



PrEP for Women:

Prep and PreP-ception

LaShonda Spencer, MD

MCA Clinic

LAC+USC Medical Center

Disclosures

- Consultant- Gilead
- Research Grant Support- Janssen

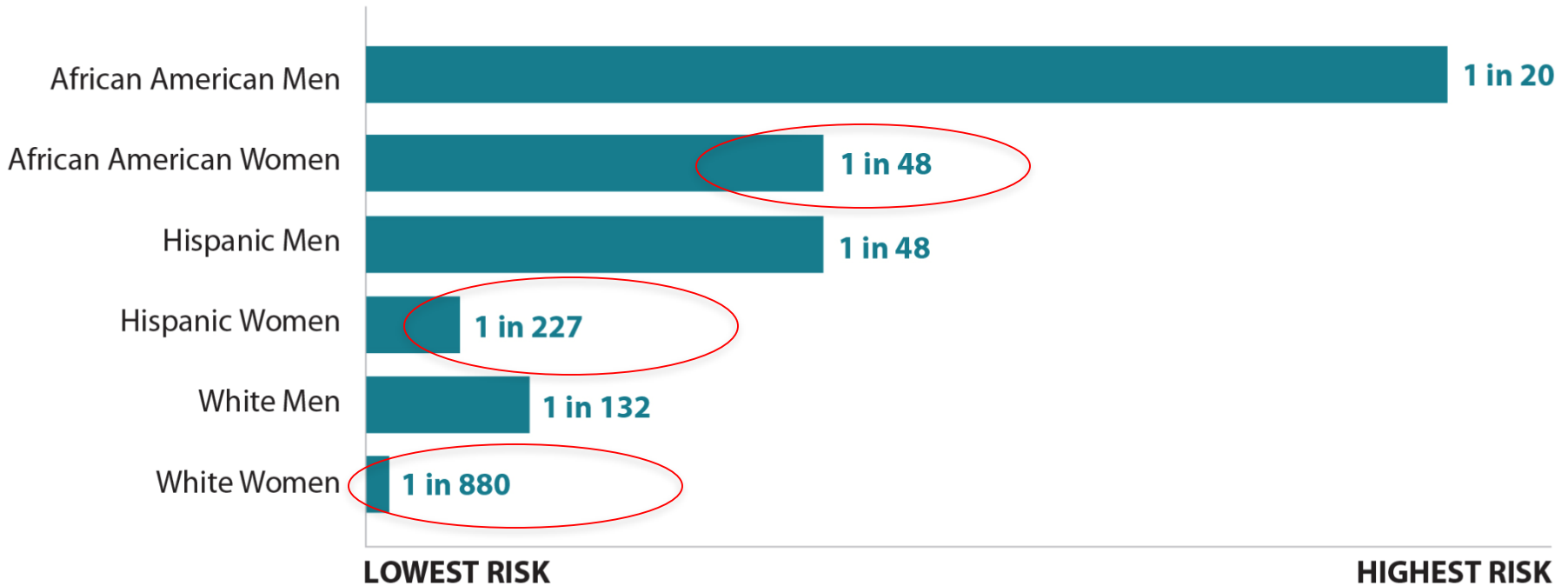


PrEP for Women

- 27 yo pregnant female with HIV + partner, tested negative in first trimester of pregnancy. At baby's 2 week follow-up, mom noted to be positive and baby tested positive.
- 17 yo female victim of commercial sex exploitation referred from JH, tested positive for gonorrhea, chlamydia and HIV.
- 53 yo female, single, dating with 2 partners in last 2 years, tested HIV+ at routine physical exam.

Women at Risk

Lifetime Risk of HIV Diagnosis by Race/Ethnicity



Source: Centers for Disease Control and Prevention



Women at Risk

2015 HIV (Cases/100,000)

	US	California
African American	26.2	18.5
AI/AN	5.6	5.6
Hisp/Lat	5.3	3.2
Asian	1.7	0.8
White	1.6	1.6



Women at Risk

- In the US, the majority of women get HIV from sex with a man.
- Best known risk factors, injection drug use and male-to-male sex, does not apply to them and many women may not know if it applies to their partners.
- Stigma, fear, discrimination and homophobia may also place many women of color at high risk for HIV

**HIV IS A VIRUS.
STIGMA
IS THE DEADLY DISEASE.**

Women at Risk

- Young women:
 - More likely to have partners whose status is unknown
 - More likely to have an STI which facilitates HIV acquisition
 - Immature reproductive tract
- Older women
 - May be unaware their partner has been sexually active with other women or men.
 - May not use condoms as not concerned about pregnancy



- ISIS Study (HPTN 064) n=2099
 - Estimate new HIV incidence in at risk women 18-44 May 2009-July 2010. (NY,NJ, MD, NC,GA).
 - Describe factors that impacted HIV risk
 - Results
 - 1.5% entered study unaware of the HIV infection
 - Annual incidence 0.32% (5x CDC estimate)
 - Factors associated with HIV:
 - Substance abuse
 - Age 27-33; 34+ (compared with 18-26)
 - HIV diagnosis of partner

Summary of relevant PrEP Trials

FEM-PrEP Trial³ South Africa, Kenya Tanzania	Phase 3 randomized, double-blind, placebo-controlled study among heterosexual women -1951 Heterosexual women	TDF/FTC Vs Placebo	- No Effect -Adherence was low -TDF detected in fewer than 50% -correlated with low efficacy -trial stopped after interim analysis determined unlikely difference in efficacy between the two groups.
Vaginal and Oral Interventions: VOICE⁴	Phase 2B randomized, open-label, placebo-controlled study . 5029 Heterosexual women -young- ave age 25 -single- 79%	oral TDF or oral TDF/FTC or topical TDF vaginal gel Vs Corresponding placebo	No Effect TDF only detected in: -30% o in TDF group -29% in TDF/FTC -25% Gel Ultimately not assoc w/ risk of reduction. -TDF/FTC- 4% increase -TDF- 49% increase -Gel- 15% decrease (not statistically significant)

Summary of relevant PrEP Trials

Study Name	Design	Medication	Key Findings
Partners Demonstration Project (Partners PrEP)¹ Africa	Open-label; daily oral PrEP among ART-naïve heterosexual serodiscordant, high-risk couples -4758 couples -38% HIV neg female -68% HIV neg male	TDF/FTC Vs TDF alone Vs Placebo	-TDF- 67% reduction -TDF/FTC- 75% reduction -detectable plasma TDF levels was associated with 90% reduction in risk of HIV acquisition -no drug resistance detected in those infected after enrollment
TDF2² Botswana	Phase 3 randomized, double-blind, placebo-controlled study in 1,219 heterosexual 55% male 45% female 90% unmarried 90% aged 21-29	TDF/FTC Vs Placebo	-62% reduction in HIV acquisition (95% CI 22-83; P=0.03) -Adherence was 84% in both arms.
HPTN 052 Africa, Brazil, India, Thailand	Randomized clinical trial designed to evaluate cART by HIV-infected individuals to prevent sexual transmission of HIV among serodiscordant couples. -1763 Heterosexual couples 50% HIV neg female	cART- immediate or delayed	cART led to a 96% reduction in transmission of HIV to the uninfected partner.

Summary of relevant PrEP Trials

Study Name	Design	Medication	Key Findings
HPTN 069/A5305 US	Randomized double-blind Women 18+ cohort (188)	MVC containing regimens vs Truvada	MVC containing regimens were safe -adherence 60-65% -no new HIV infections -low number of STI
iPrEx Brazil, Ecuador, Peru, S.Af, Thailand, US	Gay men, other MSM, Transgender women	Daily oral Truvada	44% efficacy

- Effective in Partners PrEP
 - Women were older (mean age 36)
 - All in committed relationship with a partner they knew was HIV positive
- Effective in TDF2
 - Small study size
- Effective in HPTN 069/A5305
 - Adherence was aided by personal motivation and adherence cues and reminders.
 - Few concerns about HIV-stigma or side effects
 - Mixed plans for future PrEP use

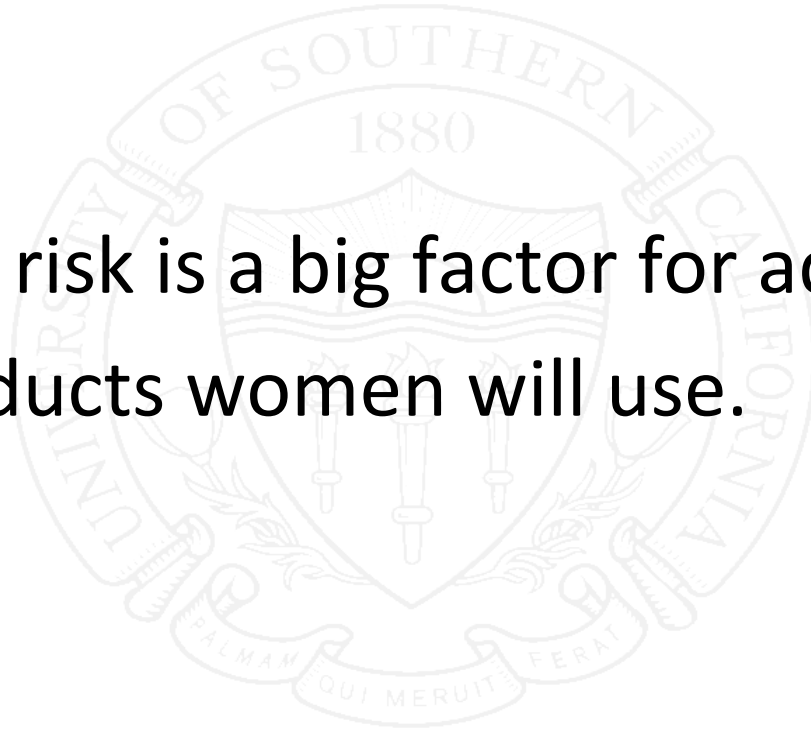


- Not effective in FEM-PrEP or VOICE
 - Young age, 59% under age 25
 - Drug detected in 21% of young, unmarried women vs 54% in older, married women (VOICES)
 - 70% perceived themselves at little or no risk of HIV



Lesson learned

- Perceived risk is a big factor for adherence
- Need products women will use.



On going Studies

- Truvada
 - AEGIS- adherence, text messaging, drug level monitoring
- Alternate regimens and modalities.
 - TAF- Oral
 - ÉCLAIR- Injectable Cabotegravir
 - -MSM/TGW
 - HPTN 083-injectable Cabotegravir
 - MSM/TGW
 - HPTN 077/084-injectable Cabotegravir
 - Cis women
 - HPTN 076- Injectable Rilpivirine
 - 136 Low risk HIV-uninfected women (NY,NY, ZIM, SA)
 - Immunotherapies- VRCO1

PrEP- C: Guidelines on Safer Conception

- US Public Health Service PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014 A CLINICAL PRACTICE GUIDELINE
 - PrEP use periconception and during pregnancy by the uninfected partner may offer an additional tool to reduce the risk of sexual HIV acquisition.
 - Both the FDA labeling information¹ and the perinatal antiretroviral treatment guidelines² permit this use.
 - However, data directly related to the safety of PrEP use for a developing fetus are limited

Reproductive Health Services for Serodiscordant Couples

- Preconception counseling
- PMTCT services
- Assisted reproductive services
 - Sperm washing
 - IUI/IVF
- Biomedical approaches
 - TasP
 - **Prep and Prep-C**
 - STI testing and treatment



Safer Conception

HIV Transmission/goal	Method	Risk Reduction
Female HIV positive Goal: decrease perinatal transmission (MTCT)	ARV in the mother ARV to child after birth	95-98%
Male positive Goal: decrease male to female transmission	Sperm washing + intrauterine insemination or IVF	100%
Either partner positive Goal: decrease transmission to negative partner	Sex without condoms limited to peak fertility ART for infected partner PrEP (oral, daily FTC/TDF) Treatment of STIs	Unknown 96% 63-73% 40%

Risk to HIV negative Woman:

- attempting to get pregnant or are already pregnant increases the risk of getting HIV from the infected partner.
 - risk of transmitting to baby is very high if seroconversion occurs during pregnancy.
 - 8x higher.

Reducing risk of HIV Transmission

- ARV therapy (TasP)
 - Goal of sustained, undetectable viral load
 - CD4 count above 350
- **PrEP**
- Are healthy
 - No opportunistic infections
 - Not using drugs or alcohol
- Screen for STI
- Safest options for becoming pregnant
 - Avoid or limit condomless sex

- **No options** have been shown to be **100% effective**, but some can greatly reduce the chance of transmission

Safest:

- Donor sperm from an uninfected HIV man with artificial insemination
- Sperm washing
- Access to sperm washing and IVF can be limited in some settings.

- TDF/FTC is FDA approved for only daily dosing
 - Guidelines: “option for serodiscordant couples during conception and pregnancy”
- Adherence is critical
- The exact time to optimal protection using daily doses of TDF/FTC is not known.
 - maximum intracellular concentrations are reached in cervicovaginal tissues at approximately 20 days
 - rectal tissue at approximately 7 days

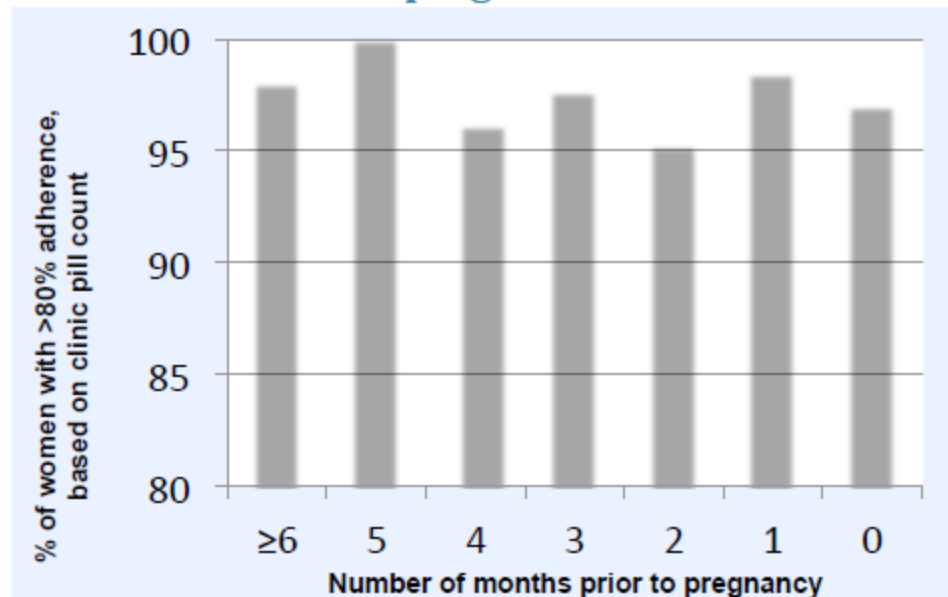
HIV treatment and planned unprotected sex

TIMED, PERIOVULATORY UNPROTECTED INTERCOURSE AFTER:

- undetectable viral load for 6 months
- no sexually transmitted infections (STIs)
- Semen analysis- to evaluate for low sperm count, low motility, low semen volume
 - Avoid unnecessary exposure for prolonged periods when likelihood of conceiving is low or nonexistent
- Daily dosing of TDF/FTC beginning one month before conception attempt, continue for 1 month after conception (or longer)
- Condomless sex **limited** to peak fertility time identified by lab tests for ovulation.

- Switzerland study:
 - Vernazza et al: 46 Heterosexual HIV-discordant couples with an HIV-uninfected female partner.
 - Males on cART with undetectable viral load
 - One dose of TDF at peak LH and 2nd dose 24hours later.
 - No HIV infections
 - High rate of pregnancy- 75% after 12 attempts
- Further studies are needed.

- 267 Women had 288 pregnancies
- Adherence: (CROI 2017,#955 Heffron)



The percentage of women with high adherence did not differ by month.

- High adherence to study drug as measured by pill count and plasma tenofovir concentrations

- In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1–4 years.
 - Decrease in bone mineral density
 - Return to pre- truvada baseline 6 months after stopping PrEP (iPrex)
 - Women more susceptible to bone loss.
- Long-term safety of PrEP has not yet been determined

- Pregnancy and breastfeeding are not contraindications to PrEP
 - Long term safety during pregnancy or during breastfeeding is not yet determined for HIV negative
 - TFV transferred in milk in very small quantities (3.2 ng/ml or 3% MP conc)
 - Infant plasma, TFV was unquantifiable in 94% of samples
 - BF infant would have exposures <0.01% of proposed infant therapeutic dose (6mg/kg)

Partners PrEP and Partners Demonstration Project pregnancy outcomes in Kenya and Uganda

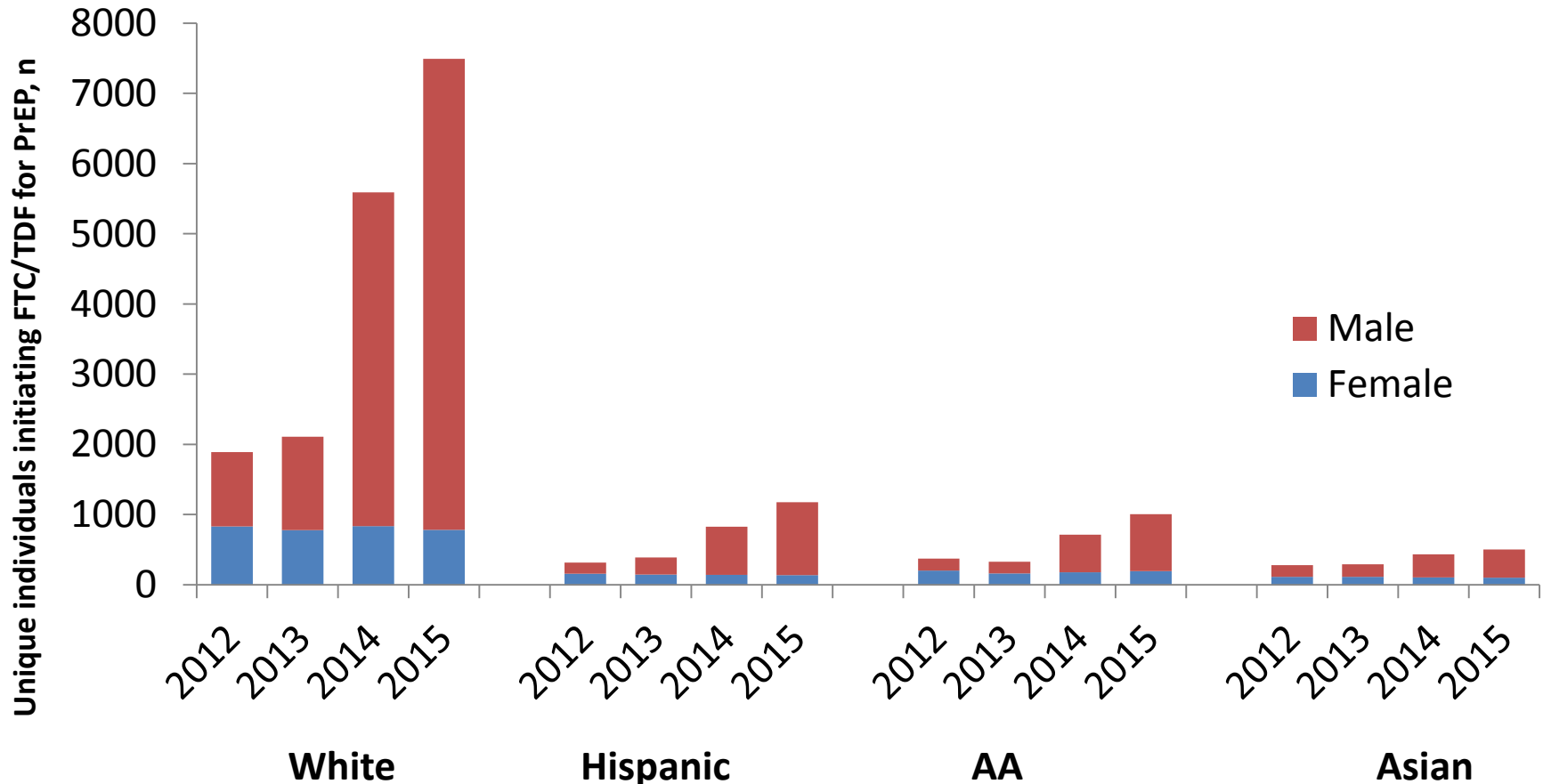
	PrEP-exposed	PrEP-unexposed	OR (95% CI)* p-value
Number of women	30	79	
Number of pregnancies	30	85	
Mean age (yrs)	25	28	
Preterm delivery	0	5 (7.7%)	0.4 (0-2.3) p=0.4
Pregnancy loss	5 (16.7%)	20 (23.5%)	0.8 (0.3-2.5) p=0.7
Congenital anomaly	0	5 (7.7%)	Fisher's exact p=0.3

**No increased poor birth outcomes in women
on TRUVADA for PrEP**

- Between 1st quarter 2013- 1st Quarter 2016 prescriptions for Truvada rose:
 - 72% for women
 - 1350% for men.
- Kaiser Research (CROI 2017, #874)
 - Cohort study on Northern CA members initiating PrEP July 2012-Dec 2014. N 972
 - 98% men
 - Factors associated with discontinuation:
 - Women: Risk ratio 2.1
 - Drug/alcohol: RR 1.6
 - Copay >\$50: RR 1.4
- DHSP PrEP/PEP Centers of Excellence (to date)
 - Enrolled 10 cis-females/ 12 transgender females

Racial Characteristics Of FTC/TDF for PrEP Users in the US

New FTC/TDF PrEP Starts by Gender* and Race



FTC/TDF for PrEP use among AA and Hispanic women was significantly less than that of White women

* These data represent 43.7% (n=21,463) of unique individuals who have started FTC/TDF for PrEP from 2012-3Q2015 .

Bush S, et al. ASM 2016. Boston, MA. Oral

MCA

- PrEP
 - Pregnant women in serodiscordant relationships
 - Non pregnant women: age range 14- 51
 - Serodiscordant
 - Victims of commercial sex exploitation
- Direct Partnerships: JH, VIP Clinic, Adolescent Clinic and new LGBTQ clinic.
- HIV Education- Treatment and Prevention:
 - Medical Students/Residents/Fellow
 - PAETC trainees
 - “Target Zero”.

Provider Education

- Educating providers on candidates for PrEP:
 - CDC: Survey HIV Provider Prescriptions for PrEP (CROI 2017 #974) Jan 2013-Jan 2014
 - 26% ever prescribed PrEP
 - 74% MSM; 30% WSM; 23% serodiscordant couples
 - Expand LAC County PrEP guidelines to include specifics on women
 - Normalize sexual health as part of Comprehensive health care.

**TOGETHER
WE WILL
END AIDS.**

- **Increase women's awareness on PrEP**
 - Most literature and social marketing targets MSM
 - Educate and utilize community stakeholders to deliver messages on PrEP in women.
 - Increase awareness to decrease stigma
 - Recognize and address factors that may interfere with uptake and adherence to PrEP
 - Stigma, intimate partner violence, Immigration status.
 - Normalize sexual health as part of comprehensive healthcare.



Challenges and Next Steps

- **Increase number of PrEP Centers of Excellence that focus on women's care**
 - Culturally competent
 - Centers that provide testing and treatment for HIV
 - Expand to family planning clinics and other family clinics where women frequent
- **Partner with research institutions and leverage public-private partnerships**
 - Knowledge from demonstration projects and real world-experience
 - New modalities for differing needs
 - Build upon locally funded efforts and drug affordability programs
 - Social determinants of health that might impeded HIV prevention programs
 - Interplay between interpersonal, social and structural factors



Special Thanks

- MCA Patients and Community Advisory Board
- MCA Providers and Staff
- LAC Medical Center
- DHSP Staff
- Commission on HIV

- MCA Clinic: PrEP referral
 - Call or text: 323 455-9454
 - Email MCAclinic@usc-mca.org

