HIV and Women's Health

Sharon Weissman, MD
Professor of Internal Medicine
University of South Carolina School of Medicine
Division of Infectious Diseases
PHUSCMG

Palmetto Health USC
MEDICAL GROUP

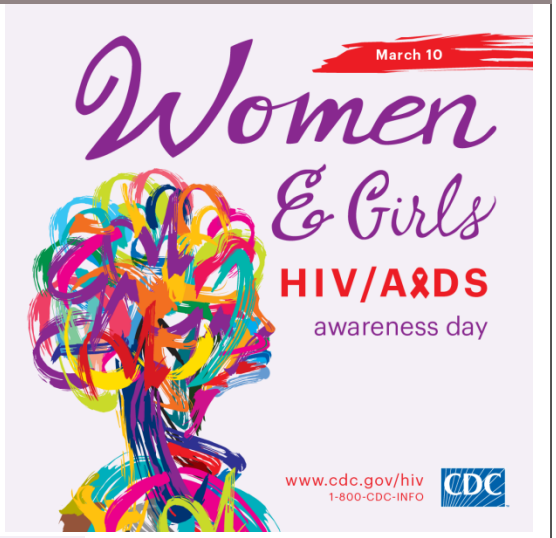
UNIVERSITY OF
SOUTH CAROLINA

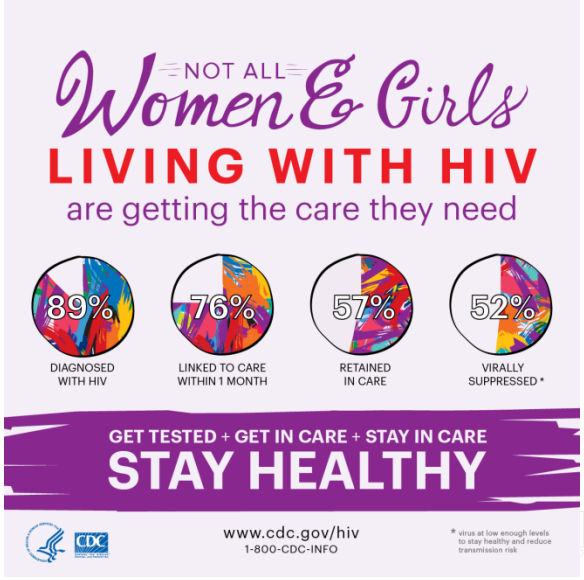
Disclosure Statement

- Nothing to disclose

Objectives: HIV and Women

1. Epidemiology
   - Global, National, Local
2. Challenges
   - Inequalities and IPV
3. Antiretroviral therapy and women
   - Prep
   - Adherence
   - Pregnancy
4. Health Screening
   - Bone health
   - Cancer
   - Vaccination





Global HIV Epidemiology

AIDS Epidemic 2015	
Adults living with HIV - Women	31.8 million [30.1 million - 33.7 million] ~50% PLWHIV
New HIV Infections Adults - Women	1.9 million [1.7 million – 2.1 million] ~48%
AIDS deaths - Women	1.9 million [1.7 million – 2.1 million] ~42%

http://aidsinfo.unaids.org
UNAIDS fact sheet 2015

World Health Organization

UNAIDS

The HIV Pandemic

New infections in adults 2005- 2015

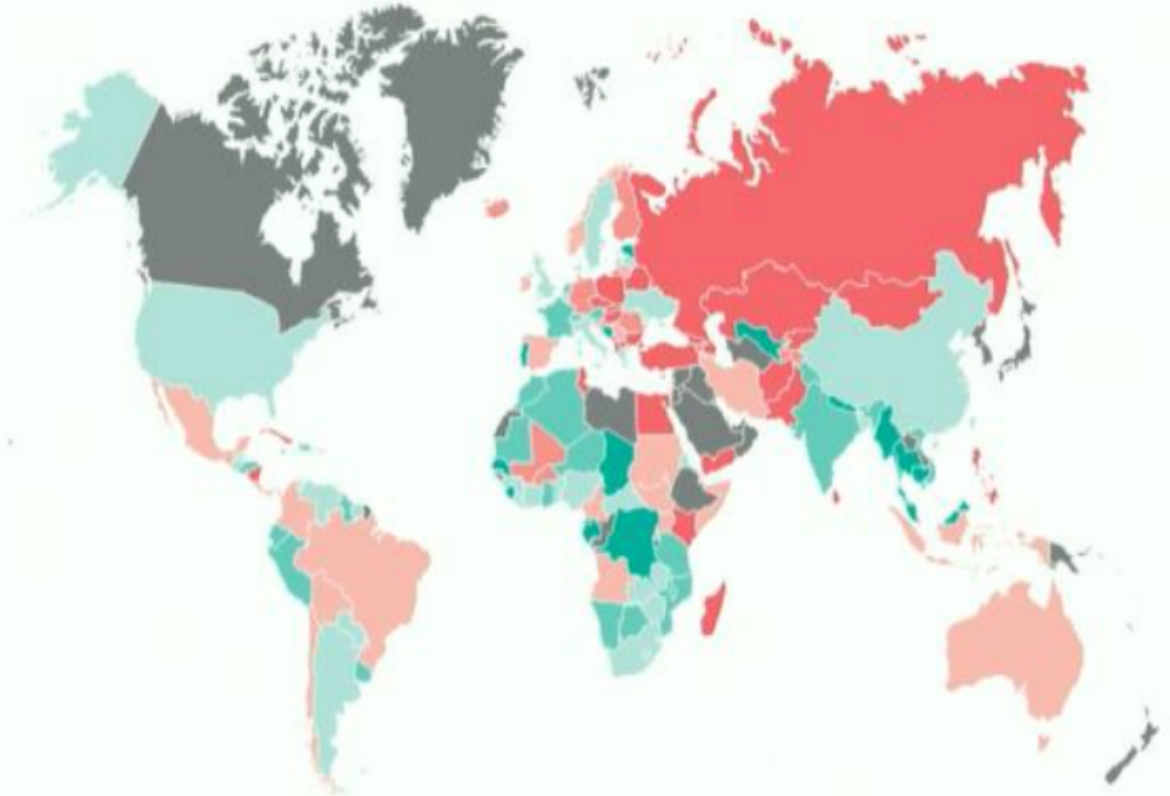
In 2015,

37 mi

people living with HIV.

1.9 mi

new infections per year.



>49% decrease
25–49% decrease
0–24% decrease
>49% increase
25–49% increase
1–24% increase
Data not available

Sources: UNAIDS 2016 estimates; European Centre for Disease Prevention and Control (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, I
Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, United Kingdom, Albania, Andorra, Bosnia and Herzegovina, Macedonia, Israel, Montenegro, San Mari
Serbia, Switzerland and Turkey); Centers for Disease Control and Prevention. HIV Surveillance Report, 2014; vol. 26. http://www.cdc.gov/hiv/library/reports/surveillance/. Published November 2015. Accessed [10
2016]. Russian Federation 2016 Global AIDS Response Progress Reporting submission. China 2016 Global AIDS Response Progress Reporting submission.

HIV and Women – US

- Women account for ~23% PLWHIV
  - ~ 246,372 women with HIV at the end of 2014
  - ~7,400 women diagnosed with HIV in 2015
  - 40% decline in new HIV diagnosis from 2005 to 2014

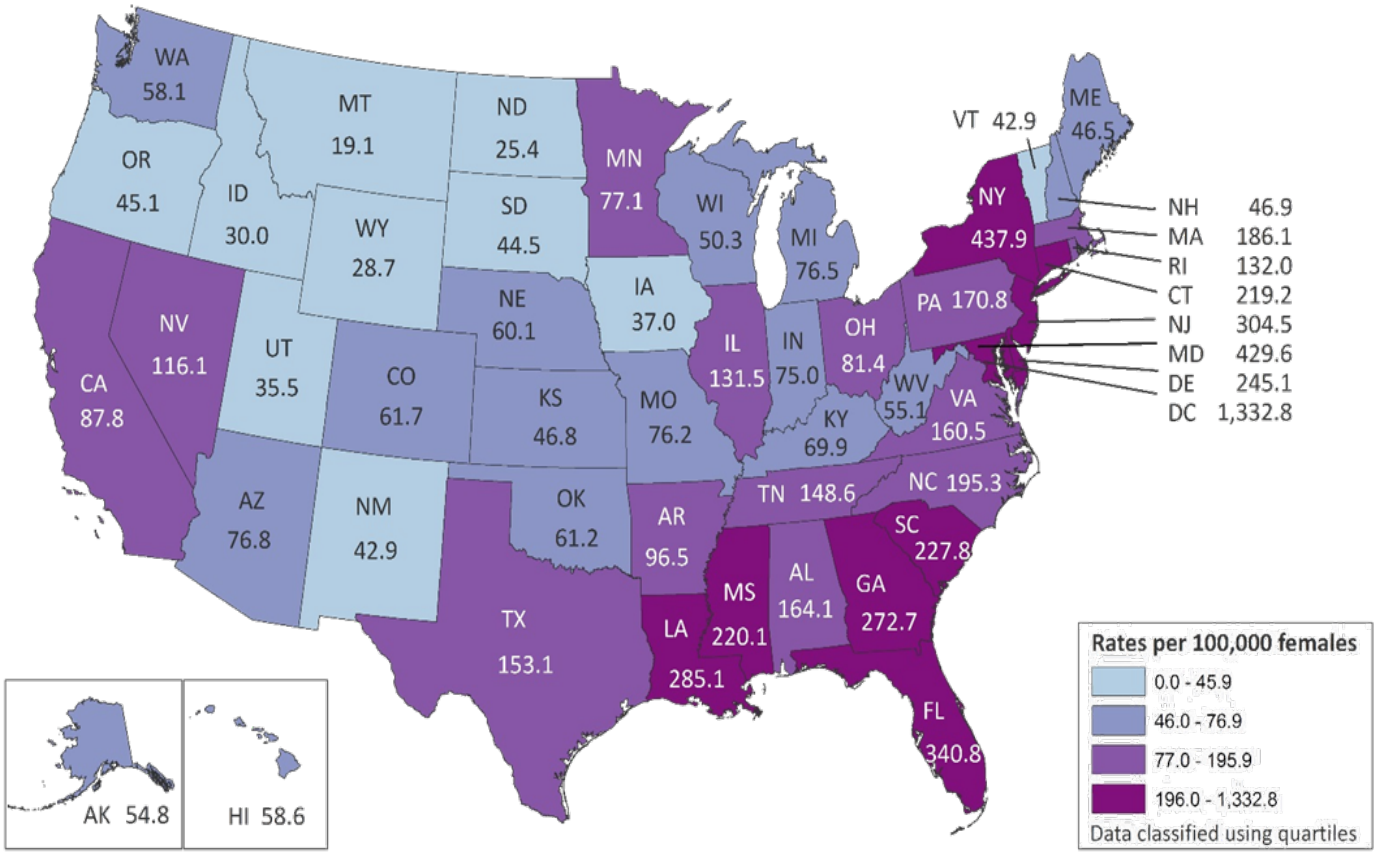
- 19% (7,402) new HIV diagnoses in 2015 were in women

- HIV was among the top 10 causes of death for AA women (ages 15 to 64) in 2010

Good news: 42% ↓ in new infections in AA women (2005→2014)

Rates of Female Adults and Adolescents Living with Diagnosed HIV Infection Year-end 2014—United States and 6 Dependent Areas

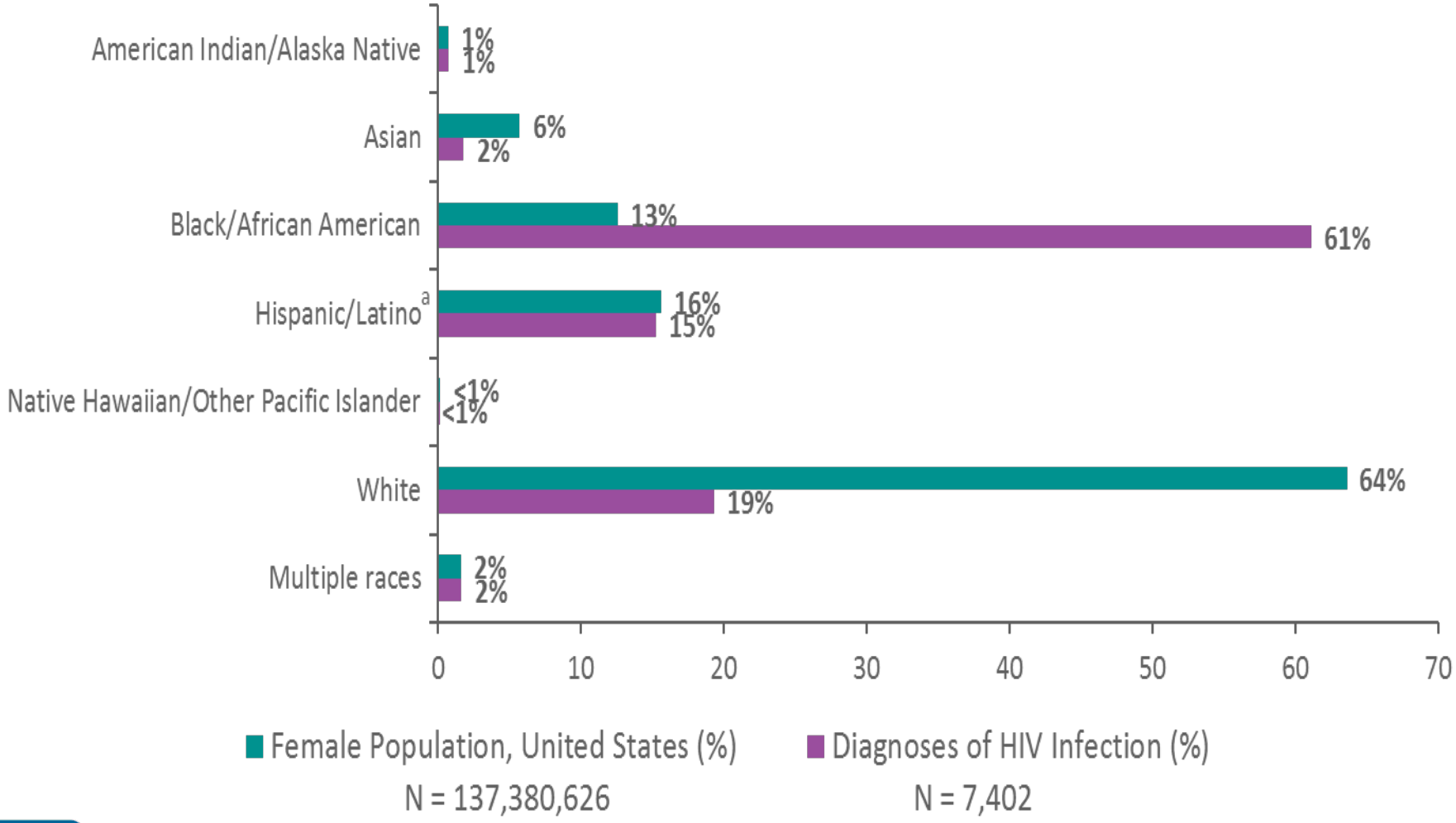
N = 235,813 **Total Rate = 171.0**



American Samoa	0.0
Guam	25.8
Northern Mariana Islands	4.8
Puerto Rico	326.6
Republic of Palau	24.0
U.S. Virgin Islands	501.7

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. Data are based on address of residence as of December 31, 2014 (i.e., most recent known address).

Diagnoses of HIV Infection and Population among Female Adults and Adolescents, by Race/Ethnicity, 2015—United States



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.

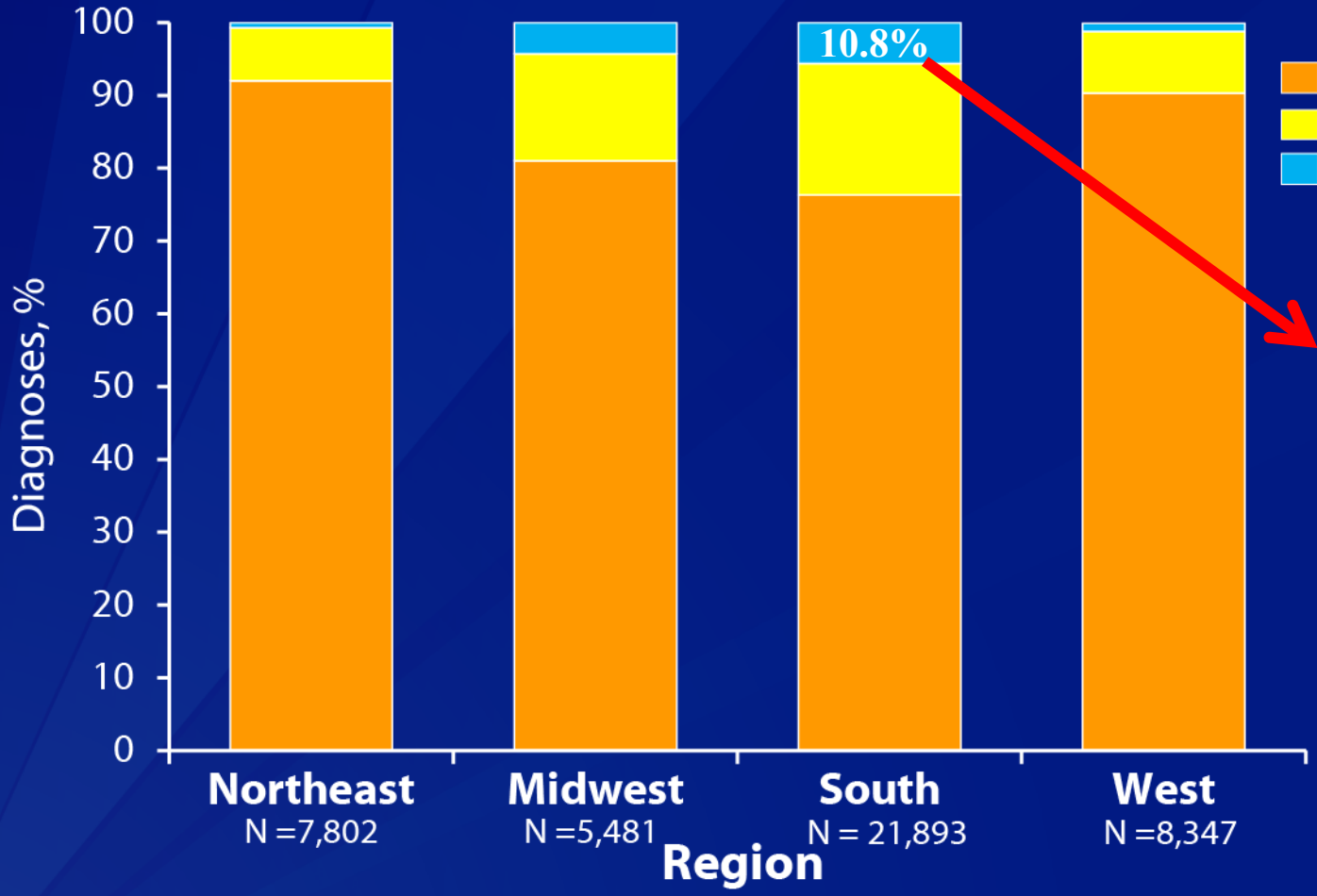
[a] Hispanics/Latinos can be of any race.

HIV in South Carolina: Women

- By the end of 2015 estimated 18,420 PLWHIV in SC
- Women account for 28.7% of PLWHIV in SC
  - Compared with 23% in U.S.
- Women with HIV in SC
  - 77% AA, 17% White, 4% Hispanic

http://www.scdhec.gov/Health/docs/stdhiv/Surveillance%20Report%202015.pdf

Diagnoses of HIV Infection among Adults and Adolescents, by Region and Population of Area of Residence, 2014—United States



South Carolina 27% new HIV cases in rural

SC ranked first in the rural prevalence of PLWHIV

Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Data exclude persons whose county of residence is unknown.

HIV and Women: Rural US Challenges

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

- Challenges of rural residents with HIV:
  - 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.;

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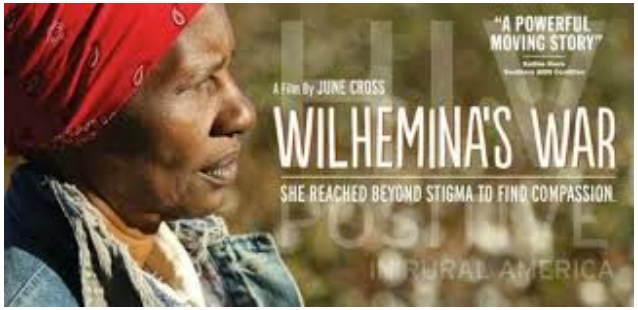

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Global Approach to HIV Elimination

Millennium Development Goals #6:

Combat HIV/AIDS, malaria, and other diseases by 2015

- Target 6A: Have halted by 2015 and begin to reverse the spread of HIV/AIDS
- Target 6B: Achieve universal access to treatment for HIV/AIDS for all those who need it

Joint United Nations Programme on HIV/AIDS (UNAIDS)

- UNAIDS: 10 approaches to achieve the Millennium Development Goals #6: Combat HIV/AIDS, malaria, and other diseases by 2015
  1. Reduce sexual transmission of HIV by 50% by 2015
  2. Halve the transmission of HIV among people who inject drugs by 2015
  3. Eliminate HIV infections among children and reduce maternal deaths
  4. Reach 15 million people living with HIV with lifesaving antiretroviral treatment by 2015
  5. Halve tuberculosis deaths among people living with HIV by 2015
  6. Close the global AIDS resource gap
  7. Eliminate gender inequalities and gender-based abuse and violence and increase the capacity of women and girls to protect themselves from HIV
  8. Eliminate HIV-related stigma, discrimination, punitive laws and practices
  9. Eliminate HIV-related restrictions on entry, stay and residence
  10. Strengthen HIV integration

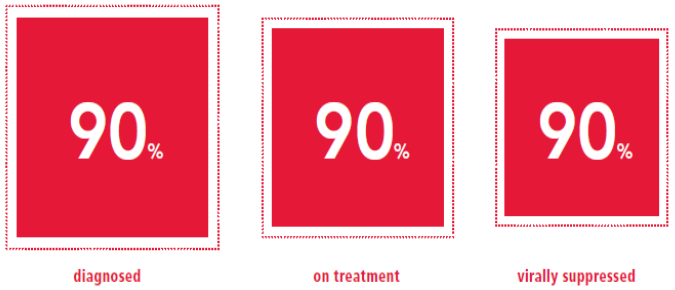
Sustainable Development Goal

In September, 2015, World Leaders at a UN Summit adopted 17 SDG to end poverty, fight inequality and injustice and tackle climate change by 2030

SDG 3: Ensure healthy lives and promote wellbeing for all

3.3: End the AIDS epidemic by 2030

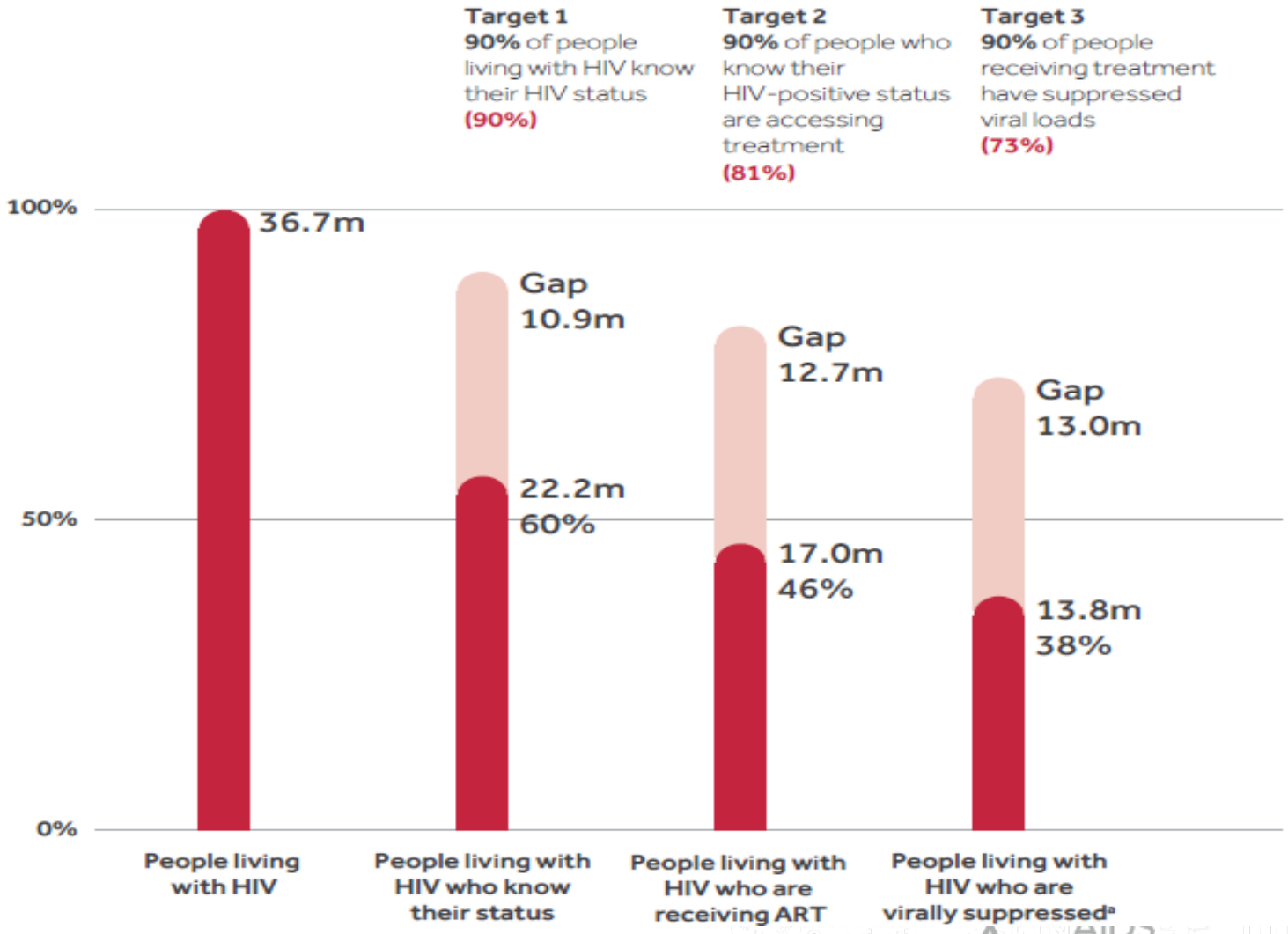
- Achieve 90-90-90 by 2020



SDG 5: Achieve gender equality and empower all women and girls

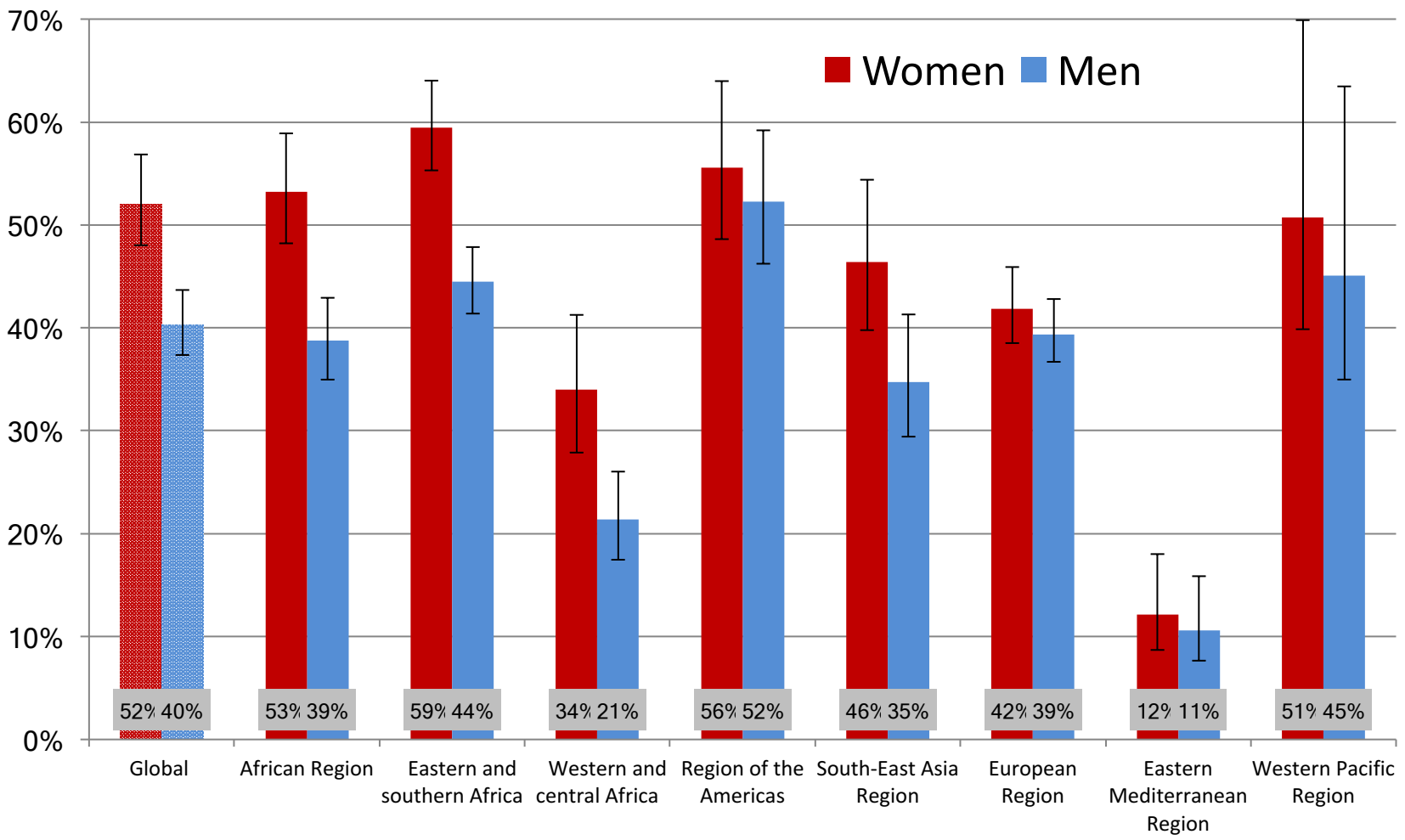
https://sustainabledevelopment.un.org/sdg

Improvements are needed at each stage of the cascade of HIV testing and treatment services, 2015



Source: UNAIDS/WHO estimates.

ART coverage by sex among adults, 2015



Source: UNAIDS/WHO estimates.

HIV and Women : Population at Risk: Challenges

Gender Inequality

- Barriers in accessing prevention, treatment and care
  - Limited decision-making power, lack of financial control , restricted mobility and 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.

HIV and Women : Population at Risk: Challenges

Violence against women and girls

- The proportion of women experiencing IPV: 15% to 71%
- Forced first sex among adolescent girls <15 years: 11% - 48%
- Hampers women's ability to protect themselves from HIV

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.

HIV and Women: IPV
SDG 5: Gender Equality

- WHO recommends health services including IPV screening, and services for counselling and care
  - Women with IPV are 50% more likely to have HIV
  - Elimination of sexual violence alone could avert 17-20% of HIV infection over the next decade*

* CROI 2015, Seattle, Abstract #135.

HIV and Women: IPV in the US

Physical/sexual violence or threats, stalking & psychological aggression

- 35.6% of women experienced IPV in their lifetime (2010 Survey)
- IPV and HIV
  - Fear of IPV can prevent testing
  - Childhood sexual abuse and forced teen sexual initiation → increased HIV risk-taking behaviors

http://www.cdc.gov/violenceprevention/intimatepartnerviolence --- Training modules
http://www.cd c.gov/violenceprevention/pdf/ipv/13_243567_green_aag-a.pdf

HIV and Women: IPV in the US

- HIV-Positive Women
  - Experience ≅ double the national rates
    - **IPV: 55%** ; Child sexual abuse: 39%; Child physical abuse 42%
  - HIV disclosure → IPV
  - Abused women have higher ART failures rates: >4 times
  - Association between IPV and decreased T cell, depression

http://www.cdc.gov/violenceprevention/intimatepartnerviolence --- Training modules
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Women and ART
Violence and Outcomes

Canadian report

- Women living with HIV are likely to have experienced violence and are at high risk for PTSD/drug use

Experienced violence in adulthood (>16 years old)	N (%)
Any type of violence	803 (80)
Physical violence	622 (62)
Sexual violence	452 (45)
Verbal violence	742 (74)
Emotional violence/control	462 (46)

CROI 2017 – Abstract # 536. Logie

Sustainable Development Goal

Goal 5: Achieving gender equality and empowering women and girls

Cash Transfer Program

- A study in rural Malawi, girls were assigned to cash payment (conditional or non-conditional) or no cash payments
  - Those receiving cash payments were:
    - 64% less likely acquire HIV
    - 33% more likely to delay their sexual debut
    - 25% fewer sexual partners
    - Chose younger partners
    - 35% less likely to drop out of school

Baird SJ, Effect of a cash transfer programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. Lancet. 2012;379:1320–9.

Pettifor A, Paying to prevent HIV infection in young women? Lancet. 2012;379:1280–2.

Sustainable Development Goal

Goal 5: Achieving gender equality and empowering women and girls

Cash Transfer Program

- The cash transfers reduced the risk of HIV infection by keeping girls in school and making them less financially dependent on older male partners
- Cost per HIV infected averted $5000

Baird SJ, Effect of a cash transfer programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. Lancet. 2012;379:1320–9.

Pettifor A, Paying to prevent HIV infection in young women? Lancet. 2012;379:1280–2.

Antiretroviral Therapy and Women

1. ART choices
2. Adherence
3. Pre Exposure Prophylaxis
4. Pregnancy

Women and HIV (US)
Disparities in HIV Care

- Several studies have shown women to be 5-10% less likely to initiate ART

- A Multicenter, observational cohort (2277 new HIV) found:
  - ART less likely to be started in women, especially non-white
  - Women, especially non-white women, were more likely to experience an AIDS-related event
  - Sex and race did not affect response to ART

Meditz AL, et al. J Infect Dis. 2011;203:442-451.
Gebo KA, et al. J Acquir Immune Defic Syndr. 2005;38:96-103
Fleishman JA, et al. Med Care. 2012; 50:419-27

Women and ART Choice

Recommended Regimen Options

(Drug classes and regimens within each class are arranged in alphabetical order.)

INSTI-Based Regimens:

- DTG/ABC/3TC[a]—**only** for patients who are HLA-B*5701 negative **(AI)**
- DTG plus TDF/FTC[a] **(AI)**
- EVG/c/TAF/FTC—**only** for patients with pre-treatment estimated CrCl ≥30 n
- EVG/c/TDF/FTC—**only** for patients with pre-treatment estimated CrCl ≥70 r
- RAL plus TDF/FTC[a] **(AI)**

PI-Based Regimens:

- DRV/r plus TDF/FTC[a] **(AI)**

Alternative Regimen (

(Drug classes and regimens within each class are arranged in alphabetical order.)

Regimens that are effective and tolerable, but that have potential disadvantages when compared with the recommended regimens listed above, have limitations for use in certain patient populations, or have less supporting data from randomized clinical trials. **An alternative regimen may be the preferred regimen for some patients.**

NNRTI-Based Regimens:

- EFV/TDF/FTC[a] **(BI)**
- RPV/TDF/FTC[a]—**only** for patients with pre-treatment HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm^3 **(BI)**

PI-Based Regimens:

- ATV/c plus TDF/FTC[a]—**only** for patients with pre-treatment estimated CrCl ≥70 mL/min **(BI)**
- ATV/r plus TDF/FTC[a] **(BI)**
- (DRV/c or DRV/r) plus ABC/3TC[a]—**only** for patients who are HLA-B*5701 negative (**BIII** for DRV/c and **BII** for DRV/r)
- DRV/c plus TDF/FTC[a]—**only** for patients with pre-treatment estimated CrCl ≥70 mL/min **(BII)**

Caution with:

Pill numbers /size

Need for food

Possibility of pregnancy

Fetal safety data available

Women and ART Recommendations

- **In general, no sex differences in virologic efficacy**

- **Increased risk of certain ART AE in women:**
  - NVP-associated hepatotoxicity (If CD4 >250 cells/µL)
  - Lactic acidosis: avoid d4T + ddI
  - Metabolic complications (eg, lipoaccumulation, elevated triglycerides, osteopenia/osteoporosis)

Women and ART Recommendations

- **In general, no sex differences in virologic efficacy**

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  - Metabolic complications (eg, lipoaccumulation, elevated triglycerides, osteopenia/osteoporosis)

- **Women of childbearing potential**
  - Offer preconception counseling/care and contraception
  - For those who wish to conceive:
    - Inform as to options for preventing transmission of HIV while attempting conception

Women and Contraception

ART interactions with hormonal contraceptives:

- Oral agents:
  - PIs, cobicistat and NNRTIs may increase or decrease levels (ethinyl estradiol, norethindrone, & norgestimate)
  - Consider alternative or additional contraceptive
- Few data on transdermal patch, vaginal ring: **caution**
- Depo-Provera: few data
  - No significant interactions with older ART
  - Associated with acquiring/ transmitting HIV (pts were not on ART)
- IUD: safe and effective

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- Oral agents:
  - PIs, cobicistat and NNRTIs may increase or decrease levels (ethinyl estradiol, norethin
  - Consider
- Few data
- Depo-Pro
  - No signif
  - Associate
- IUD: safe and effective

Consistent condoms (male or female) regardless of contraceptive !!!!!!!
To reduce risk of:
- HIV transmission &
- STD acquisition

Women And ART
Choice of ART

Weight gain in women vs men after ART initiation (ACTG –US)

- Women had greater increases in weight after initiating ART
- ART- Raltegravir, darunavir, reyataz

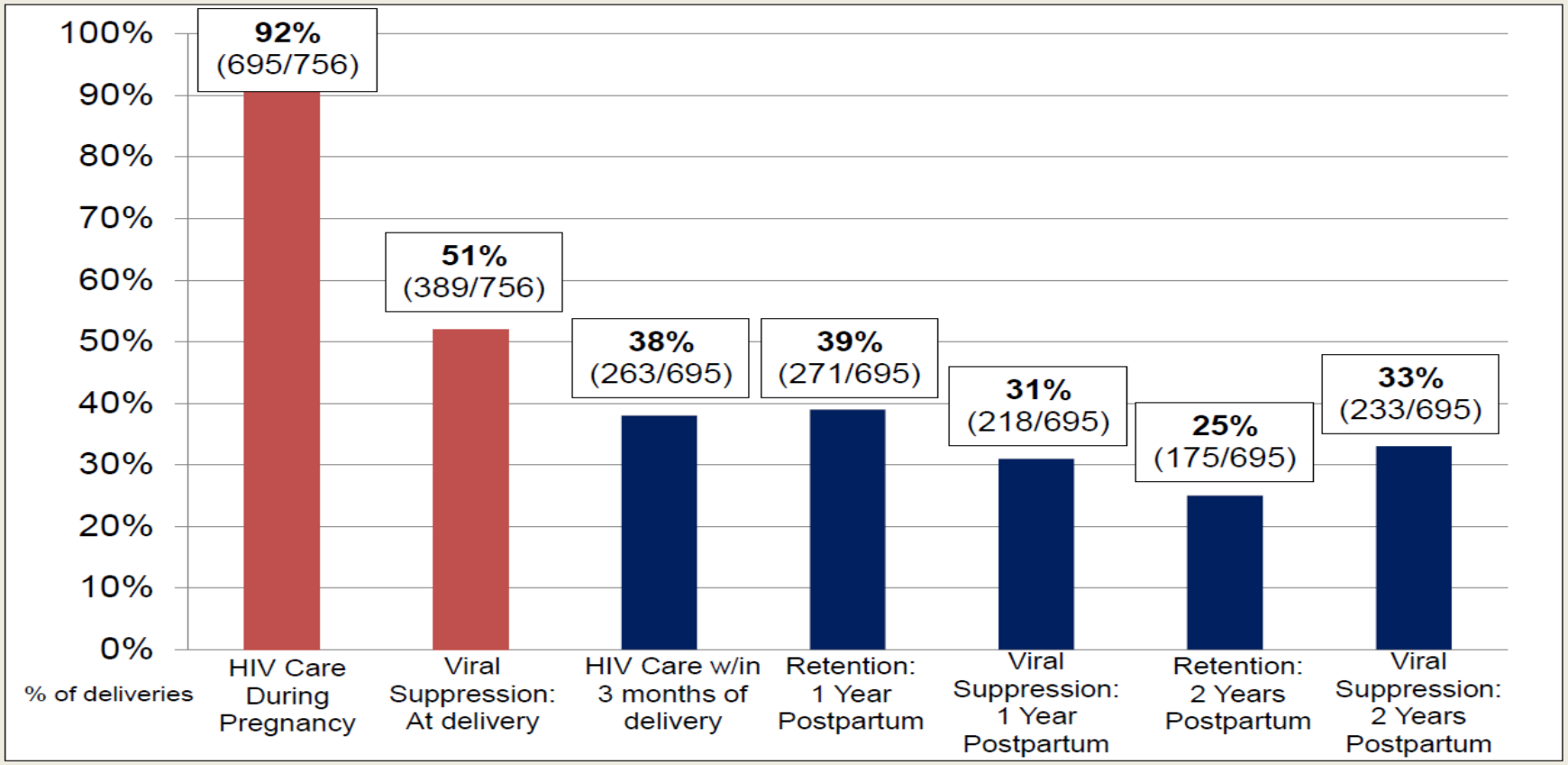
Table 2: Mean Body Mass Index (BMI in kg/m²) change					
	n (%)	Women (n=760)	Men (n=3041)	Sex difference	p-value (t-test)
Overall Observed (i.e. unadjusted)					
Thru week 48	3801 (100%)	1.53	1.15	0.38	0.002
Thru week 96	3801 (100%)	1.91	1.39	0.52	<0.001
Overall Model-based (i.e. adjusted) thru week 96					
				0.59	<0.001
Observed By Pre-ART Initiation BMI Category, thru week 96					
Underweight (< 18.5)	126 (3%)	3.51	2.12	1.4	0.016
Normal (18.5 -< 25)	1802 (47%)	2.37	1.68	0.69	0.003
Overweight (25-< 30)	1230 (32%)	1.71	1.04	0.67	<0.001
Obese (≥ 30)	643 (17%)	1.42	0.99	0.43	<0.001

CROI 2017 – Abstract # 1153. Bares

Women and HIV (US)
Adherence Post Partum

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)



CROI 2015, Abstract #890

HIV Prevention

- Women and PrEP

What is PrEP?

- Daily oral TDF/FTC
  - TDF= Tenofovir, 300mg
  - FTC= Emtricitabine, 200mg
- Most common side effects
  - GI (diarrhea, nausea)
  - May decrease bone density
  - Decreased Cr clearance

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 •Men 84% •Women 66%
3. TDF2 n=1219	Botswana	Hetero men or women	TDF-FTC or placebo	62.2% all •80% men •49% women (NS)
4. FEM-PrEP n=2120	Kenya, South Africa, Tanzania	Women	TDF-FTC or placebo	Stopped early due to lack of efficacy
5. VOICE n=5021	Uganda, South Africa, Zimbabwe	Heterosexual women	TDF gel, placebo gel, TDF, TDF-FTC, placebo pill	TDF gel and TDF pill stopped due to lack of efficacy
6. CAPRISA 004 n=889	South Africa	Hetero women	Topical vaginal TDF gel or placebo gel	39% TDF gel
7. Bangkok TDF study n=2413	Thailand	IVDU	TDF or placebo	48.9% TDF

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3. TD n=1				(NS)
4. FE n=2				y due to cy
5. VO n=5				DF pill to lack
6. CAPRISA 004 n=889	South Africa	Hetero women	Topical vaginal TDF gel or placebo gel	39% TDF gel
7. Bangkok TDF study n=2413	Thailand	IVDU	TDF or placebo	48.9% TDF

- Summary of studies
  - Yes it works: Efficacy between 39-80%
  - Studies show conflicting results for women
  - Adherence is important

PrEP Guidelines: (CDC May, 2014)

- PrEP be considered for people who are HIV-negative and at substantial risk for HIV
  - Heterosexual or same sex transmission
  - Intravenous drug users
  - Discordant couples
- Recommend
  - HIV monitoring every 3 months
  - PrEP refills 90 days with HIV testing
  - Ongoing risk reduction counseling
  - STI screening
  - Medication adherence counseling

Every visit:

- Assess adherence
- Risk reduction counseling
- Provide condoms

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

Women and Adherence

PrEP

- Was not effective in preventing HIV in at risk women[1,2]
  - Reason : **NON – adherence !!!!!!!!!!!!**

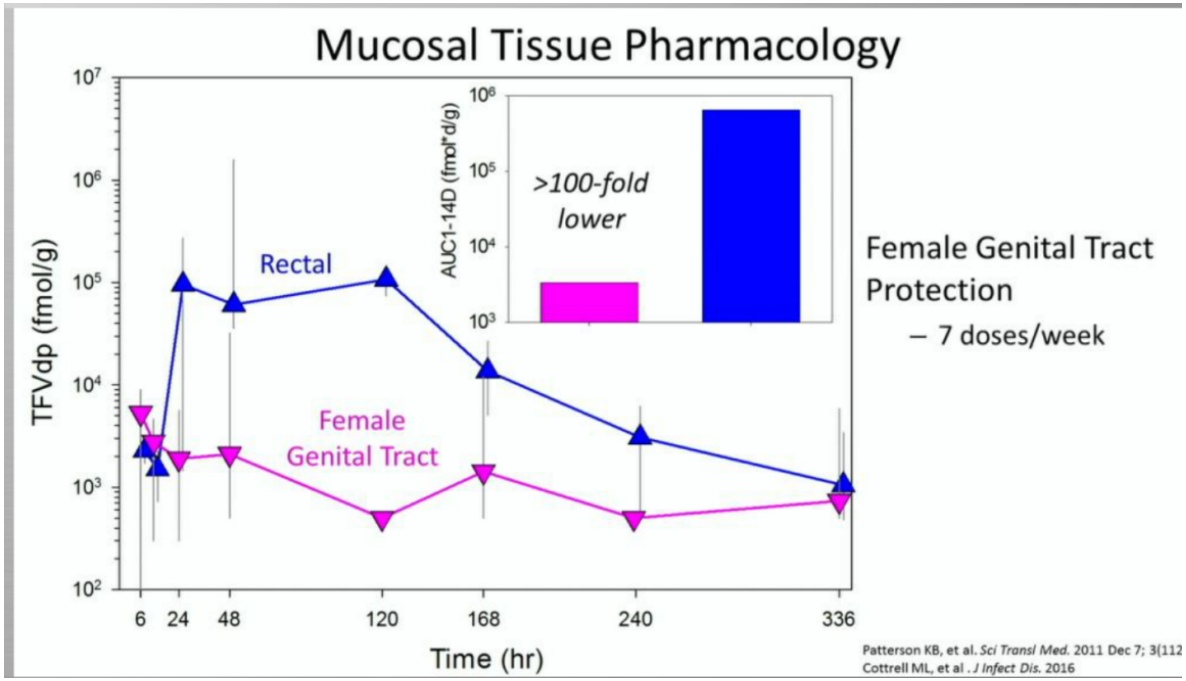
IPV, PrEP and Adherence[3,4,5]

- IPV (past 3 months) associated with a lower adherence
- VOICES trial
  - Women reported taking pills/pill counts confirmed this
    - **BUT** Serum drug level was undetectable
  - They experienced stigma, fear, relationship conflict and lack of understanding → non adherence

[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

Women and PrEP

- Differences in vaginal (versus rectal) concentrations of drug levels may cause decreased efficacy of PrEP



CROI 2016 Concentrations of TFV and TFVdp in Female Mucosal Tissues After a Single Dose of TAF

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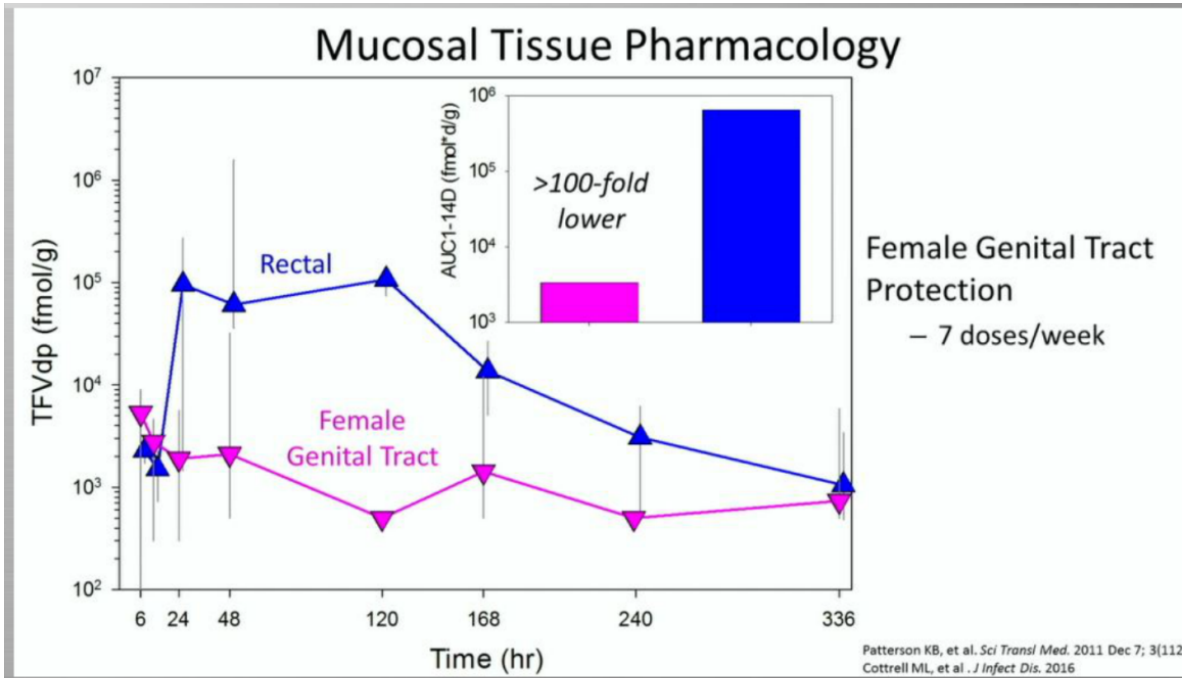


Women just have to work harder

CROI 2016 Concentrations of TFV and TFVdp in Female Mucosal Tissues After a Single Dose of TAF

What is New in PrEP: Dapivirine Vaginal Ring

A Phase III Trial of the Dapivirine Vaginal Ring for HIV-1 Prevention in Women (ASPIRE)

Safety and Efficacy of Dapivirine Vaginal Ring for HIV-1 Prevention in African Women (The Ring Study)

N Engl J Med 2016 Feb 22; [e-pub]
CROI 2016. Boston, MA. Oral Abstract 110LB

A Phase III Trial of the Dapivirine Vaginal Ring for HIV-1 Prevention in Women

- Women randomized 1:1 to dapivirine ring or placebo ring
  - Ring placed every 4 weeks
  - 2629 women enrolled
  - 91% attendance at f/u
  - 2 measures for adherence (plasma levels and residual drug levels in returned rings)

N Engl J Med 2016 Feb 22; [e-pub]

A Phase III Trial of the Dapivirine Vaginal Ring for HIV-1 Prevention in Women

- Excluded 2 sites with low adherence efficacy 37% in preventing HIV
- Disappointing results for younger women
  - Adherence and efficacy lower in women <21 year

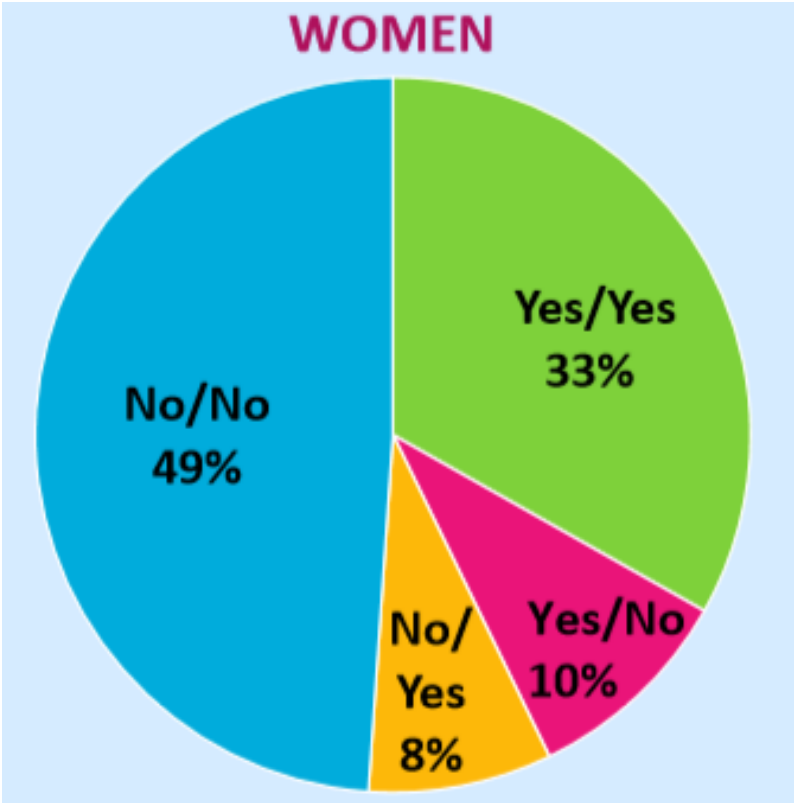
	Age 18-21	Age 22-26	Age 27-45
HIV Protection (65% CI)	-27% (-133, 31)	56% (19, 76)	51% (8,74)

N Engl J Med 2016 Feb 22; [e-pub]

HIV and Pregnancy

Women and Fertility Desires

- Secondary analysis of phase 3 trial of 3 ART regimens
- Completed questionnaire regarding desire for children
- **Primary outcome**: desire to have children in the future
- Baseline and at 96 week data



CROI 2017 abstract 1134-Cohn et al

HIV & Women: Reproductive Options

Reproductive Options for HIV-Concordant and Serodiscordant Couples (Last updated October 26, 2016; last reviewed October 26, 2016)

Panel's Recommendations

For Couples Who Want to Conceive

For Concordant (Both Partners are HIV-Infected) and Discordant Couples:

- Expert consultation is recommended so that approaches can be tailored to couples' specific needs **(AIII)**.
- Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**.
- Both partners should attain maximum viral suppression before attempting conception **(AIII)**.

For Discordant Couples:

- The couple should be counseled and only attempt conception after the HIV-infected partner has initiated antiretroviral therapy and have achieved sustained suppression of plasma viral load below the limits of detection **(AI)**.
- Administration of antiretroviral pre-exposure prophylaxis 30 days before and 30 days after conception for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission, particularly if the HIV-infected partner's plasma viral load is unknown or detectable **(BII)**. It is not known whether pre-exposure prophylaxis for the uninfected partner confers additional benefit when the infected partner receiving antiretroviral therapy has demonstrated sustained viral suppression.

Discordant Couples with HIV-Infected Women:

- The safest conception option is assisted insemination at home or in a provider's office with a partner's semen during the peri-ovulatory period **(AIII)**.

Discordant Couples with HIV-Infected Men:

- The use of donor sperm from an HIV-uninfected man with artificial insemination is the safest option **(AIII)**.
- When the use of donor sperm is unacceptable, the use of semen preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered **(BII)**.
- Semen analysis is recommended for HIV-infected men before conception is attempted to prevent unnecessary exposure to infectious genital fluid. Semen abnormalities appear to be more common among HIV-infected men than HIV-uninfected men **(AIII)**.

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*

DHHS Perinatal Guidelines, Updated Aug 2015

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Panel's Recommendations
For Couples Who Want to Conceive *For Concordant (Both Partners are HIV-Infected) and Discordant Couples:* • Expert consultation is recommended so that approaches can be tailored to couples' specific needs **(AIII)**. • Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**. • Both partners should attain maximum viral suppression before attempting conception **(AIII)**. *For Discordant Couples:* • The couple should be counseled and only attempt conception after the HIV-infected partner has initiated antiretroviral therapy and have achieved sustained suppression of plasma viral load below the limits of detection **(AI)**. • Administration of antiretroviral pre-exposure prophylaxis 30 days before and 30 days after conception for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission, particularly if the HIV-infected partner's plasma viral load is unknown or detectable **(BII)**. It is not known whether pre-exposure prophylaxis for the uninfected partner confers additional benefit when the infected partner receiving antiretroviral therapy has demonstrated sustained viral suppression. *Discordant Couples with HIV-Infected Women:* • The safest conception option is assisted insemination at home or in a provider's office with a partner's semen during the peri-ovulatory period **(AIII)**. *Discordant Couples with HIV-Infected Men:*

For discordant couples:

- HIV+ partner should be on ART & sustained suppression of VL **(AI)**
- Periconception PrEP for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission. (CIII)

DHHS Perinatal Guidelines, Updated Aug 2015

Reproductive Options for HIV

Discordant couples with HIV-infected male:

- Donor sperm from an HIV-uninfected male with artificial insemination - safest option
- If this is unacceptable, sperm preparation techniques coupled with either intrauterine insemination or in vitro fertilization should be considered
- Semen analysis is recommended for HIV-infected males before conception, to reduce exposure if the likelihood of getting pregnant is low because of semen abnormalities

PrEP :Reproductive Options
Other Cost

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

- For many, these options are not acceptable or affordable

Reproductive Options for HIV

Periconception PrEP

- Studies under way
- Infected partner should be on ART with fully suppressed HIV VL
- Couples should use condoms at all times except during periovulatory intercourse
- No reported increase in congenital anomalies for children whose mothers were exposed to Truvada® during pregnancy

Risk of Transmission: Treatment as Prevention

HPTN 052: Preventing Sexual Transmission of HIV with ARTs

- Phase III RCT
- 1,763 serodiscordant couples (890 HIV+ men and 873 HIV+ women)—Africa, Asia, South America and US
- Immediate ART vs delay until CD4 fell below 250
- **Earlier ART initiation = 96% reduction in HIV transmission**

(M. Cohen et al. NEJM, vol 365, 2011)

Risk of Transmission: Treatment as Prevention

HPTN 052: Preventing Sexual Transmission of HIV with ARTs

- Phase III RCT
- 1,763 serodiscordant couples (890 HIV+ men and 873 HIV+ women)—Africa, Asia, South America and US

Encouraging data when advising discordant couples but remember when advising couples trying to get pregnant that in this study condom use was encouraged

(M. Cohen et al. NEJM, vol 365, 2011)

Risk of Transmission: Treatment as Prevention

Observational study of discordant couples(1989-2008)

- 424 heterosexual couples
- In 83% of couples, the man was the HIV+ partner
- 95,000 acts of intercourse
- 20,000 acts of intercourse without condoms
- No HIV transmission in couples where HIV+ partner was taking combination ART
  - On ART risk of HIV transmission estimated 1 in 2000 risk exposure

Del Romero, J, et al. BMJ 2010; 340 doi: http://dx.doi.org/10.1136/bmj.c2205

Risk of Transmission: Treatment as Prevention

Observational study of discordant couples(1989-2008)

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  - Encouraging results suggesting that the risk of HIV transmission is low if the HIV+ partner is on fully suppressive ART even without condom use BUT the risk is NOT zero.

    Several studies have shown ongoing HIV detection in semen and vaginal fluids even on fully suppressive ART

g

Del Romero, J, et al. BMJ 2010; 340 doi: http://dx.doi.org/10.1136/bmj.c2205

WHO Millennium Development Goal(2000)

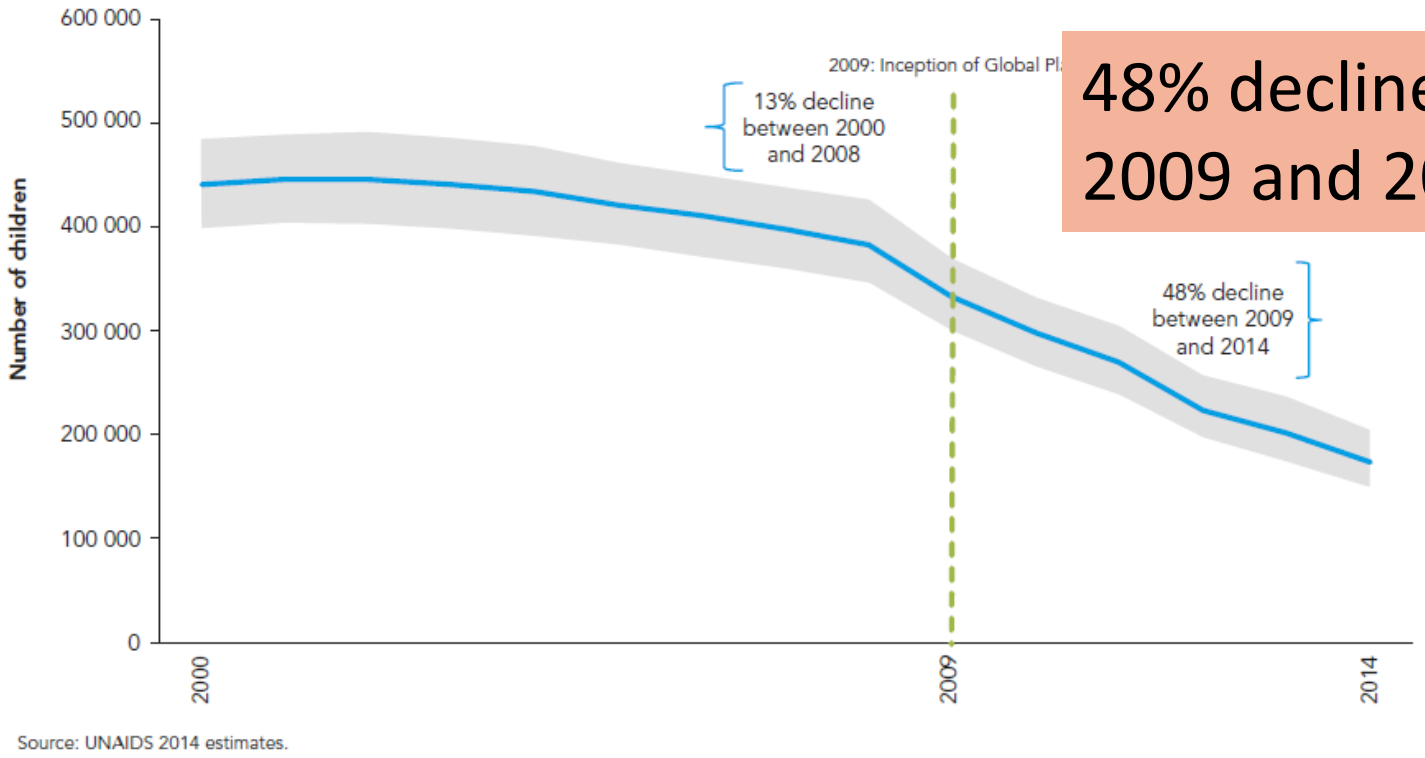
UNAID approach to eliminating perinatal HIV

- To reduce new HIV infections in children by 90% by 2015
  - <40,000 new mother to child transmission /yr
- To achieve this goal:
  - 95% of pregnant women should be tested
  - 90% of pregnant HIV-infected women need ART

NAID approach to eliminating perinatal HIV

Where we were in 2014 globally

Figure 1
Number of new HIV infections among children in 21 Global Plan priority countries, 2000–2014



48% decline between 2009 and 2014

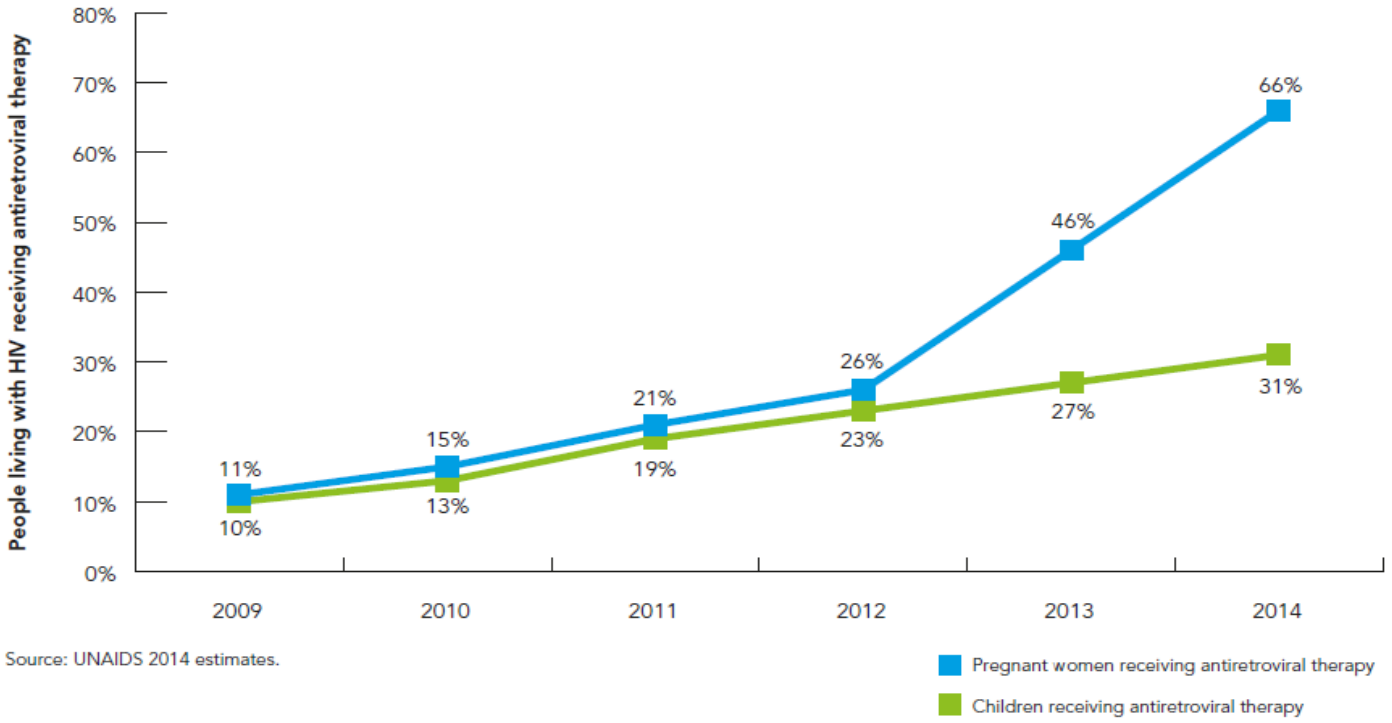
Source: UNAIDS 2014 estimates.

http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf

2014: Worldwide 66% Pregnant Women with HIV Received ART therapy to Prevent MTCT

Figure 9

Percentage of pregnant women and children (aged 0–14 years) living with HIV who are receiving antiretroviral therapy in 21 Global Plan priority countries, 2009–2014

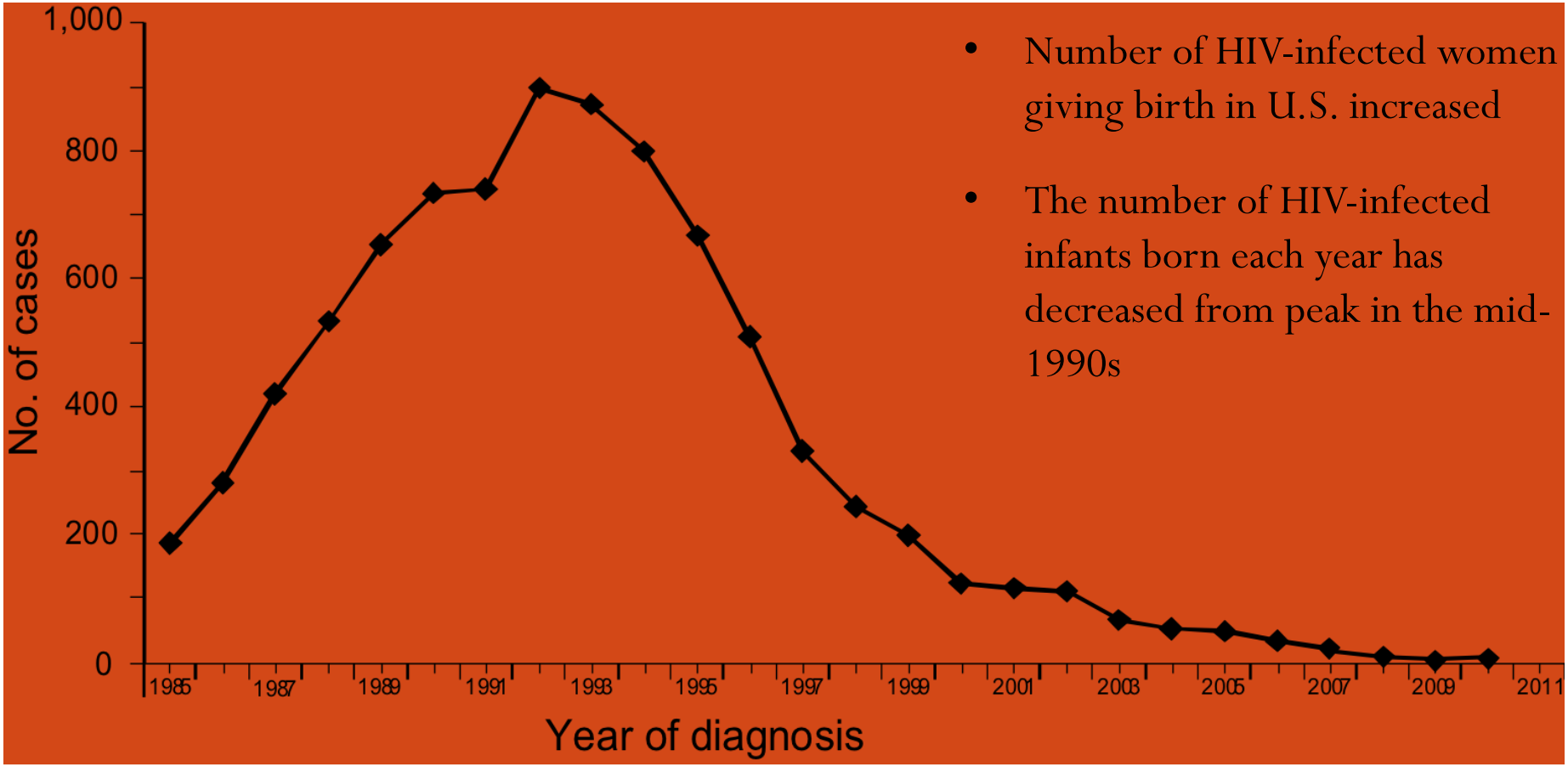


Source: UNAIDS 2014 estimates.

http://www.unaids.org/sites/default/files/media_asset/JC2774_2015ProgressReport_GlobalPlan_en.pdf

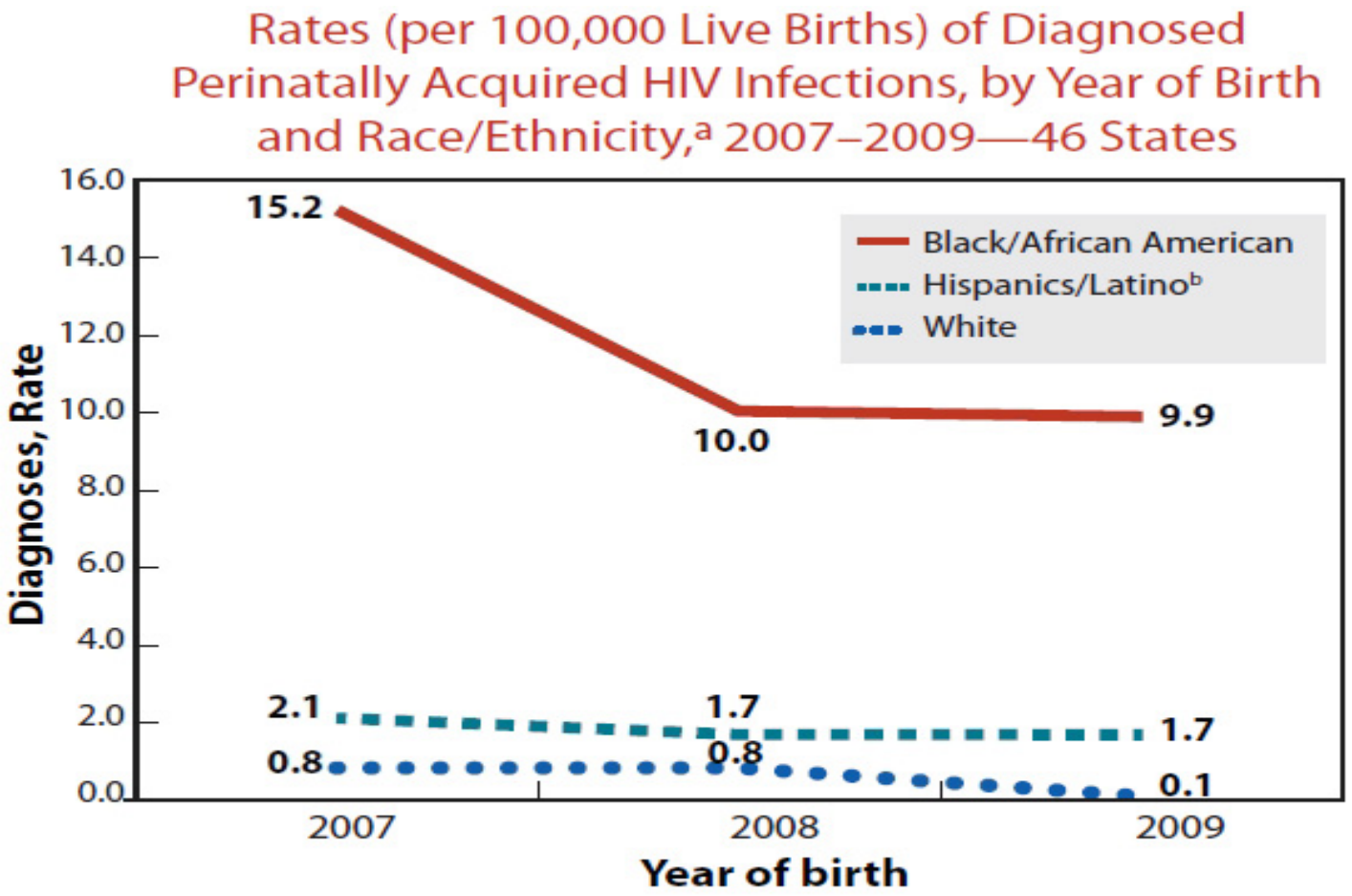
HIV and Perinatal transmission (U.S.)

Estimated Numbers of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2010 — United States and Dependent Areas



Note: Data have been adjusted for reporting delays and missing risk-factor information.

Risk of Transmission



Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
[a]Live birth data reflect race/ethnicity of the infant's mother.
[b]Hispanics/Latinos can be of any race.

CDC reports

No Perinatal HIV Transmission with ART Before Conception

- Analysis of the French Perinatal Cohort from 2000-2011
- Included 8075 mother-infant pairs
- MTCT transmission occurred in 56 cases (0.7%)
- No HIV transmissions if mothers started ART before conception and had undetectable VL at delivery

MTCT	Pre-conception	1st Trimester	2nd Trimester	3rd Trimester	P value
Rate	0.2%	0.4%	0.9%	2.2%	< .0001

CID. 2015;61:1715-1725

Pregnant Women and ART

Recommendations for Use of Antiretroviral Drugs during Pregnancy: Overview (Last updated October 26, 2016; last reviewed October 26, 2016)

Panel's Recommendations
• Multiple factors must be considered when choosing an antiretroviral (ARV) drug regimen for a pregnant woman, including comorbidities, convenience, adverse effects, drug interactions, resistance testing results, pharmacokinetics (PK), and experience with use in pregnancy (**AIII**).
• In general, the same regimens as recommended for treatment of non-pregnant adults should be used in pregnant women if appropriate drug exposure is achieved in pregnancy, unless there are known adverse effects for women, fetuses, or infants that outweigh benefits (**AII**).
• In most cases, women who present for obstetric care on fully suppressive ARV regimens should continue their current regimens (**AIII**).
• PK changes in pregnancy may lead to lower plasma levels of drugs and necessitate increased dosages, more frequent dosing, or boosting, especially of protease inhibitors (**AII**).
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*

"A dual NRTI combination: Epzicom, Truvada, or TDF/3TC

and either

- A ritonavir-boosted PI: atazanavir/ritonavir or darunavir/ritonavir

OR

- An integrase inhibitor: Raltegravir

Women And ART: Efavirenz

Efavirenz

Atripla

- Teratogenic in nonhuman primates

- Risk of neural tube defects occurs during the first 5-6 wks of pregnancy; pregnancy usually not recognized before 4-6wks

  Changes in ARTs may increase risk of loss of viral control and risk of perinatal transmission →

  EFV can be continued in pregnant women

- Use alternative ART agent in women who are trying to conceive or who are not using effective contraception, if feasible

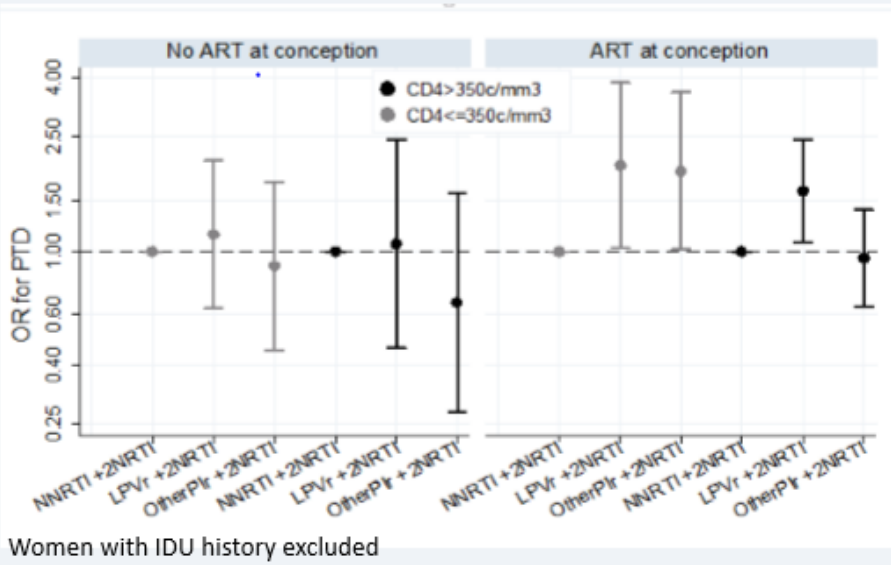
Women And ART
Lopinavir and Pre-Term Delivery

Increased risk of PTD in:

- Women on LPV/r-regimens had higher risk of PTD vs. women on NNRTI regimens

- Lopinavir seldom used in the U.S. anymore but worldwide it is still the preferred PI

Fig 1 Adjusted OR for PTD stratified by ART at conception and CD4 count (≤350 and >350 cells/mm^3)



Women with IDU history excluded

CROI 2017 – Abstract #778. Favarato. (UK /Ireland data)

Pregnant Women: Intrapartum

Zidovudine and C-sections:

Update **October, 2016**

- IV ZDV infusion recommended during labor if maternal HIV RNA is **≥1000 copies/mL** (or is unknown) near delivery
- Consider omitting IV ZDV during labor if maternal HIV RNA is <1000 copies/mL
- Scheduled cesarean delivery at 38 weeks' gestation is recommended for women who have HIV RNA >1,000 copies/ml near delivery

http://aidsetc.org/resource/guidelines-use-antiretroviral-agents-adults-and-adolescents-training-slide-sets

AETC NATIONAL RESOURCE CENTER

Pregnant Women and ART Postpartum Management

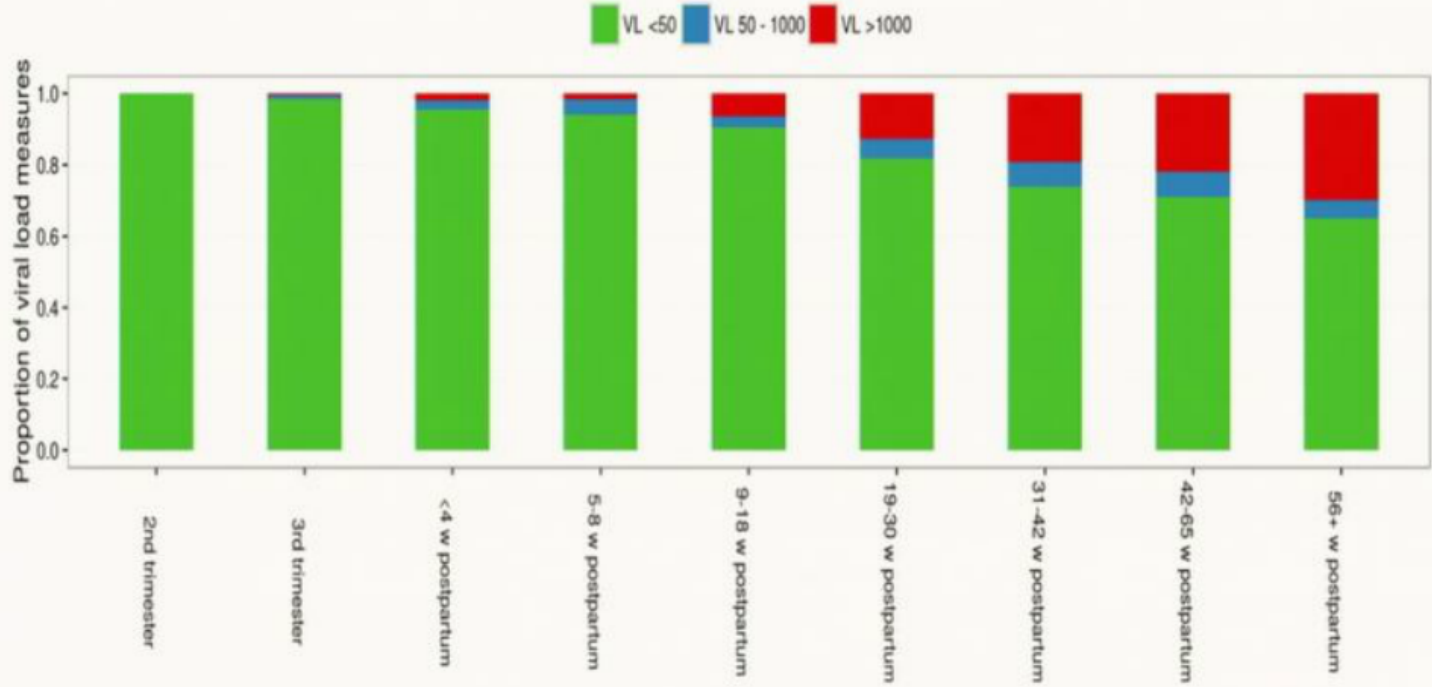
- Continuation of ART for maternal health
- ART adherence may worsen postpartum;
  - Specifically address and support adherence
- To reduce risk of post natal transmission
  - No breast-feeding
  - No premastication of food for the infant

Pregnant Women and ART Postpartum Management

Viremia increases post-partum

Myer et. al. Frequency of Viremic Episodes in HIV-Infected Women Initiating Antiretroviral Therapy During Pregnancy: A Cohort Study

Clin Infect Dis. 2017;64(4):422-427. doi:10.1093/cid/ciw792

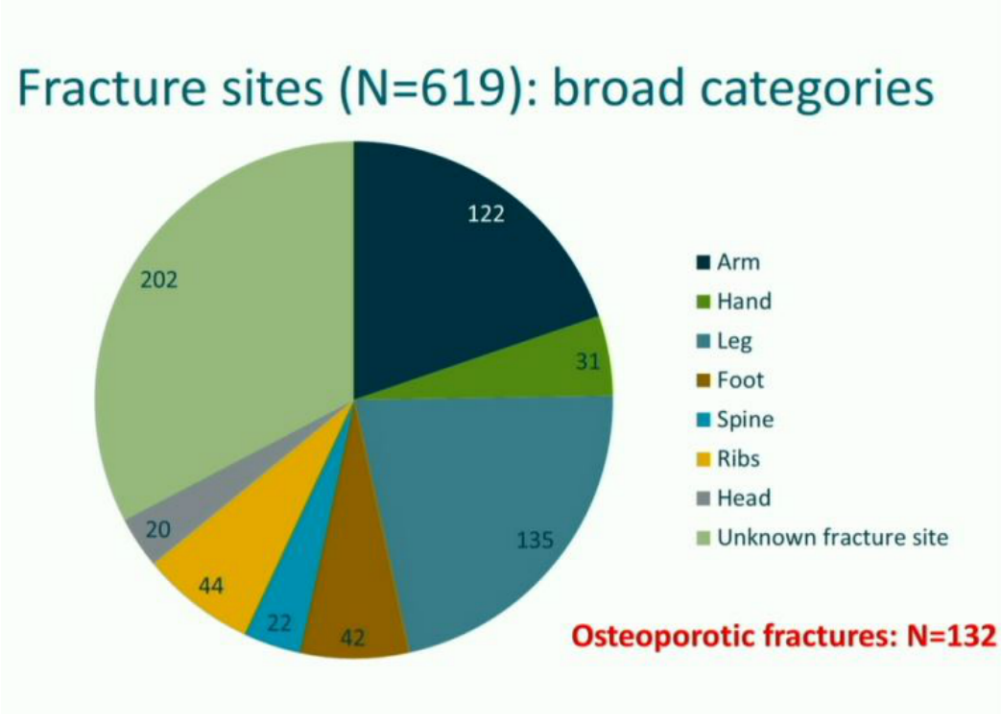


Distribution of viral load (VL) test results during select intervals of time during pregnancy and postpartum; each column shows results for all tests conducted in the cohort during that interval.

Bone Health

HIV and Bone Health

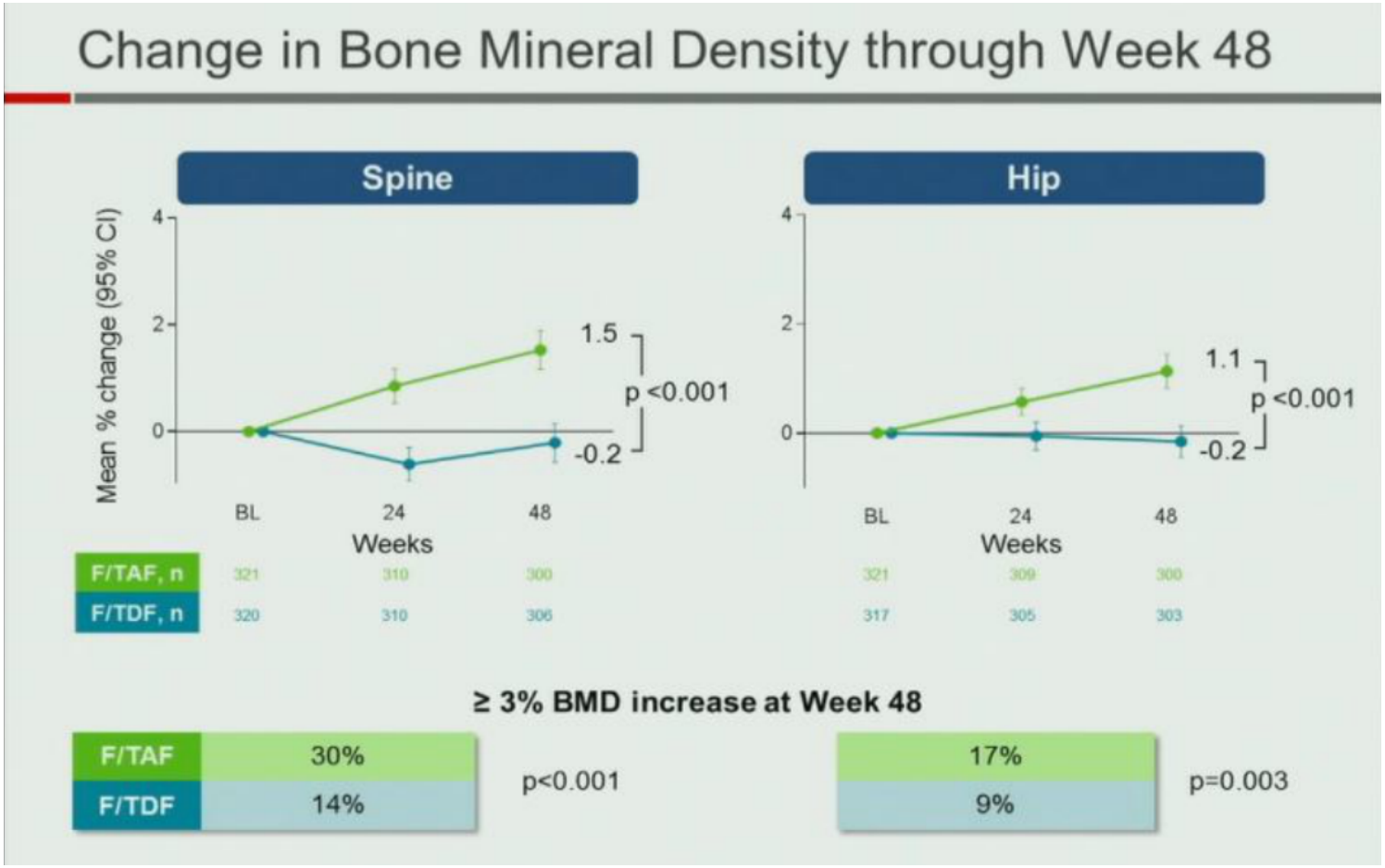
Initiation of ART associated with 1-6% loss of BMD
Occurs with all ART, especially TDF



- Fractures 3x more common in HIV+
- Associated factors:
  - TDF exposure(current or past)
  - White race, IVDU, older age,
  - Lower BMI,
  - HCV
  - Prior ON or facture,
  - Recent CVD

CROI Abstract #46: ART, Fractures and Osteonecrosis in Large European HIV Cohort

HIV and Bone Health :
Recovery after switching TDF → TAF

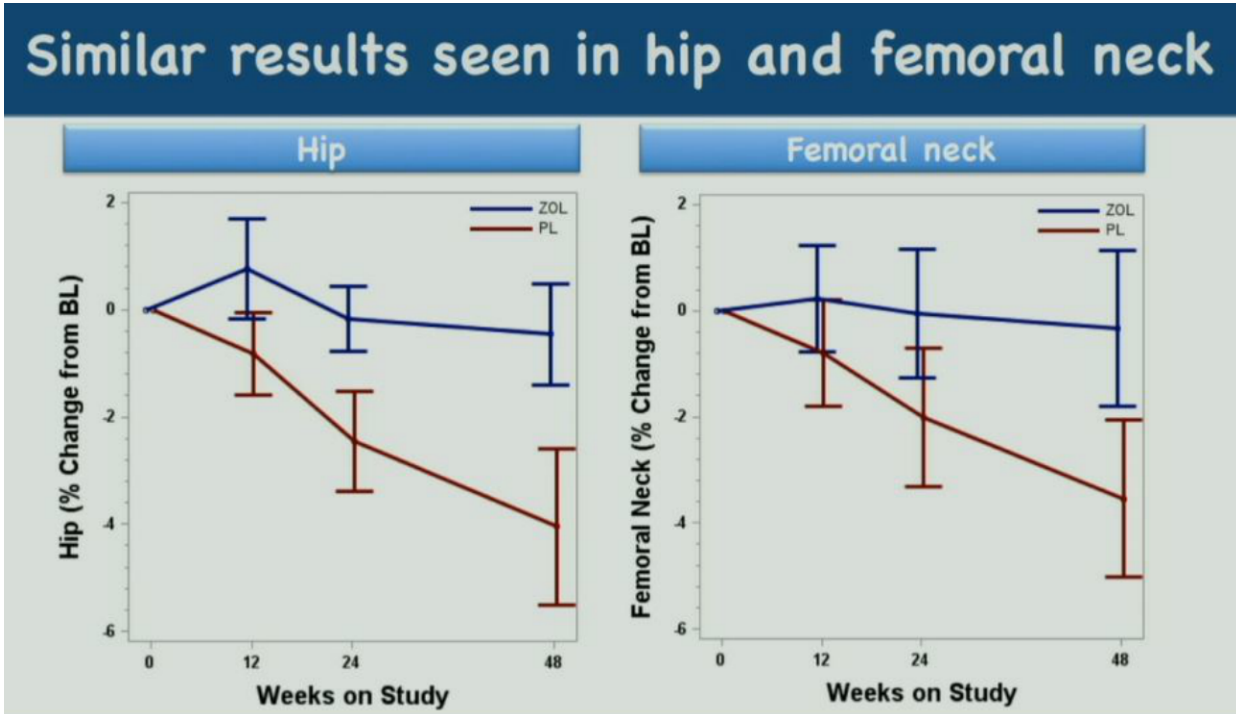


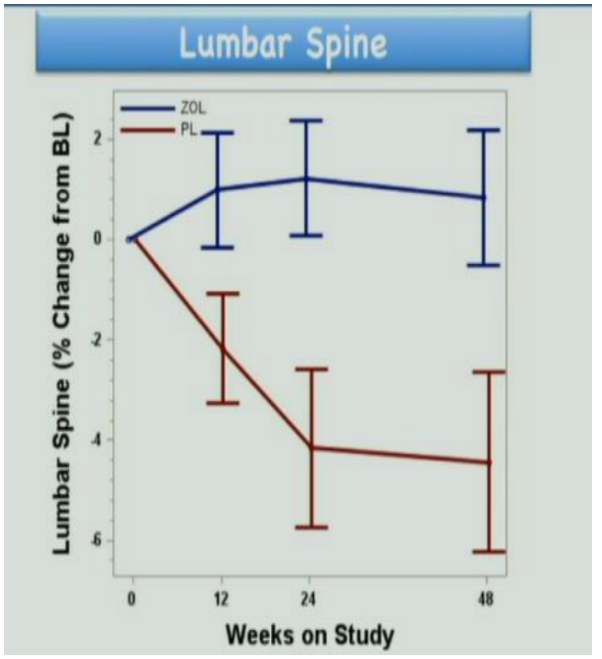
CROI 2016 Oral Abstract #29: Switching Tenofovir DF to Tenofovir Alafenamide in Virologically Suppressed Adults

HIV and Bone Health : The Future

A single dose of zolendronic acid at initiation of ART can ameliorate bone loss

- 63 ART naïve age 30-50 years, no bone disease and vit D3 level ≥12 ng/ml





CROI 2016Oral Abstract #47: A Single Dose Zolendronic Acid Prevents ART Induced Bone Loss

Cancer Screening

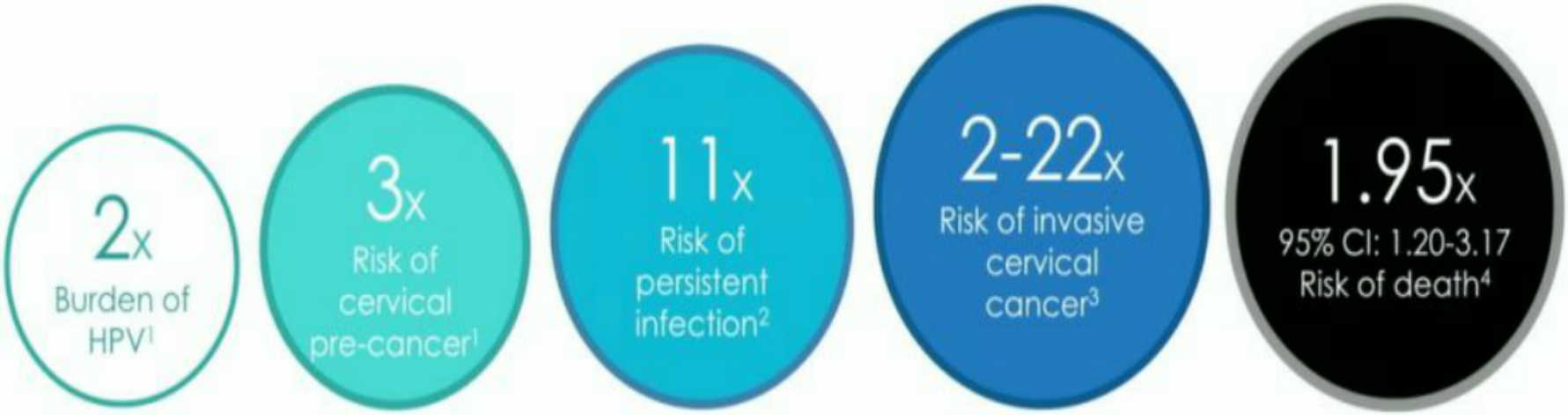
Breast Cancer Screening

- ACOG in 2012 in conjunction with ACS/NCCN
  - Clinical breast exam
    - Age 40 and older: annually
    - Age 30-39: 1-3 years
  - Mammogram @ age 40

- ACS Oct 2015 update (for average risk women)
  - Breast exam (medical/self) no longer recommended
  - Mammograms
    - Annual mammograms at age 45
      - Women can start at age 40 if they want to
    - Every other year beginning at age 55

HIV & Cervical Cancer Burden

- HIV-infected women are disproportionately affected by cervical cancer.



1. Jamieson DJ, et al. Characterization of genital human papillomavirus infection in women who have or who are at risk of having HIV infection. Am J Obs Gynecol **2002**
2. Ellerbrock, TV, et al. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. JAMA **2000**
3. Denny LA, et al.. Human papillomavirus, human immunodeficiency virus and immunosuppression. Vaccine **2012**
4. Dryden-Peterson S, et al. HIV Infection and Survival Among Women With Cervical Cancer. J Clin Oncol **2016**.

Cervical Cancer Screening: Gen Population

ACOG Jan 2016 bulletin

Table 1. Screening Methods for Cervical Cancer for the General Population: Joint Recommendations of the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology*

Population	Recommended Screening Method	Comment
Women younger than 21 years	No screening	
Women aged 21–29 years	Cytology alone every 3 years	
Women aged 30–65 years	Human papillomavirus and cytology cotesting (preferred) every 5 years Cytology alone (acceptable) every 3 years	Screening by HPV testing alone is not recommended*
Women older than 65 years	No screening is necessary after adequate negative prior screening results	Women with a history of CIN 2, CIN 3, or adenocarcinoma in situ should continue routine age-based screening for a total of 20 years after spontaneous regression or appropriate management of CIN 2, CIN 3, or adenocarcinoma in situ
Women who underwent total hysterectomy	No screening is necessary	Applies to women without a cervix and without a history of CIN 2, CIN 3, adenocarcinoma in situ, or cancer in the past 20 years
Women vaccinated against HPV	Follow age-specific recommendations (same as unvaccinated women)	

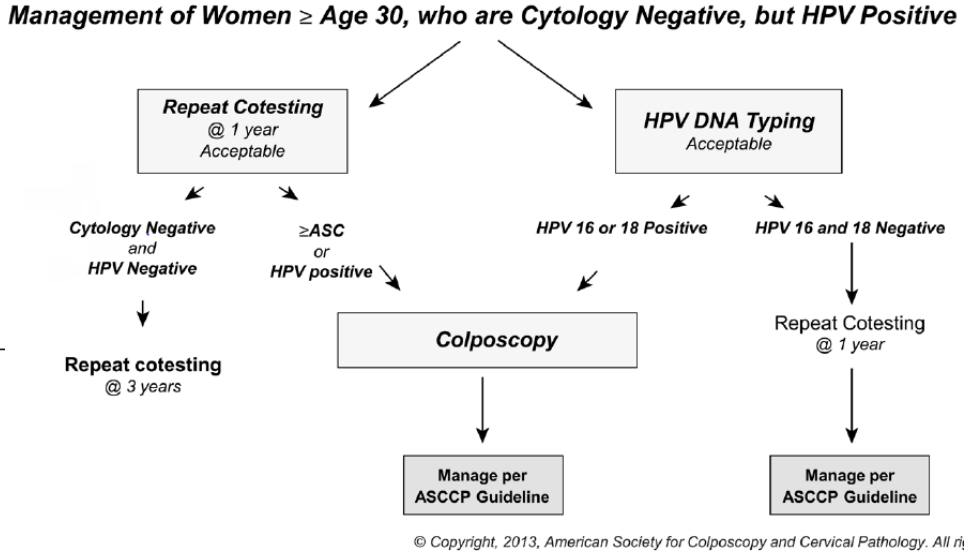
Resource : ASCCP Mobile app $ 10

Cervical Cancer Screening: Gen Pop

ACOG Jan 2016 bulletin

Table 2. Management of Cervical Cancer Screening Results ⇦

Screening Method	Result	Management
Cytology screening alone	Cytology negative	Screen again in 3 years
	ASC-US cytology and reflex HPV negative	Cotest in 3 years
	All others	Refer to ASCCP guidelines*
Cotesting	Cytology negative, HPV negative	Screen again in 5 years
	ASC-US cytology, HPV negative	Screen again in 3 years
	Cytology negative, HPV positive	
	All others	



Resource : ASCCP Mobile app $ 10

HIV and Cervical Cancer Screening

ACOG Jan 2016 bulletin

- Screening
  - Starts at age of sexual activity
  - **At time of HIV dx (cytology) then q 12 months, if 3 consecutive normal then q 3 yrs**
  - Screen DOES NOT stop at 65 years

- Age >30yrs: cytology alone or cotesting
  - If cytology alone: as above
  - If Co-testing: Once negative then **next screen in 3 yrs**

HIV and Cervical Cancer Screening

ACOG Jan 2016 bulletin

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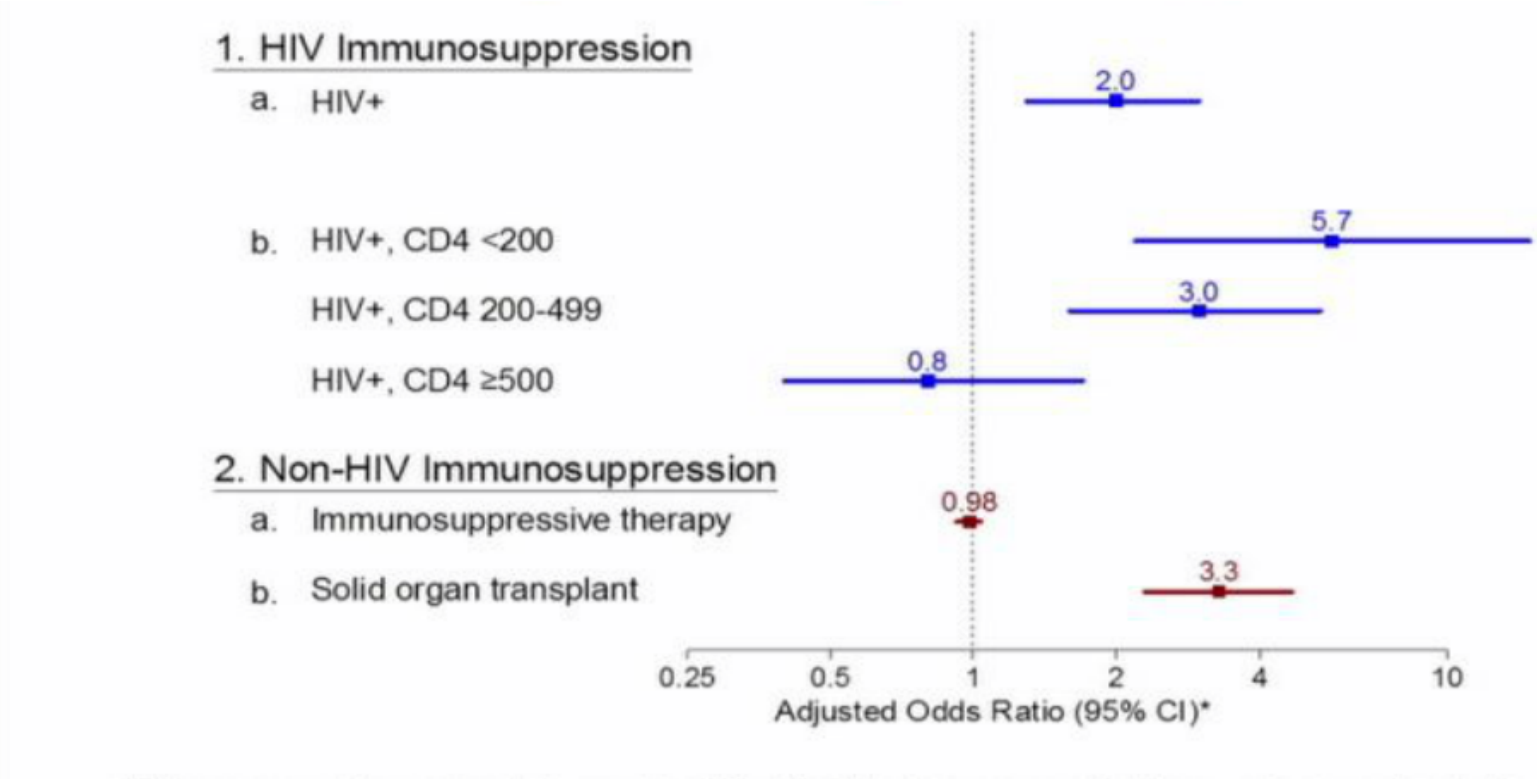
  - Starts at age of sexual activity
  - **At time of HIV dx (cytology) then q 12 months, if 3 consecutive normal then q 3 yrs**
  - Screen DOES NOT stop at 65 years

- Age >30yrs: cytology alone or cotesting
  - If cytology alone: as above
  - If Co-testing: Once negative then **next screen in 3 yrs**

- Scenarios
  - If cytology neg & HPV positive → then as general pop
  - If ASC-US & HPV positive → colposcopy
  - If ASC-US (and no HPV available) then rpt in 6-12 months
    - If ASC-UC or worse on rpt cytology → colposcopy

HIV and Cervical Cancer Screening

- HIV+ women had a 2 fold higher risk of CIN2+ and CIN3+ compared with HIV-uninfected
- Higher risk only observed among those with CD4 <500 cells



CROI Oral Abstract # 162: Is Intensive Cervical Cancer Screening Justified in Immunosuppressed Women?

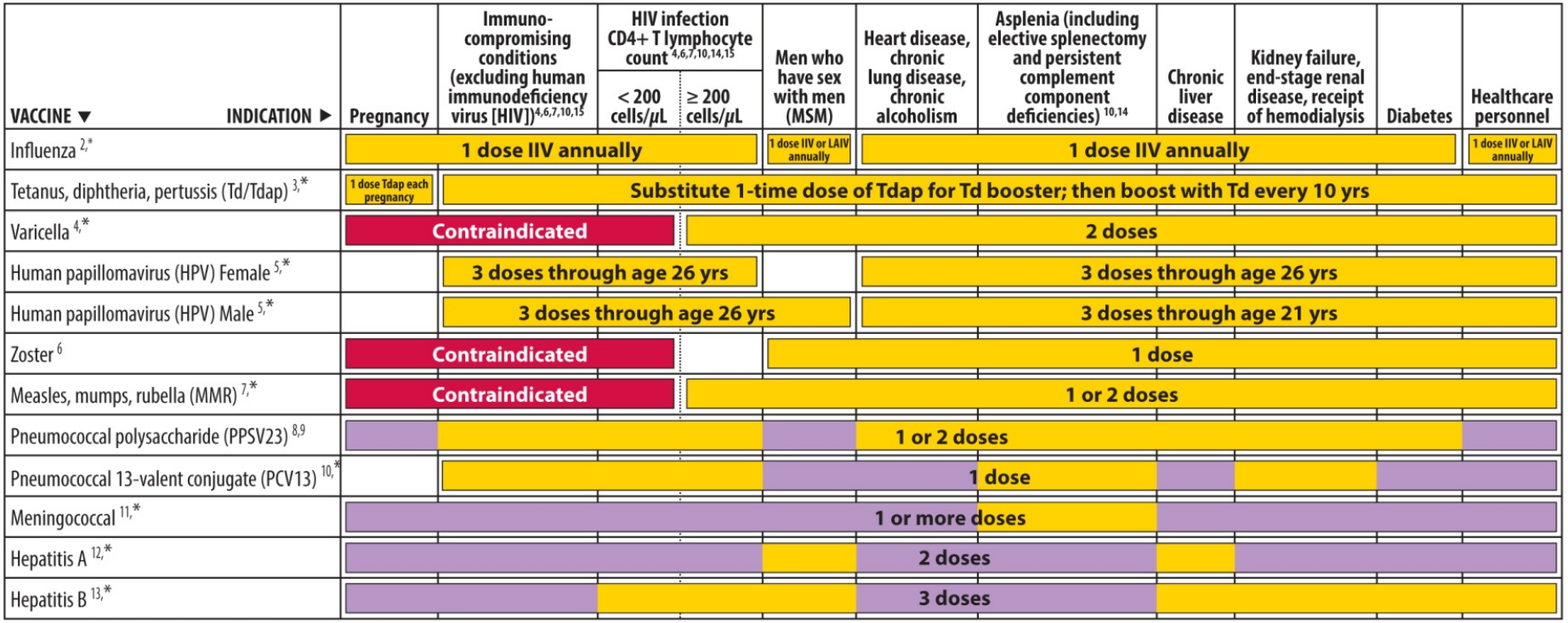
HIV and Cervical Cancer Outcomes

WIHS Cohort: Natural history study of CIN2 progression in HIV (US data)

- 74% of HIV+ women with CIN2 regressed without treatment
  - 15% progressed and 11% stable
- Median time to progression in HIV+ women: 3 years
- Sustained ART used and increased CD4 cells were significantly associated with decreases in the hazard of CIN2 progression

CROI 2017. Abstract # 23, Colie .

Women and HIV: HPV Vaccination



*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

These schedules indicate the recommended age groups and medical indications for which administration of currently licensed vaccines is commonly indicated for adults ages 19 years and older, as of January 1, 2013. For all vaccines being recommended on the Adult Immunization Schedule: a vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Licensed combination vaccines may be used whenever any components of the combination are indicated and when the vaccine's other components are not contraindicated. For detailed recommendations on all vaccines, including those used primarily for travelers or that are issued during the year, consult the manufacturers'

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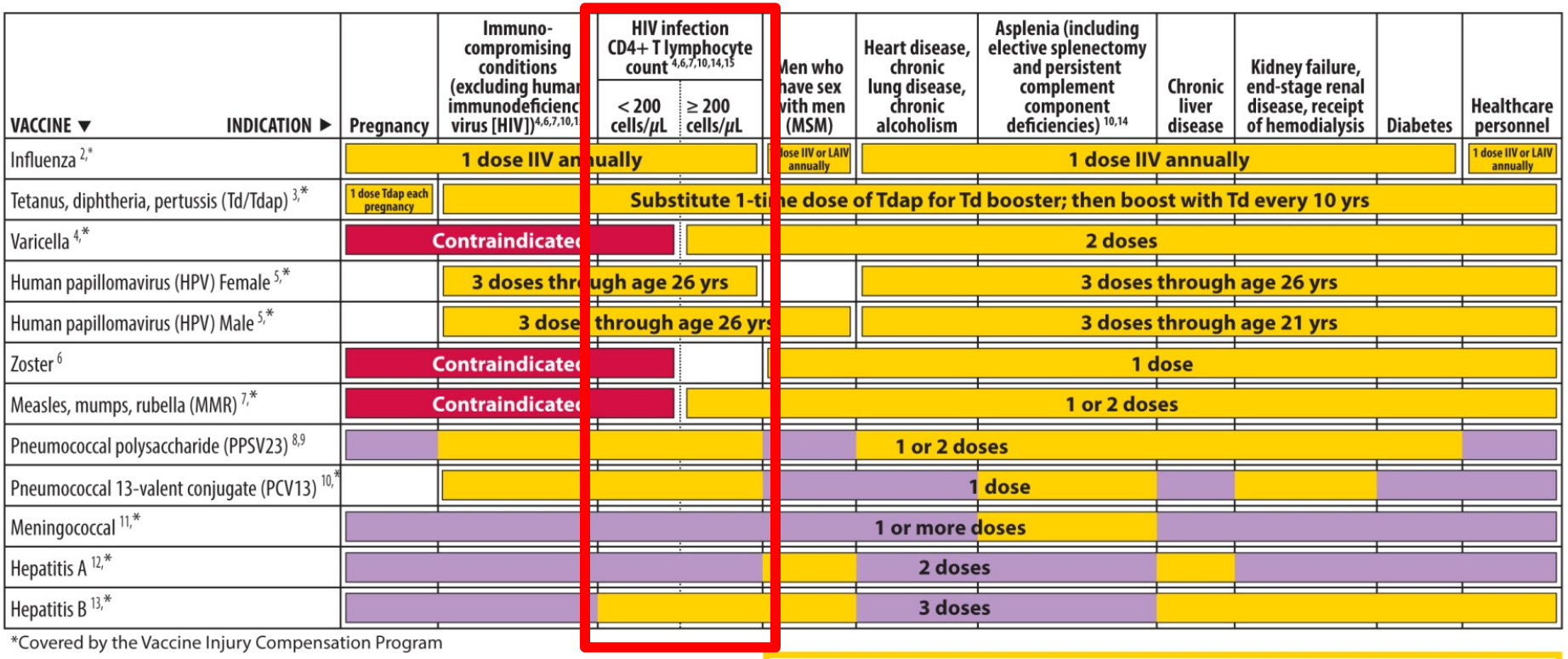
Any HPV vaccine (bivalent, quadrivalent, or 9-valent), whichever is readily available should be given to females aged 9-26 years (ACOG)

Centers for Disease Control and Prevention

Women and HIV: HPV Vaccination



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Centers for Disease Control and Prevention

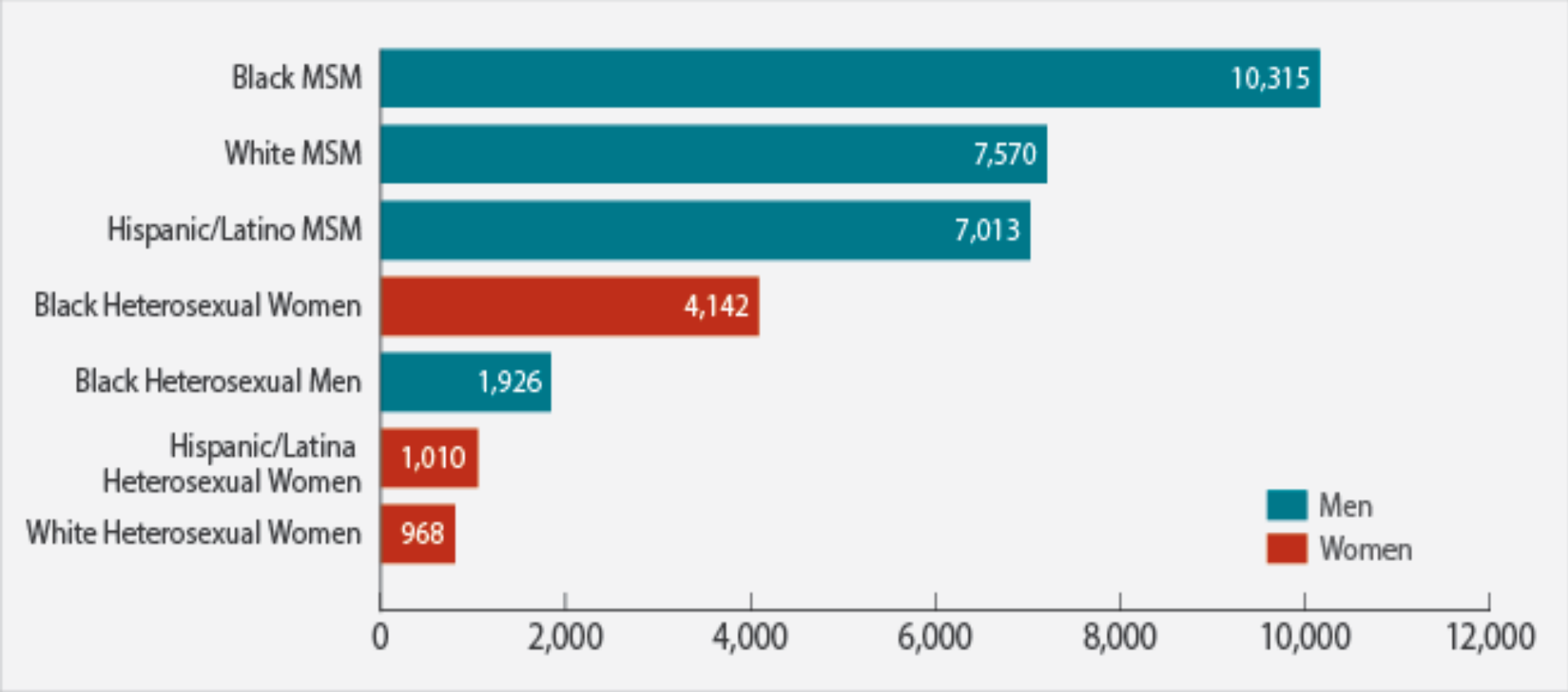
Thank you

Questions ?

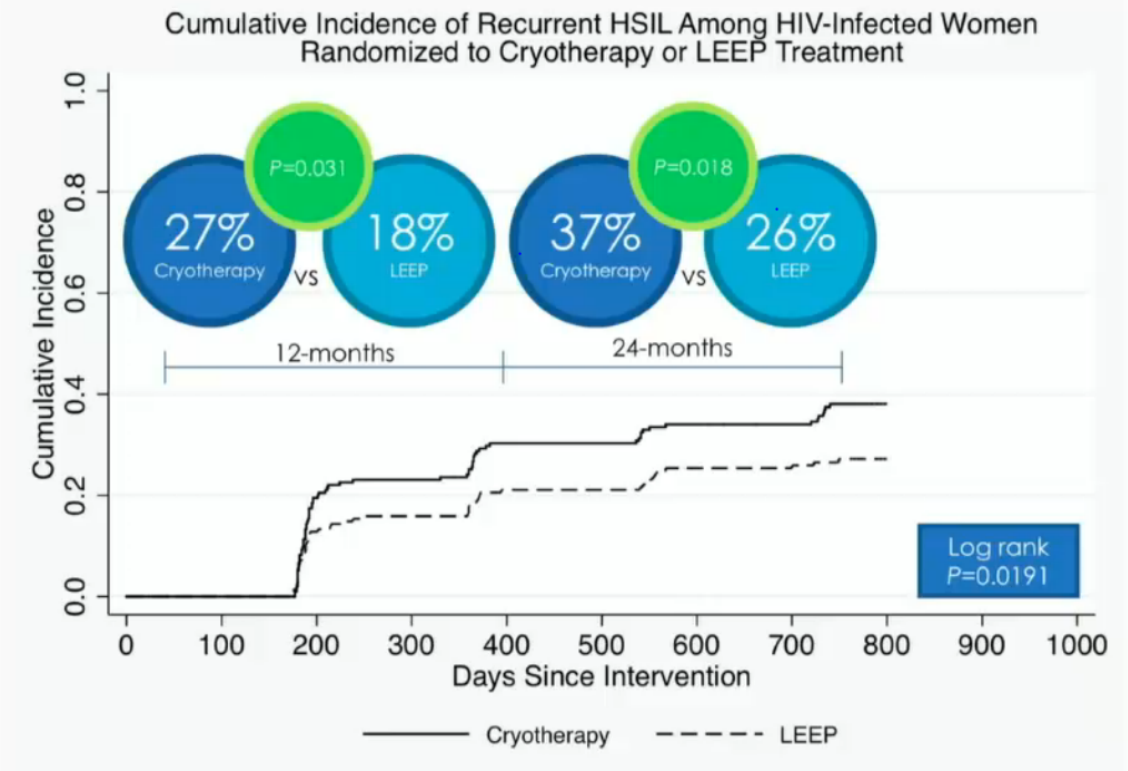
Contact info:
sharon.weissman@uscmed.sc.edu
Office#: 803-545-5350

Women and HIV : US 2015

Sex and Race distribution



HIV and Cervical Cancer
Cryo vs LEEP- Nairobi



Cryotherapy was associated with a 52% higher risk of recurrence compared to LEEP.

Adjusting for ART, baseline plasma, and CD4 count, cryotherapy was associated with a 64% higher risk of recurrence.

Croi 2017,
Abstract#22. Greene