



Care of Pregnant People with HIV: Preventing Perinatal Transmission

Jennifer Janelle, MD
Clinical Associate Professor
University of Florida, Gainesville

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Objectives

At the completion of this presentation, participants should be able to

1. Describe testing for HIV in people who are pregnant
2. Recognize risks for perinatal HIV transmission
3. Develop patient centered, team based, treatment and delivery plans to prevent perinatal HIV transmission

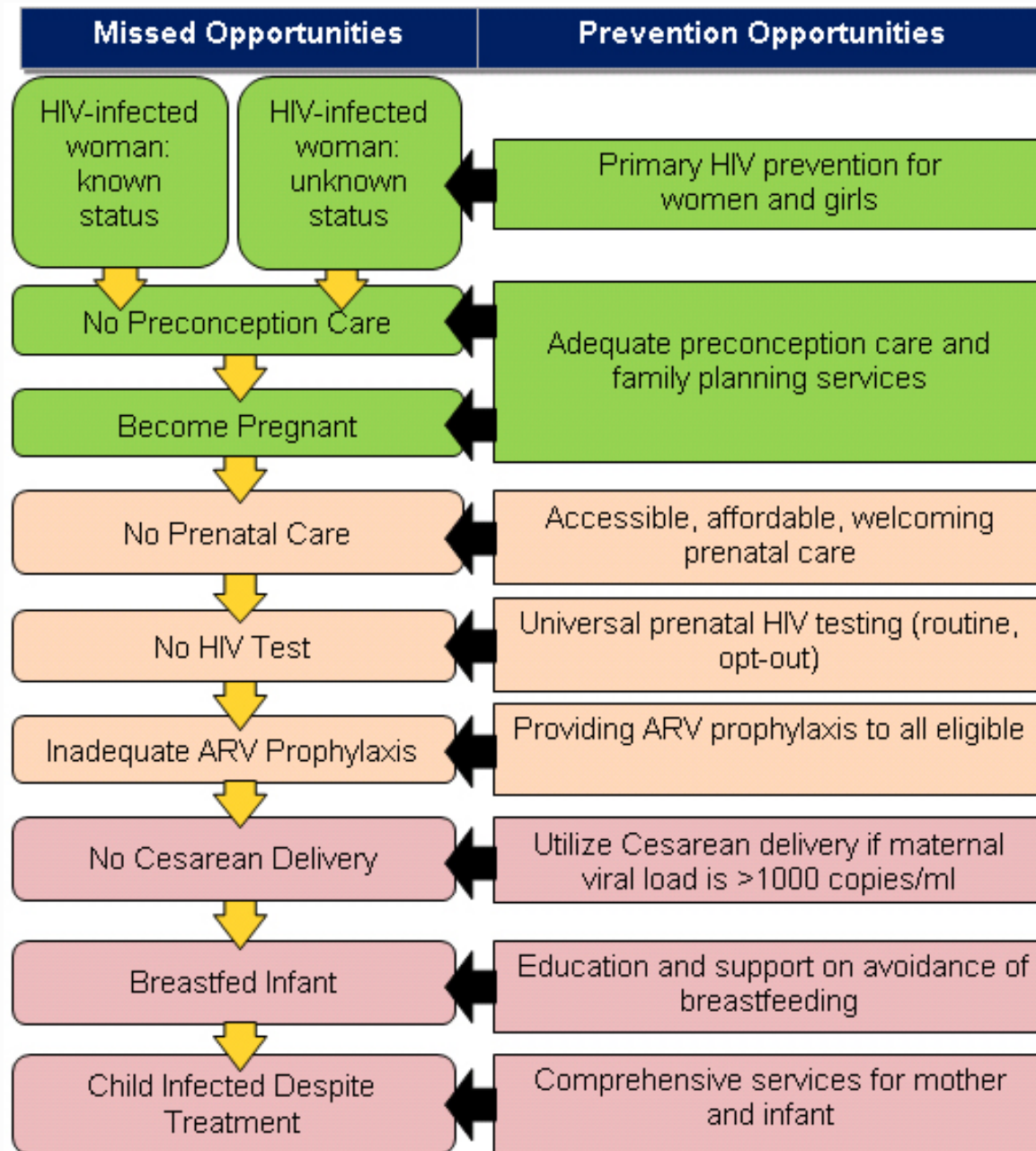


Case

- Brandi is a 32 year old woman who presents in her 4th pregnancy with rupture of membranes at an estimated 24 weeks' gestation
- No prenatal care
- Testing done at admission
 - Positive for gonorrhea, but negative for chlamydia and syphilis
- 4th generation Ag/Ab HIV test had an indeterminate result
 - Ag/Ab test positive
 - Ab differentiation was negative
 - HIV viral load pending

Case

- Vaginal delivery 6 days after presented to hospital
 - No intrapartum AZT administered
- Baby fed formula and mother's breast milk was expressed and stored until the HIV viral load resulted
- Viral load 14 million copies/mL
 - Resulted 12 days after test drawn
- Baby acquired HIV infection



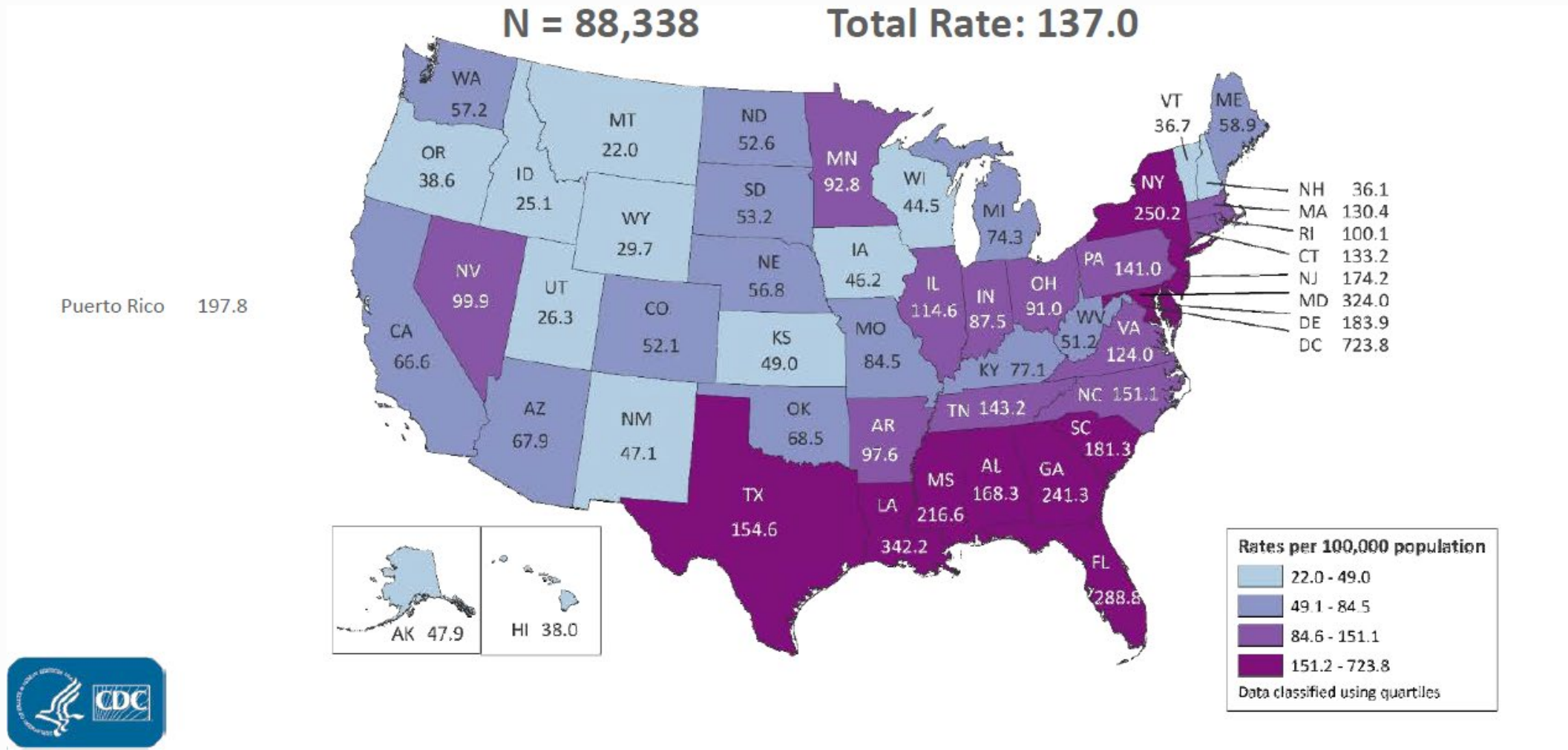
Missed Opportunities for Preventing Perinatal Transmission of HIV: Florida 2007 – 2014

- Retrospective review of de-identified data from Florida's Enhanced HIV/AIDS Reporting System (eHARS)
- 70/4337 (1.6%) of exposed babies were perinatally infected
- Among the infected maternal-infant pairs **over 1/3 of mothers used street drugs or acquired an STD during pregnancy**

Missed Opportunities for Preventing Perinatal Transmission of HIV: Florida 2007 – 2014

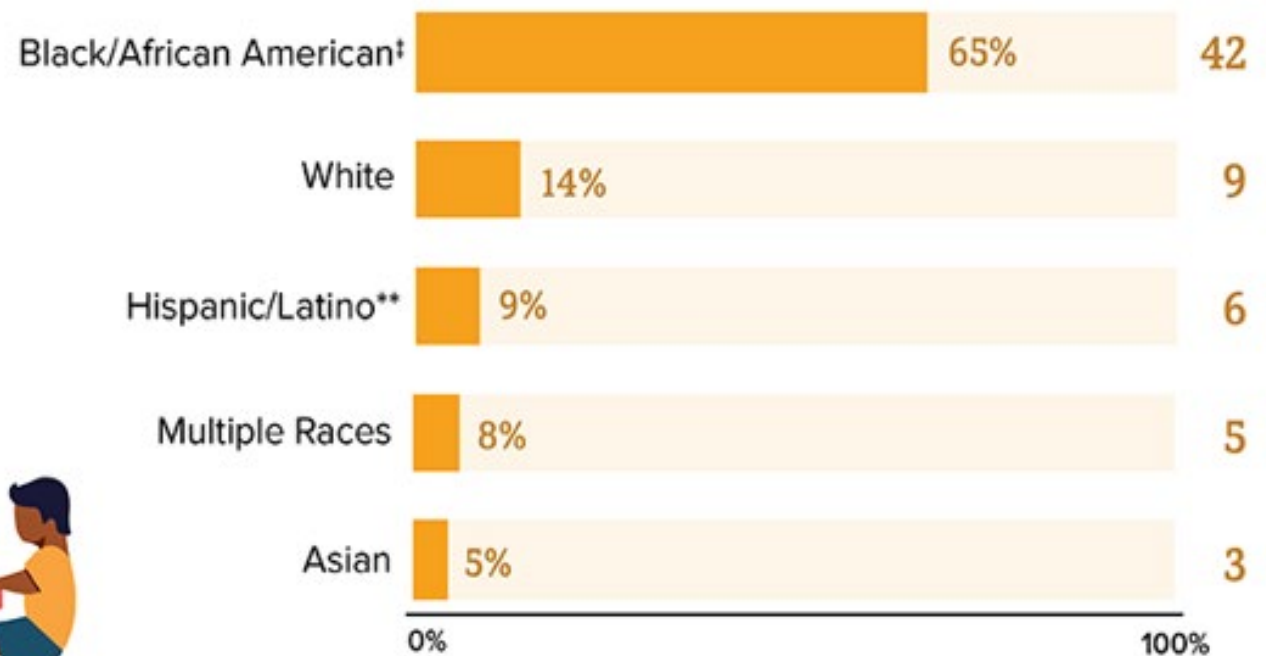
- Relative Risk of Perinatal Transmission
 - **Maternal HIV Diagnosis during labor and delivery**
 - RR = 5.66, (95% CI 2.31-13.91) (compared with prenatal diagnosis)
 - **Maternal HIV Diagnosis after birth**
 - RR = 26.50, (95% CI 15.44-45.49)
- Factors associated with perinatal transmission of HIV
 - **Late diagnosis**
 - **Maternal acute HIV infection**
 - **Poor or late prenatal care**

Rates of Females Aged 15-44 Years Living with Diagnosed HIV Infection by Area of Residence, 2017



Diagnoses of Perinatal HIV Infections in the US and Dependent Areas by Race/Ethnicity, 2018

Most perinatal HIV diagnoses were among Black/African American children.



25% Risk of Perinatal HIV Transmission Without Intervention

An **HIV+ pregnant woman** can transmit HIV to her baby **3 WAYS**:

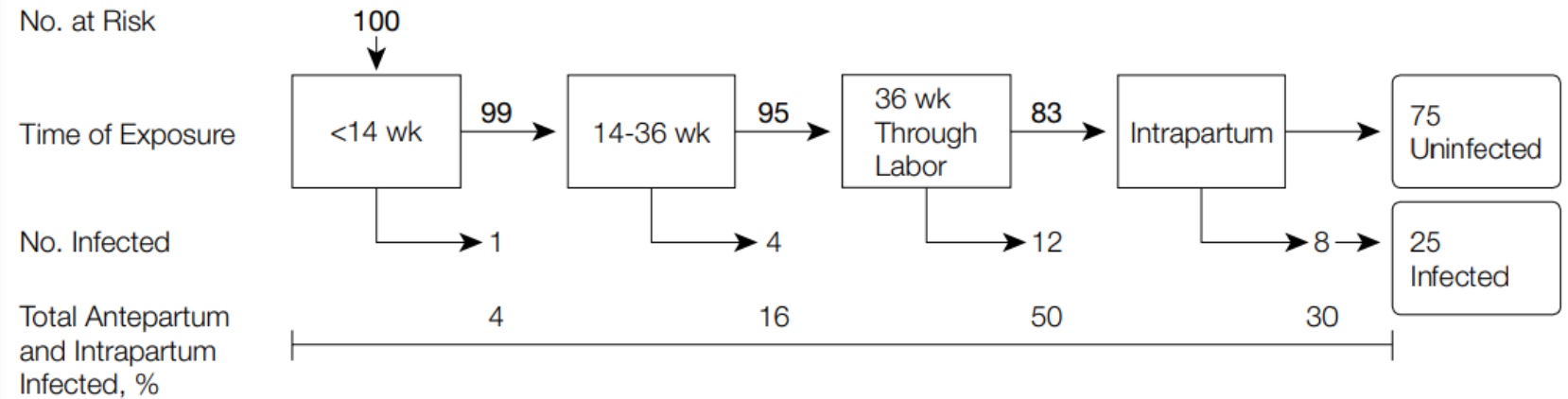
+ During pregnancy

+ During vaginal childbirth

+ Through breastfeeding



Figure. Estimation of Timing of Perinatal HIV Transmission Rates



Estimated rates are for different times of gestation and delivery in non-breastfeeding populations. Estimates are based on a hypothetical cohort of 100 children born to HIV-infected women without any interventions. HIV indicates human immunodeficiency virus. Boldface numbers indicate number of children at risk for infection.

Kourtis AT et al. JAMA. 2001;285:709-12.

HIV in Pregnancy

- Less than 1% risk if
 - Suppressive antiretroviral therapy (ART) throughout pregnancy
 - Postnatal infant antiretroviral prophylaxis
 - C-section & zidovudine (AZT) if indicated
 - Avoidance of breastfeeding

Viral Load During Pregnancy is the Strongest Predictive Factor for Transmission

- WITS – published in 1999
- 552 mother-infant pairs at 8 US sites from 1990-1995
- Mothers evaluated 3 times during pregnancy and at delivery

TABLE 2. RATES OF PERINATAL TRANSMISSION OF HIV-1 ACCORDING TO MATERNAL PLASMA HIV-1 RNA LEVELS AND THE USE OF ZIDOVUDINE THERAPY DURING PREGNANCY.*

ZIDOVUDINE THERAPY	MATERNAL PLASMA HIV-1 RNA COPIES/ml					P VALUE†
	<1000	1000-10,000	>10,000-50,000	>50,000-100,000	>100,000	
	no. of infants infected/total no. (%)					
Yes	0/22	10/83 (12.0)	13/75 (17.3)	5/16 (31.2)	7/34 (20.6)	0.02
No	0/35	22/110 (20.0)	26/108 (24.1)	12/38 (31.6)	19/30 (63.3)	<0.001
Total	0/57	32/193 (16.6)	39/183 (21.3)	17/54 (30.9)	26/64 (40.6)	<0.001

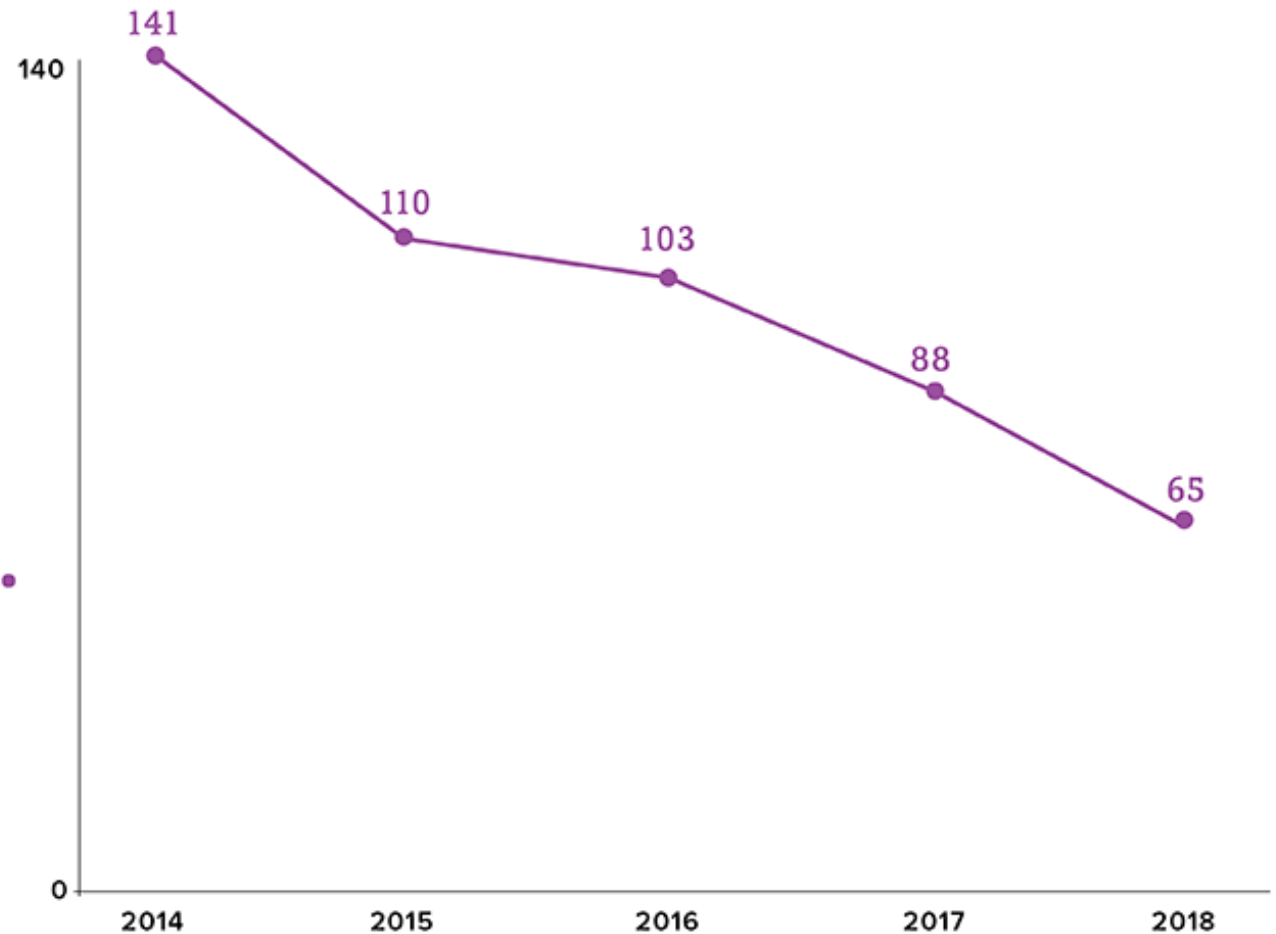
*Values are the geometric means of measurements obtained throughout pregnancy. For each woman, levels were measured up to three times during pregnancy and once at delivery. The treatment status of one woman was not known.

†The P values were calculated with use of the Mantel extension test for trend.

Diagnoses of Perinatal HIV Infections in the US and Dependent Areas, 2014-2018

HIV diagnoses declined
54% among children
overall from 2014 to 2018.

CDC goal: less than 1 per
100,000 live births and < 1%
among HIV exposed infants



Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

Question

When should pregnant women be screened for HIV?

- A) At entry into care for pregnancy
- B) Anytime they have any signs or symptoms suggestive of acute HIV
- C) In the 3rd trimester if at risk of HIV acquisition
- D) All of the above



Screening for HIV

- At presentation for pregnancy care
- Repeat in 3rd trimester (<36 weeks)
 - If at risk of acquiring HIV during pregnancy
 - Area/hospital with high number of people with HIV
 - Transactional sex
 - Drug use
 - Sex partner with HIV
 - New sex partner or more than 1 sex partner
 - Suspected or diagnosed sexually transmitted infection
- At labor and delivery if HIV status is unknown
- Mandated by law

Labor and Delivery Testing

- Expedited or rapid testing
 - Goal is to have results within 1 hour
- Needed if:
 - Prior negative HIV test(s) but mother at high risk for HIV acquisition
 - Ongoing illicit drug use
 - New STD diagnoses during pregnancy
 - Sex partners have HIV infection
 - Exchange sex for money or drugs
 - New or more than one sex partner during the current pregnancy
 - Teenage mother

HIV Acquisition Probability and Relative Risk: 2751 African Women with HIV-Infected Male Partners, by Reproductive Stage

Table 5. HIV Acquisition Probability and Relative Risk (RR) of HIV Acquisition Among 2751 African Women With HIV-Infected Male Partners, by Reproductive Stage

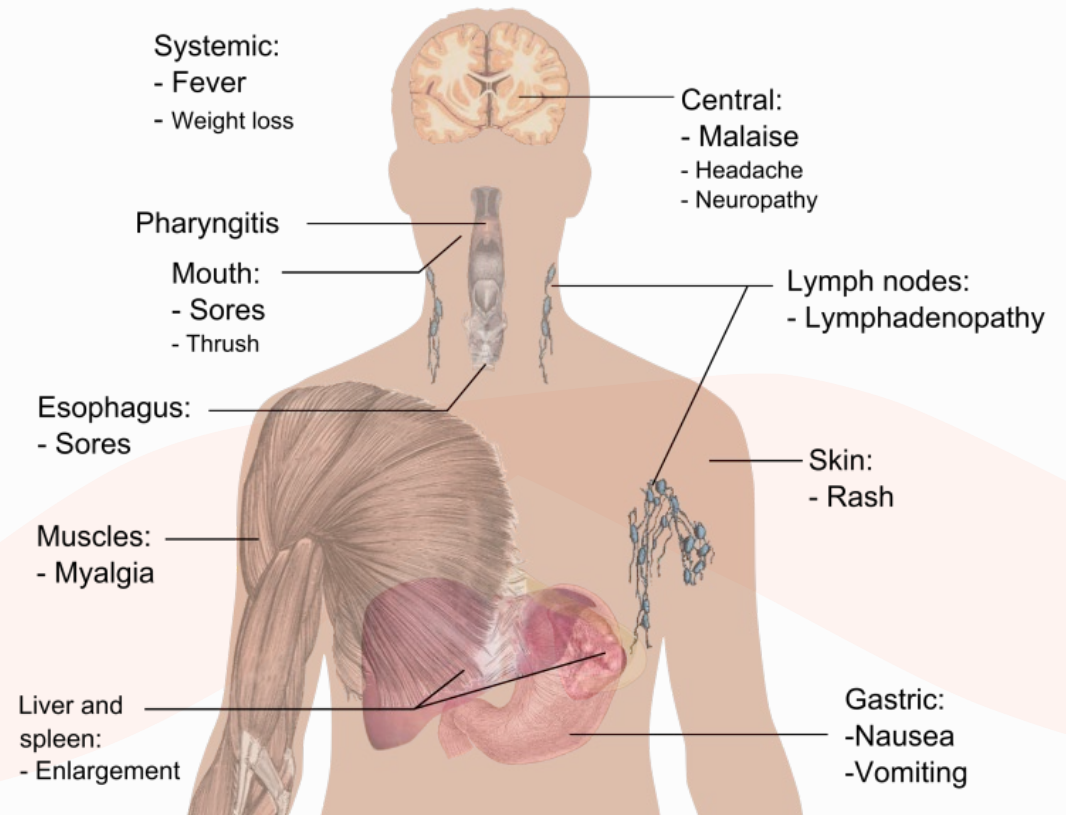
Reproductive Stage	Base Model ^a			Adjusted Model ^b		
	Probability ^c of HIV Acquisition per Condomless Sex Act (95% CI)	RR ^d for per-Act Probability of HIV Acquisition (95% CI)	<i>P</i>	Probability ^c of HIV Acquisition per Condomless Sex Act (95% CI)	RR ^d for per-Act Probability of HIV Acquisition (95% CI)	<i>P</i>
Early pregnancy through postpartum period	0.0027 (0.0009, 0.0074)	4.97 (2.95, 8.38)	<.001	0.0029 (0.004, 0.0093)	2.76 (1.58, 4.81)	<.001
Early pregnancy	0.0018 (0.0003, 0.0070)	3.20 (1.24, 8.25)	.02	0.0022 (0.0004, 0.0093)	2.07 (0.78, 5.49)	.14
Late pregnancy	0.0031 (0.0008, 0.0102)	5.54 (2.62, 11.69)	<.001	0.0030 (0.0007, 0.0108)	2.82 (1.29, 6.15)	.01
Postpartum period	0.0044 (0.0008, 0.0167)	7.80 (3.04, 20.02)	<.001	0.0042 (0.0007, 0.0177)	3.97 (1.50, 10.51)	.01
Nonpregnant/nonpostpartum periods	0.0005 (0.0003, 0.0009)	1.00	...	0.0011 (0.005, 0.0019)	1.00	...

Thomson K et al. J Infect Dis. 2018;218:16-25

Screening for HIV

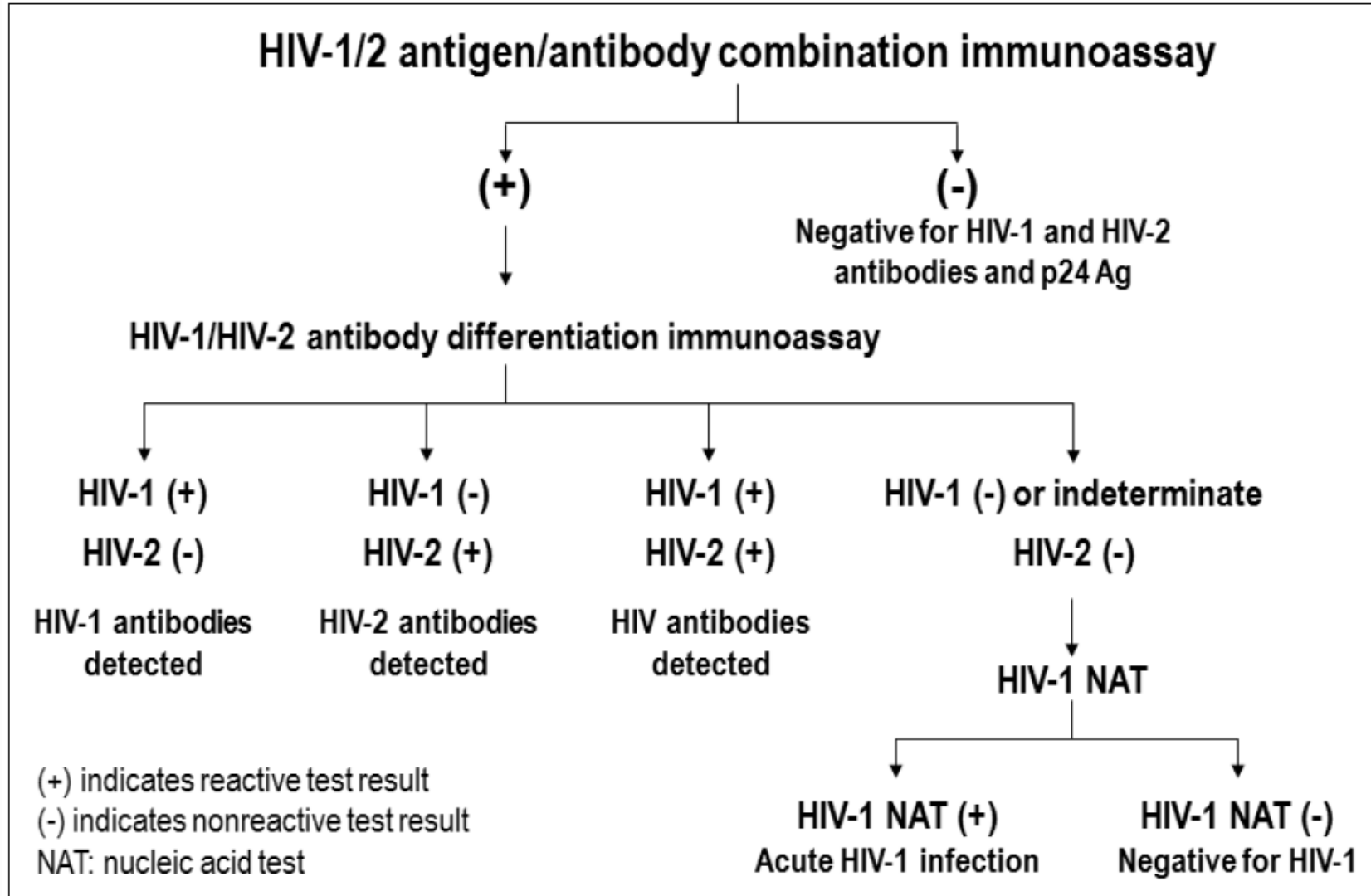
- Signs or symptoms of acute HIV if pregnant or breastfeeding
 - Check HIV viral load as well as 4th generation Ag/Ab test
- Partners of all pregnant people should be referred for HIV testing when their status is unknown

Main symptoms of Acute HIV infection



https://commons.wikimedia.org/wiki/File:Symptoms_of_acute_HIV_infection.svg

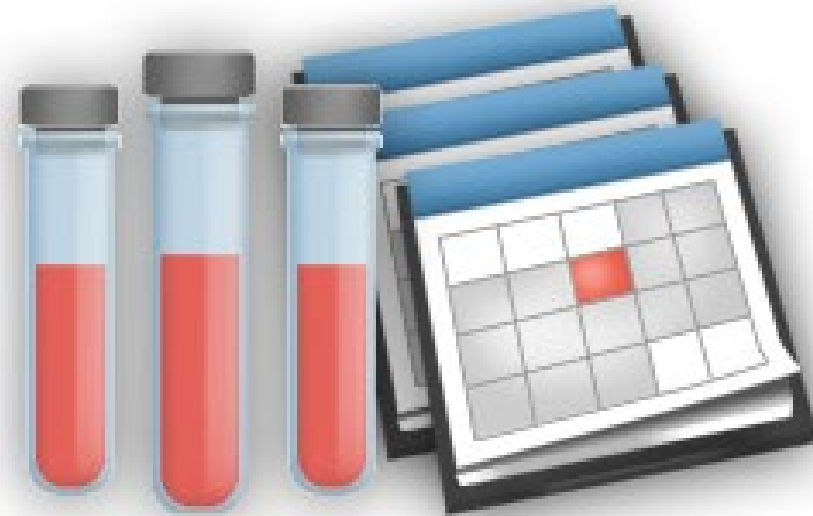
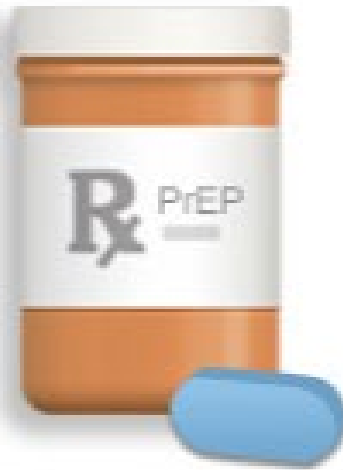
HIV Testing Algorithm



Question

- What should occur in the event of a positive HIV Ag/Ab test and a negative HIV Ab differentiation assay while awaiting the result of an HIV viral load in a pregnant woman?

Pre-exposure Prophylaxis



PrEP IS AN HIV PREVENTION METHOD IN WHICH **PEOPLE WHO DO NOT HAVE HIV INFECTION TAKE A PILL DAILY TO REDUCE THEIR RISK** OF BECOMING INFECTED

ONLY PEOPLE WHO ARE HIV-NEGATIVE SHOULD USE PrEP. AN HIV TEST IS REQUIRED BEFORE STARTING PrEP AND THEN EVERY 3 MONTHS WHILE TAKING PrEP.

Care for the Pregnant Person with HIV

Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection *and* Interventions to Reduce Perinatal HIV Transmission in the United States



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

<https://clinicalinfo.hiv.gov/en/guidelines>

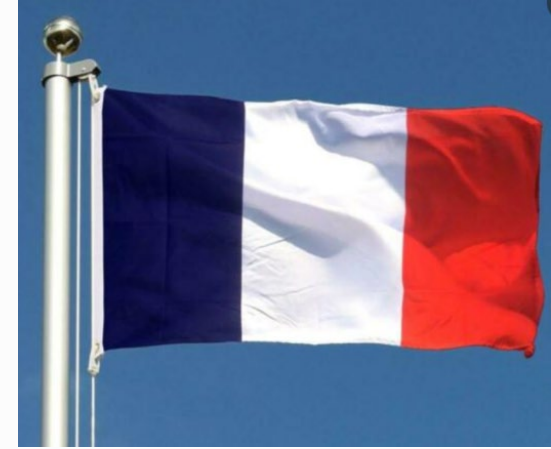
Last update 12/30/2021

CLINICAL INFO
HIV.gov

Antiretroviral Therapy in Pregnancy

- Start as soon as possible, regardless of HIV RNA level of CD4 count - even prior to results of genotype
 1. For health of the mother of the baby and to prevent perinatal HIV transmission and secondary sexual transmission
 2. Earlier viral suppression is associated with reduced risk of transmission to the fetus
 3. Modify therapy later if needed
 4. Goal: Maintain HIV viral load level below the limit of detection during pregnancy and postpartum and throughout life
 5. “PrEP” for the fetus

French Perinatal Cohort



- 8075 HIV-infected mother-infant pairs
- 2000 to 2011
- Mothers received ART, delivered live-born children with determined HIV status, and did not breastfeed

Mandelbrot L, et al. Clin Infect Dis, 2015 Dec 1;61(11):1715-25.

French Perinatal Cohort

- Overall rate of perinatal transmission 0.7%
- 2651 children born to women on ART prior to conception, ART throughout pregnancy, HIV viral load < 50 copies/mL at delivery
 - No HIV transmission
- Regardless of viral load at birth, risk of transmission varied based on when ART was started
 - ART prior to conception 0.2%
 - ART started in first trimester 0.4%
 - ART started in second trimester 0.9%
 - ART started in third trimester 2.2%

P < .001

Medications in Pregnancy

- Many physical changes occur in pregnancy that affect drug pharmacokinetics
 - Decrease in serum proteins
 - Increased plasma volume
 - Increase in kidney filtration
 - Delayed stomach emptying
- What does this mean for the pregnant woman?
 - May have to take higher doses or take ART more often to get appropriate blood and placental levels



Preferred Initial Therapy for Antiretroviral Naïve Pregnant People

2 NRTIs + **OR** **INSTI**

PI/r

NRTI = Nucleoside Reverse Transcriptase Inhibitor
INSTI = Integrase Strand Transfer Inhibitor
PI/r = Ritonavir boosted protease inhibitor

Preferred 2-NRTI Backbones

- 1. Abacavir (ABC)/lamivudine (3TC) = Epzicom**
 - Must be HLA-B*5701 negative
 - If HIV viral load > 100,000 don't combine with atazanavir or efavirenz
 - 2. Tenofovir alafenamide (TAF) /emtricitabine (FTC) = Descovy**
 - 3. TAF + 3TC**
 - 4. Tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) = Truvada**
 - 5. TDF/3TC = Cimduo, Temyxis**
- **Tenofovir in pregnancy**
 - Both TAF and TDF are preferred in pregnancy
 - TAF associated with fewer adverse birth outcomes and slightly higher gestational weight
 - TDF has potential renal toxicity
 - Either form appropriate for treatment of HIV/hepatitis B co-infection

Preferred INSTIs

INSTIs rapidly decrease HIV viral load

1. Dolutegravir (Tivicay)

- Once daily dosing
- Specific timing and/or food recommendations if taken with calcium or iron
- Preferred for treatment of acute HIV during pregnancy

2. Raltegravir (Isentress)

- Must be dosed 400 mg twice daily in pregnancy
- HD formulation not studied in pregnancy, so do not use
- Well-tolerated, few drug interactions

Preferred PIs

1. Darunavir/r (Prezista + Norvir)

- Dose in pregnancy: darunavir 600 mg + ritonavir 100 mg twice daily with food

2. Atazanavir/r (Reyataz + Norvir)

- 300 mg once daily + ritonavir 100 mg daily with food – many would increase atazanavir dose to 400 mg daily in 2nd and 3rd trimesters
- Maternal hyperbilirubinemia but no clinically significant neonatal hyperbilirubinemia or kernicterus
- Interactions with acid reducing agents

Alternative ART for Initial Therapy in Pregnancy

- NRTI backbone
 1. **Zidovudine/3TC (Combivir)**
- NNRTI
 1. **Efavirenz**
 2. **Rilpivirine**
 - Take with food
 - Interacts with acid reducing agents
 - Don't use if HIV viral load > 100,000 copies/mL or CD4 < 200 cells/mm³
 - PK data suggests lower drug levels and risk for viral rebound in second and third trimesters – monitor closely

Acute HIV in Pregnancy

- Preferred regimen
 - Dolutegravir + tenofovir + emtricitabine (or lamivudine)
- Alternative regimen
 - Darunavir/r + tenofovir + emtricitabine (or lamivudine)

DHHS Perinatal Guidelines Available at <https://clinicalinfo.hiv.gov/en/guidelines/perinatal>. Accessed 1/23/2022.

Insufficient Data in Pregnancy to Recommend for Initial Regimens in People Who Are ART-Naive

These drugs are approved for use in adults but lack adequate pregnancy-specific PK or safety data.

BIC/TAF/FTC (FDC)	Limited data on the use of BIC in pregnancy.
DOR	No data on the use of DOR in pregnancy.
IBA	No data on the use of IBA in pregnancy.

DHHS Perinatal Guidelines Available at <https://clinicalinfo.hiv.gov/en/guidelines/perinatal>. Accessed 1/23/2022.

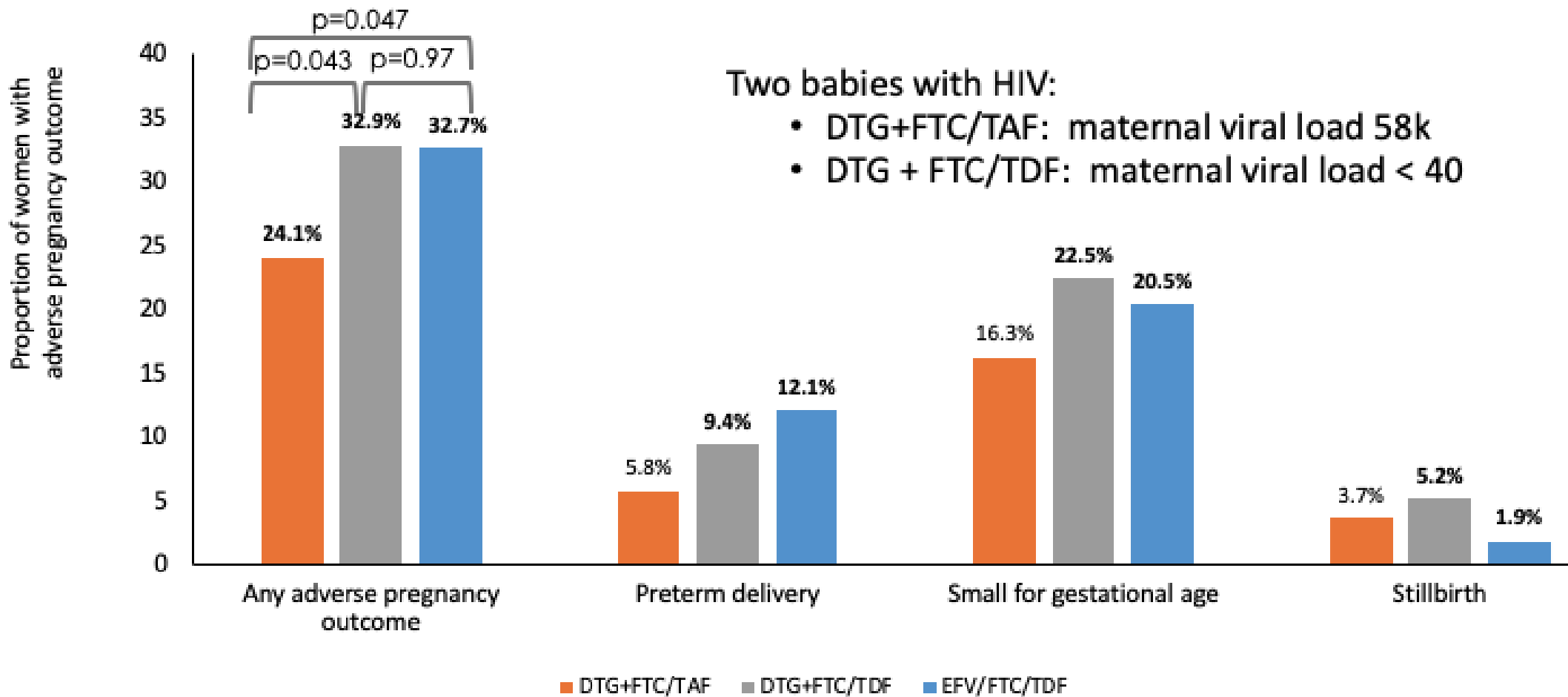
Antiretrovirals **Not** Recommended In Pregnancy

- Cobicistat containing regimens due to pharmacokinetic changes that can reduce medication efficacy
 - (Atazanavir/c, darunavir/c, elvitegravir/c)
- Long acting injectable cabotegravir/rilpivirine
 - Limited data
- Stavudine (d4T), Didanosine (ddI), Fosamprenavir, indinavir, nelfinavir, ritonavir (as sole PI), saquinavir, tipranavir, **two-drug antiretroviral regimens**, or a three NRTI regimen

ART Not Recommended Except in Special Circumstances or for Treatment Experienced People in Pregnancy

- Etravirine
- Fostemsavir
- Lopinavir/ritonavir
- Maraviroc
- Nevirapine
- T-20

IMPAACT 2010: DTG + TAF/FTC associated with *fewest* adverse pregnancy outcomes when started during pregnancy



Chinula L, et al. 27th CROI; Boston, MA; March 8-11, 2020. Abst. 130LB.

Antiretroviral Therapy in Pregnancy

Key Points

1. In most cases, women who present for obstetric care on fully suppressive HIV therapy should continue their current regimen
2. The same regimens recommended for treatment of nonpregnant adults should be used in pregnant people when sufficient data suggests appropriate drug exposure, efficacy, and safety
3. There are often incomplete data on safety of HIV drugs in pregnancy

Table 5. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive

ART Regimen Component	ART for Pregnant People Who Have Never Received ARV Drugs and Who Are Initiating ART for the First Time	Continuing ART for People Who Become Pregnant on a Fully Suppressive, Well-Tolerated Regimen	ART for Pregnant People Who Have Received ARV Drugs in the Past and Who Are Restarting ART ^a	New ART Regimen for Pregnant People Whose Current Regimen Is Not Well Tolerated and/or Is Not Fully Suppressive ^a	ART for Nonpregnant People Who Are Trying to Conceive ^{a,b}
Integrase Strand Transfer Inhibitor (INSTI) Drugs Used in combination with a dual-nucleoside reverse transcriptase inhibitor (NRTI) backbone ^c					
DTG	Preferred	Continue	Preferred	Preferred	Preferred
RAL	Preferred	Continue	Preferred	Preferred	Preferred
BIC	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
EVG/c^d	Not recommended	Continue with frequent viral load monitoring or consider switching	Not recommended	Not recommended	Not recommended

Important Conversations

- Importance of lifelong antiretroviral therapy for the pregnant person
 - Before, during and after pregnancy
- Risks/benefits of antiretroviral therapy for mother and infant
 - Appendix C in perinatal guidelines: Counseling guide
- Infant feeding and ART prophylaxis
 - Breastfeeding and pre-mastication are not recommended in the US for people with HIV
- Timing of infant diagnostic testing

Family Planning Conversations

- Women with HIV can use all available contraceptive methods, including hormonal contraception

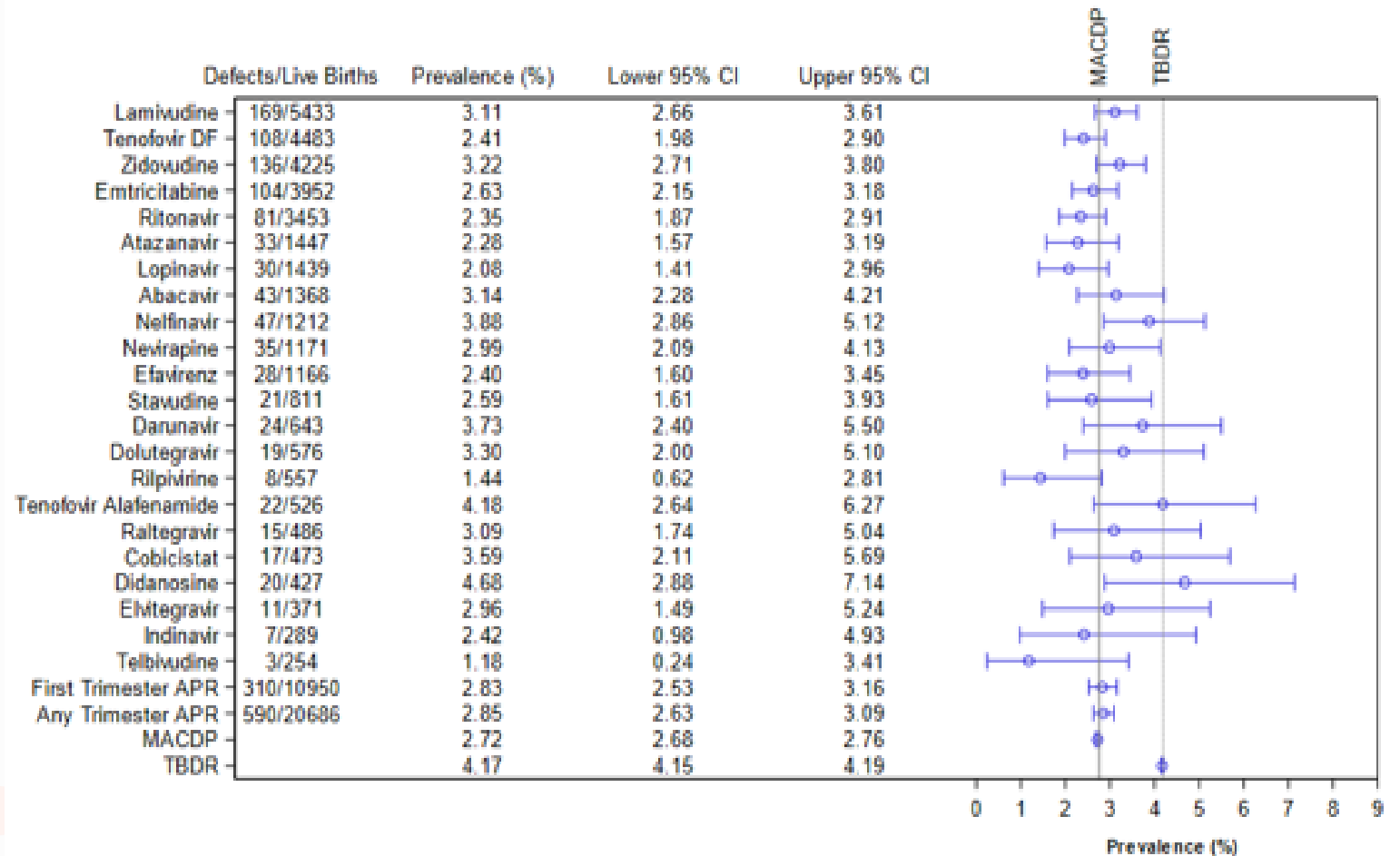
Integrase Strand Transfer Inhibitors (INSTIs)	
Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA ^a , Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	No significant drug interactions with EE or norgestimate.
Clinical Studies	N/A
Justification/Evidence for Recommendation	No clinical data.
Dolutegravir (DTG)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA ^a , Etonogestrel Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	<p>COC</p> <ul style="list-style-type: none"> No significant effect on etonogestrel implants⁵⁸ No significant effect on norgestimate or EE No change in DTG AUC⁴⁰
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE or progestin. No clinical data. No data on POPs.

THE ANTIRETROVIRAL PREGNANCY REGISTRY INTERIM REPORT

1 JANUARY 1989 THROUGH 31 JANUARY 2021

(Issued: June 2021 / Expiration: 6 months after issue)

- Annually enrolls approximately 1300-1700 pregnant women
- Total number of women involved as of 1/31/21: 24,876



Monitoring of HIV During Pregnancy

- HIV viral load testing
 - Initial visit
 - 2-4 weeks after starting or changing ART
 - Monthly until HIV viral load is below limit of detection of test (“undetectable”)
 - Every 3 months during pregnancy
 - 34-36 weeks’ gestation to inform delivery decisions
- Antiretroviral resistance testing
 - Prior to starting ART if never on treatment
 - Prior to changing regimen if HIV RNA above threshold for resistance testing (> 500 to 1,000 copies/mL)

Support Pregnant People with HIV So They Stay in Care and on Therapy

- Coordination of services helps:
 - Prenatal care providers
 - Primary care and HIV specialty care providers (Adult and Peds ID)
 - Mental health and substance use disorder treatment, if needed
 - Intimate partner violence support services
 - Public assistance programs
 - Perinatal coordinator, case manager, peer, and/or support groups

Engaging Pregnant People with HIV

- Involve their support system if patient allows
 - Father of the baby, or current partner
 - Family
 - Friends
- Be available and answer questions
- Give hope

What You Can Do If You Are Pregnant and Have HIV



Visit your health care provider regularly.



Take HIV medicine as prescribed to stay healthy, protect your partner, and protect your baby.

Taking HIV medicine reduces the amount of HIV in the body (viral load) to a very low level, called *viral suppression* or an *undetectable viral load*.^{*} Getting and keeping an undetectable viral load is the best thing you can do to stay healthy and help prevent transmission to your baby.



The risk of transmitting HIV to your baby can be 1% or less if you:

- Take HIV medicine daily as prescribed throughout pregnancy, labor, and delivery.
- Give HIV medicine to your baby for 4-6 weeks after giving birth.



If your HIV viral load is not adequately reduced, a Cesarean delivery can also help prevent HIV transmission.



Do not breastfeed or pre-chew your baby's food.

Keeping an undetectable viral load substantially reduces, but does not eliminate, the risk of transmitting HIV through breastfeeding. The current recommendation in the U.S. is that mothers with HIV should not breastfeed their babies.

What if virologic suppression is not attained?

1. Test for drug resistance
2. Assess drug adherence, tolerability, dosing, potential problems with absorption, lack of attention to food requirements
3. Consider ART modification

Adherence to ART, labs and appointments (both OB and HIV care) are critical to success in preventing mother to child transmission!

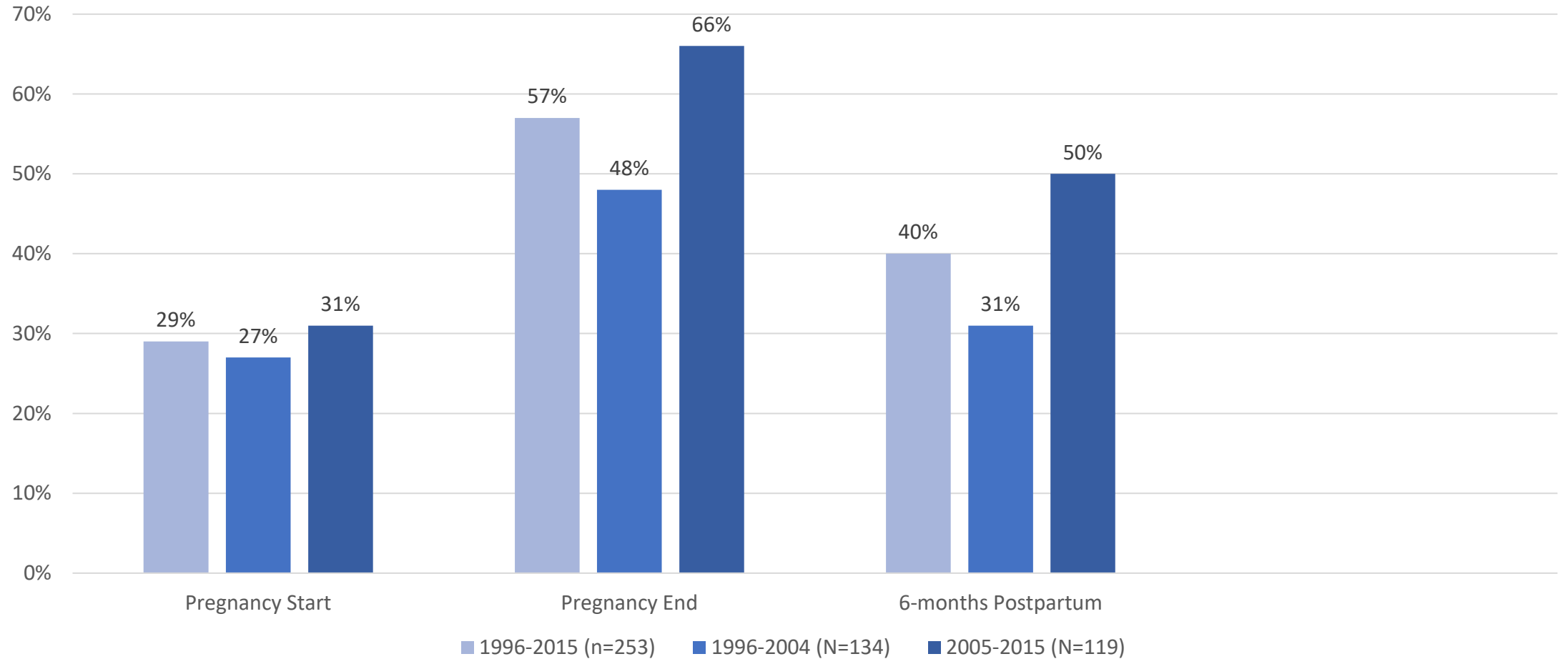
Virologic Failure Near Delivery

- HIV RNA > 1,000 copies/mL or unknown viral load
 - Scheduled cesarean section at 38 weeks
 - Intravenous zidovudine
 - 2 mg/kg dose followed by a continuous infusion of 1 mg/kg/hour until delivery
 - Some providers would give IV zidovudine if last HIV viral load > 50 or any concern for non-adherence

The Fourth Trimester: Postpartum Care

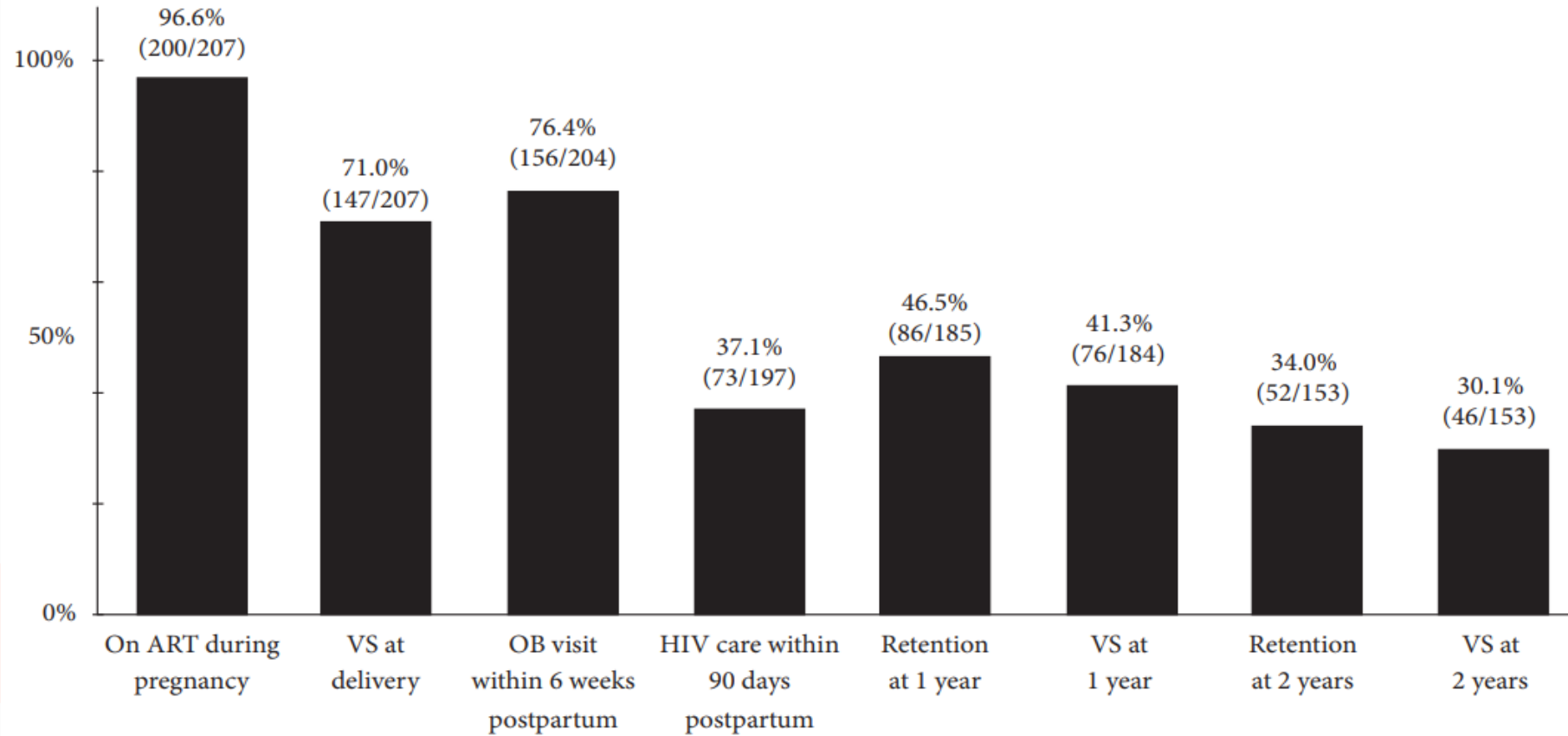
- The 12 weeks postpartum are referred to as “the fourth trimester”
- Address the following
 - Mood and emotional wellbeing
 - Infant care and feeding
 - Sleep, fatigue and physical recovery from birth
 - Sexuality, contraception, birth spacing
 - Chronic disease management and coordination of care with PCP
 - Health Maintenance
- Women living with HIV are often lost to HIV follow-up during this time period

Viral suppression among women on antiretroviral therapy (ART) at time points during and after pregnancy, HIV Outpatient Study, 1996 to 2015



Virally Suppressed (≤ 500 copies/mL)

Postpartum HIV Care Continuum Atlanta 2011 - 2016



Postpartum HIV Care:

- Cross-disciplinary approach to integrate HIV obstetric care during pregnancy
- Enhanced care coordination for transition between obstetric and HIV services postpartum
- Co-locate HIV primary care for mother and pediatric care of infant

Case

- C is a 28 year old woman with perinatal HIV infection.
- Raised by foster family from age 2.
- Nonadherent to therapy throughout childhood and adolescence. At age 20 diagnosed with cutaneous lymphoma and became adherent and engaged in care.
- Stopped depo-medroxyprogesterone acetate after a longstanding relationship ended.
- Became pregnant during a short relationship.
- Adherent to ART, accepted peer and group support, was engaged in her care and had a suppressed viral load throughout pregnancy.
- Vaginal delivery of a healthy son who is now in kindergarten.



Summary

- Recognizing HIV infection in people who are pregnant is critical for protection of the pregnant person's health and to prevent transmission to the baby
- Viral load during pregnancy is best predictor of HIV transmission
- There are multiple effective, safe and well tolerated options for antiretroviral treatment in pregnancy
- Support before, throughout, and after pregnancy is critical for the health of people with HIV and their babies

Resources

- National HIV Curriculum
 - HIV.uw.edu
- DHHS Perinatal Guidelines
 - <https://clinicalinfo.hiv.gov/en/guidelines/perinatal/>
- National Clinician Consultation Center
 - <http://nccc.ucsf.edu/clinician-consultation/perinatal-hiv-aids/>

Perinatal HIV/AIDS



Rapid perinatal HIV consultation from practicing providers

- HIV testing in pregnancy
- Treating HIV-infected pregnant women
- Preventing transmission during labor and delivery and the post-partum period
- HIV-exposed infant care

Call for a Phone Consultation

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24 hours,
Seven days a week

CALL