HIV in Pregnancy

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Objectives

- Review epidemiology of Perinatal HIV
- Overview of options for serodiscordant couples
- Brief Overview of PrEP
- Discussed methods of prevention of Maternal to Child Transmission antepartum, intrapartum and postpartum
- Discuss HIV testing algorithm

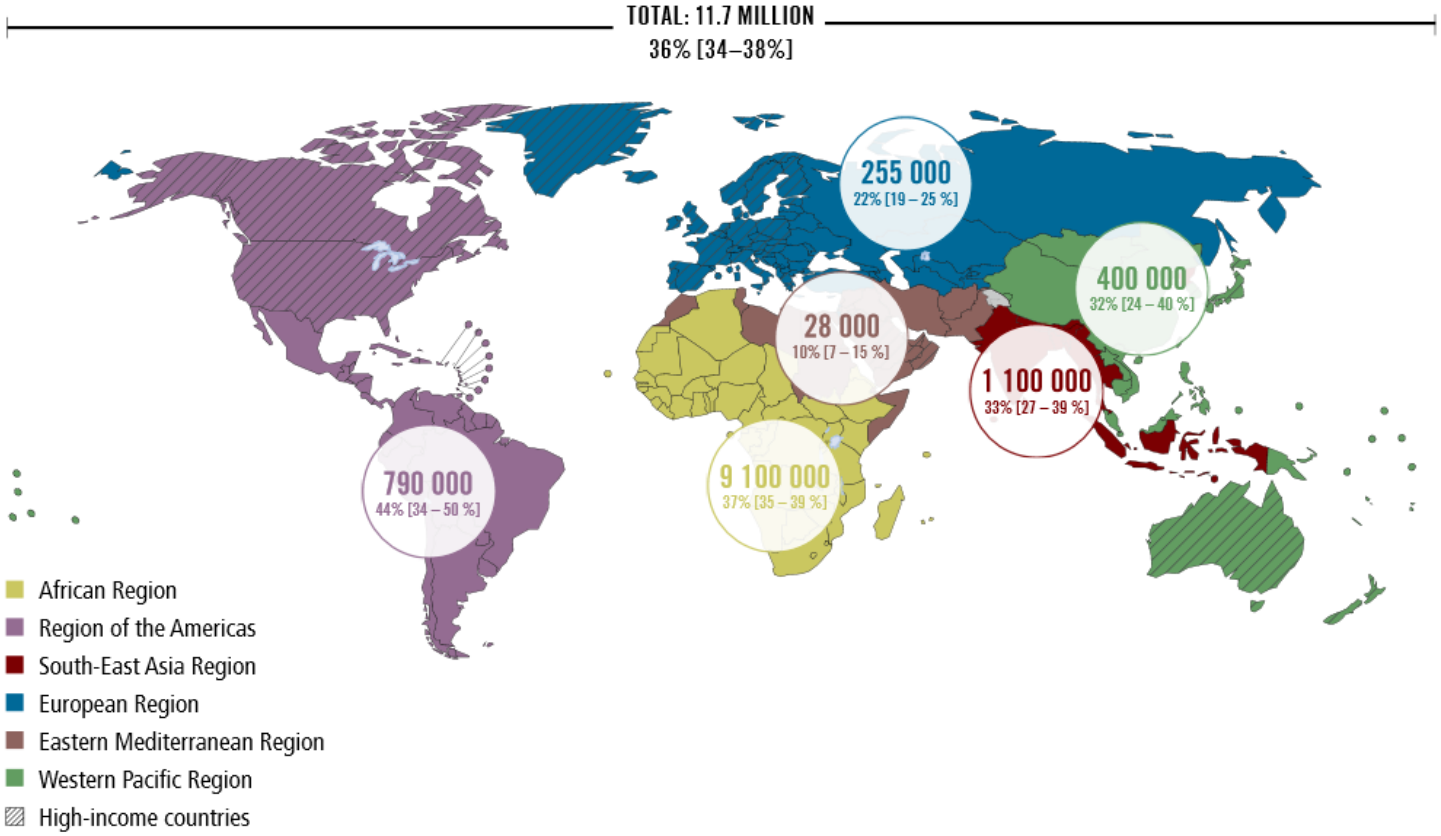
Global summary of the AIDS epidemic | 2014

Number of people living with HIV in 2014	**Total**	36.9 million [34.3 million – 41.4 million]
	Adults	34.3 million [31.8 million – 38.5 million]
	Women	17.4 million [16.1 million – 20.0 million]
	Children (<15 years)	2.6 million [2.4 million – 2.8 million]
People newly infected with HIV in 2014	**Total**	2.0 million [1.9 million – 2.2 million]
	Adults	1.8 million [1.7 million – 2.0 million]
	Children (<15 years)	220 000 [190 000 – 260 000]
AIDS deaths in 2014	**Total**	1.2 million [980 000 – 1.6 million]
	Adults	1.0 million [890 000 – 1.3 million]
	Children (<15 years)	150 000 [140 000 – 170 000]

World Health Organization UNAIDS unicef

http://www.who.int/hiv/data/en/

Number of people receiving ART and percentage of all people living with HIV receiving ART in low- and middle-income countries overall and by WHO region, 2013[a]



[a]Country income classification by the World Bank at the time of the 2011 Political Declaration on HIV and AIDS.

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS).

http://www.who.int/hiv/data/en/

Maternal Mortality

- 6-20% of all maternal deaths worldwide are related to HIV (Lathrop, Jameison et al, HIV and Maternal mortality. Int J Gynaecol Obstet. 2014)

United States Incidence

State/Dependent Area	Number of Diagnoses of HIV Infection, 2013
Florida	5,377
California	5,334
Texas	4,854
New York	3,803
Georgia	3,020
New Jersey	2,177
Maryland	2,174
Illinois	2,091
North Carolina	1,578
Pennsylvania	1,425

http://www.cdc.gov/hiv/statistics/overview/

CDC Perinatally Infected Infants

- HIV-infected women delivering infants annually
  - ≈ 8700 in 2006[1]
  - ≈ 30% increase since 2000
- HIV-infected children < 13 years old diagnosed per year in 50 states (estimated)[2]
  - 224 (180 are perinatal) in 2009
  - 187 (107 are perinatal) in 2013
- HIV-infected infants born in 50 states
  - ≈ 151 (95CI, 135-174) in 2009[3]

[1]Whitmore, Pediatrics JAIDS 2011;57:p218; [2]NHSS Surveillance Report 2013, vol 25; [3]Taylor, 2012 CROI, abst 103

What do we know (estimate)?

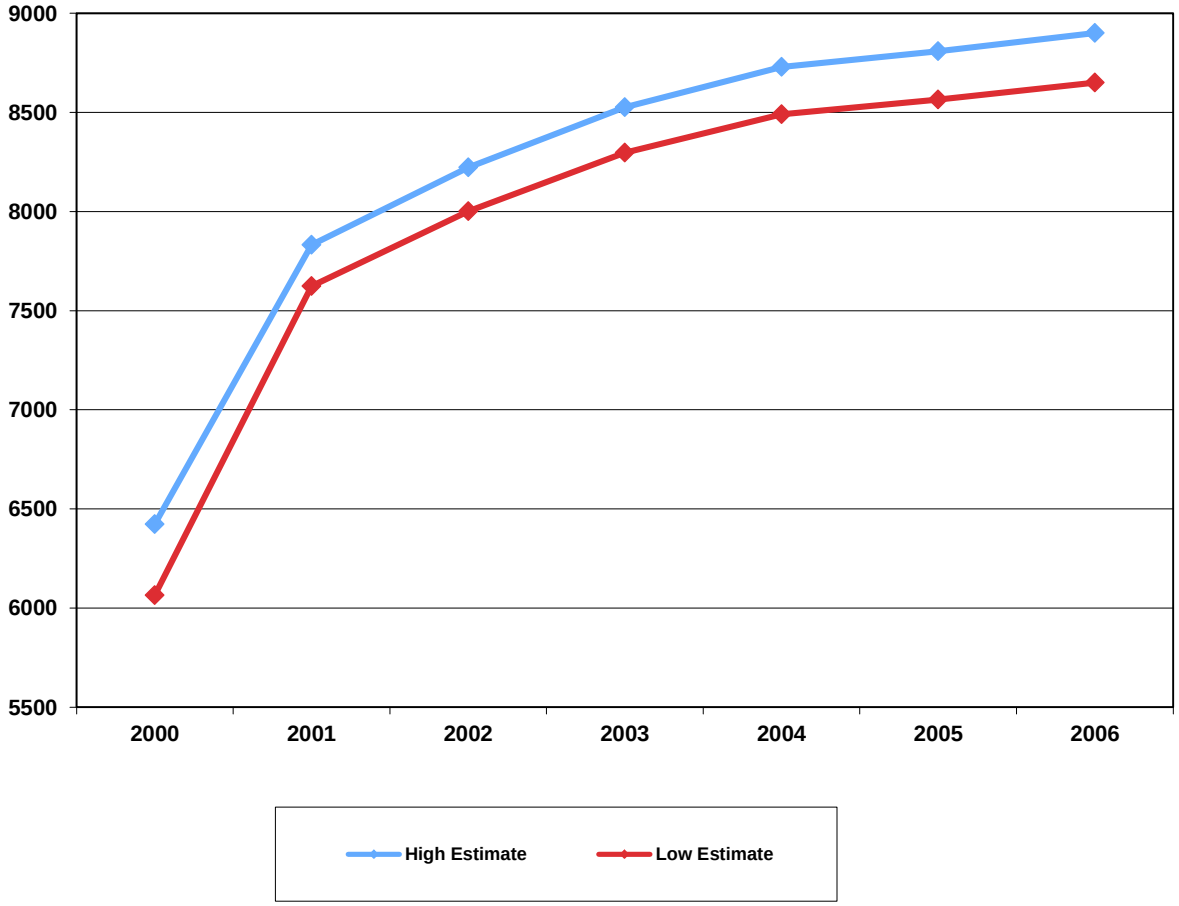
- Mother-to-Child transmission rate:
  - 2-3%[4]
  - No significant difference by race, (mirrors the tremendous racial disparity among women with HIV)

Year	Number of Cases	Incidence
2008	168	4.0
2009	150	3.6
2010	118	3.0
2011	102	2.6
2012	123	3.1

[4]CDC HIV Surveillance Supplemental Report, EPS 2005-2008. 2011; vol 16 (2).

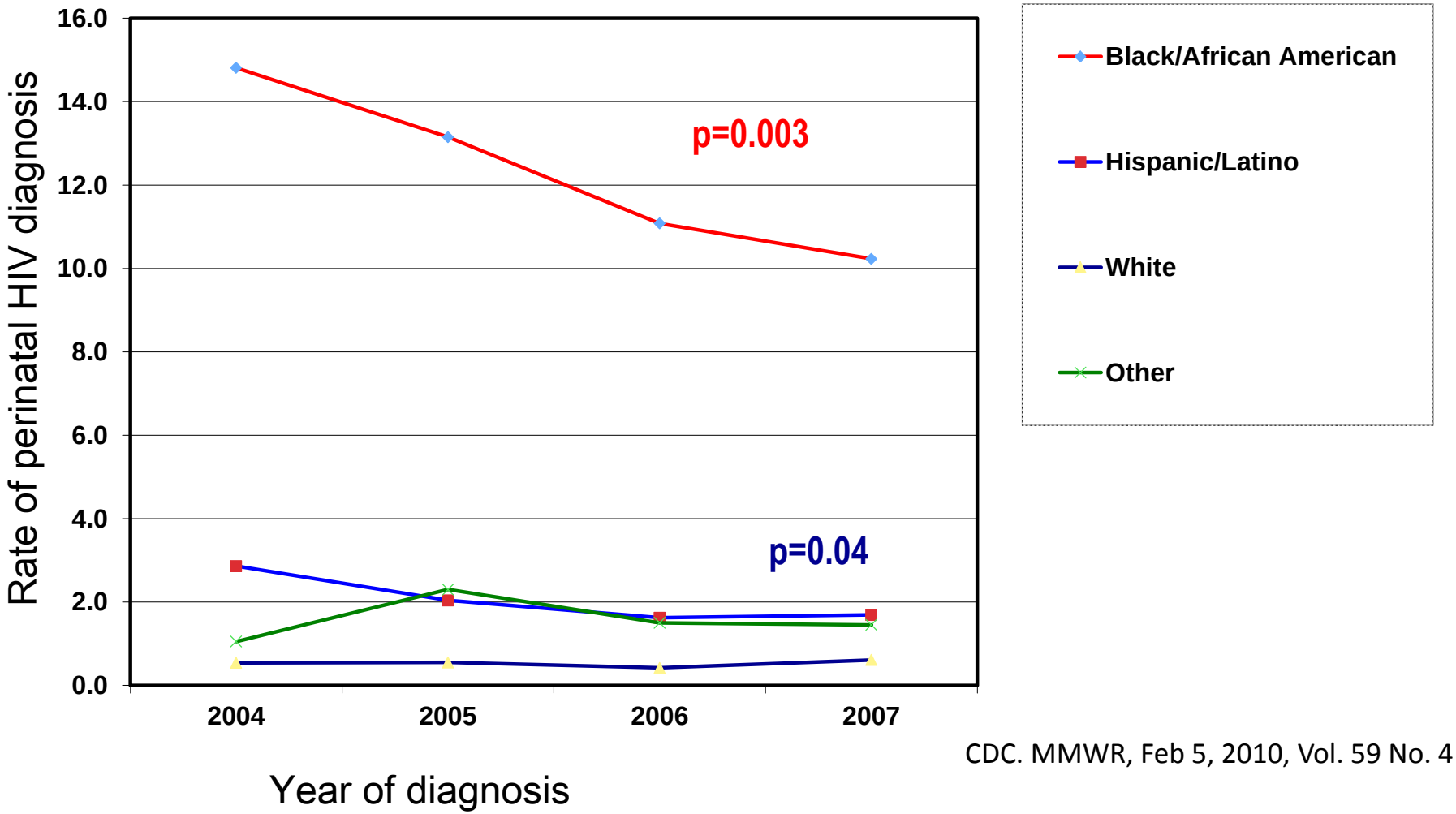
[5]CDC. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data—United States and 6 Dependent Areas—2013. 2015;20(2)

Estimated number of births to women living with HIV infection, 2000-2006, United States



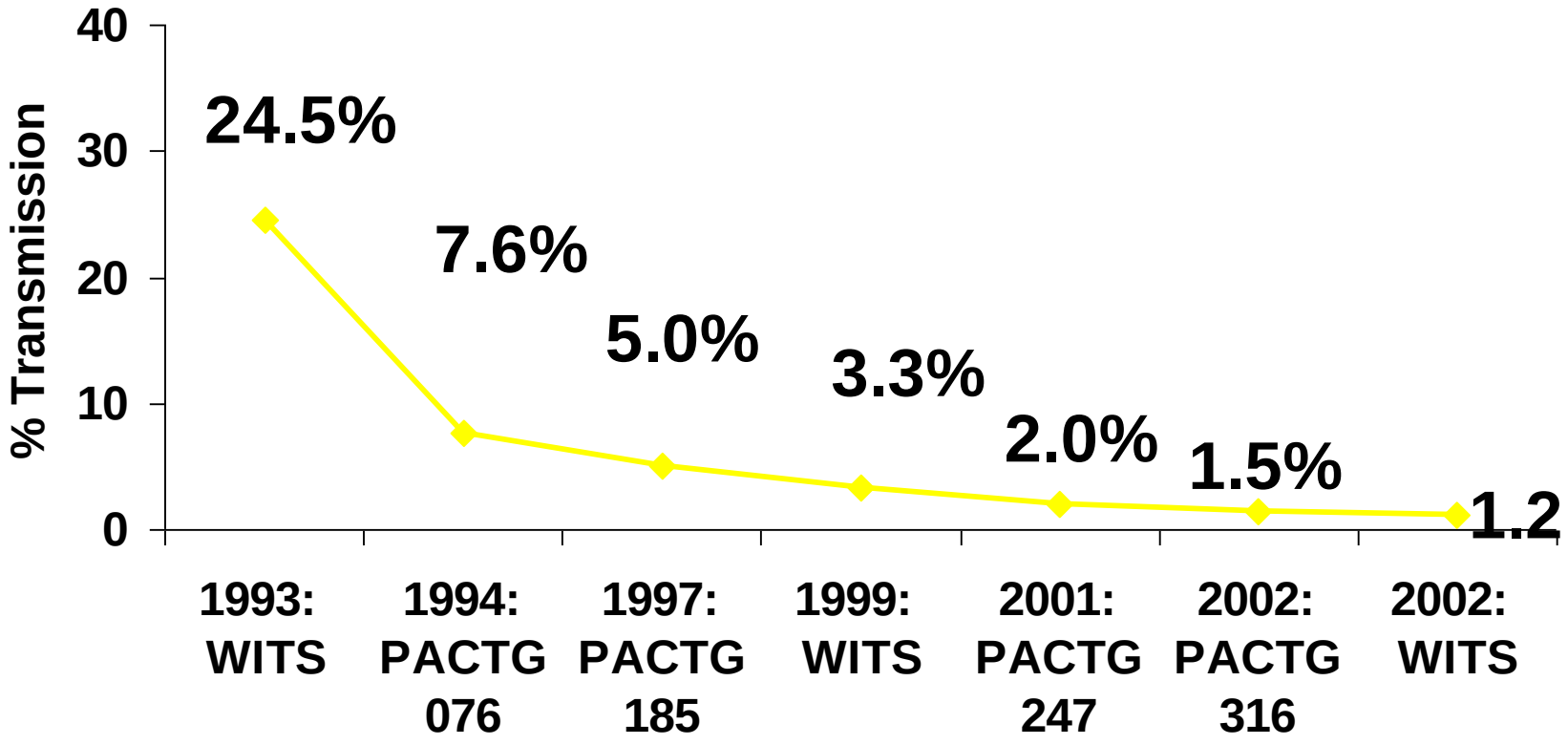
Office of Inspector General (Fleming), 2002
Whitmore, et al. CROI, 2009

Annual rate of diagnoses of perinatal HIV infection per 100,000 infants aged ≤1 year, by race/ethnicity — 34 states, 2004-2007

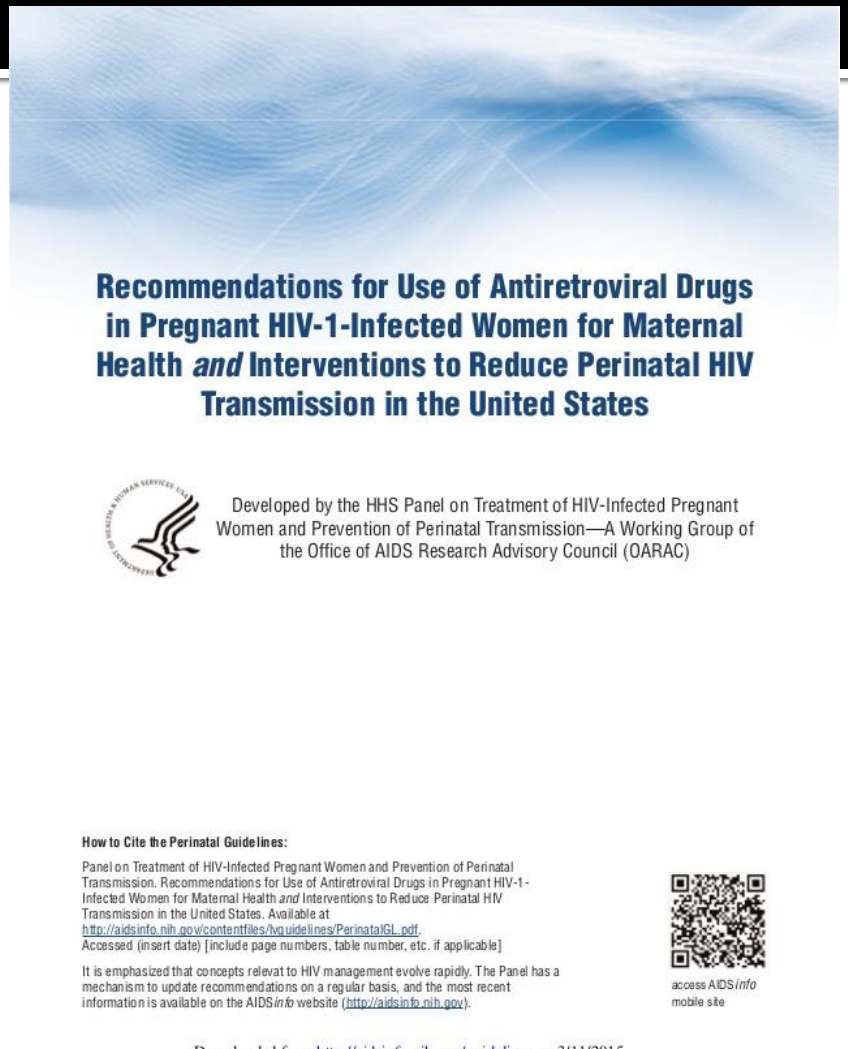


CDC. MMWR, Feb 5, 2010, Vol. 59 No. 4

Mother to Child Transmission in the U.S. Over Time



Perinatal HIV Guidelines



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States

Developed by the HHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission—A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Perinatal Guidelines:

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed (insert date) [include page numbers, table number, etc. if applicable]

It is emphasized that concepts relevat to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDS*info* website (http://aidsinfo.nih.gov).

access AIDS*info* mobile site

www.aidsinfo.nih.gov

Preconception Care for Women with HIV or Serodiscordant Couples

PreConception

- Preconception counseling/care for HIV-infected women
- Reproductive options for HIV serodiscordant couples
- PrEP
- PrEPception

PreConception Counciling

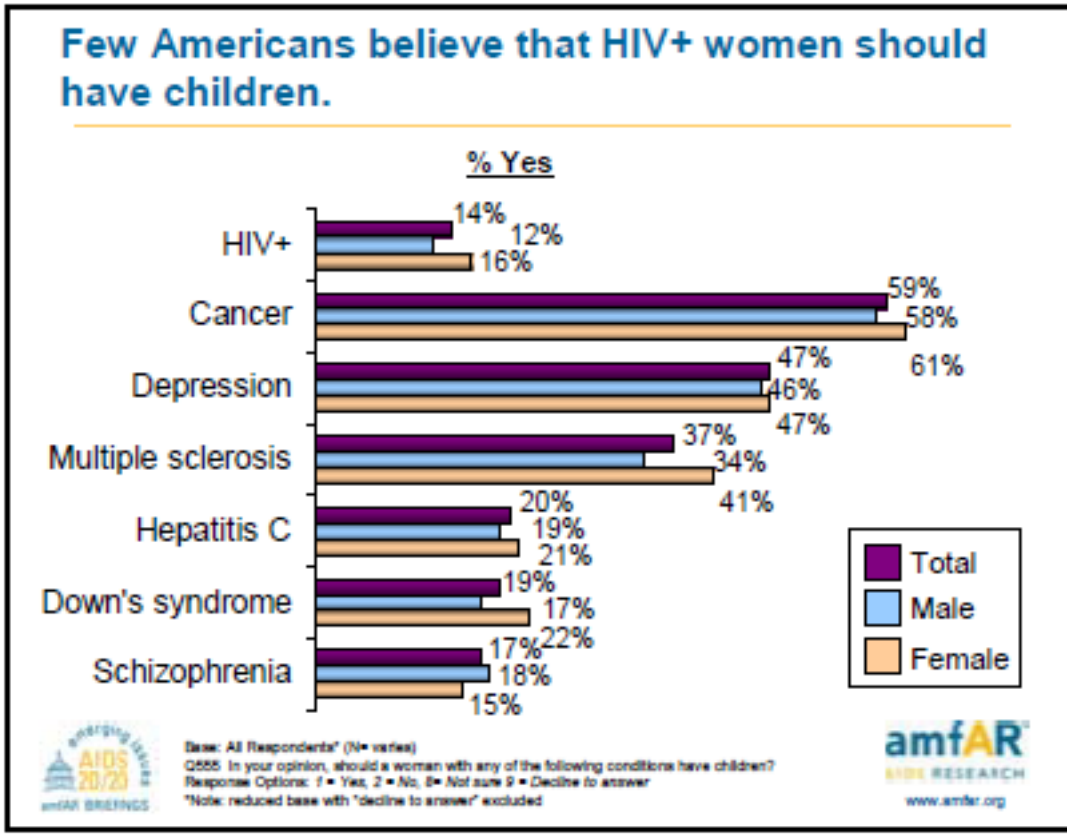
- Optimize cART regimen
- Minimize Viral Load (undetectable)
- Contraception
- Discussion of safe methods of conception for serodiscordant couples

Preconception counseling is not being addressed

- Data suggests that reproductive counseling does not often occur until after conception
  - Study of 181 women with HIV: Only 31% reported a personalized discussion with their provider specific to their childbearing plans.
  - Of those who had a personalized discussion, most were initiated by the client rather than the provider.

S. Finocchario-Kessler, et al., AIDS Patient Care and STDS, 24(5), 317-23, 2010

In your opinion, should a woman with any of the following conditions have children?



Foundation for AIDS Research (2008) email survey, n=4831

Fertility desires and intentions… trends over time

- 1998: Interviews with 1421 HIV-infected men and women in the U.S.
  - 28-29% desired pregnancy in the future
- Survey of 450 HIV+ women in the UK in 2011
  - 75% stated they wanted more children

Chen J et al. Family Planning Perspectives. 2001;33(4):144-152
Cliffe S et al. AIDS Care. 2011 Sep;23(9):1093-101

LOGISTICS for the serodiscordant couple who desire pregnancy

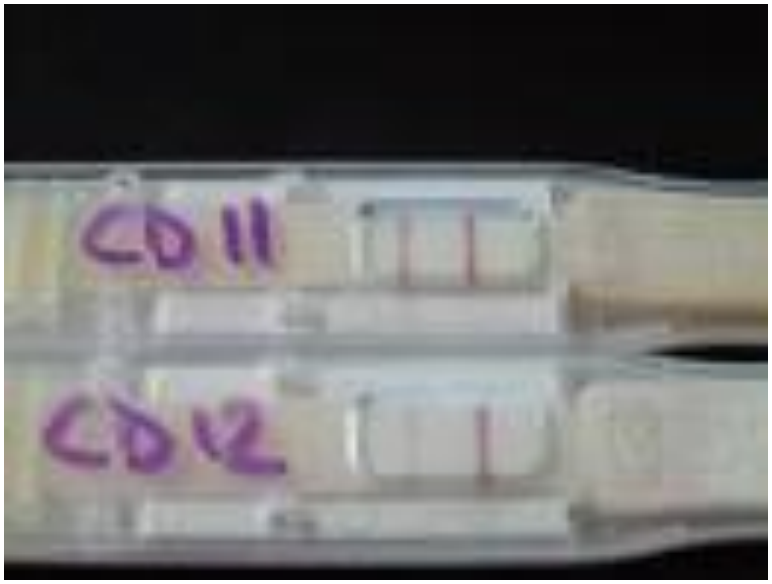
- Woman with HIV/ man without HIV
- Man with HIV/woman without HIV

Serodiscordant couples

- If the woman has HIV and the man does not
  - Viral suppression (ideally for at least 6 months) to protect partner AND prevent transmission to baby
  - Ovulation predictor kits
  - Home insemination ("turkey baster method")

Perinatal Guidelines 2014. www.aidsinfo.nih.gov
www.hiveonline.org

Ovulation predictor kits



These test kits replace the old basal body temperature charts

Alternatives

- Insemination in a doctor's office with partner's semen
- Penile/vaginal intercourse only during the 24 hours after the LH surge and using condoms the rest of the month. Placing the woman on ARVs prior to attempted conception will further protect her partner
- Pre-exposure prophylaxis for male (PrEP)? If yes, how many doses?

www.hiveonline.org

Baeten, J. et al (2012). NEJM: 367:399-410
http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf

Serodiscordance

- If the man has HIV and the woman does not, consider:
  - Maximal viral suppression of the male
  - Ovulation predictor kit/timed intercourse
  - Pre-exposure prophylaxis (PrEP) for female
  - (Assisted reproductive technology including intracytoplasmic sperm injection--ICSI)

Risk of transmission to partner

- Barreiro
  - 62 serodiscordant couples (40 HIV+ men and 22 HIV+ women)
  - HIV+ partner on ART and VL < 500 for 6 months
  - Timed intercourse
  - No transmission of HIV to partner

Barreiro et al. (2006). JAIDS 43(3):324-326.
Barreiro et al. (2007). Human Reproduction 22 (9), 2353-2358.

What if both partners are HIV-positive?

- When a couple is not attempting conception, we recommend condoms to avoid superinfection and sharing of antiretroviral resistant virus

- If pregnancy desired: Ovulation predictor kit, maintaining an undetectable viral load, and once monthly unprotected sex is a reasonable approach

Expert opinion

PrEP

- Pre-exposure prophylaxis
- If used around conception, also known as "PrEPception"

Pre-exposure prophylaxis (PrEP) for the uninfected partner

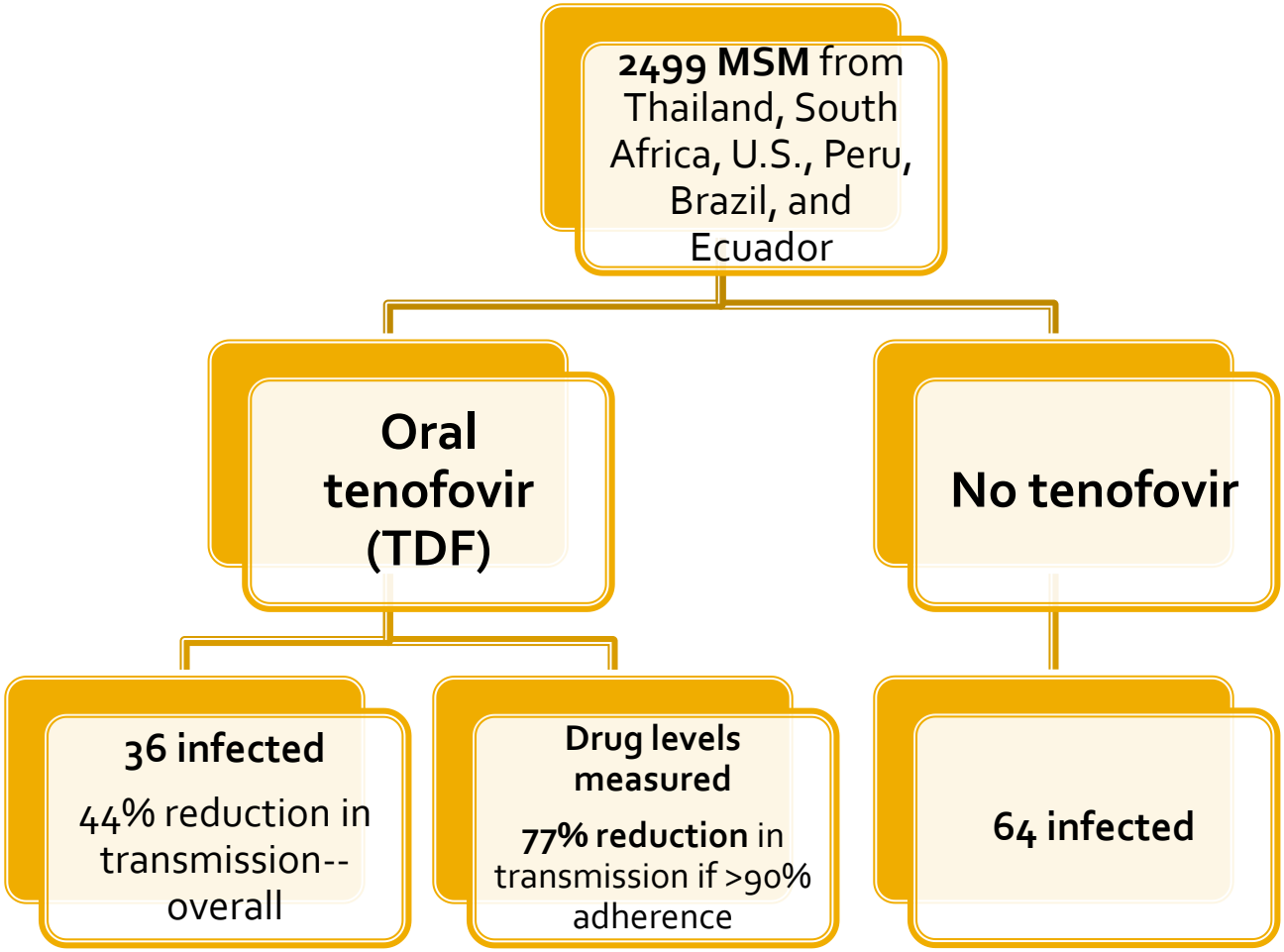
- Once daily tenofovir/emtricitabine (Truvada)
- FDA approved since 2012
- Basic requirements:
  - Baseline HIV, renal function, pregnancy test, HepBsAg and HBsAb
  - HIV test and pregnancy test q 3months
  - Renal function q 6 months
  - Immunize against Hep B if not immune
- Pregnancy and breastfeeding are not contraindications to PrEP

Treatment as Prevention

HIV Prevention Trials Network (HPTN) O52 *2011*

- Randomized controlled trial of 1763 HIV mostly heterosexual serodiscordant couples
- Sub-Saharan Africa, Asia and the Americas
- Early ART at CD4 count 350–550 vs. 200–250
- **96%** decrease in HIV-1 sexual transmission

HIV prophylaxis in serodiscordant couples: iPrex study 2010



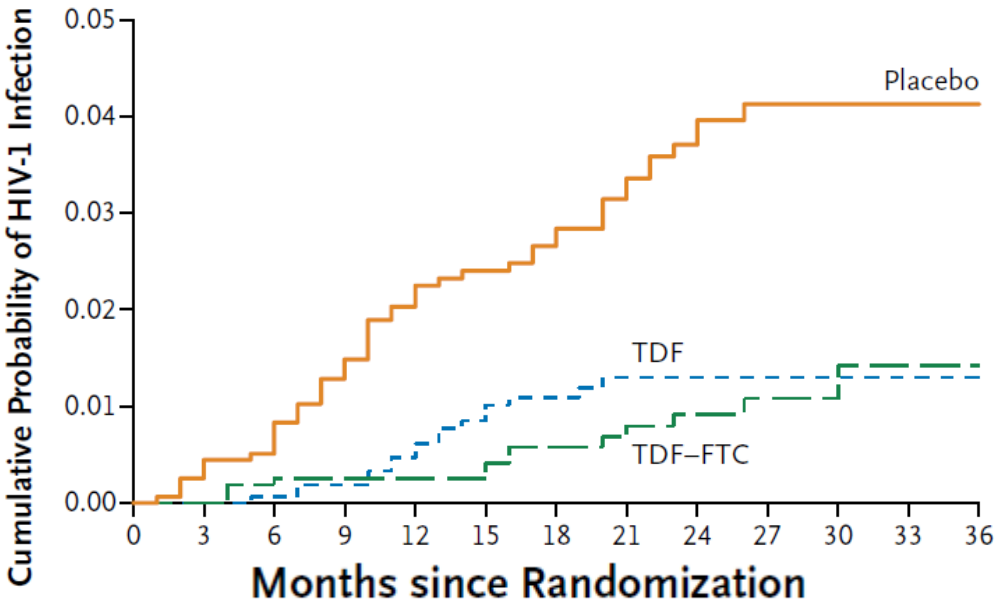
Grant R et al. NEJM 2010; 263(37):2587-99.

HIV prophylaxis in serodiscordant couples: Partners Trial

- Pre-Exposure Prophylaxis (PrEP)
  - 4578 serodiscordant (*heterosexual*)couples
  - 3 arms: HIV-negative partner treated with once daily tenofovir, tenofovir/emtricitabine, or placebo
  - 62% reduction in HIV transmission with tenofovir
  - **73% reduction** with tenofovir/emtricitabine

Baeten, J. et al (2012). NEJM: 367:399-410

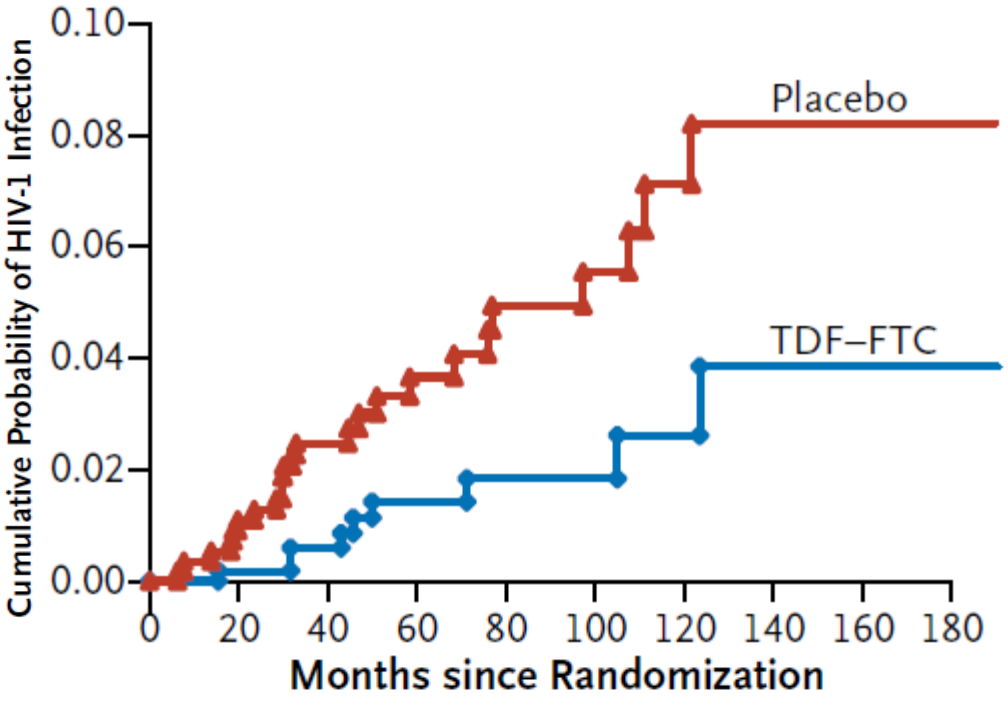
Oral PrEP
Partners PrEP



- TDF → 62% fewer infections
- FTC-TDF→73% fewer infections

- 4758 HIV sero-discordant heterosexual couples
  - Kenya & Uganda
  - TDF vs. FTC-TDF vs. placebo
  - Pregnancy rate was high (10.3 per 100 person –years) with no diff between groups

Oral PrEP
TDF2-CDC



- 63% reduction in the risk of HIV acquisition

- Randomized Control Trial
- 1200 men and women
  - Botswana
  - Daily oral
  - FTC-TDF vs. placebo

Thigpen, M.C., et al.. N Engl J Med, 2012. 367(5): p. 423-34.

Long term drug safety considerations

From the iPrEx study:

-- nausea and mild inadvertent weight loss (in about 1-2% of the study participants)

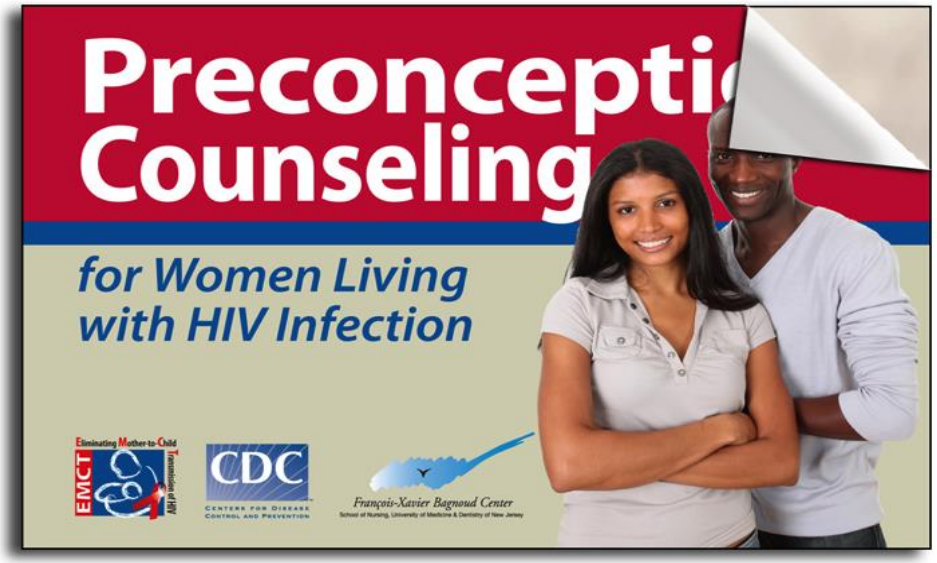
- 1% BMD loss at the total hip and femoral neck
- rate of bone fractures was no different

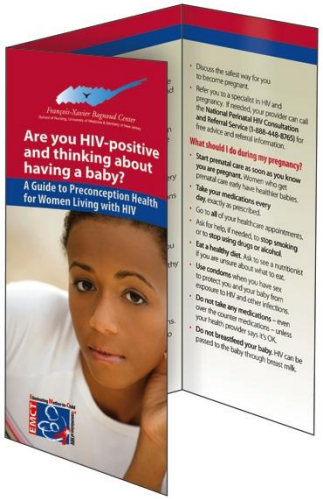
And , for the HIV uninfected female partner, once pregnant:

- HIV testing at first visit and in third trimester
- Rapid testing in labor if third trimester test was not done
- Consider continuing PrEP during pregnancy and breastfeeding if not consistently using condoms

Perinatal Guidelines. www.aidsinfo.nih.gov

Integrating preconception and HIV care





Guides to
- preconception counseling

-- for the HIV care provider

-- for clients

http://fxbcenter.org/downloads/Counseling_Tool_HIV_Preconception_Care.pdf

Practical references

- Preconception counseling toolkit: client and provider information including brief questionnaire for women with HIV about their pregnancy desires http://www.womenandhiv.org/francois-xavier
- **HIV/AIDS Management Warmline www.nccc.ucsf.edu (800) 933-3413** Monday – Friday, 9 a.m. – 8 p.m. EST
- http://www.hiveonline.org/
- Men with HIV and options for conception including surrogacy https://gayswithkids.com/**positively-dads**

Interactions of ARVs with Hormonal Contraceptives

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (CIII)
(page 1 of 3)

ARV Drug	Effect on Contraceptive Drug Levels	Dosing Recommendation/ Clinical Comment for Combined Hormonal Methods and Progestin-Only Pills	Dosing Recommendation/ Clinical Comment for DMPA[a]	Dosing Recommendation/ Clinical Comment for Etonogestrel Implants
NNRTIs				
EFV	Oral Ethinyl Estradiol/ Norgestimate: • No effect on ethinyl estradiol concentrations • ↓ active metabolites of norgestimate (levonorgestrel AUC ↓ 83%; norelgestromin AUC ↓ 64%) Implant: • ↓ etonogestrel Levonorgestrel (Emergency contraception) AUC ↓ 58%	Use alternative or additional contraceptive method.	No additional contraceptive protection is needed.	Use alternative or additional contraceptive method.

Case #1

- 29 yo G1P1011 presents for preconception counseling. Her partner was just diagnosed with HIV last week and they had been planning to have another child.

Case #1

- 29 yo G1P1011 presents for preconception counseling. Her partner was just diagnosed with HIV last week and they had been planning to have another child.
  - Have you been tested for HIV?

Case #1

- 29 yo G1P1011 presents for preconception counseling. Her partner was just diagnosed with HIV last week and they had been planning to have another child.
  - Have you been tested for HIV?
  - Is your partner on cART?

Case #1

- 29 yo G1P1011 presents for preconception counseling. Her partner was just diagnosed with HIV last week and they had been planning to have another child.
  - Have you been tested for HIV?
  - Is your partner on cART?
  - Has your partner had semen analysis?

Antepartum Care for Women with HIV

Antepartum Care

- Goal of cART is to maintain a viral load below the limit of detection throughout pregnancy
- May start cART before genotype result returns and adjust accordingly after genotype available
- In labor: continue oral cART and give IV AZT if VL>1000

Teratogenicity

- Lack of clear association between first-trimester exposure to any ARV drug and increased risk of birth defects
- The clinical significance of lower bone mineral density in newborns exposed to tenofovir is unknown

Combination antiretroviral therapy (cART)

- **cART naïve:**
  - Initiate cART as soon as HIV is diagnosed/earlier viral suppression is associated with lower risk of transmission.
  - Consider RAL if high VL late in pregnancy (expect 1-log decrease per week)
- **Monitoring in pregnancy:**
  - Check VL 2-4 weeks after initiating rx, monthly until undetectable, every 3 months, and at 34-36 weeks to inform decision regarding mode of delivery *and optimal management of newborn*

Antepartum Care

Lack of viral suppression

- Resistance vs. adherence
- Consider adding raltegravir
- Consider directly observed therapy
- Scheduled Cesarean if VL>1000 at 38 weeks

Intrapartum Care for Women with HIV

Intrapartum Care

- Epidural is safe regardless of cART regimen

International Journal of Obstetric Anesthesia (2014) 23, 45–51
0959-289X/$ - see front matter
http://dx.doi.org/10.1016/j.ijoa.2013.08.011

CrossMark

ELSEVIER
www.obstetanesthesia.com

ORIGINAL ARTICLE

Effect of ritonavir-induced cytochrome P450 3A4 inhibition on plasma fentanyl concentrations during patient-controlled epidural labor analgesia: a pharmacokinetic simulation

C.R. Cambic, M.J. Avram, D.K. Gupta, C.A. Wong
Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Intrapartum Care

- Ritonavir inhibits CYP450 and decreases elimination of fentanyl
- Recent pharmacokinetic simulation study suggest this inhibition is unlikely to produce plasma fentanyl concentrations at levels that would cause respiratory depression

Intrapartum

- IV zidovudine should be given intrapartum to women with a **VL >1000 copies/mL**
- Scheduled cesarean delivery is recommended at 38 weeks for women who fail to achieve virological suppression **(VL > 1000 copies/mL)**
- Scheduled cesarean delivery performed solely for prevention of HIV transmission in women receiving cART and with HIV RNA <1000 copies/mL is not routinely recommended

Intrapartum

- Insufficient evidence to determine whether cesarean delivery after rupture of membranes or onset of labor reduces risk of transmission

- Providers may contact the **National Perinatal HIV Hotline** (1-888-448-8765), which provides free clinical consultation on perinatal HIV care

Postpartum Care for Women with HIV

Postpartum

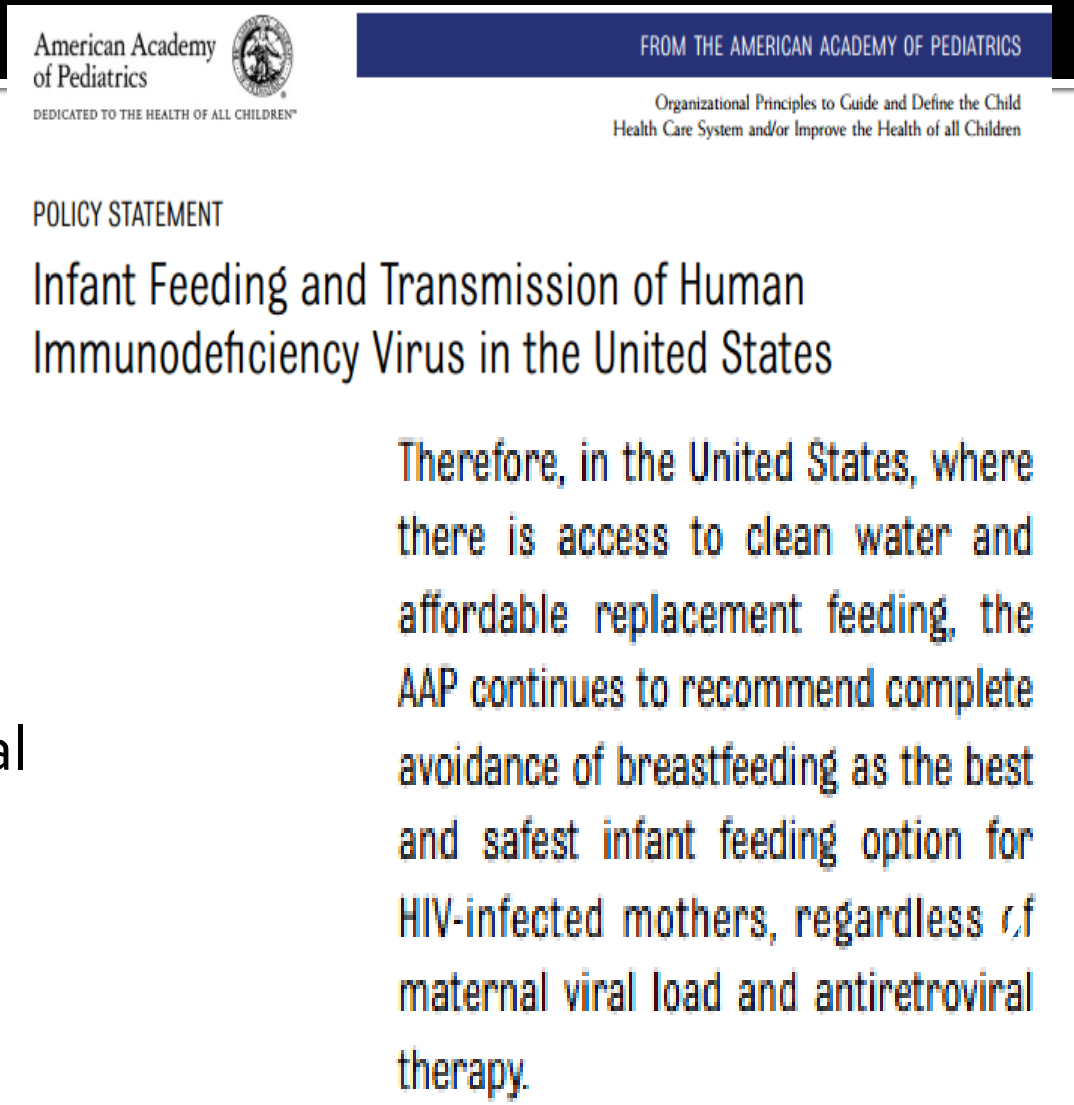
- Decisions regarding cART after delivery should be made between the patient and her HIV provider, before delivery
- Contraceptive counseling is a critical step
- *The postpartum period creates challenges to antiviral adherence, therefore a plan for postpartum should be made prior to delivery and discharge*
  - Supportive services, transportation
  - Linkage to care
  - Appointments should be made prior to discharge

Postpartum

- **In discussing the avoidance of breastfeeding as the strong, standard recommendation for HIV-infected women in the United States, the Panel notes that women may face social, familial, and personal pressures to breastfeed despite this recommendation and that it is important to begin addressing possible barriers to formula feeding during the antenatal period.**

US Recommendations

- With current interventions MTCT of HIV <1%
- BF transmission rates with ART 1%-5%
- MTCT can occur despite undetectable maternal viral load



American Academy of Pediatrics
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Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

POLICY STATEMENT

Infant Feeding and Transmission of Human Immunodeficiency Virus in the United States

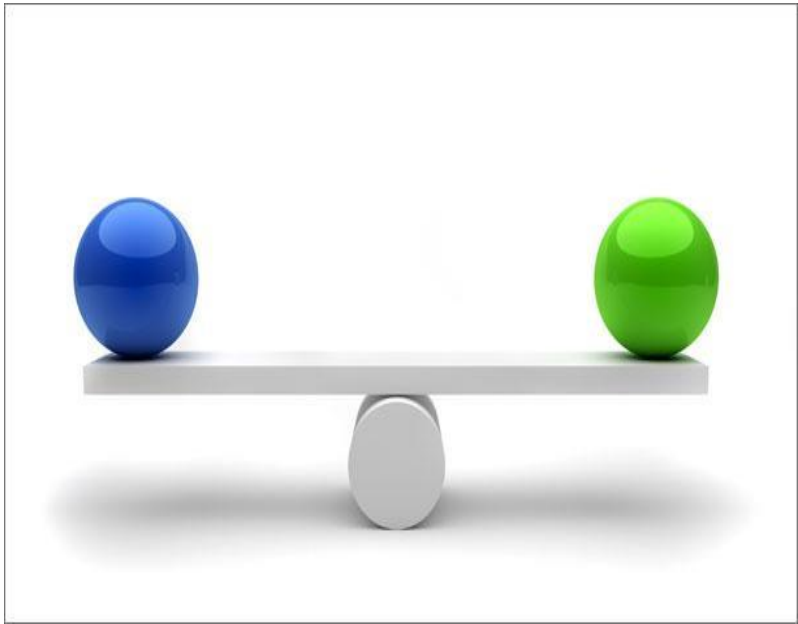
Therefore, in the United States, where there is access to clean water and affordable replacement feeding, the AAP continues to recommend complete avoidance of breastfeeding as the best and safest infant feeding option for HIV-infected mothers, regardless of maternal viral load and antiretroviral therapy.

WHO – Infant feeding in Resource Limited Settings

Exclusive breastfeeding for first 6 months of life followed by complementary foods and breastfeeding through 12 month of age

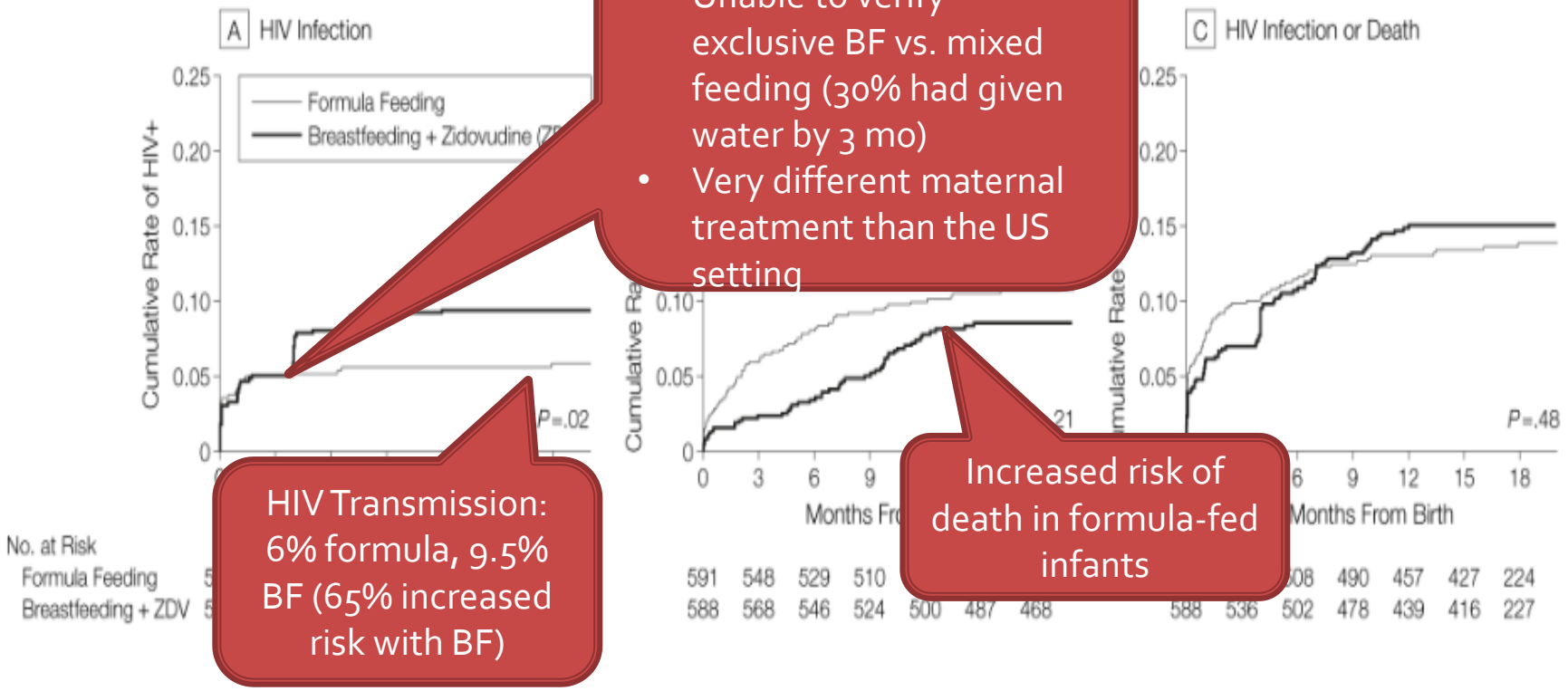
+

Postnatal infant prophylaxis or maternal antiretroviral treatment



Mashi Study (Botswana 2001-03)

- Infant: BF + 6 months ZDV vs. Formula + 1 mo ZDV
- No maternal trea



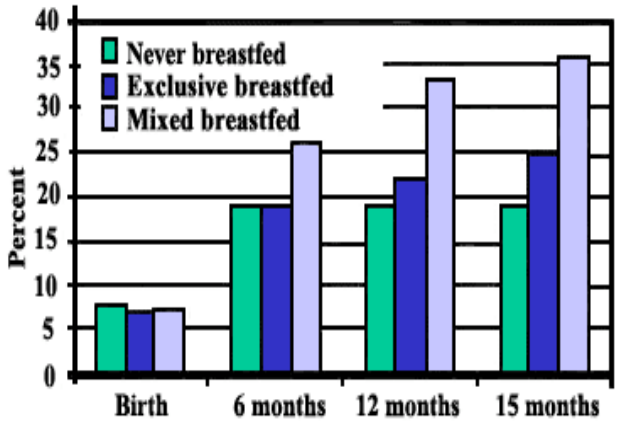
- Differences in transmission greater at >3 months of age
- Unable to verify exclusive BF vs. mixed feeding (30% had given water by 3 mo)
- Very different maternal treatment than the US setting

HIV Transmission: 6% formula, 9.5% BF (65% increased risk with BF)

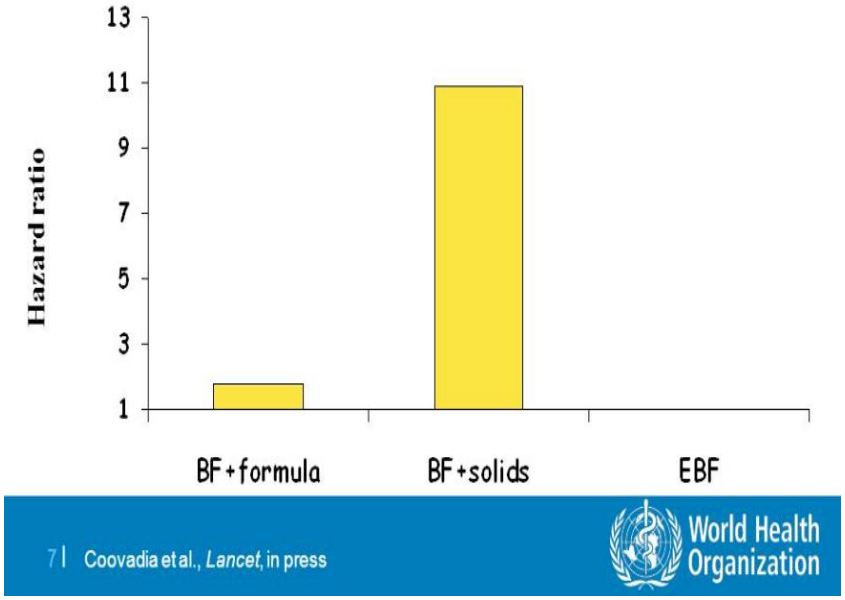
Increased risk of death in formula-fed infants

Thior I, et al. *JAMA.* 2006;296(7):794-805

Exclusive BF vs. Mixed Feeding

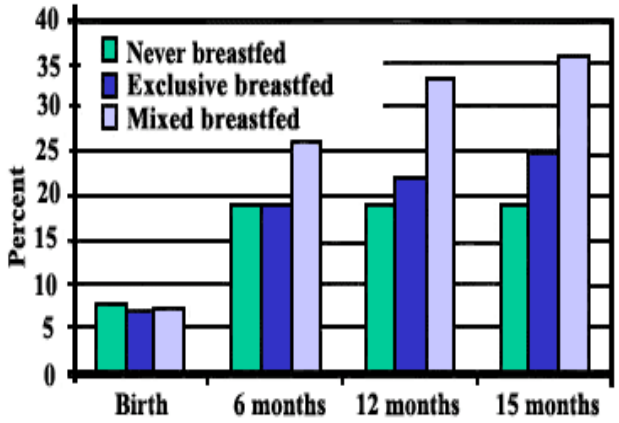


A. Coutsoudis, K. Pillay, L. Kuhn, E. Spooner, W.-Y. Tsai, H. M. Coovadia, *AIDS* **15**, 379 (2001)

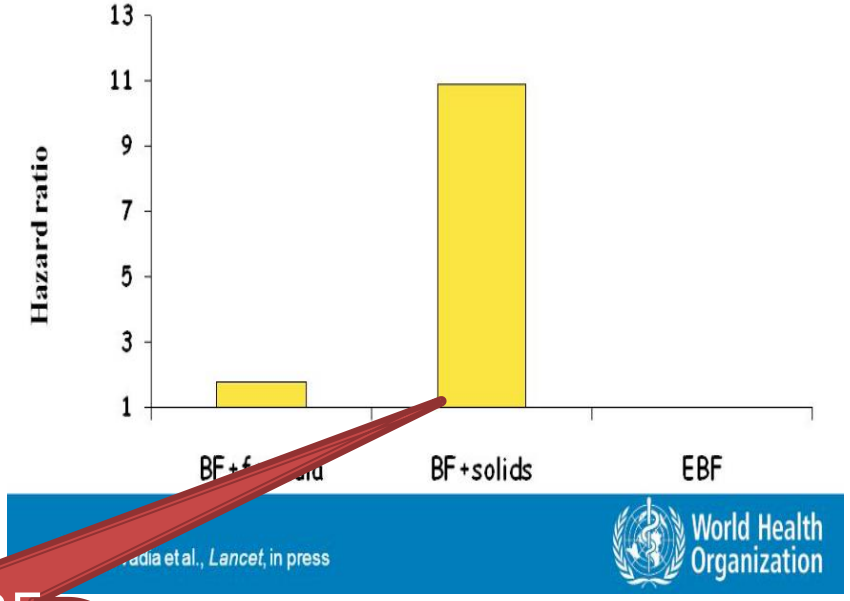


Coovadia, Hoosen M et al.
The Lancet , Vol 369:9567, 1107 – 1116 (2007)

Exclusive BF vs. Mixed Feeding



A. Coutsoudis, K. Pillay, L. Kuhn, E. Spooner, W.-Y. Tsai, H. M. Co[illegible]
AIDS **15**, 379 (2001)



Infants given BF + solids >10 times more likely to become HIV-infected

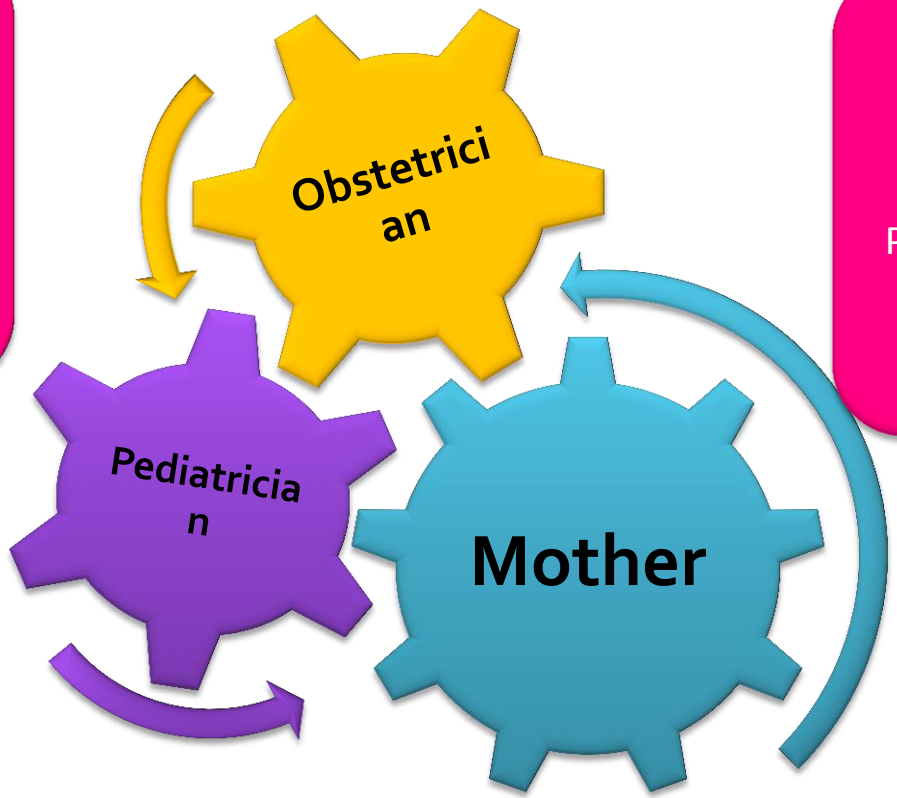
Coovadia, Hoosen M et al.
The Lancet , Vol 369:9567, 1107 – 1116 (2007)

Collaborative Harm Reduction Strategy

Ensures optimal maternal treatment

Prenatal referral to Pediatrician

Coordinates feeding with birth hospital



Understands risks

Virologic suppression

Prepares ahead for complications

Family support

Educates mother on risks/benefits

Guides nursery pediatricians

Addresses feeding/weaning issues

Infant testing

Infant prophylaxis

- **Standard:** 4-6 weeks of ZDV

- **High Risk:** (no antepartum ARVs +/- intrapartum) then ZDV x 6 weeks PLUS NVP at birth, 48 hours and 96 hours after second dose

Infant anti-retroviral prophylaxis

- Despite the paucity of available data, the use of combination ARV prophylaxis for infants in high risk situations is increasing.

- Canadian investigators have reported outcomes in 136 infants who received treatment-level dose of triple ARV prophylaxis within 72 hours of birth. 12/136 were infected and no major toxicities were identified

Pediatric Treatment Guidelines

- The risks associated with use of a three-drug ARV regimen in neonates as well as the potential benefits, including the possibility of prolonged remission in infected neonates, require further study before a general recommendation can be made
- Contact a **pediatric HIV expert for guidance and individual case assessment** of the risk/benefit ratio of treatment and for the latest information on neonatal drug doses
- Providers may contact a local pediatric HIV expert or **National Perinatal HIV Hotline** (1-888-448-8765), which provides free clinical consultation on perinatal HIV care

Case #2

- 23 yo G5P2112 presents to L&D without previous prenatal care, with the chief complaint of abdominal pain.

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  - HIV test in triage is positive
  - FHT is category 1 and toco shows contractions q 2min
  - Membranes are intact and her cervix is 2cm dilated

Case #2

- Start Zidovudine IV

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- Determine gestational age

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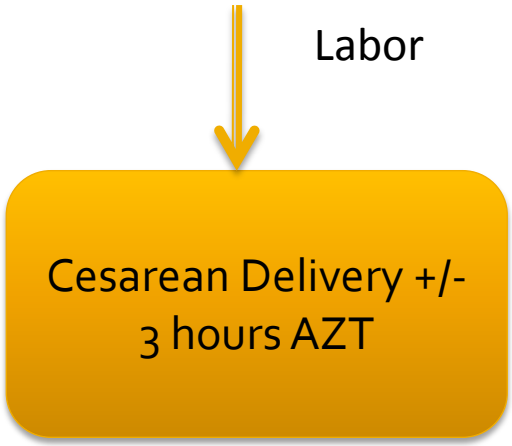

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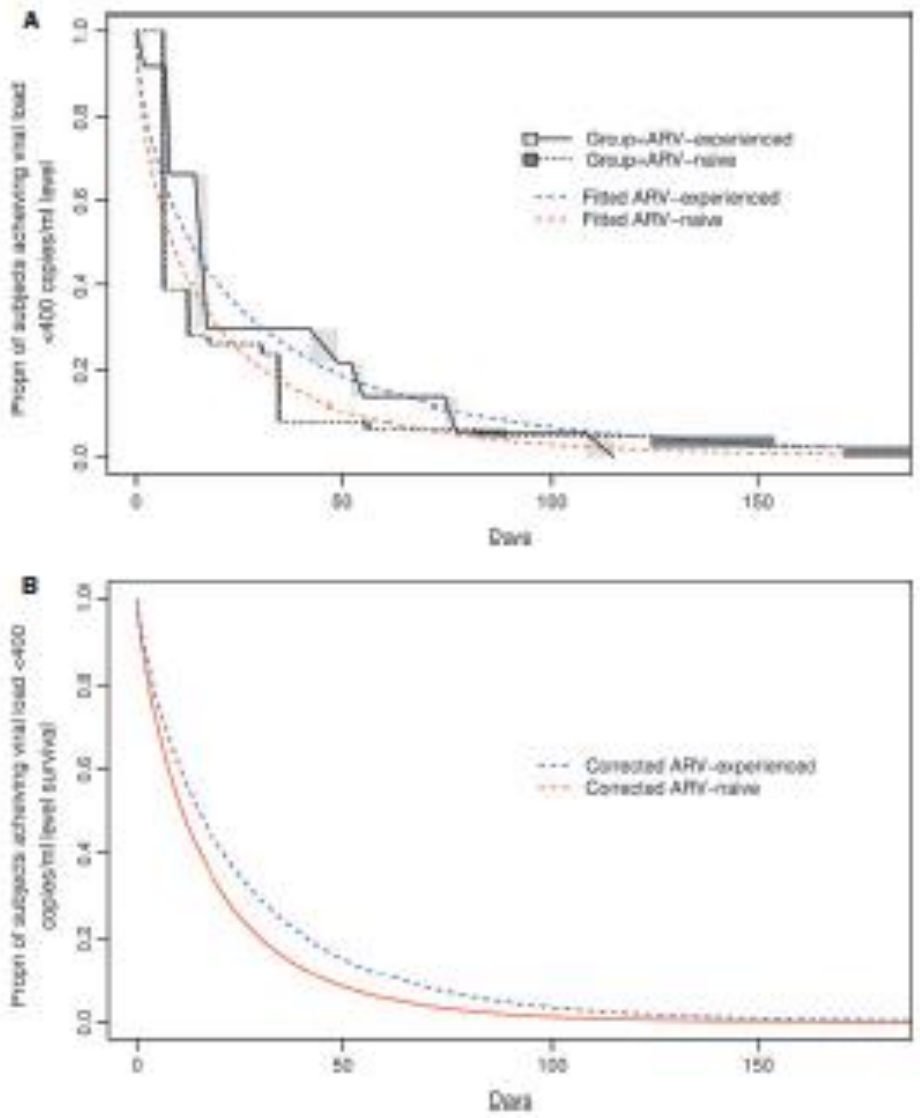


Figure 1. Time to HIV viral load <400 copies/ml for ARV-naive versus ARV-experienced pregnant women on HAART. A, Unadjusted; B, adjusted for all covariates in the final multiple predictor model.

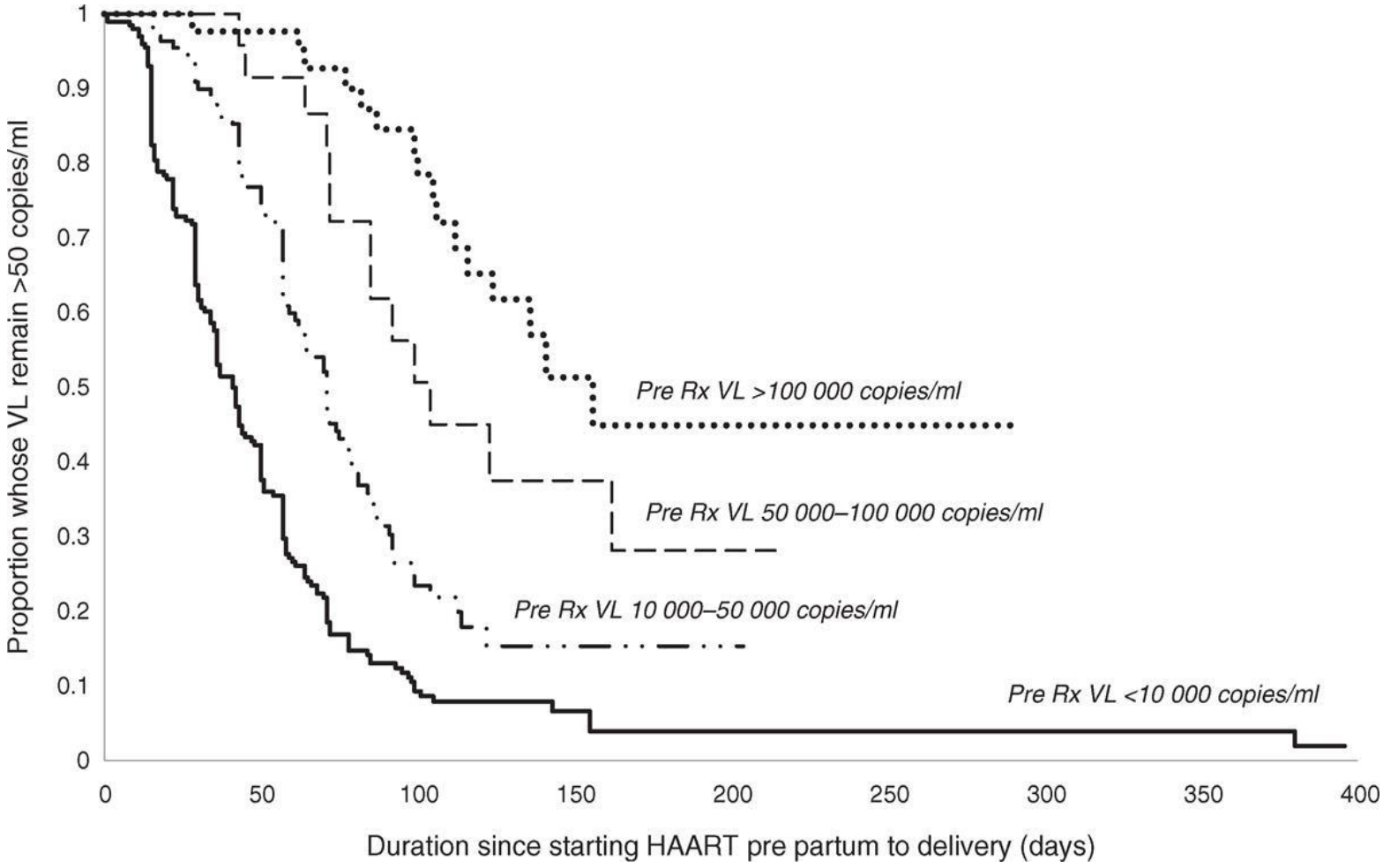
Aziz N et al.. BJOG 2013 Nov;120(12):1534-47

More on time to viral suppression

- *Read et al (2012)*: It depends on pretreatment viral load
  - 77% had a VL <50 by delivery
  - If baseline VL <10 000 copies/ml, most women achieved VL <50 by delivery if they had started ARVs by 26 weeks gestation.
  - If VL > 10 000 copies/ml, deferring HAART past 20.4 weeks reduced the probability of reaching less than 50 copies/ml by delivery (P<0.011)
  - If initial VL >100,000, chance of reaching VL <50 by delivery was 37%.

Read et al. AIDS 2012, 26:1095–1103

Viral suppression as a function of initial VL



Read et al. AIDS 2012, 26:1095–1103

What if time is short?

- Consider adding raltegravir (integrase inhibitor) to standard regimen
- Estimate is 1.12 log VL decline per week
- Westling et al (Sweden):
  - Mean VL decline per week was 1.12 log (range, 0.94–1.22), which is estimated to occur (based on literature) after 1–2 months with standard ART.

Westling et al. AIDS Patient Care STDS. 2012;26(12):714-7.

More on raltegravir

- Nobrega:
  - 14 cases (Brazil): raltegravir added to at least 2 other ARVs
  - Median gestational age 36 weeks (range 34-38)
  - Median maternal plasma HIV-1 RNA viral load was 35,364 copies/ml (range 636-391,535)
- At delivery, the median gestational age was 38 weeks (range 37-40). The median exposure time to RGV was 17 days (range 7-32), with a mean maternal VL decay of 2.6 log.
- At delivery,
  - 7 women had undetectable (<50 copies/ml) VL
  - 4 had between 64 and 457 copies/ml
  - 3 VL was not available

Nobrega et al.AIDS Res Hum Retroviruses. 2013 Nov;29(11):1451-4.

21 Integrase strand transfer inhibitors given to HIV-infected women late in pregnancy decrease HIV viral load more quickly than other antiretroviral therapy (ART)

Lisa Rahangdale[1], Jordan Cates[1], JoNell Potter[2], Martina L. Badell[3], Dominika Seidman[4], Emily S. Miller[5], Jenell S. Coleman[6], Gweneth B. Lazenby[7], Judy Levison[8], William R. Short[9], Sigal Yawetz[10], Andrea Ciaranello[11], Elizabeth Livingston[12], Lunthita Duthely[2], Bassam H. Rimawi[13], Jean R. Anderson[6], Elizabeth Stringer[1]

[1]University of North Carolina, Chapel Hill, NC, [2]University of Miami, Miami, FL, [3]Emory University, Atlanta, GA, [4]University of California San Francisco, San Francisco, CA, [5]Northwestern University Feinberg School of Medicine, Chicago, IL, [6]Johns Hopkins University, Baltimore, MD, [7]Medical University of South Carolina, Charleston, SC, [8]Baylor College of Medicine, Houston, TX, [9]University of Pennsylvania, Philadelphia, PA, [10]Brigham & Women's Hospital, Boston, NC, [11]Massachusetts General Hospital, Boston, MA, [12]Duke University, Durham, NC, [13]Emory University, Atlanta, GA

OBJECTIVE: Minimizing time to HIV viral suppression is critical in pregnancy. Integrase strand transfer inhibitors (INSTIs), like raltegravir, are known to rapidly suppress plasma HIV RNA in nonpregnant adults. We describe time to clinically relevant reduction in HIV RNA in pregnant women using INSTI-containing and non-INSTI-containing ART options.

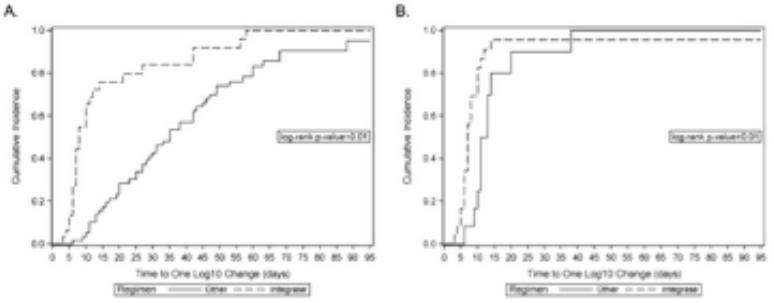
STUDY DESIGN: We conducted a retrospective cohort study of pregnant HIV-infected women in the U.S. from 2009 to 2015. We included women who initiated ART, intensified their regimen or switched to a new regimen due to detectable viremia (HIV RNA > 40c/mL) at > 20 weeks gestation. Among women with a baseline HIV RNA permitting 1-log reduction, we estimated time to 1-log RNA reduction using the Kaplan-Meier estimator comparing women starting/adding an INSTI in their regimen versus other ART. To compare groups with similar follow-up time, we also conducted a subgroup analysis limited to women with <14 days between baseline and follow-up RNA data.

RESULTS: Maternal characteristics of 101 women from 11 U.S. clinics are shown in Table 1. 76/101 (75%) women were not taking ART at baseline. 39/101 (39%) women started/added an INSTI in their ART regimen. Among 90 women with a baseline HIV RNA permitting 1-log reduction, the median time to 1-log RNA reduction was 8 [IQR: 6, 14] days in the INSTI group versus 35 [IQR: 20, 53] days (p<0.001) in the non-INSTI ART group. In a subgroup of 39 women with first and last RNA measurements <14 days apart, median time to 1-log reduction was 7 [IQR: 6, 10] days in the INSTI group versus 11 [IQR: 10, 14] days (p=0.01) in the non-INSTI group. (Figure 1)

TABLE 1. Characteristics of 101 HIV-infected pregnant women from 11 US clinics post 20 weeks gestation at time of starting/including a new ART regimen, 2009-2015.
Categorical variables are expressed as N (%), and continuous variables are expressed as median (IQR).
*** Missing data, N=1**

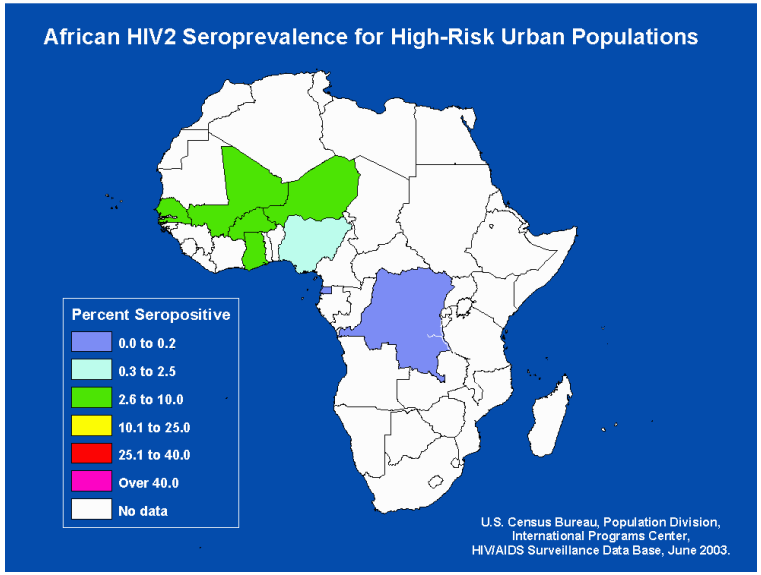
	Integrase (N=39)	Other ART (N=62)	p-value
Race & Ethnicity			
White, non-Hispanic	5 (13)	11 (18)	0.47
White, Hispanic	4 (11)	6 (10)	
Black	28 (72)	45 (73)	
Other	2 (5)	0 (0)	
Parity*			
0	17 (44)	21 (34)	0.63
≥1	22 (56)	40 (65)	
Maternal Age (years)	29 (23, 34)	26 (23, 31)	0.33
Median Gestational Age (weeks)	33.6 (29.9-36.1)	27.5 (25.4-30.7)	<0.01
Body Mass Index (kg/m^2)	28.2 (24.4-35.0)	30.5 (26.6-35.3)	0.33
No ART at baseline	20 (51)	56 (90)	<0.01
Initial HIV RNA (log_{10})	4.3 (3.5-4.9)	4.1 (3.3-4.6)	0.17
(copies/mL)	21,278 (3,370-71,660)	13,015 (2,050-35,570)	
AIDS Diagnosis	23 (60)	20 (32)	<0.01

FIGURE 1. Cumulative incidence of time to 1-log_{10} change among A) 90 HIV-infected pregnant women from 11 U.S. clinics and B) a subset of 39 of the 90 HIV-infected pregnant women with baseline and follow up HIV RNA measurement of less than 14 days, stratified by drug regimen intervention.

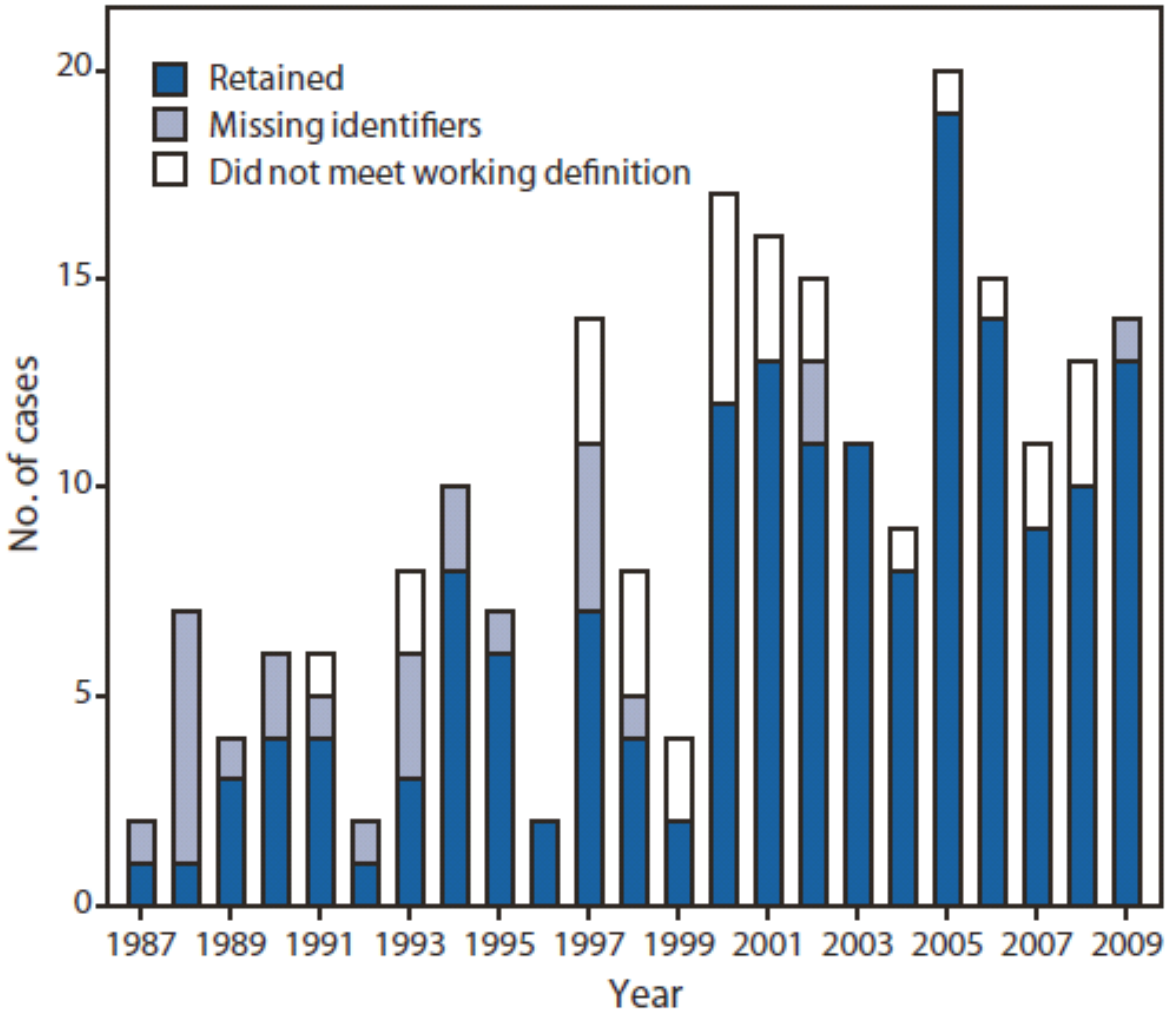


HIV 2 infection

- Should be considered in women who are from (or have partners from) countries where HIV2 is endemic AND who have positive results on an HIV1/HIV2 antibody or HIV1/HIV2 immunoassay



Number of reported cases of HIV-2 infection and year of diagnosis --- United States, 1987--2009



http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6029a3.htm#fig

HIV 2 infection and pregnancy

- Women who require treatment for their own health because they have significant clinical disease or CD4 <500 cells/nm^3 should be treated with 2 NRTIs and a boosted protease inhibitor

- **Preferred regimens:**
  - Lopinavir/ritonavir *plus*
    - zidovudine/lamivudine
    - or
    - abacavir/lamivudine
    - or
    - tenofovir/emtricitabine

HIV 2 infection

- Optimal treatment regimens for women with CD4>500 and no significant disease are unknown

- **Expert opinion:**
  - A boosted PI based regimen with 2 NRTIs

    OR

  - Zidovudine prophylaxis alone during pregnancy and intrapartum

4th generation HIV-1/2 immunoassay

(+)

(-)

Negative for HIV-1 and HIV-2 antibodies and p24 Ag

HIV-1/HIV-2 antibody differentiation immunoassay

HIV-1 (+)

HIV-2 (-)

HIV-1 antibodies detected

HIV-1 (-)

HIV-2 (+)

HIV-2 antibodies detected

HIV-1 (+)

HIV-2 (+)

HIV antibodies detected

HIV-1 (-) or indeterminate

HIV-2 (-)

NAT

NAT (+)

Acute HIV-1 infection

NAT (-)

Negative for HIV-1

Perinatally-infected pregnant women

- *A significant number of pregnancies are unintended in this population*
- *Components of healthcare do not differ —however, unique issues to be aware of include*:
  - Adherence is often a problem
  - Overall younger (adolescent)
  - Higher chances of drug resistance due to prolonged exposures

Perinatally-infected Pregnant Women

- *May have increased psychosocial challenges*
  - Depression
  - Loss of parents
  - Presence of long term chronic illness
- *Addressing mental health is critical*

SMFM HIV Checklists

Preconception and Antepartum Checklist
for Management of Pregnant Women with HIV

This checklist is a general guide to care for an HIV positive prenat
haven't treated a HIV positive pregnant patient in the past year, i
recommended you consult with a physician experienced in care fo
women

Pre-Conception

- Discuss methods of safe conception
- Ensure an undetectable HIV viral load prior to attempting
- Ensure combined antiretroviral therapy (cART) medicati
  use during pregnancy
- Discuss disclosure of patient's HIV status to her partner a
  if the partner is HIV negative
- Offer partner(s) testing (is/are her partner(s) aware of he
  positive? Is their viral load undetectable?)
- Discuss PreP
- Ensure vaccines are up to date (pneumococcal, hepatitis
  influenza, MMR, chickenpox, HPV, tDAP, seasonal influen

Antepartum

First visit:

- If new diagnosis:
  - Determine:

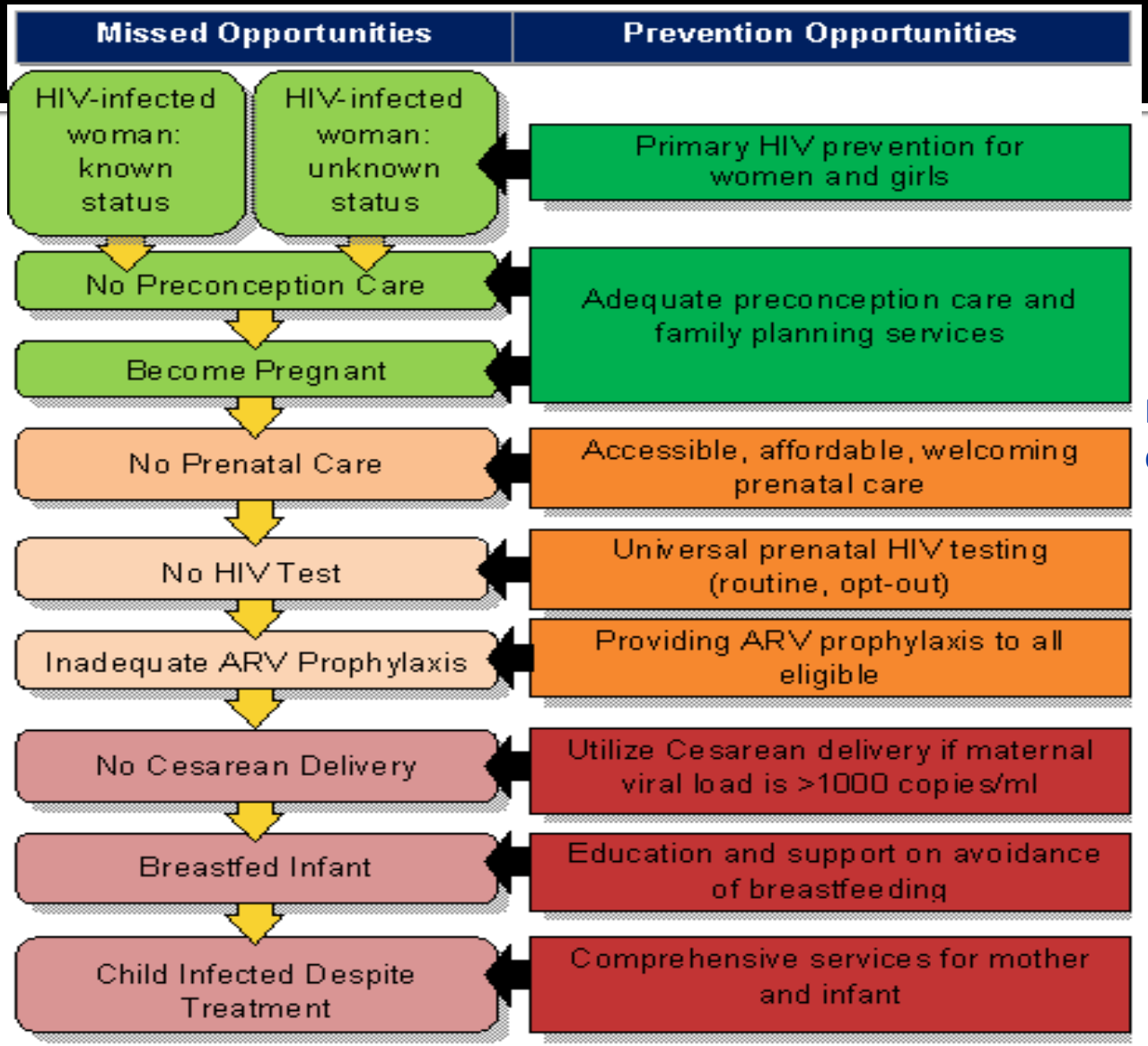
Intrapartum and Postpartum Checklist for Management of Women with HIV

This checklist is a general guide to care for an HIV positive patient. If you haven't treated a HIV positive pregnant patient in the past year, it is strongly recommended you consult with a physician experienced in care for HIV positive pregnant women

Intrapartum

- All patients
  - Combined antiretroviral therapy (cART) should be continued in labor
  - Notify pediatric team and confirm plan for pediatric prophylaxis, consideration of expanded neonatal therapy or treatment after delivery
  - No fetal scalp electrode (relative contraindication)
  - Avoidance of early rupture of membranes, unless viral load consistently <50 copies/mL
  - Operative vaginal delivery should be avoided in most circumstances
  - In case of PPH:
    - ❑ Preferred 1st line uterotonic agent is Oxytocin
    - ❑ Preferred 2nd line uterotonic agent is Prostaglandin (such as carboprost or misoprostil)
    - ❑ Methergine is the least preferred option due to potential interactions with protease inhibitors and other antiretroviral agents
- If viral load greater than or equal to 1000 copies/mL
  - Begin zidovudine 2g/kg load over first hour and 1g/kg hour infusion
  - If patient is not in labor and has intact membranes, perform cesarean delivery 3 hours after zidovudine infusion has begun
  - If patient presents in labor or with ruptured membranes, management should be individualized based on the patient's labor course, parity, and likely progression in labor. (Resources available for consultation include the national perinatal HIV hotline: 1-888-448-8765[2])
- If viral load is <1000 copies/mL
  - If the patient has been adherent to cART and consistently had viral load

Perinatal HIV Prevention Cascade



Pre-exposure prophylaxis

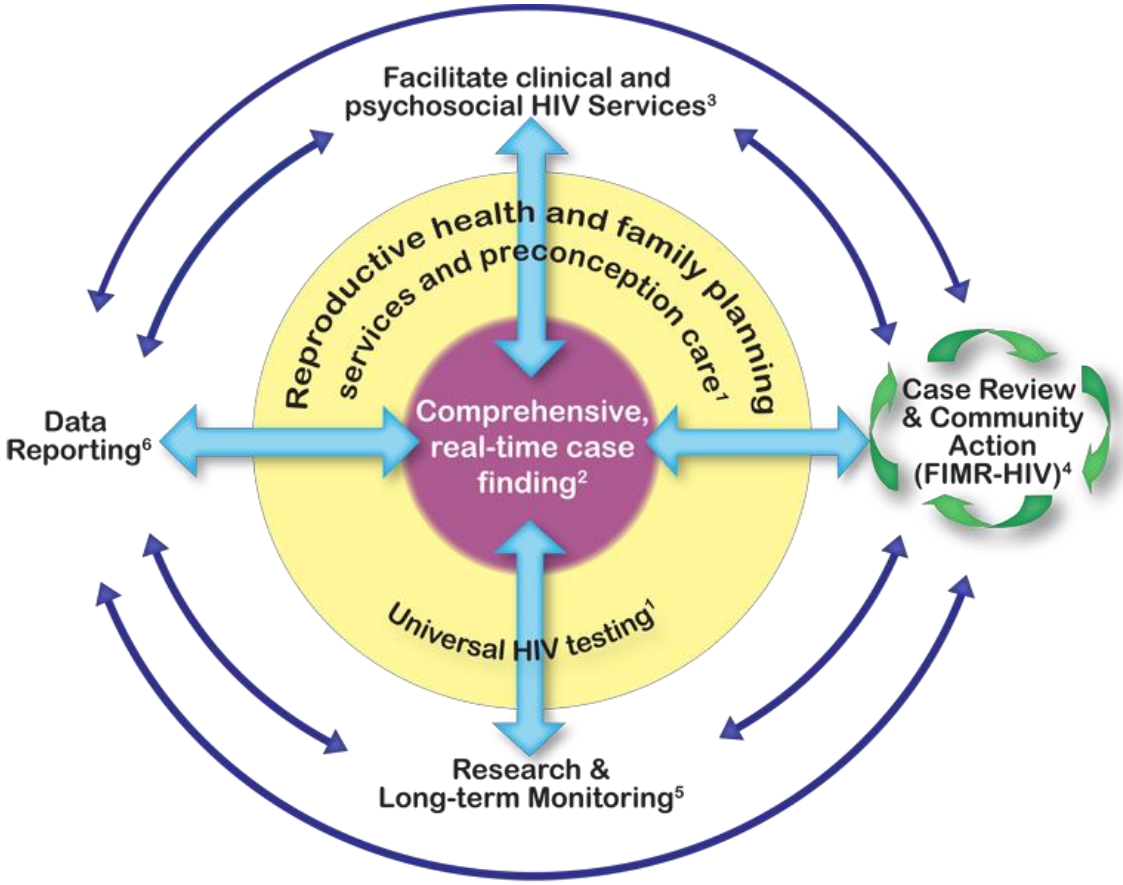
Treatment as Prevention (TasP)

Proposed new diagnostic algorithm

Acute HIV infection & repeat testing

Potential curative therapy for infants

Framework to Eliminate Mother-to-Child HIV Transmission in the United States



Nesheim SR, Taylor A, Lampe MA, et al. Pediatrics. 2012 Oct;130(4):738-44.

http://www.fimrhiv.org

Thank you!

Questions?