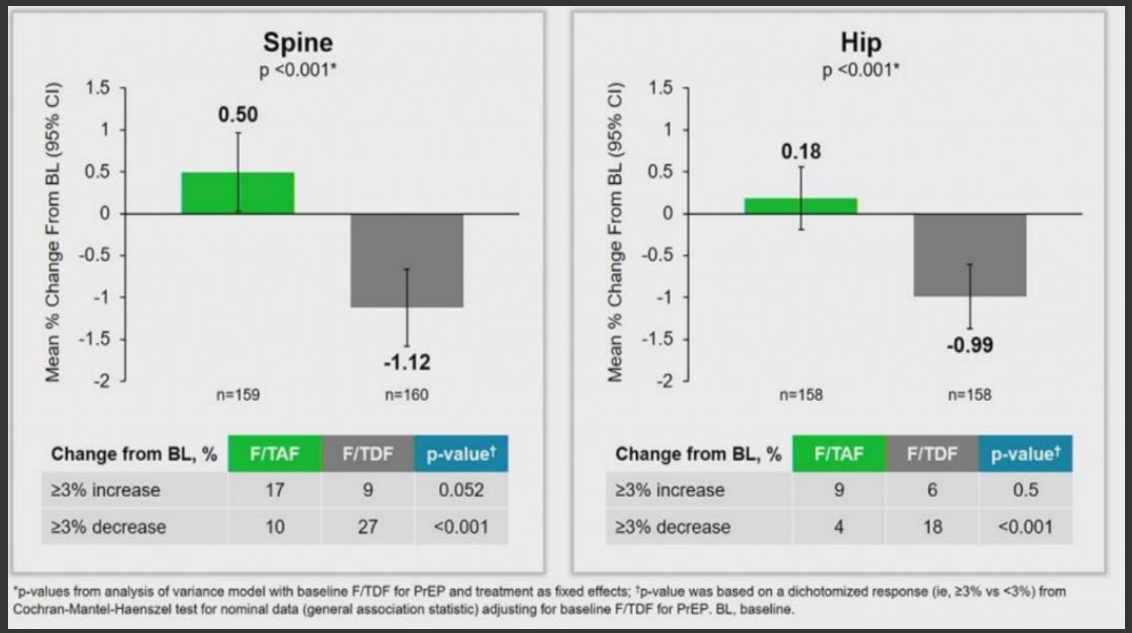


Need efficacy data on F-TAF for PrEP in women and youths

PrEP: An Option for the Future

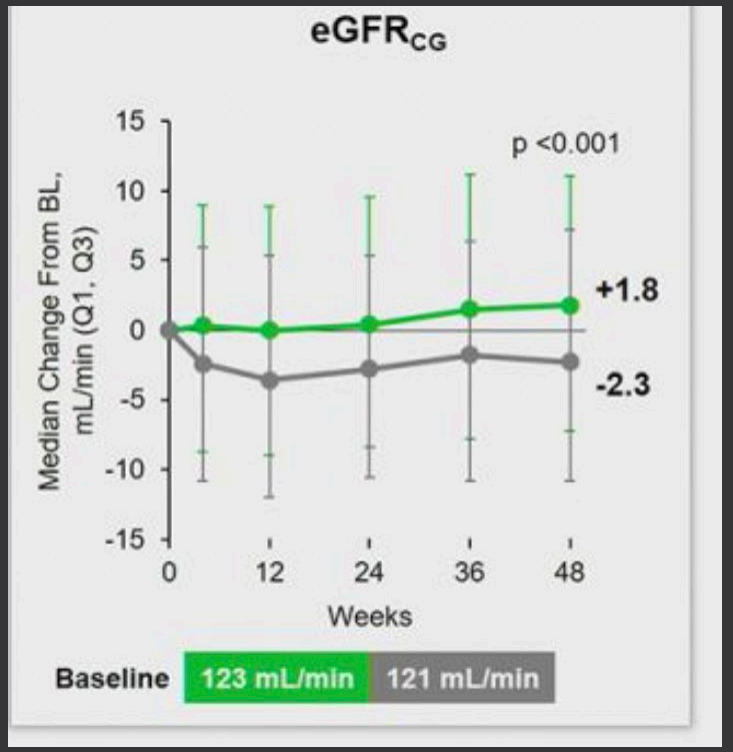
F-TAF safer for bone and kidney health



Change from BL, %	F/TAF	F/TDF	p-value†
≥3% increase	17	9	0.052
≥3% decrease	10	27	<0.001

Change from BL, %	F/TAF	F/TDF	p-value†
≥3% increase	9	6	0.5
≥3% decrease	4	18	<0.001

*p-values from analysis of variance model with baseline F/TDF for PrEP and treatment as fixed effects; †p-value was based on a dichotomized response (ie, ≥3% vs <3%) from Cochran-Mantel-Haenszel test for nominal data (general association statistic) adjusting for baseline F/TDF for PrEP. BL, baseline.



CROI 2019-Discover: Phase III RCT of F-TAF vs. F-TDF for PrEP

PrEP: An Option for the Future

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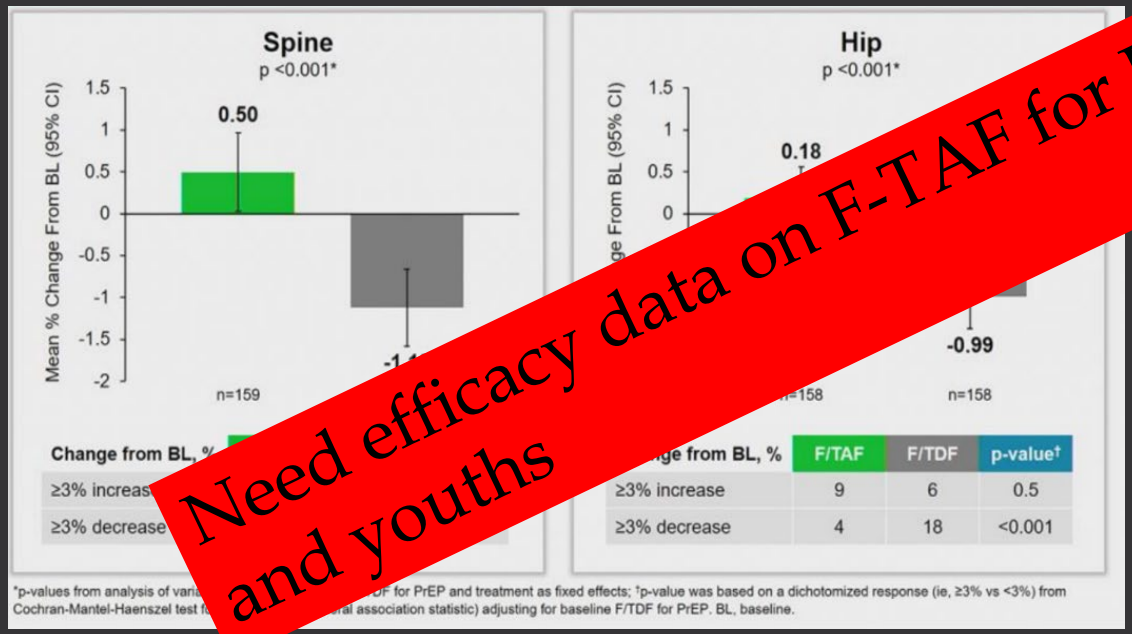

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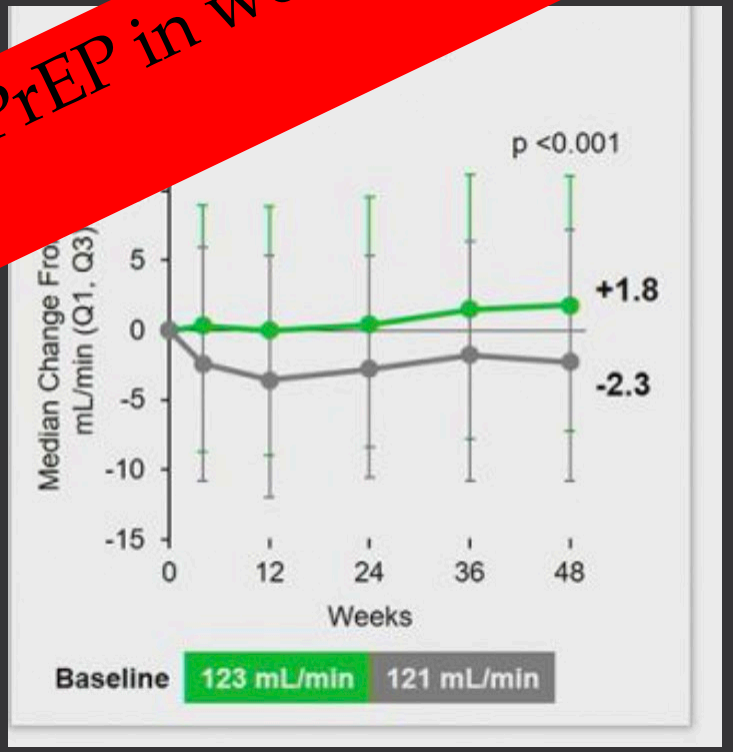


CROI 2019-Discover: Phase III RCT of F-TAF vs. F-TDF for PrEP

Case 2

- 17 y/o cis gender female presents to your FM clinic
- For pre- college work up (College in the South)
- During sexual hx
  - Bisexual – oral, anal, vaginal
  - Pap smear last month, chlamydia positive*1

- Exam
  - Vital normal , weight 50kg
  - Normal well-developed young woman

Case 2

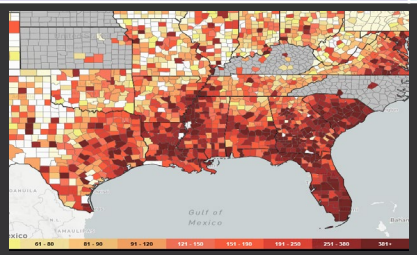
- In addition to updating her meningococcal vaccine, should PrEP be offered?
  1) yes
  2) no

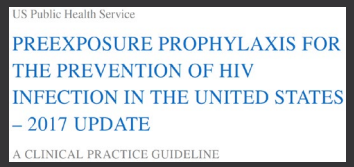
PrEP: Who Needs It?

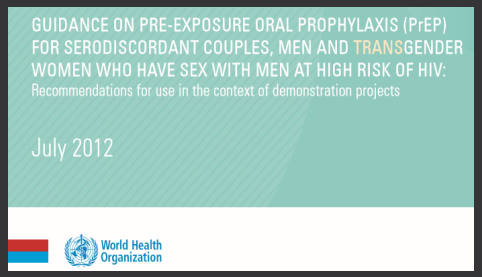
	MSM	Heterosexual Men and Women	Injection Drug Users
RISK	• Commercial sex workers • HIV+ partner • Recent STI • Multiple partners • Inconsistent/ No condoms	• Commercial sex workers • HIV+ partner • Recent STI • Multiple partners • Inconsistent/ No condom use • High prevalence area	• HIV positive injecting partner • Sharing needles/ injection equipment

Transgender People

Trans women of color[2]
(National HIV/AIDS Strategy 2010, 2015)







1. https://www.cdc.gov/hiv/risk/prep/index.html (2017 guidelines)
2. Herbst JH, Jacobs ED, Finlayson TJ, et al. Estimating HIV prevalence and risk behaviors of transgender persons in US . AIDS Behav 2008
3. https://www.cdc.gov/mmwr/volumes/68/wr/mm6827a1.htm?s_cid=mm6827a1_
4. AIDSVU

Ending the HIV Epidemic: An American Plan

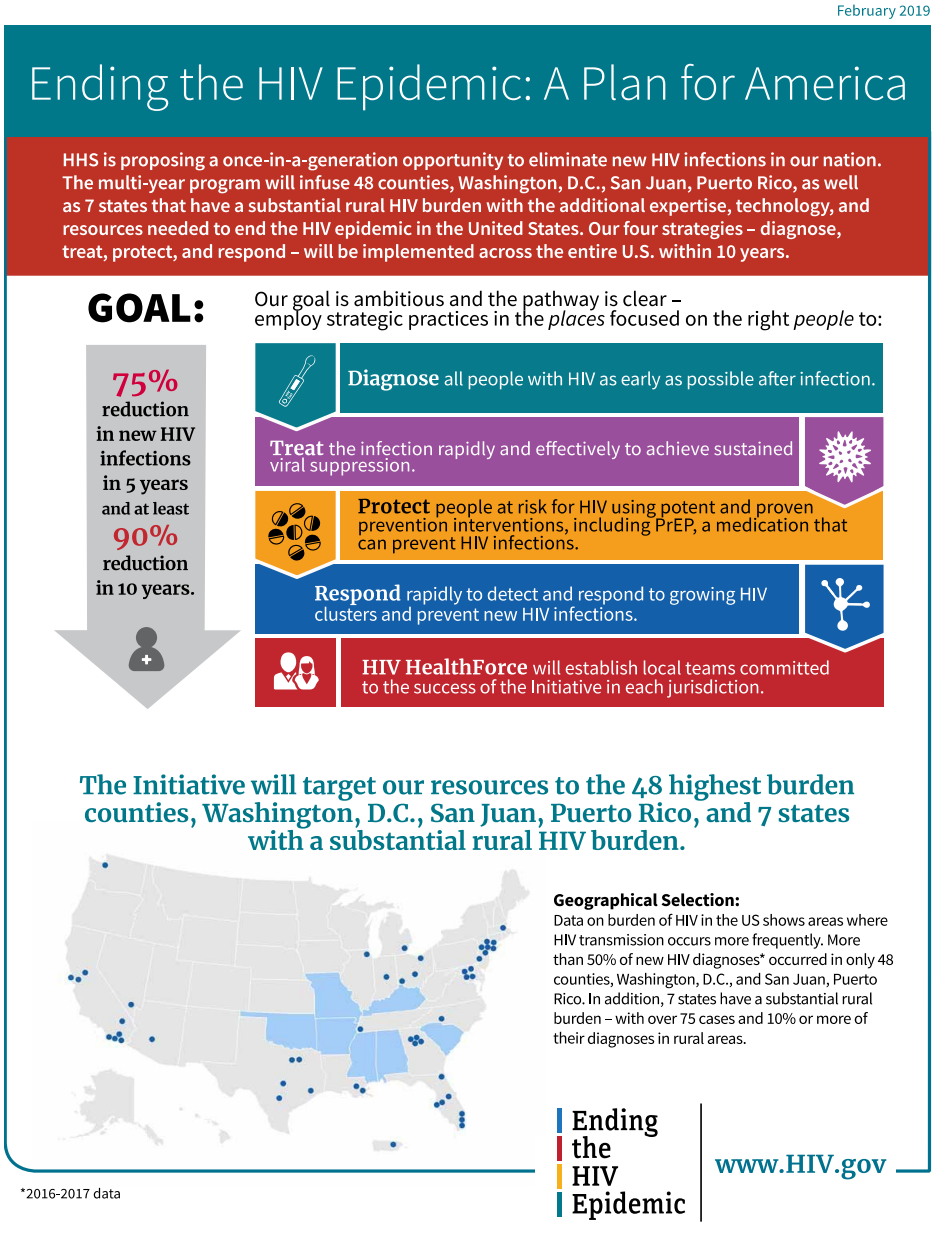
Goal :

- 75% reduction in new HIV infections in 5 years
- 90% reduction by 10 years

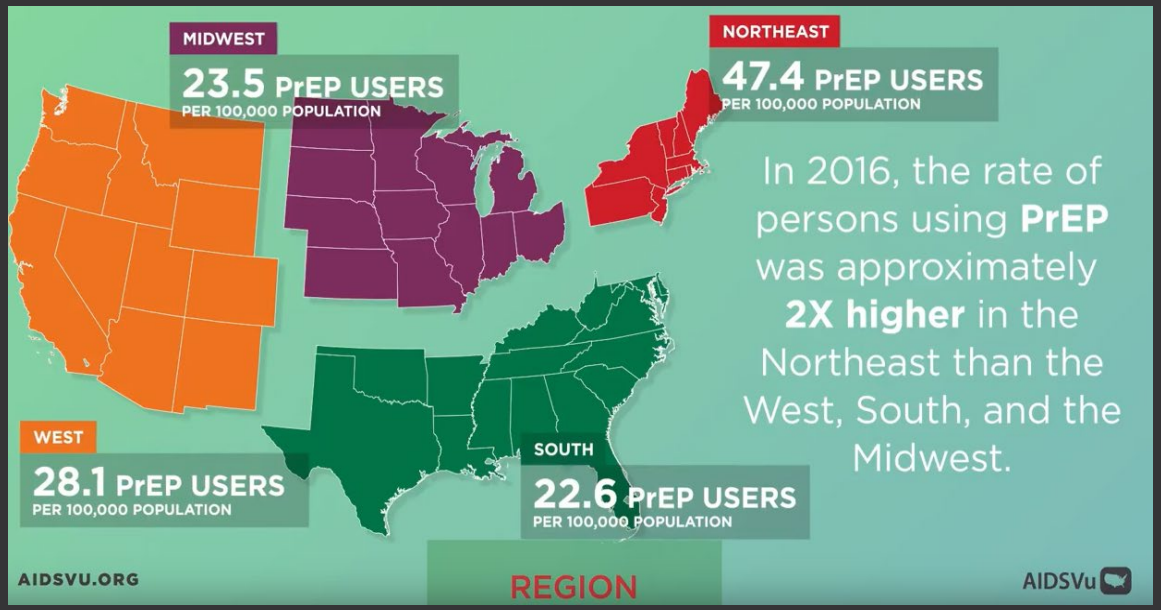
Plan :

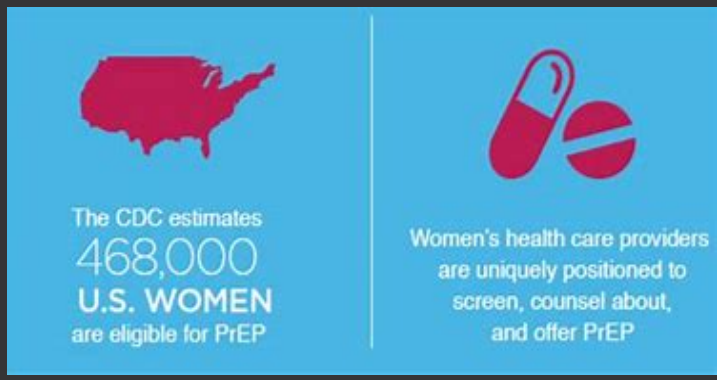
Target areas disproportionally effected by HIV

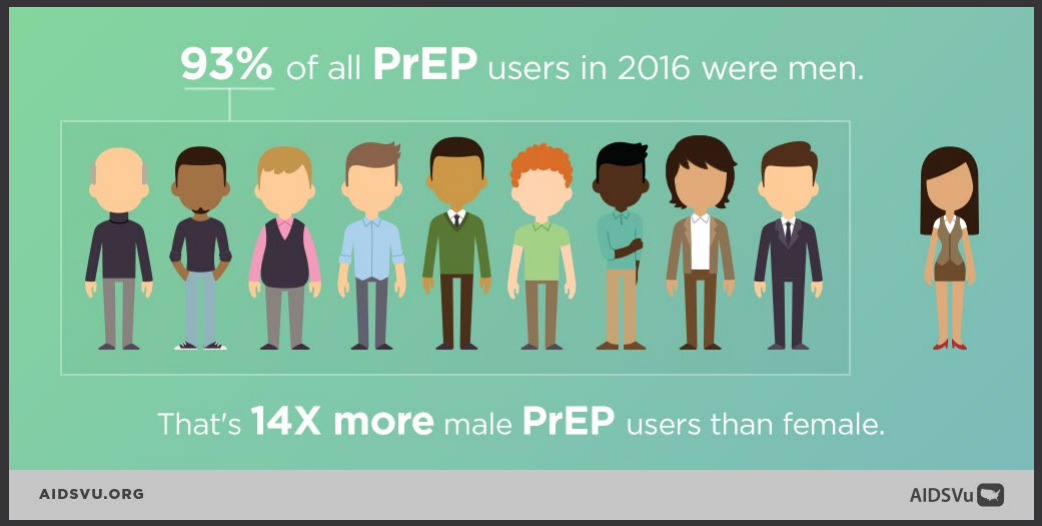
- 48 of 3007 counties in U.S. account for >50% new HIV infections
- 7 states with a substantial rural burden of HIV



PrEP in Women







1. https://hiveonline.org/prep4women-disparities/-UCSF
2. DC'S PrEP AWARENESS CAMPAIGN

Trends in PrEP Use In the US

Age Group

Gender

Region

Lowest rates in youth ≤24 year

Lower rates in women

Lowest rates in Southern U.S.

Age groups, yr

24 and younger (EAPC=+55.3%)

Overall (EAPC=+60.6%)

South (EAPC=+59.6%)

West (EAPC=+59.0%)

PnR*

Year

Sullivan Et. Al. Ann Epi.https://doi.org/10.1016/j.annepidem.2018.06.009

Missed Opportunities to Prescribe PrEP (SC 2013-2016)

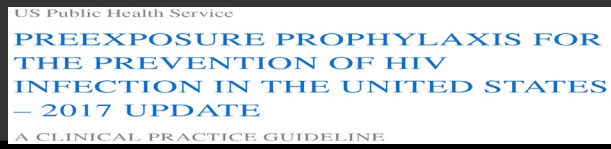
- 885 new HIV+ pts had 4029 healthcare visits in the months prior to diagnosis
- 2/3rd had missed opportunities for PrEP engagement
- **Women, Black race and younger** individuals were more likely to have had missed opportunity
- Location
  - 84% of missed opportunities occurred in the ED
  - 10% occurred in outpatient clinics
- 46% had no insurance coverage

Clinical Infectious Diseases· May 2018. DOI: 10.1093/cid/ciy441

Learning Outcome 2

1. Discuss data supporting HIV PrEP in cis and transgender women

PrEP: Does it Work?



Trial	Where	Who	What	Efficacy
1. iPrEx n=2499	SA, US, South Africa, Thailand	MSM high risk	TDF-FTC or placebo	44% TDF-FTC
2. Partners PrEP n=4747	**Kenya, Uganda**	**Discordant hetero couples**	**TDF, TDF-FTC or placebo**	**67 -75% (TDF, TDF/FTC) •Men 84% •Women 66%**
3. US MSM safety Trial, n=400	US	MSM	TDF or placebo Early vs delay	Not reported ; 0 infections on TDF
4. TDF2 n=1219	**Botswana**	**Hetero men or women**	**TDF-FTC or placebo**	**62.2% all •80% men •49% women (NS)**
5. FEM-PrEP n=2120	**Kenya, South Africa, Tanzania**	**Women**	**TDF-FTC or placebo**	**Stopped early due to lack of efficacy**
6. VOICE n=5021	**Uganda, South Africa, Zimbabwe**	**Heterosexual women**	**TDF gel, placebo gel, TDF, TDF-FTC, placebo pill**	**TDF gel/pill stopped, lack of efficacy**
7. West African Trial n=859	**West Africa**	**Hetero women**	**TDF vs placebo**	**65% (NS, stopped early)**
8. Bangkok TDF n=2413	Thailand	IVDU	TDF or placebo	49% TDF

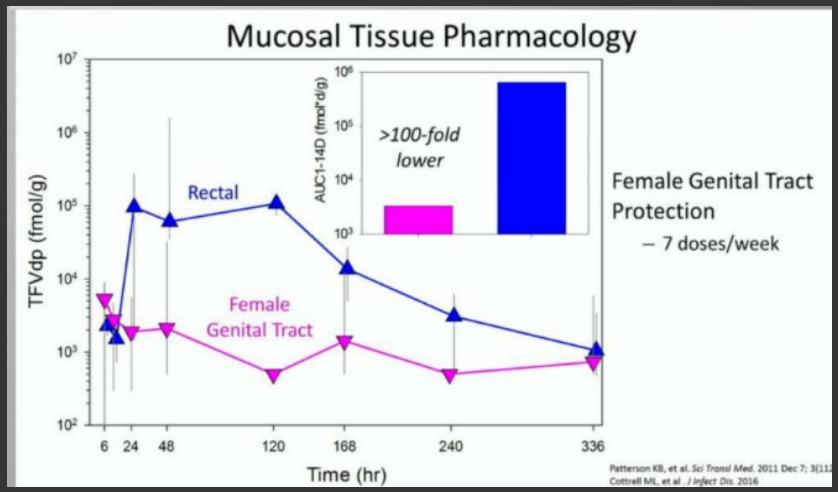
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

PrEP in Women: Why didn't it work?

- 2 large studies (FEM-PrEP and VOICE trials), PrEP was not effective in preventing HIV

- Women need to work harder!
- Focus counselling efforts on cultural barriers

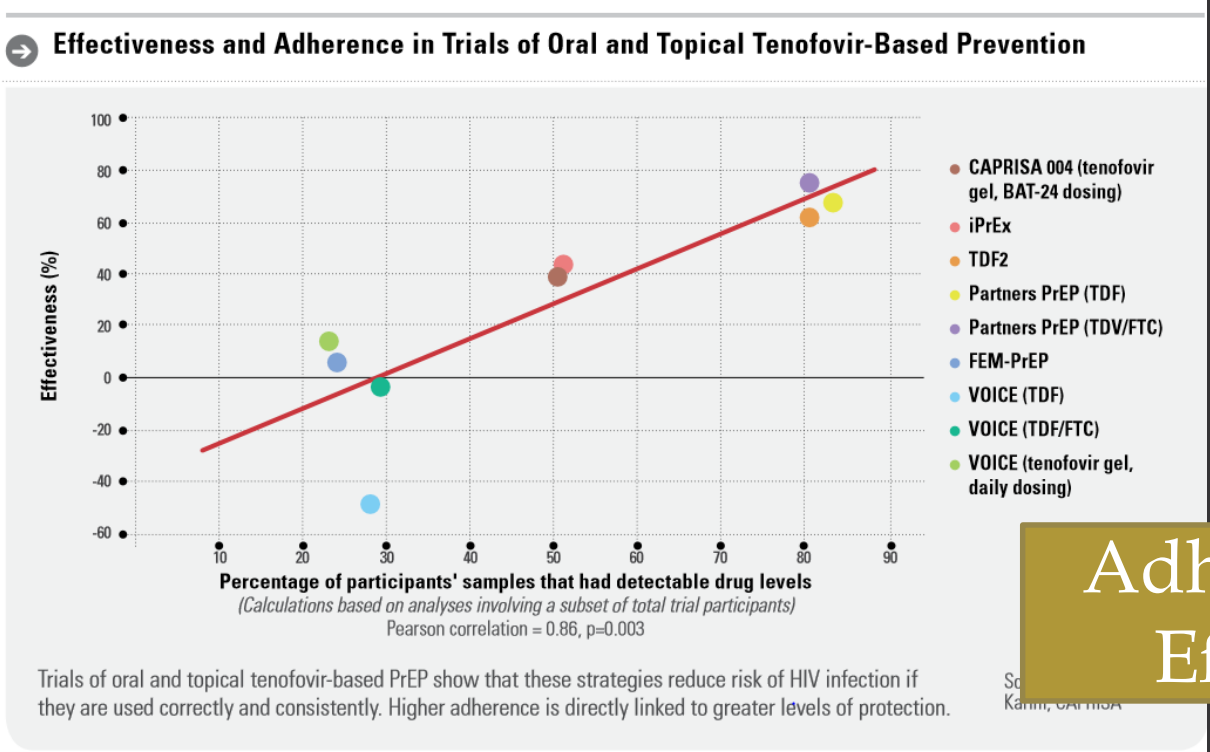
  - Differences in vaginal concentrations of drug is a plausible role in lack of efficacy



Van Damme L, et al. N Engl J Med. 2012;367:411-422
Marrazzo JN, et al. N Engl J Med. 2015;371:509-518.

PrEP: Efficacy and Adherence

- If drug detected in blood, effectiveness of PrEP = **90-92%**
  - 92-100% if levels equivalent to daily use[2] (Post Hoc iPrEx)
  - 0 conversions if at least 4 doses taken[3]



Adherence= Efficacy

AVAC Report. 2013
2 Anderson . Intracellular TDF/FTC driedbloodspots following DOT .Antimicrob AgentsChemother.2017
3 Anderson iPrExStudyTeam. PrEP efficacyinmenwhohavesexwithmen.SciTransl Med.2012

Case 3

- 23 y/o transwoman (MtF) , unemployed on feminizing hormones
- Sources of income intermittent gas station work
- Occ prostitution
- Seeing you in FMC for rectal pain and drainage
- Diagnosed with gonorrhea

Case 3

In addition to treating her GC , what else can we offer?

1) Nothing , too busy
2) Condoms and counselling on risk reduction only
3) Condoms, counselling and PrEP
4) Condoms and no PrEP due to lack of data to support PrEP in trans people

PrEP: TDF/FTC in Transgender The Earlier Studies

Trial	Where	Who	What	Efficacy	Efficacy by blood detection of drug
1. iPrEx[1] n=2499 (2010)	SA, US, South Africa, Thailand	MSM high risk+ **Trans women**	TDF-FTC or placebo	**44**% TDF-FTC	0 conversations in those with levels consistent with daily use[2]

Open Label Studies with good outcomes- TDF/FTC

What, where, when	Participants (n)	Efficacy Estimates %	Efficacy by blood detection of drug
Demo (3 centers, US)	MSM (552^) **MtF (5)**	HIV incidence 0.43 per 100 py	2 seroconverters had levels equivalent to <2 doses/wk

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf
1. Grant PrEP for HIVpreventioninmenwhohavesexwithmen. NEnglJMed.2010
2 Anderson iPrExStudyTeam. PrEP efficacyinmenwhohavesexwithmen.SciTransl Med.2012
Demo - Liu JAMA.2016^

PrEP: TDF/FTC in Transgender

iPrEx Trial had 339 Transwomen (MtF) only

- Compared with MSM, MtF more frequently reported transactional sex, receptive anal intercourse without a condom, or >5 partners in the past 3 months
  - PrEP did not affect behavior
- Overall adherence, less for MtF
- 11 MtF converted vs 10 in placebo group
  - At time of conversion, none had detectable drug levels (n=6)
- **if > 4 tablets/week, rate of infection per 100,000 pt/yr = 0**

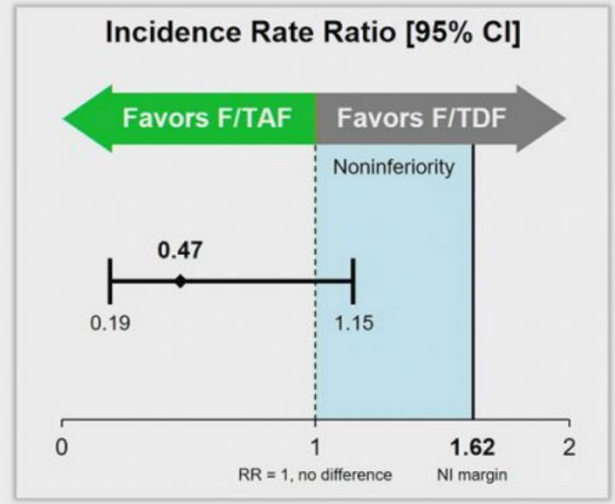
Similar barriers to adherence as women

Deutsch HIV PrEP in transgender women: iPrEx trial. Lancet HIV. 2015

PrEP: An Option for the Future TAF/FTC in Transgender

- RCT of Truvada® versus Descovy® for PrEP
  - MSM and TGW
  - Enrolled ~6000
    - **74 TGW**
  - Followed- 96 wks
  - 9% black
  - High rates STI and chem-sex

- 22 HIV transmission
- 7 TAF and 15 TDF



CROI 2019-Discover: Phase III RCT of F-TAF vs. F-TDF for PrEP

PrEP: The Reality for Transgender

- Does PrEP interfere with gender affirming hormones? No
  - PrEP does not affect the efficacy of sex hormones[1,2]
    - But hormones can drop PrEP levels→ Ensure Compliance

Don't let this be a deterrent

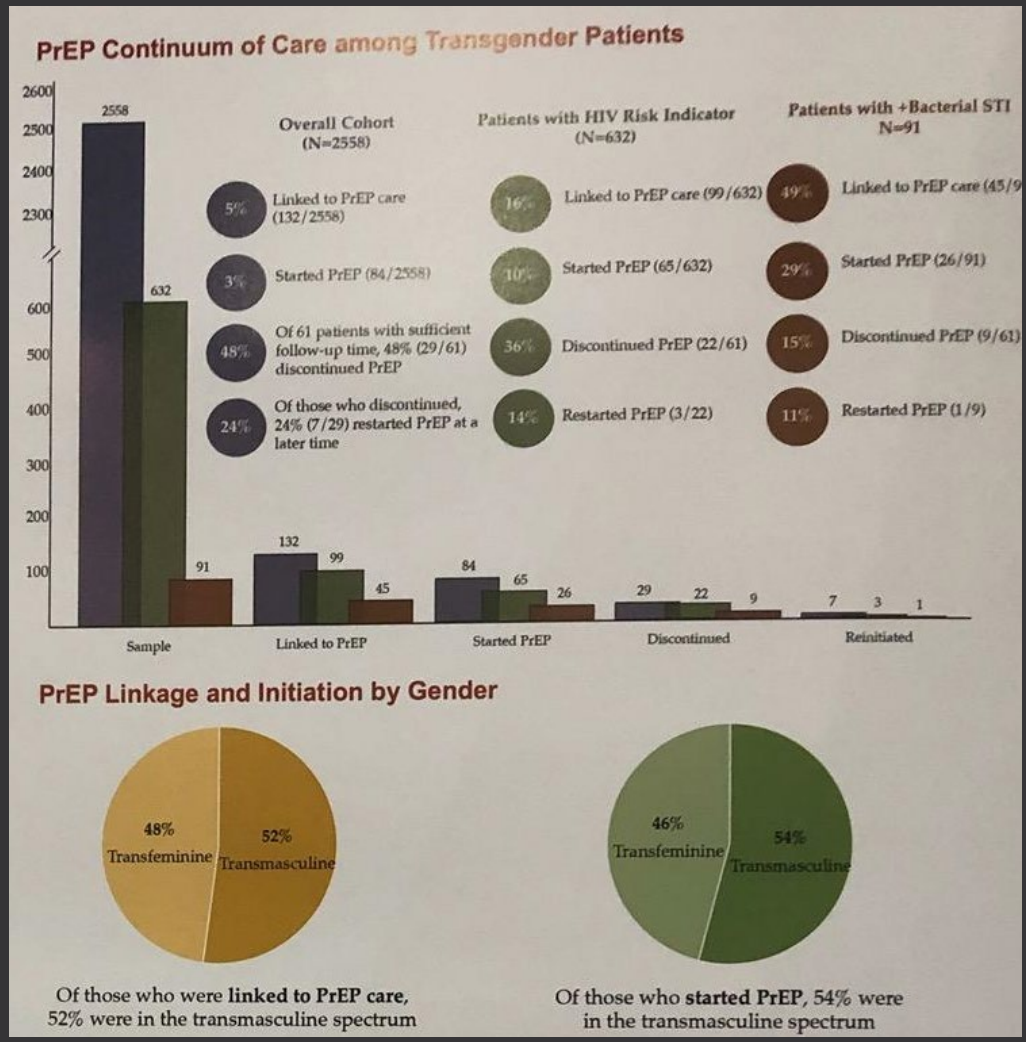
  - When not addressed with patients, adherence with PrEP declined due to fear of drug-drug interaction with hormones[3]

1 WHO endorsed
2 *Kearney* Lack of effect of TDF on pharmacokinetics of hormonal contraceptives. *Pharmacotherapy. 2009*
3 Deutsch HIV PrEP in transgender women: iPrEx trial. Lancet HIV. 2015

PrEP Continuum of Care

PrEP Continuum in Transgender

- Kaiser gp (2012-2019)- n=2558 pts (HIV negative)
- Majority of trans pt in care – white, average age 33, 51% trans woman
- Higher rates of discontinuation in those with ETOH/ Substance abuse

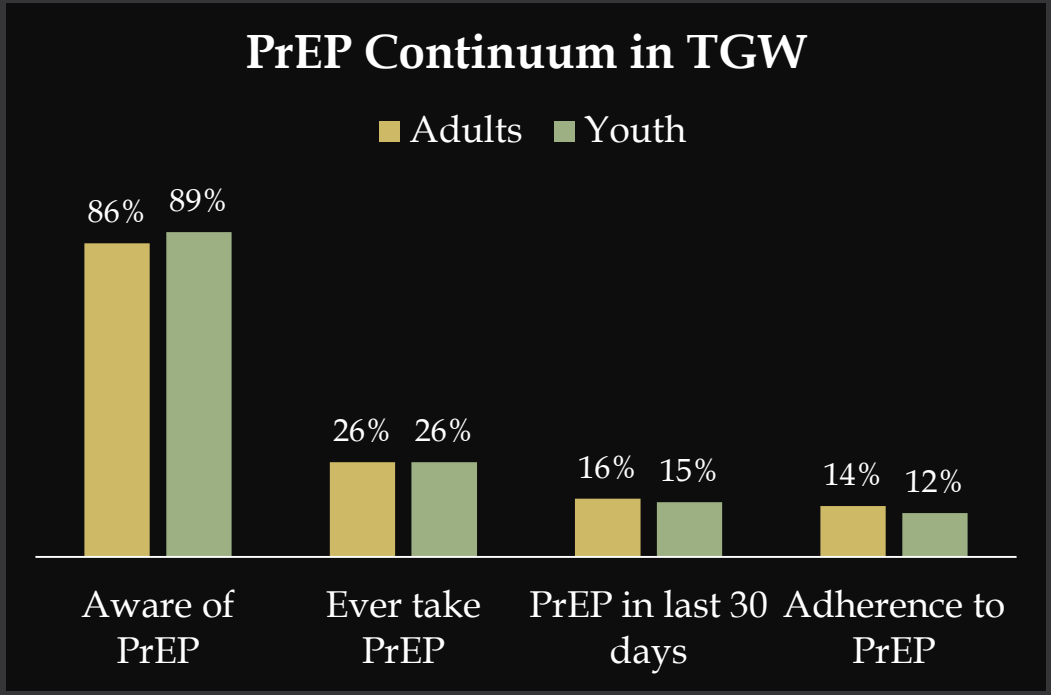


Hojitia, Volk et al IAS 2019

PrEP Continuum in Transgender Women

The LITE Study

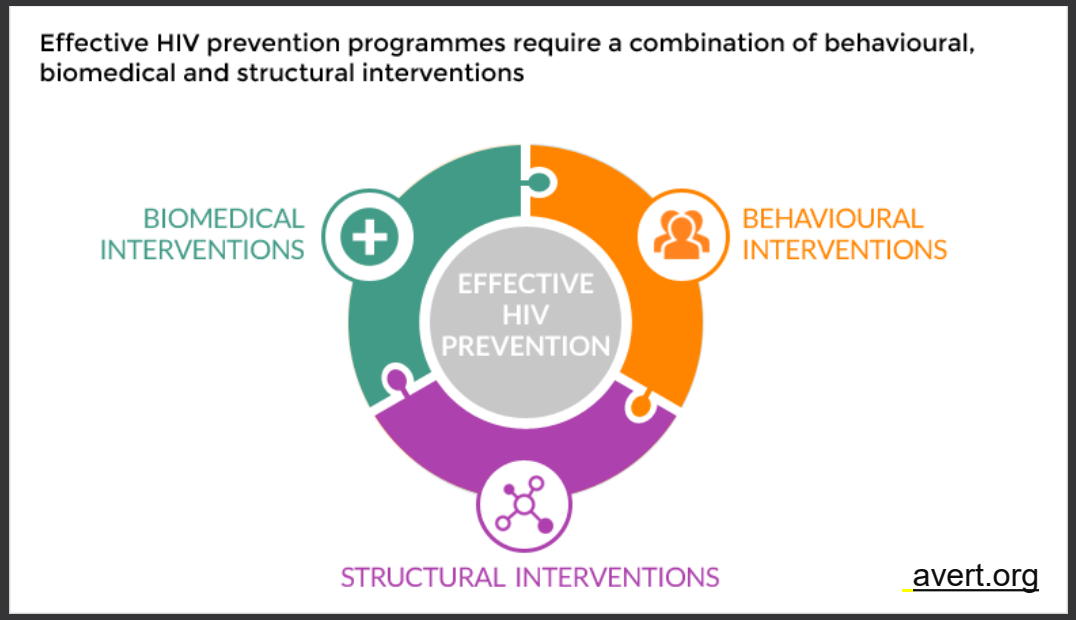
- HIV uninfected MtF(TGW) in 6 cities (incl. South)
- 3 months visits with testing and survey
- App-based GPS data collection, some self testing



http://www.croiwebcasts.org/console/player/41371?mediaType=audio&

Learning Outcome 3

1. Describe the process of overcoming the barriers to providing PrEP for cis and transgender women



I. How to modify practice to meet the needs

Perceived Barriers

Top Concerns of Transgender Pts:

1. Gender affirming and **non discriminatory care** (59%)
    I. 37% of those who saw a health care provider in SC had at least 1 negative experience[2]
2. Hormone therapy and side effects (53%)
3. Mental Health care, including trauma recovery (49%)
4. Personal care (nutrition, healthy living (47%)
5. ART and side effects (46%)

    .....

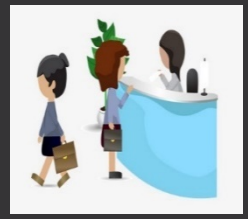
    PrEP and post-exposure prophylaxis (16%)

1. Chung, et al. Positively Trans: Initial report of a national needs assessment ... Oakland, California: Transgender Law Center. 2016 (n=159)
2. 2015 US Transgender Survey

National Center for TRANSGENDER EQUALITY Celebrating 15 Years

Providing Non-discriminatory/ Culturally Competent Care: A Welcoming Environment

1. No assumptions: gender identity, sexual orientation, or behavior
   - HCP should be nonjudgmental
2. Inclusive language on records
   - Appropriate pronouns /preferred name
   - Adding a 'Transgender' or 'Agender' or 'Other' option
3. Assurance of confidentiality
4. Training **staff to increase their knowledge and sensitivity**
   - Including front desk, phlebotomist
5. The adoption and posting of a nondiscrimination policy (organizational support)



Gay and Lesbian Medical Association. Guidelines for care of lesbian, gay, bisexual, and transgender patients. Washington, DC: GLMA; 2006.

*http://www.glma.org/_data/n_0001/resources/live/GLMA%20guidelines%202006%20FINAL.pdf

Activity 1: Getting Comfortable

- Disclose your pronouns
  - Around the office
  - Write it somewhere
  - Add to email signature

Slurs/it/he-she =
Offensive =
Missed opportunity for
PrEP initiation/ retention or
Suicide prevention

1	2	3	4	5
(f)ae	(f)aer	(f)aer	(f)aers	(f)aerself
e/ey	em	eir	eirs	eirself
he	him	his	his	himself
per	per	pers	pers	perself
she	her	her	hers	herself
they	them	their	theirs	themself
ve	ver	vis	vis	verself
xe	xem	xyr	xyrs	xemself
ze/zie	hir	hir	hirs	hirself

Providing Non-Discriminatory Care -Provider Biases

- Sexual history usually deferred: Primary care[3], STI care[4] ,HIV care[5-7]
- 40% of Physicians were uncomfortable with lesbian/gay pts (1986)[2]
  - If aware of trans status, likelihood of discrimination ⬆(2011)[1]
- Perceived Risk
  - Persons with greater heterosexism, more strongly anticipated increased risk behavior and adherence problems to PrEP → lower prescribing intention[8]

1 2011 The National Gay and Lesbian Task Force and the National Center for Transgender Equality.
[2] Matthews *et al., 1986*
3.Wimberly YH et al . Sexual history-taking among primary care physicians. *J Natl Med Assoc.* 2006
4. Kurth AE. A national survey of clinic sexual histories for sexually transmitted infection and HIV screening STD 2005
5. Laws MB, Discussion of sexual risk behavior in HIV care is infrequent and appears ineffectual: *AIDS Behav.* 2011
6. Metsch LR,. Delivery of HIV prevention counseling by physicians at HIV medical care settings in 4 US cities. *Am J Public Health.* 2004
7. Duffus WA, Effect of physician specialty on counseling practices /referral patterns among physicians caring for disadvantaged HIV populations. *CID 2003*
8. Sarah K. Calabrese**A Closer Look at Racism and Heterosexism in Medical Students' Clinical Decision-Making Related to HIV (PrEP): Implications for PrEP Education** AIDS 2018

Providing Non-Discriminatory Care: Assess Patients' Risk Behavior

- In the past 6 mos: (Heterosexual men and women)
  - Have you had sex with men, women, or both? (if opposite sex or both sexes) How many men/women have you had sex with?
  - How many times did you have vaginal or anal sex when neither you nor your partner wore a condom?
  - How many of your sex partners were HIV-positive?

    (if any positive) With these HIV +partners, how many times did you have vaginal or anal sex without a condom?

The five "P"s stand for:

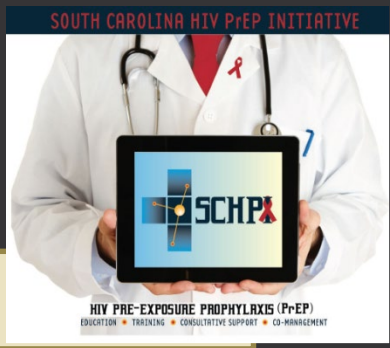
- **Partners**
- **Practices**
- **Protection from STDs**
- **Past history of STDs**
- **Prevention of pregnancy**

CDC. PrEP Guidelines. 2017.

Engaging Trans Patients (Extrapolating for HIV data)

- **Transgender people might not fully engage in medical care**
  - Lack of medical gender affirmation/stigma in HIV care associated with missing appointments[1] → risk of HIV transmission
    - 40% of FtM in care for HIV had detectable VL over prior 12 mths[2]
    - 50% of MtF had detectable VL over the prior 12 mths [3]

1 Reisner Characterizing the HIV Prevention and Care Continua in a Sample of Transgender Youth in the U.S. AIDS Behav. 2017
2 Lemons, Characteristics of HIV-Positive Transgender Men Receiving Medical Care: United States, 2009–2014 . ajph 2018
3 Mizuno , Characteristics of Transgender Women Living with HIV LGBT Health. 2015
https://www.cdc.gov/hiv/group/gender/transgender/index.html



Barriers	Solutions
Access[2]	Training providers
Cost[2] /Insurance	Medication assistance programs
Resistance[1]	HIV testing while on PrEP
Adherence	Counseling/Reminders/Behavioral Intervention
Side effects	OTC meds, Revisit need for PrEP Q 12 months
Heterosexism[2]	Training, Education on HIV public health burden, checking biases
Risk compensation	Emphasize condom use and screen for STIs frequently

1. 2017 HIV PrEP guidelines; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4308722
2. Calabrese. Racism and Heterosexism in Medical Students' Clinical Decision-Making Related to HIV PrEP: AIDS 2018

Adherence and Women

- Baseline studies
  - In at-risk women: PrEP not effective[1,2] Non – adherence

- Intimate Partner Violence (IPV) and PrEP [3,4,5]
  - Recent IPV (past 3 mths) associated with a lower adherence
  - VOICES trial
    - Women reported taking pills and pill counts (unused) pills suggested they took their PrEP
      - BUT serum drug levels undetectable
    - Revealed themes of stigma, fear, relationship conflict and lack of understanding

[1] Van Damme L, et al. N Engl J Med. 2012;367:411-422 ; [2] Marrazzo JN, et al. N Engl J Med. 2015;371:509-518
[3]Roberts ST, et al. CROI 2015. Abstract 980; [4]Saag MS. N Engl J Med. 2015; 372:564
[5]van de Straten A, et al. JIAS. 2014;17 (supple):19146

Adherence: An Interdisciplinary Approach

- Retention/adherence rates varies – higher in multidisciplinary scenarios 75%- 90%[1,3]
  - Pharmacist[1] and nurse models[4]

- **Text messaging**[2] service or PrEPmate(**app**)[5]
  - Those who opted for text were more likely to remain in clinic (76% vs. 53%)[2]
  - App had better adherence to visits/ therapeutic levels (56 vs 40% @ 36 wks)

- Brief **behavioral intervention** (sexual health or adherence) →less missed pills/higher drug levels (96.6%vs 84%; p = 0.02)- NYC[3]

1. CROI 2017 Tung et al FEASIBILITY OF A PHARMACIST-RUN HIV PREP IN A COMMUNITY PHARMACY
2. CROI 2017 (Abstract 964)- Khosropour et al
3. CROI 2017 (Abstract 965) – Sarit
4. Gibson, S. et al. AIDS 2016 (Strut)
5. *Clinical Infectious Diseases*, ciy810, https://doi.org/10.1093/cid/ciy810

Medication and Adherence Counseling
Role of Interdisciplinary Team: PharmD, CM

PrEP barriers: 31% concerned about potential adverse events

- Counseling - AE typically resolve within 1 mth of starting therapy ("start-up syndrome")
  - Discuss OTC meds for headache, nausea, flatulence
  - Counsel regarding symptoms requiring urgent evaluation
- Drug–drug interactions
- Missed doses
- Remind the patient that PrEP does not prevent STIs!

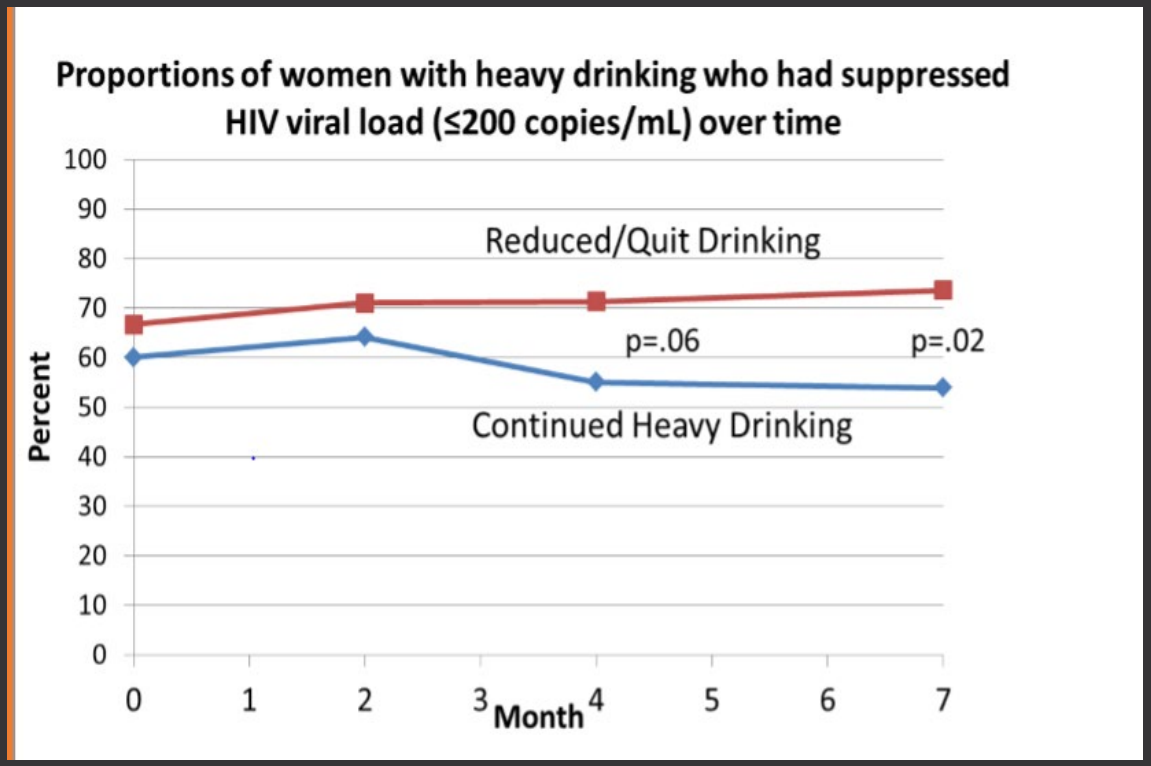
- Stress the importance of adherence and coming to all follow-up visits
- Discuss tools for adherence support: reminder apps, pill boxes, refill reminder calls, scheduling f/u visits, etc
- Discuss behavioral risk reduction at every visit

Mayer KE. IAS 2017. Abstr MOPEC0648. CDC. PrEP Guidelines. 2017.

Slide credit: clinicaloptions.com

Could Behavioral Intervention affect Adherence? Extrapolated from ETOH and Virologic Suppression

- Women with baseline 7 drinks /weeks or 2 binges/mth
- Quitting heavy drinking was significantly associated with achieving HIV viral suppression (Adjusted OR: 2.62, 95% CI: 1.02, 6.69)



CROI 2017 – Abstract # 874 . Cook (UF)

Barrier

Do We Need to Discuss Risk Compensation?

- Baseline STI rates
  - 60% with STI in 12 mths prior(PROUD)
  - 38% of trans had STI in prior 6 mths (iPrEX Trans[3])
  - 27 % had STI at beginning of study (IPERGAY)

- During studies
  - Risk compensation[4]
    - **30% had more condomless sex @4 mths**
    - STI overall increased
  - 30-35% had STI[1,2]
    - Rectal chlamydia & urethral GC

- PrEP independently associated with new STI[5]
  - Rate:24.6 per 100 person yrs, vs 10.4 per 100 person-yrs in non-PrEP users

Screen more !!!!!

1 Volk JE,MarcusJL, NonewHIVinfectionswithincreasinguseofHIV PREP. CID .2015
2. Volk, J et al. JAIDS 2016;73(5):540–46 (Kaiser:)
3 Deutsch HIV PrEP in transgender women: iPrEx trial. Lancet HIV. 2015
4. STRUT Gibson, S. et al. AIDS 2016
5 Mayer STI in MSM Boston community healthcenter (2005-2015).OpenForumInfectDis.2017

Other Barriers for Women

Challenges: Gender Inequality

- Barriers in accessing prevention, treatment and care
  - Limited decision-making power
  - Lack of financial control
  - Restricted mobility
  - Child-care responsibilities
- Usually the primary care-givers → limit economic opportunities
- Denial of property and inheritance rights for women
- Early marriage is still common worldwide

Garcia-Morena et al. WHO. Prevalence of intimate partner violence: Lancet 2006; 368: 1260–69
WHO multi-country study on women's health and domestic violence Geneva, World Health Organization, 2005
Jewkes, et al Lancet, published online 16 June 2010.

Rural US Challenges

- Rural residence is a risk factor for late HIV diagnosis
  - Less likely to **obtain HIV testing** and Rx

- Challenges of rural pts with HIV (Can extrapolate to PrEP care):
  - Stigma and social isolation
  - Long travel distances to care
  - Lack of transportation
  - Lack of providers with "HIV" expertise
    - 95% of rural counties lack "HIV" providers compared to 69% of urban counties

Vyavaharkar, M. (2013). HIV in Rural America. A technical report by the SCRural Health Research Center. Ohl ME, et al. BMC Public Health. 2011; 11:681.; Weis KE, et al. J Rural Health. 2010; 26(2):105-12.;

The Work Flow

PrEP Algorithm/Workflow

Step 1 – 1 vs 2 visits

UNIVERSITY OF SOUTH CAROLINA

Palmetto Health USC MEDICAL GROUP

HIV PrEP Implementation Toolkit

2 visits vs 1 visit (Same day PrEP)

Bolded items mandatory

PrEP Orientation Visit:

- Discuss PrEP use
- Review insurance coverage/med. assistance
- Perform baseline laboratory tests:
  - **HIV Ab/Ag screen^ (4th generation)**
  - **Cr**
  - **Hepatitis Bs Ag/Ab** and cAb
  - Hepatitis C Antibody
  - RPR/Trep Ab
  - Triple site GC/CH testing- Urine, Rectal, Oral (based on exposure)
  - **Pregnancy test** (if female)

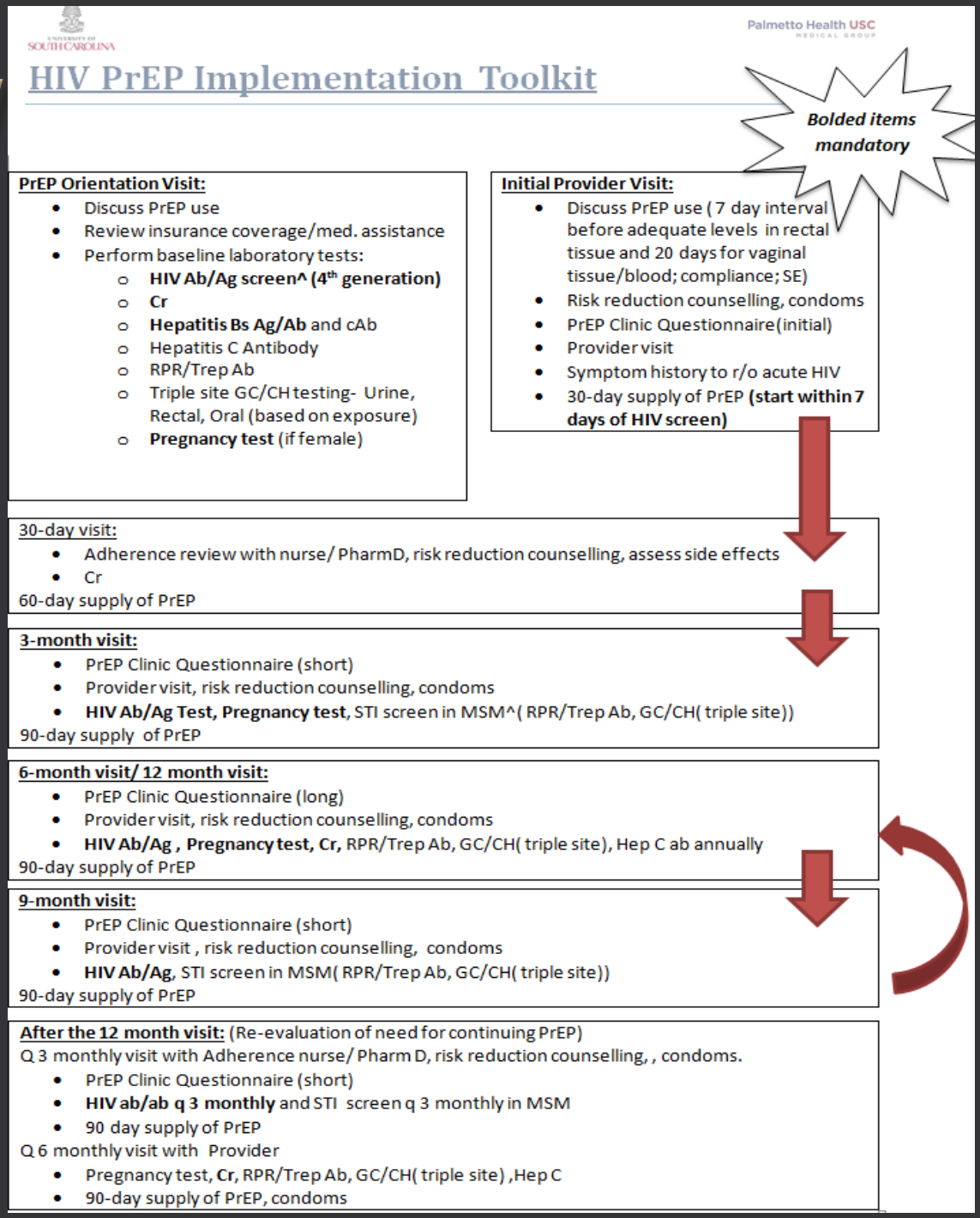
Initial Provider Visit:

- Discuss PrEP use (7 day interval before adequate levels in rectal tissue and 20 days for vaginal tissue/blood; compliance; SE)
- Risk reduction counselling, condoms
- PrEP Clinic Questionnaire(initial)
- Provider visit
- Symptom history to r/o acute HIV
- 30-day supply of PrEP **(start within 7 days of HIV screen)**

PrEP Algorithm/ Workflow

Every visit(Q 3mths):

- Greet appropriately
- Assess adherence
- Risk reduction counseling
- Provide condoms
- **HIV Screen → refills**
- STI screen



Case 4

- 26 y/o woman presents inquiring about PrEP
- 7 weeks gestation
- Her HIV ab/ag test= negative
- Male Partner HIV positive
  - HIV Viral load unknown , non compliance with ART
  - Continue to have unprotected sex with partner

Case 4

- If she is HIV negative, should PrEP be offered to her?
  1. No; because we are beyond 30 days after conception
  2. Yes; PrEP is safe in pregnancy and she has ongoing risk
  3. No; PrEP is not safe in pregnancy
  4. Unsure

PrEP: For Pregnancy

Reproductive Options for Couples in Which One or Both Partners are Living with HIV (Last updated December 7, 2018; last reviewed December 7, 2018)

Panel's Recommendations

For Couples Who Want to Conceive When One or Both Partners are Living with HIV:

- Expert consultation is recommended to tailor guidance to couples' specific needs (**AIII**).
- Partners should be screened and treated for genital tract infections before attempting to conceive (**AII**).
- Partners living with HIV should attain maximum viral suppression before attempting conception to prevent HIV sexual transmission (**AI**) and, for women living with HIV, to minimize the risk of HIV transmission to the infant (**AII**).
- For couples with differing HIV statuses, **when the partner living with HIV is on ART and has achieved sustained viral suppression**, sexual intercourse without a condom limited to the 2 to 3 days before and the day of ovulation (peak fertility) is an approach to conception with effectively no risk of sexual HIV transmission to the partner without HIV (**BII**).
- For couples with differing HIV statuses who attempt conception via sexual intercourse without a condom (despite counseling) **when the partner living with HIV has not been able to achieve viral suppression or when the viral suppression status is not known**, administration of antiretroviral pre-exposure prophylaxis (PrEP) to the partner without HIV is recommended to reduce the risk of sexual transmission of HIV (**AI**). Couples should still be counseled to limit sex (without condoms) to the period of peak fertility (**AIII**).
- When the woman is living with HIV, assisted insemination at home or in a provider's office with semen from a partner without HIV during the periovulatory period is an option for conception that eliminates the risk of HIV transmission to the partner without HIV (**AIII**).
- When the man is living with HIV, the use of donor sperm from a man without HIV is an option for conception that eliminates the risk of HIV transmission to the partner without HIV (**BIII**).
- For couples with differing HIV statuses who attempt conception (sexual intercourse without a condom limited to peak fertility) when the partner living with HIV has achieved viral suppression, it is unclear whether administering PrEP to the partner without HIV further reduces the risk of sexual transmission (**CIII**).

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines
DHHS Perinatal Guidelines, Updated Oct 2016

PrEP: For Pregnancy

Reproductive Options for Couples in Which One or Both Partners are Living with HIV (Last updated December 7, 2018; last reviewed December 7, 2018)

For discordant couples:

- HIV+ partner should be on ART and attain suppression of VL (AI)
- Once suppression of VL, Peri-ovulatory sex without condom, an option with effectively no risk of HIV transmission (BII)
- If HIV+ partner not suppressed or VL unknown:
  - PrEP (AI) to reduce the risk of sexual transmission and limit sex without condom in peri-ovulatory period (AIII)

- When the woman is living with HIV, assisted insemination at home or in a provider's office with semen from a partner without HIV during the periovulatory period is an option for conception that eliminates the risk of HIV transmission to the partner without HIV (**AIII**).
- When the man is living with HIV, the use of donor sperm from a man without HIV is an op… transmission to the partner without HIV (**BIII**).
- For couples with differing HIV statuses who attempt conception (sexual intercourse witho… partner living with HIV has achieved viral suppression, it is unclear whether administering … the risk of sexual transmission (**CIII**).

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or valid… designed, nonrandomized trials or observational cohort studies with long-term clinical outc…*

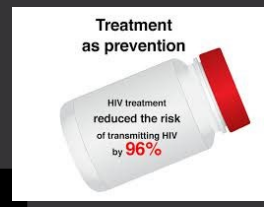
https://aidsinfo.nih.gov/guidelines/html/3/perinata…
DHHS Perinatal Guidelines, Updated Oct 2016

Safer options= cost

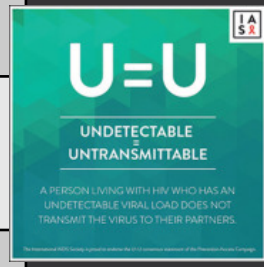
- Artificial insemination can cost per cycle - $1,500 to $4,000
- Cheap method of insemination
- Sperm washing – $100-300
- Semen analysis $85-135

PrEP: For Pregnancy, Support data

Treatment as Prevention TasP & PrEP



Trial	When	Who (sero-Discordant)	What	Efficacy
1. Observational	1989-2008- Madrid Spain	424 heterosexual couples . 83% male+	20,000 acts of intercourse w/out condoms	0 transmission if +partner on ART Risk: 1 in 2000 exposure
2. HPTN 052	9 countries	1763 couples (homosexual + heterosexual)		0 transmission if the + partner were suppressed
3. Partners	14 countries Europe	1166 couples (homosexual + heterosexual)	58 000 instances of unprotected sex	0 of the 11 who converted were linked to their partners
4. Opposites Attract	3 countries (Aust, tia, Bra)	358 HIV+ homosexual men	17 000 acts of sex	3 new cases, 0 linked
5. Timed, peri ovulatory sex with PrEP	**2005-2008**	**53 couples**	**244 unprotected intercourse Preg. rate: 75%**	**0 sero- conversions**
6. Timed, peri ovulatory sex with PrEP	**HIV+ suppressed 08-16 (China)**	**91 couples (43 with men living with HIV**	**196 unprotected intercourse, 97 live births**	**0 seroconversion**



Joined by CDC 10/2017

1. Del Romero, J, et al. BMJ 2010; 340

2. HPTN 052 Cohen NEJM- 9/2016

3. Partner – Rodger JAMA 7/2016

*4.. **Grulich- IAS 2017***

5. Vernazza PR, et al. AIDS. 2011- 2005-2008

6. Sun et al. Natural conception may be an acceptable option in HIV-serodiscordant couples in resource limited settings. *PLoS One*. 2015;

PrEP for Pregnancy
Baby Safety

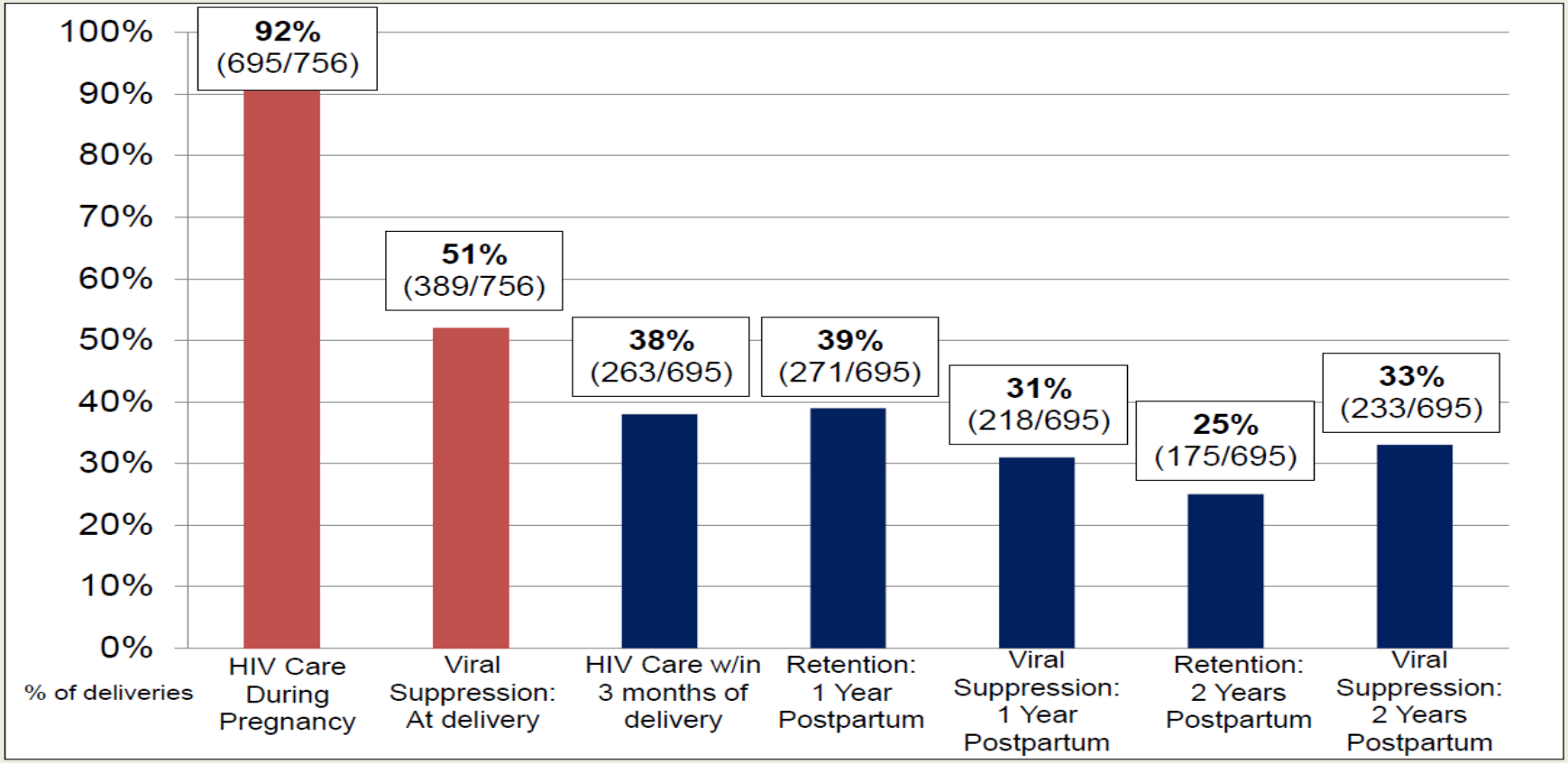
- TDF and FTC - FDA Pregnancy Category B medication[1]
- Risks and limited information should be discussed
  - In-utero studies with only low concentration of drug getting to umbilical cord[2,3]
- Pregnant women followed on tenofovir [4]
  - Infants at 6 months- No effects on their weight, length and head circumference

1. DHHS. HIV Perinatal Guideline. 2015
2. Ehrhardt Breastfeeding While Taking Lamivudine or Tenofovir Disoproxil Fumarate CID 2015
3. Mofenso TenofovirPre-exposure Prophylaxisfor Pregnant and Breastfeeding Womenat Risk ofHIVInfection PLOS 2015
4. CROI 2017 # 584 – Jourdain **TDF TO PREVENT PERINATAL HEPATITIS B VIRUS TRANSMISSION – RCT**

What happens to PrEP after delivery
Extrapolated from Postpartum HIV care

HIV Care Continuum for Postpartum Women in Philadelphia: 2005-2011

Figure 1. HIV Care Engagement During Pregnancy and for Two Years Postpartum for 598 HIV-Infected Women (n=756 deliveries)



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Palmetto Health USC MEDICAL GROUP

UNIVERSITY OF SOUTH CAROLINA

PrEP for Cis & Transgender Women

Questions!!

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