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**Perinatal HIV and Hepatitis C
Where We Were, Where We Are Now, and
Where We Are Going
10th Viral Hepatitis Conference
Ending the Epidemic
July 26, 2023**

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Disclosures

- **I have participated in advisory board meetings as a consultant for Gilead and Sanofi**
- **I have participated as principal investigator or sub-investigator in multiple sponsored clinical trials with multiple companies including Gilead, AstraZeneca, Novavax, Merck, and Jansen and Jansen**



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Human Immunodeficiency Virus (HIV)

Where we were?

- **Highly effective interventions to prevent perinatal transmission of HIV have been recommended over time**
 - In 1985, testing high risk women and avoidance of breastfeeding in HIV-infected women
 - In 1994, routine administration of antiretroviral (ARV) medication for prophylaxis, (zidovudine)
 - In 1995, routine offer of prenatal HIV testing to all pregnant women

Where we were?

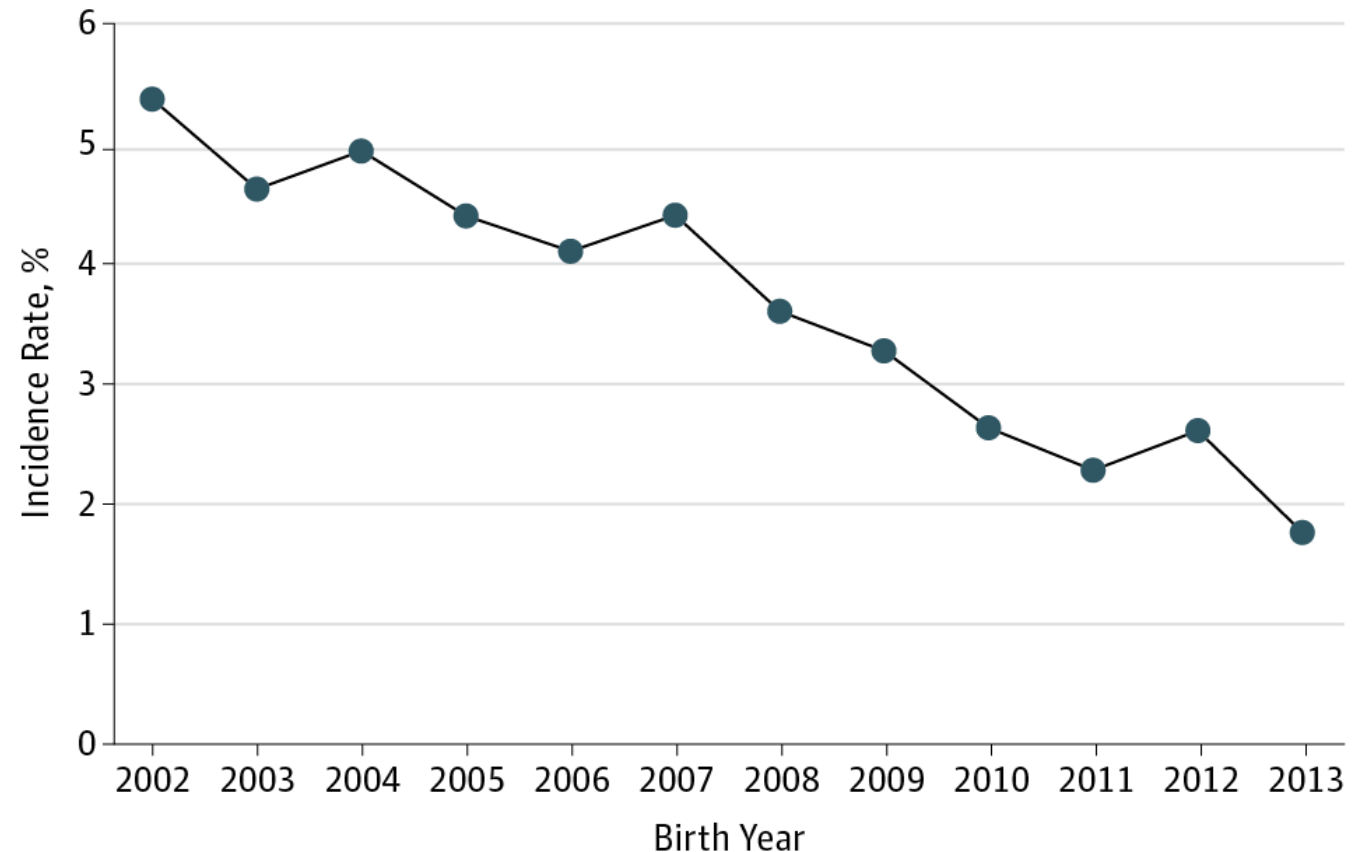
- The percentage of HIV-infected pregnant women receiving ARV prophylaxis rapidly increased after 1995
- In 2006, the CDC recommended universal HIV testing—using an opt-out approach—to increase screening and reduce perinatal HIV transmission

Rate of perinatal transmission of HIV

- Perinatal transmission occurs in 18-32% of cases without any intervention during the prenatal period or labor and delivery
- Combination of ARV therapies and the use of elective cesarean delivery, when appropriate, the number of perinatally infected infants declined by >95%
- Rates of perinatal HIV transmission have been reduced to <1% when non-breastfeeding women and infants receive all appropriate interventions and women's plasma HIV viral load is suppressed to undetectable levels

Estimated Perinatal HIV Infection Among Infants Born in the U.S., 2002-2013

- Estimated number of infants born with perinatal HIV infection decreased from **216** in 2002 to **69** in 2013
- Maternal and infant factors associated with infant HIV infection include:
 - **Late maternal diagnosis**
 - **Lack of antiretroviral treatment and prophylaxis**



Transmissions continue

- **Most new infections are attributable to failures to perform well-established interventions (ie, “missed opportunities”)**
- **Improve implementation of those interventions would further reduce the annual number of infections**
- **Improving HIV prevention of mother-to-child transmission, elimination of mother-to-child transmission will be possible**



Cascade of events for the successful prevention of MCT of HIV

• Prevention of HIV infection in women and girls of childbearing potential
• Identification of infection among women of childbearing potential
• Assurance of adequate preconception care and family planning services for HIV-infected women
• Early identification of HIV infection of pregnant women through universal prenatal screening
• Provision of adequate prenatal care for women who have HIV infection
• Maximal reduction of maternal viral load through appropriate use of ARV drugs
• Cesarean delivery when maternal viral load is not maximally suppressed
• Provision of neonatal ARV prophylaxis
• Neonatal replacement feeding as well as maternal support for lactation suppression

Where we are now?

- **Most people with HIV who give birth in the U.S. do not transmit HIV to their babies**
- **We don't know exactly how many people with HIV give birth annually in the U.S**
- **In 2017, the CDC estimated that the number is less than 5,000**

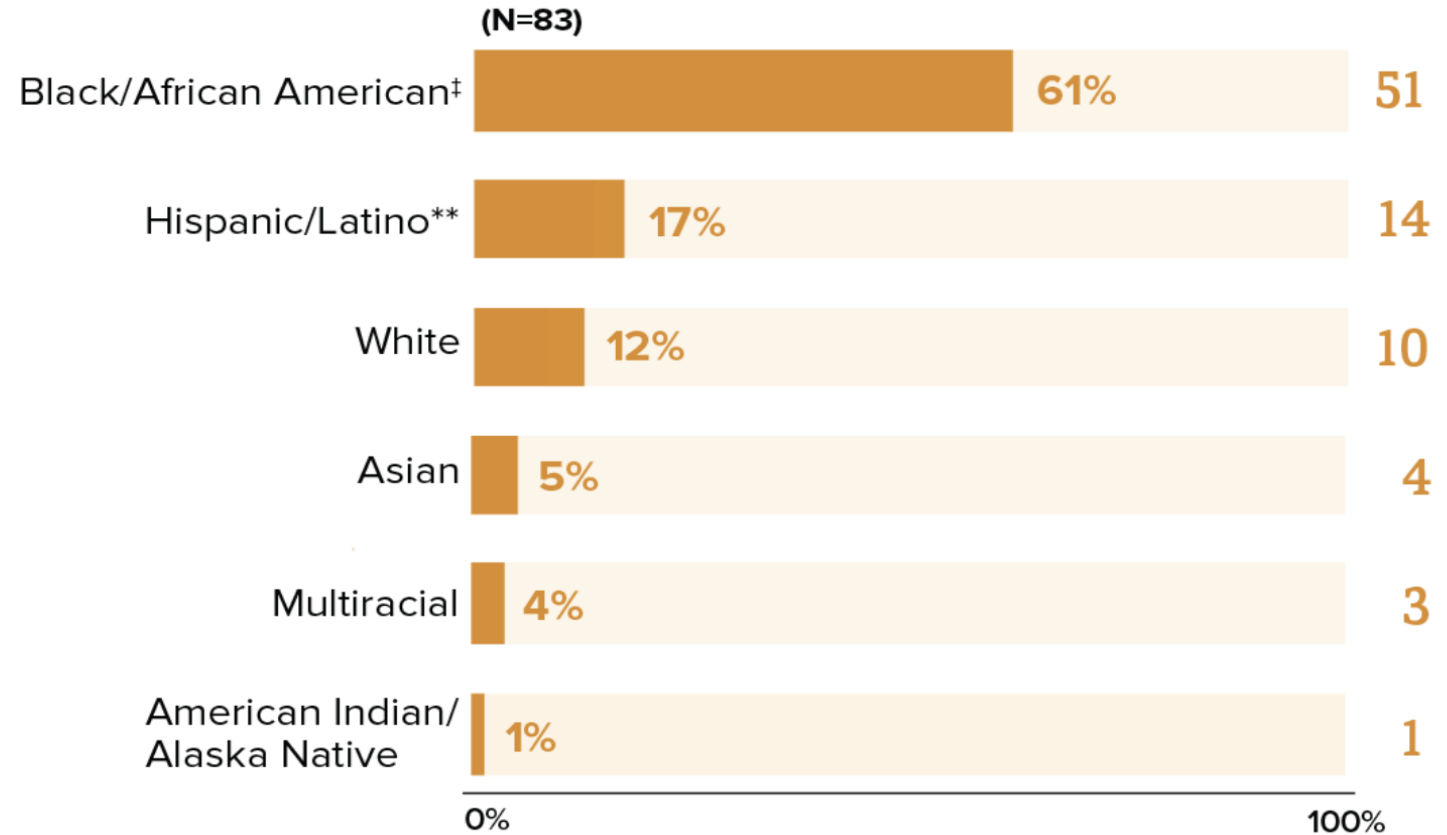


Of the **36,801 new HIV diagnoses** in the US and dependent areas in 2019, <1% (84) were due to perinatal transmission.*

*Includes HIV diagnoses attributed to perinatal transmission among adults, adolescents, and children.

New Perinatal HIV Diagnoses in the US and Dependent Areas by Race and Ethnicity, 2019*†

New perinatal HIV diagnoses disproportionately affect certain racial and ethnic groups.



* In 2019, there were no cases of perinatal HIV among Native Hawaiian and other Pacific Islander people.

† Includes HIV diagnoses attributed to perinatal transmission among adults, adolescents, and children. Data have been statistically adjusted to account for missing transmission category.

‡ *Black* refers to people having origins in any of the Black racial groups of Africa. *African American* is a term often used for people of African descent with ancestry in North America.

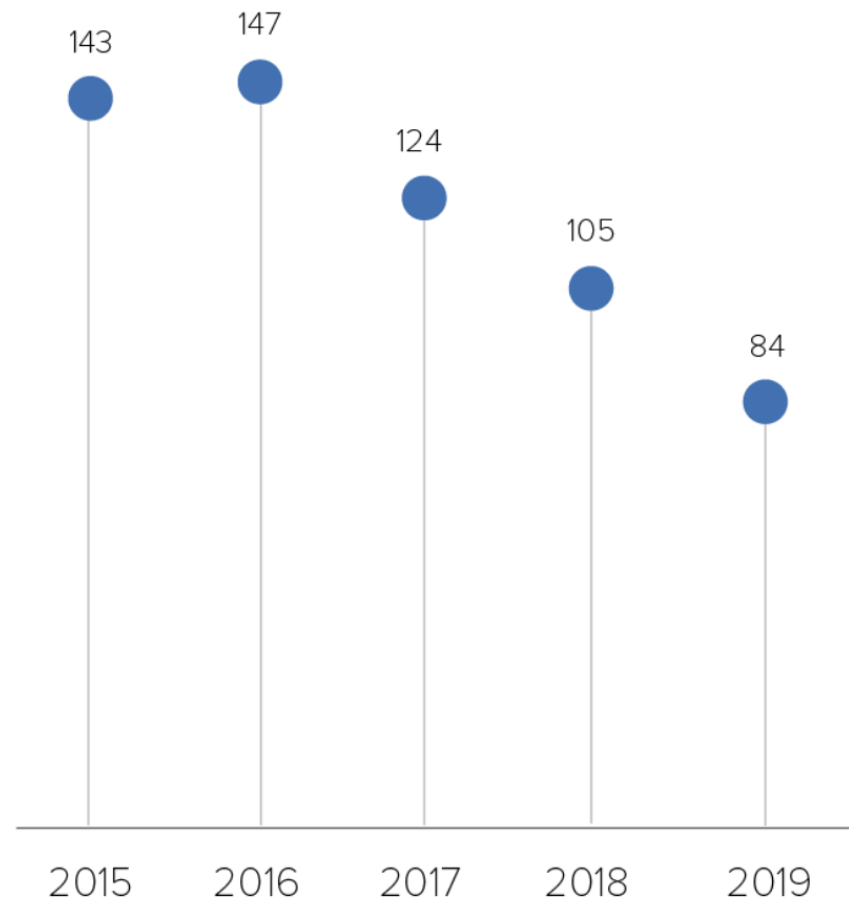
** Hispanic/Latino people can be of any race.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.



Trends in New Perinatal HIV Diagnoses in the US and Dependent Areas, 2015-2019*

Perinatal HIV diagnoses decreased 41% from 2015 to 2019.



*Includes HIV diagnoses attributed to perinatal transmission among adults, adolescents, and children.

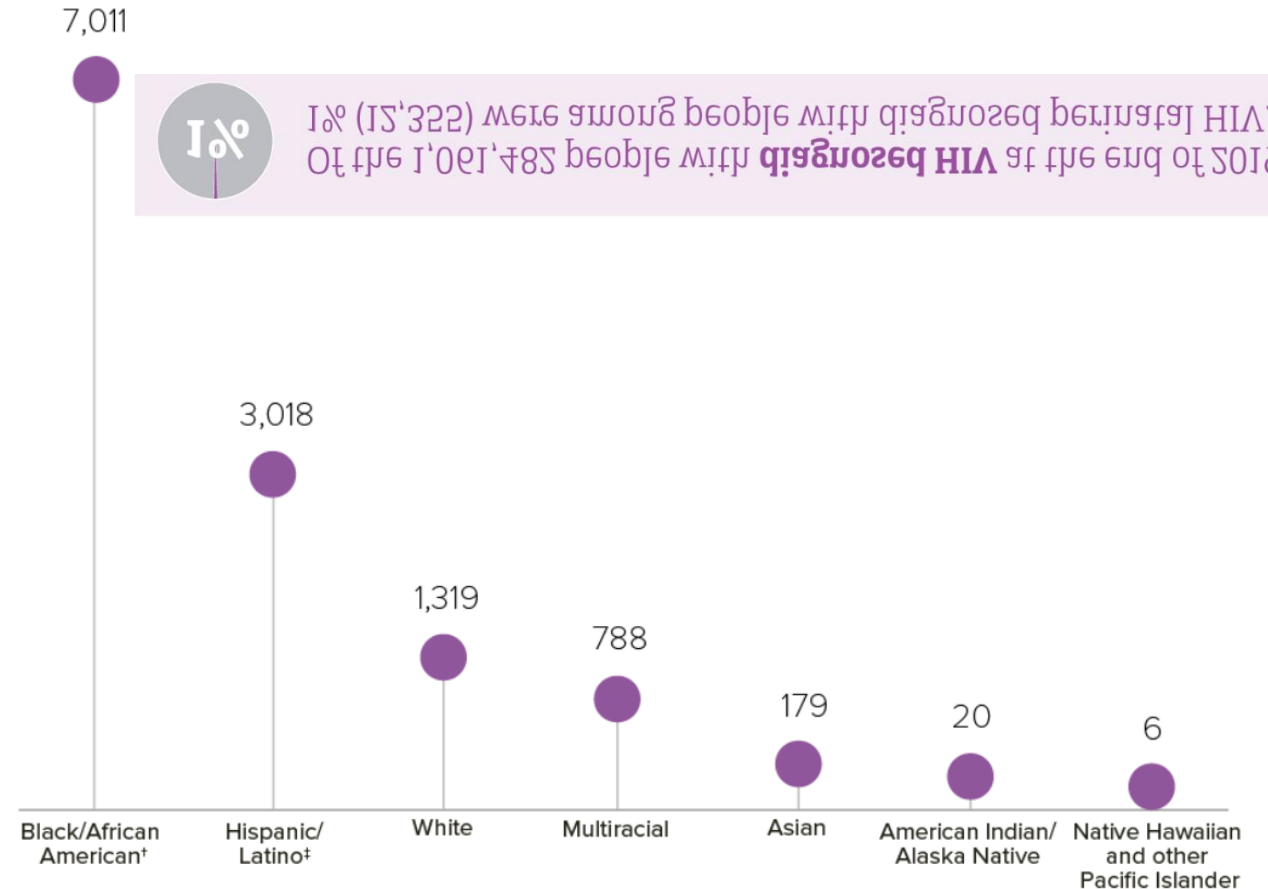
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.



<https://www.cdc.gov/hiv/images/group/pregnant-people/infographics/cdc-hiv-pregnant-people-new-diagnosis-race-infographic.png>

Total Number of People with Diagnosed Perinatal HIV in the US and Dependent Areas by Race and Ethnicity, 2019*

Perinatal HIV disproportionately affects certain racial and ethnic groups.



*Includes adults, adolescents, and children.

†Black refers to people having origins in any of the Black racial groups of Africa. *African American* is a term often used for people of African descent with ancestry in North America.

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Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

<https://www.cdc.gov/hiv/images/group/pregnant-people/infographics/cdc-hiv-pregnant-people-new-diagnosis-race-infographic.png>





Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States

The information in the brief version is excerpted directly from the full-text guidelines. The brief version is a compilation of the tables and boxed recommendations.

Search Guidelines

Guideline Search Term...

Search



Open ▼

Version:

BRIEF

FULL

What's New in the Guidelines

What's New

Updated: January 31, 2023

Reviewed: January 31, 2023

<https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new>



Update to Clinical Guidelines for Infant Feeding Supports Shared Decision Making: Clarifying Breastfeeding Guidance for People with HIV

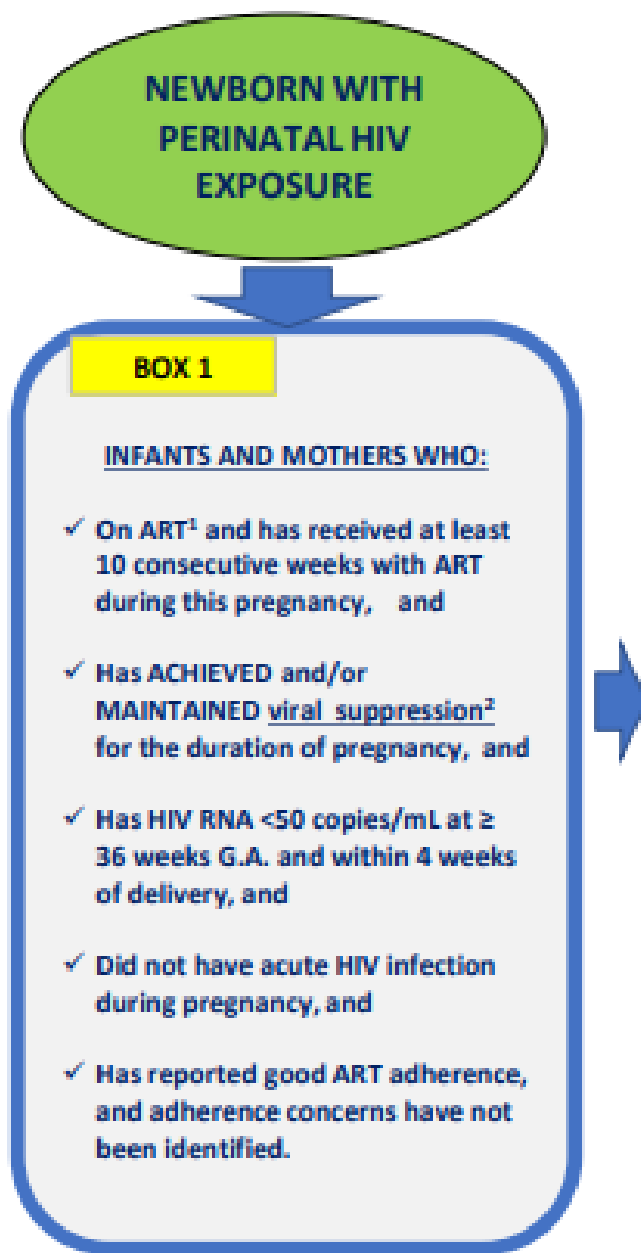
January 31, 2023

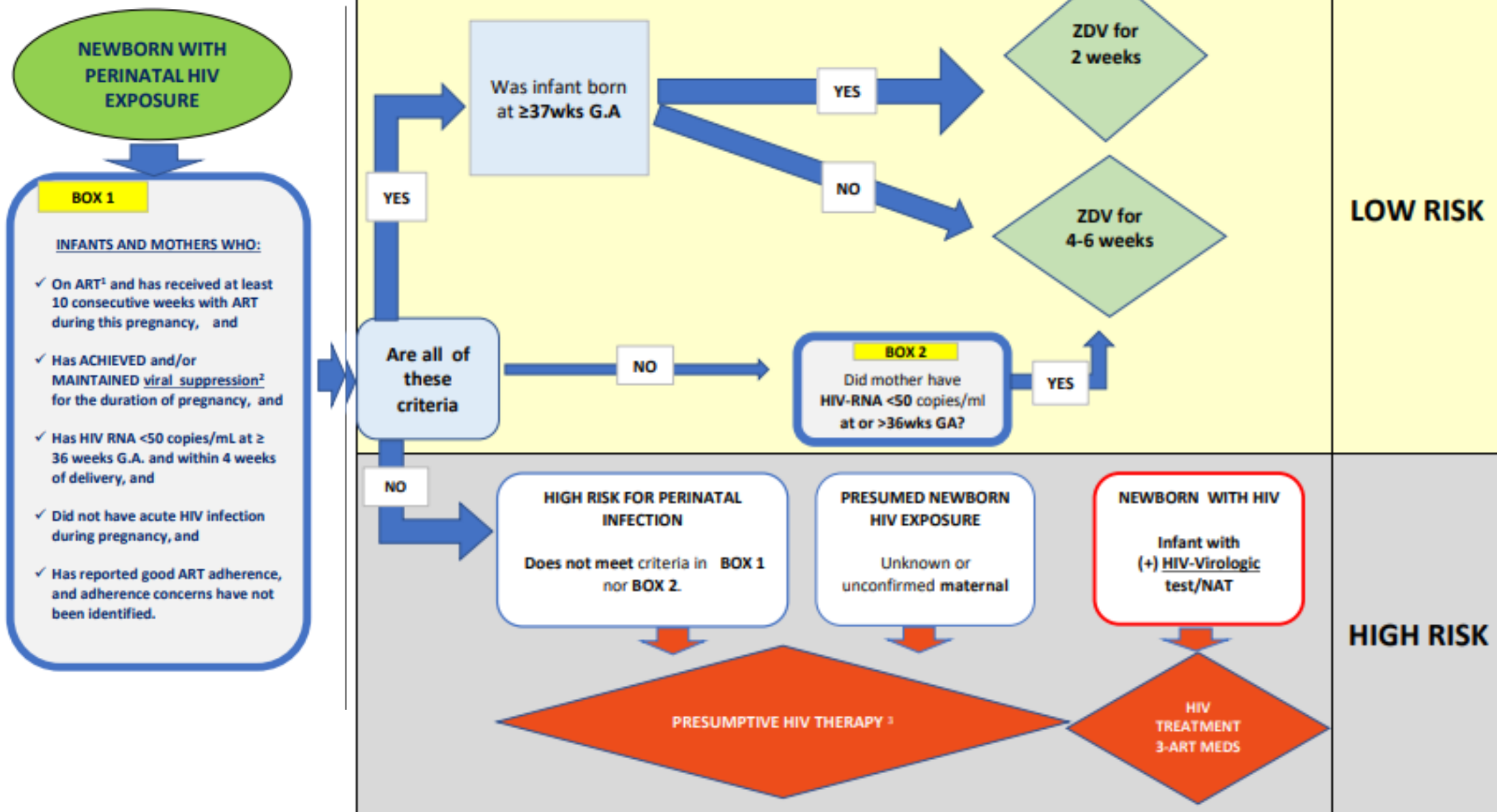
HHS HIV clinical practice guidelines now incorporate breastfeeding options for people with HIV on antiretroviral therapy with sustained undetectable viral load (levels of virus in the blood).

Clinical guideline for infant feeding

People with HIV (PWH) who are considering conception, are pregnant, or in the postpartum period should receive evidence-based counseling to support decision making about infant feeding. The updated guidelines note that:

- **The risk of postnatal HIV transmission to an infant is zero with the use of formula**
- **The risk of HIV transmission while breastfeeding is <1% (but not zero) for PWH on ART with sustained undetectable VL through pregnancy and postpartum**
- **Clinicians should support the choices of people with HIV to breastfeed (if they are virally suppressed) or to formula/replacement feed**
- **It is inappropriate to engage Child Protective Services (CPS) or similar services in response to infant feeding choices of PWH**





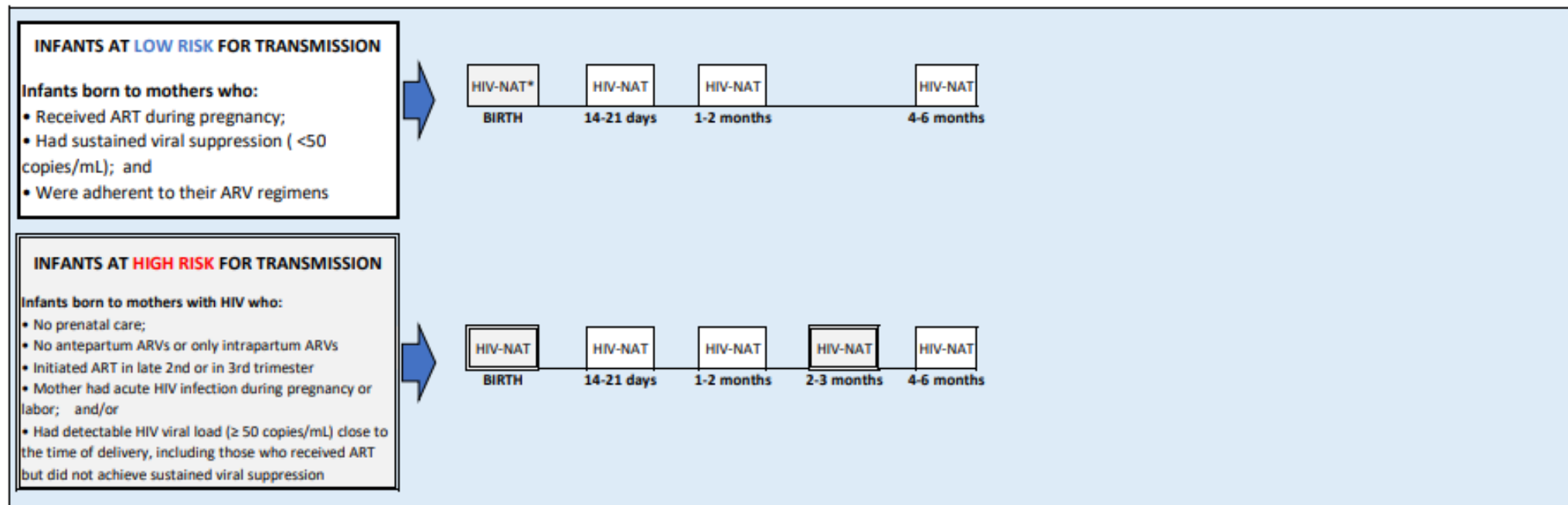
**ART REGIMENS FOR BREASTFEEDING BASED****ON RISK LEVEL FOR ACQUIRING INFECTION**

LOW RISK	Meets criteria in BOX 1.	ZDV for 2 weeks
	Meets criteria in BOX 2 but not in BOX 1.	ZDV for 4-6weeks
	Alternative regimen	NVP daily for 26weeks
HIGH RISK	BREASTFEEDING IS NOT RECOMENDED If mother still chooses to breastfeed against advice: Place infant on PRESUMPTIVE HIV THERAPY for 6wks followed by daily NVP throught breastfeeding and until 1-4 weeks after weaning.	

1	ART	Anti-retroviral medications. Doses are based on G.A., age, weight and risk level.
2	VIRAL SUPPRESSION	≥ 2 consecutive HIV- RNA levels <50 copies/mL obtained at least 4 weeks apart
3	PRESUMED HIV THERAPY	ZDV + 3TC+ either NVP or RAL. (NVP needs to be given at treatment doses)
4	TREATMENT FOR HIV INFECTION	Using 3 ART medications, all meds at treatment dosages. Recommended regimens ZDV+3TC+ (NVP or RAL)
5	PRESUMED NEWBORN WITH HIV EXPOSURE	Discontinue ART meds if mother is confirmed HIV negative

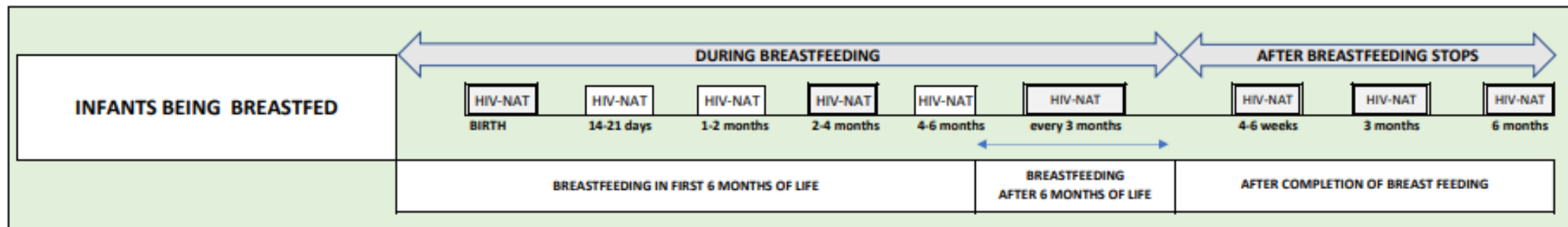


PERINATAL HIV EXPOSURE RECOMMENDED VIROLOGIC TESTING FOR INFANTS



HIV-NAT: Includes quantitative or qualitative virologic tests using Polymerase Chain Reaction (PCR) or Nucleic Acid Amplification Tests (NAATs) for HIV-RNA or HIV-DNA

*Birth HIV-NAT for LOW-RISK transmission is an added recommendation from UF-JAX Peds ID.



HIV-NAT: Includes quantitative or qualitative virologic tests using Polymerase Chain Reaction (PCR) or Nucleic Acid Amplification Tests (NAATs) for HIV-RNA or HIV-DNA



Where are we going?

**Elimination of perinatal
transmission of HIV**



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Hepatitis C

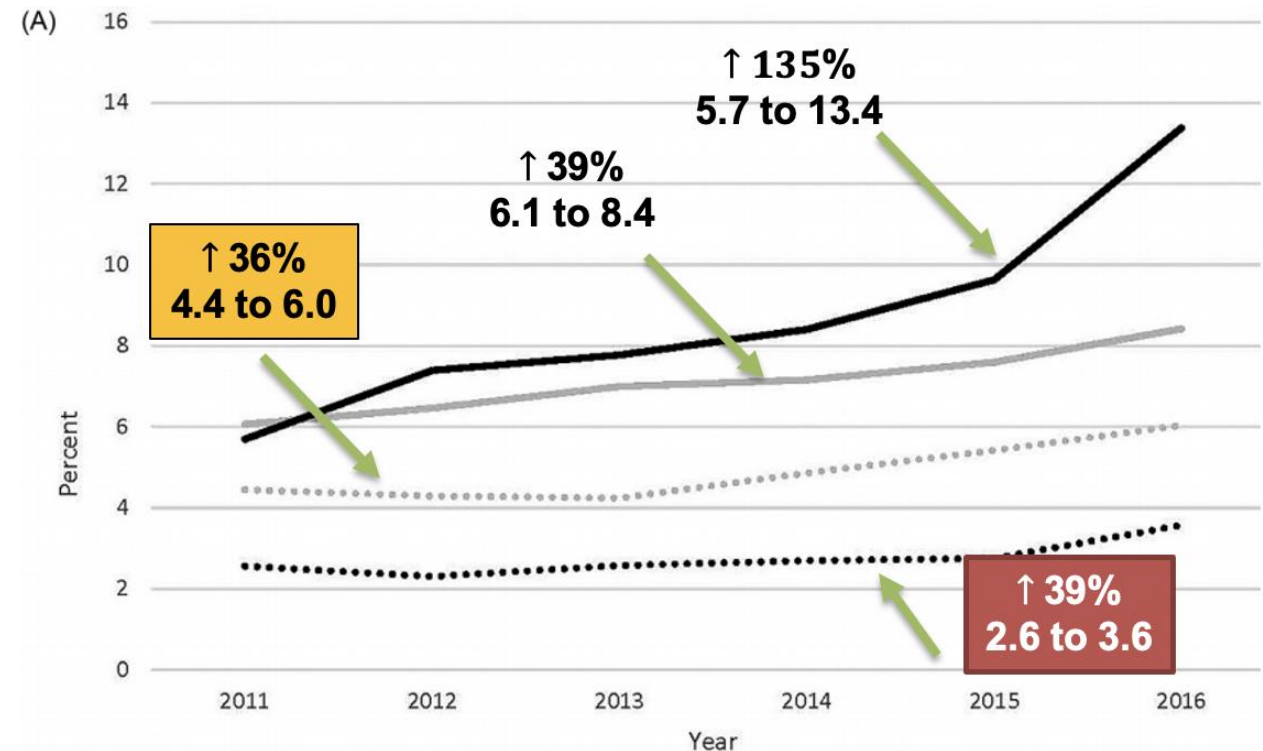
Where we were?

- **Injection drug use is the primary risk factor for HCV transmission among adults**
- **In children, the main route of transmission is vertical**
- **HCV cases tripling in the U.S. between 2010 and 2015**
- **HCV cases increased parallel with increased heroin (second wave) and synthetic opioid (third wave) overdose deaths during the opioid epidemic**
- **More than one-third of newly reported HCV cases were among women, and the highest incidence occurred among persons aged 20 to 39 years**

Where we were?

- Antepartum opioid use disorder has quadrupled since the start of the opioid epidemic in the late 1990s
- HCV cases among pregnant women from 2014 to 2017, exceeded cases of hepatitis B and syphilis combined, using HCV targeted screening during prenatal care

HCV testing trends among U.S. women of childbearing age and pregnant women, 2011-2016



Where we were?

HCV infected pregnant are at higher rate of:

- **Cesarean section and vacuum delivery**
- **Pre and postpartum hemorrhagic anemia**
- **Premature rupture of the membranes**
- **Need for blood transfusion**
- **Gestational diabetes**
- **Hypertension**
- **Hospitalizations**

HCV exposed infants are at higher rate of:

- **Intrauterine fetal death**
- **Small for gestational age**
- **Low birthweight**
- **Low Apgar score at 5 minutes**
- **Admission to the NICU**
- **Increase in neonatal mortality**

Where we were?

- **Mother-to-child transmission of HCV during pregnancy occurs in approximately 6% of children delivered by women with HCV viremia**

Increased risk

Rupture of membranes > 6 hours

Invasive procedures

Internal fetal monitoring

Maternal IV drug use during pregnancy
(peripheral mononuclear cells)

Controversial factors

Co-infection with HIV

High viral load

Transfer of maternal neutralizing
antibody

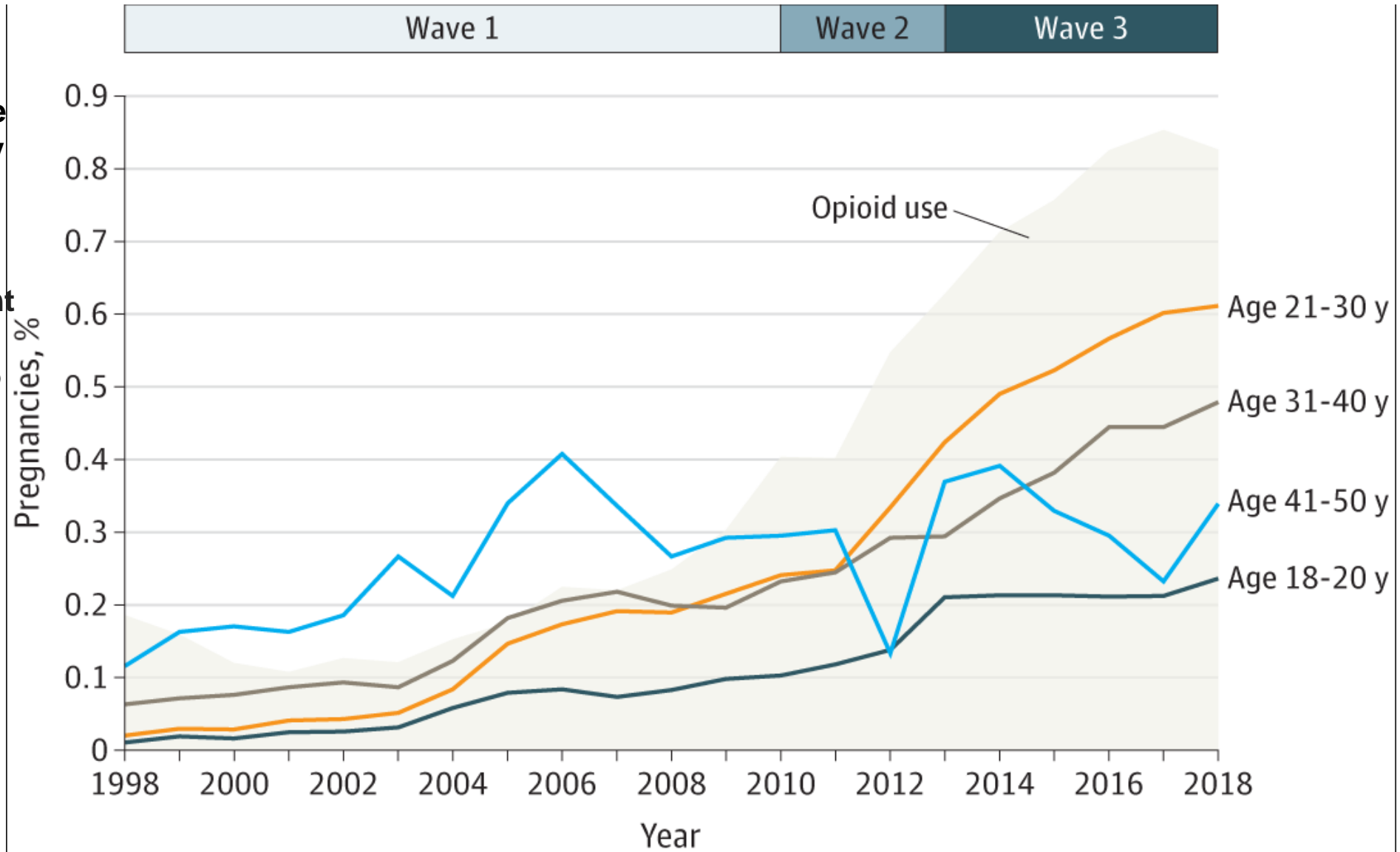
A national survey

- **The National Inpatient Sample (NIS) -largest publicly available all-payer inpatient care database in the US**
- **Contains discharge data: demographics, dx, procedures, payers, hospital characteristics, total charges, and LOS**
- **NIS is a stratified random sample of ~20% of hospitals**
- **As of 2017, 47 states contribute to the NIS**
- **Their data are weighted to allow the calculation of national estimates**
- **Data from 1998 to 2018 was analyzed using ICD9 &10 codes**



Prevalence of Hepatitis C-Positive or Opioid Use Status Among Pregnancies in the US, Across the First 3 Waves of the Opioid Epidemic

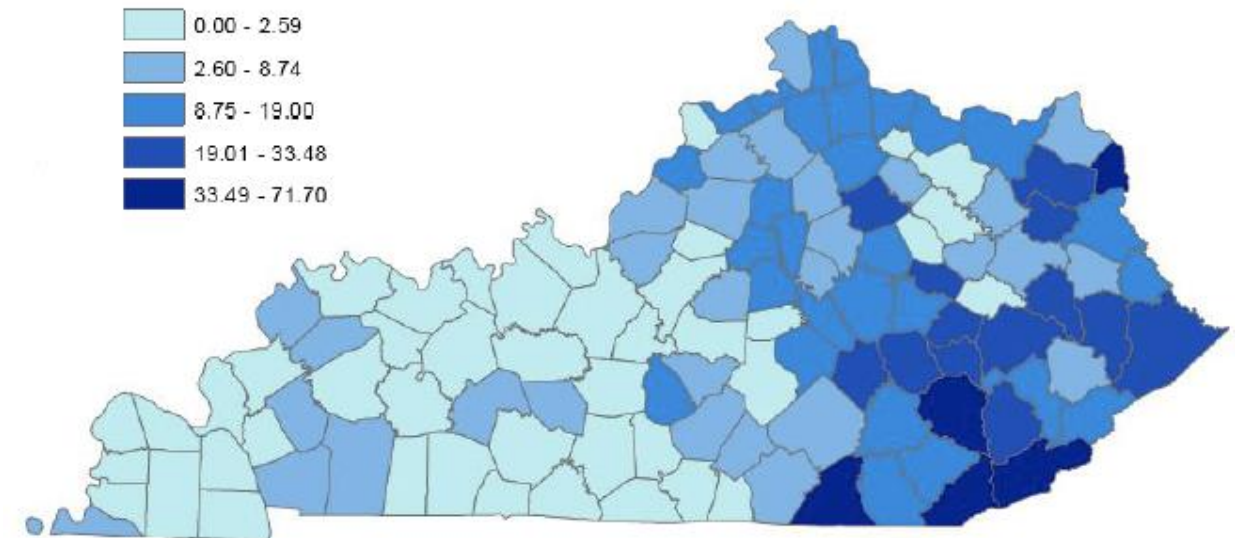
- 1998-2018, >70 million hospital admissions in the cohort resulted in delivery and 137,259 (0.20%) were HCV
- HCV infections in pregnant women increased 16-fold over 21-years from 0.34 to 5.3 cases per 1000 pregnancies
- HCV increased in all age groups
 - 22-folds in 18-20
 - 31-folds in 21-30
 - 8-folds in 31-40



KY Viral Hepatitis Prevention Program

- 2013, voluntary reporting of HCV positive pregnant women, their infants, and children <5 yr
- 2015 (Feb), mandatory reporting
- 2017 (May), expansion of harm reduction efforts
- 2018 (Jul), universal screening of pregnant women mandated

Rate of HCV infection among pregnant/post-partum women per 1000
(live births, by county – KY 2014-2016)



- 10.6 per 1,000 live births per KVHPP
- 19.3 per 1,000 live births per birth certificate data

Successful universal screening implementation

- Increased number of pregnant women with HCV risk factors in 2016 led to implementation of universal screening
- Implementation achieved by EMR (standing order)
 - *HCV Antibody at initial OB visit*
 - *HCV antibody may be repeated in the third (3rd) trimester at the discretion of the provider*
- HCV reflex RNA PCR for all antibody positive test

Hepatitis C virus testing in pregnant women

In May 2021, ACOG updated their recommendations: universal testing of all pregnant women is now recommended

Epstein & Espinosa. Clin Perinatol, 2021

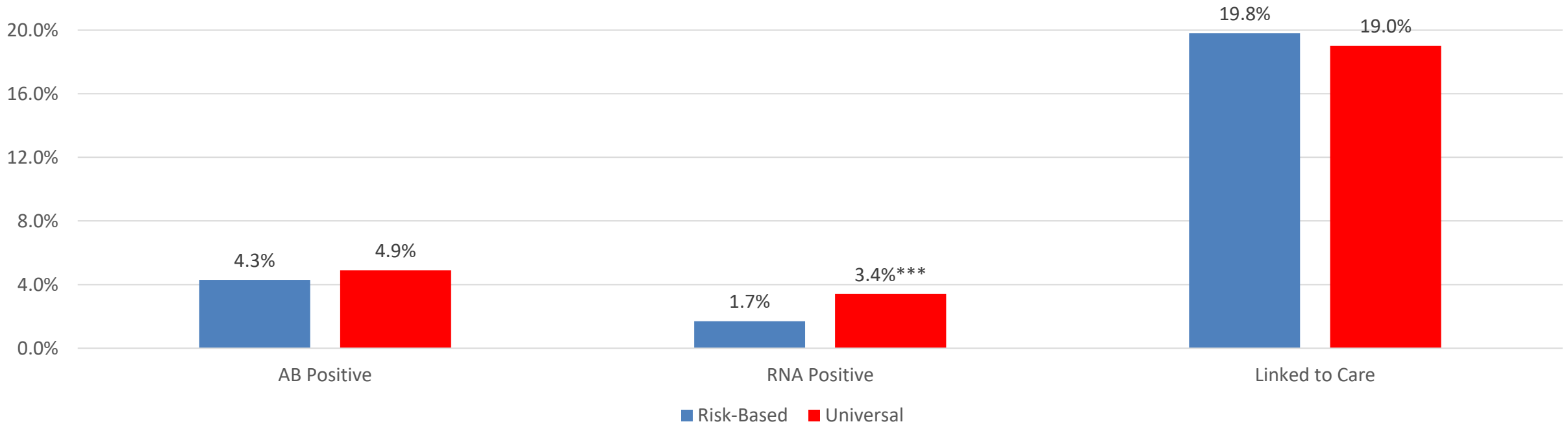
Table 1
HCV testing recommendations during pregnancy

Guiding Body	Recommendation	Year Updated	Source
US Centers for Disease Control and Prevention (CDC)	Test in each pregnancy, except if community prevalence <0.1%	2020	Schillie, ¹⁶ 2020
US Preventative Services Task Force (USPSTF)	Test all adults 18–79 years old once in their lifetime, consider in pregnant women <18 y, unclear benefit in low-risk pregnant women who have previously been tested	2020	Owens et al, ¹⁷ 2020
American Association for the Study of Liver Disease (AASLD)/ Infectious Diseases Society of America (IDSA)	Test in each pregnancy, ideally at the initial prenatal visit	2018	AASLD-IDSA HCV Guidance Panel, ¹⁸ 2018, AASLD-IDSA, ⁶⁰ 2020
Society for Maternal-Fetal Medicine	Test only if risk factors present, at first prenatal visit, and retest later in pregnancy if ongoing or new risk present	2017	Hughes et al, ²⁰ 2017
American College of Obstetricians and Gynecologists (ACOG)	Test only if risk factors present	2007 ^a	ACOG, ¹⁹ 2007

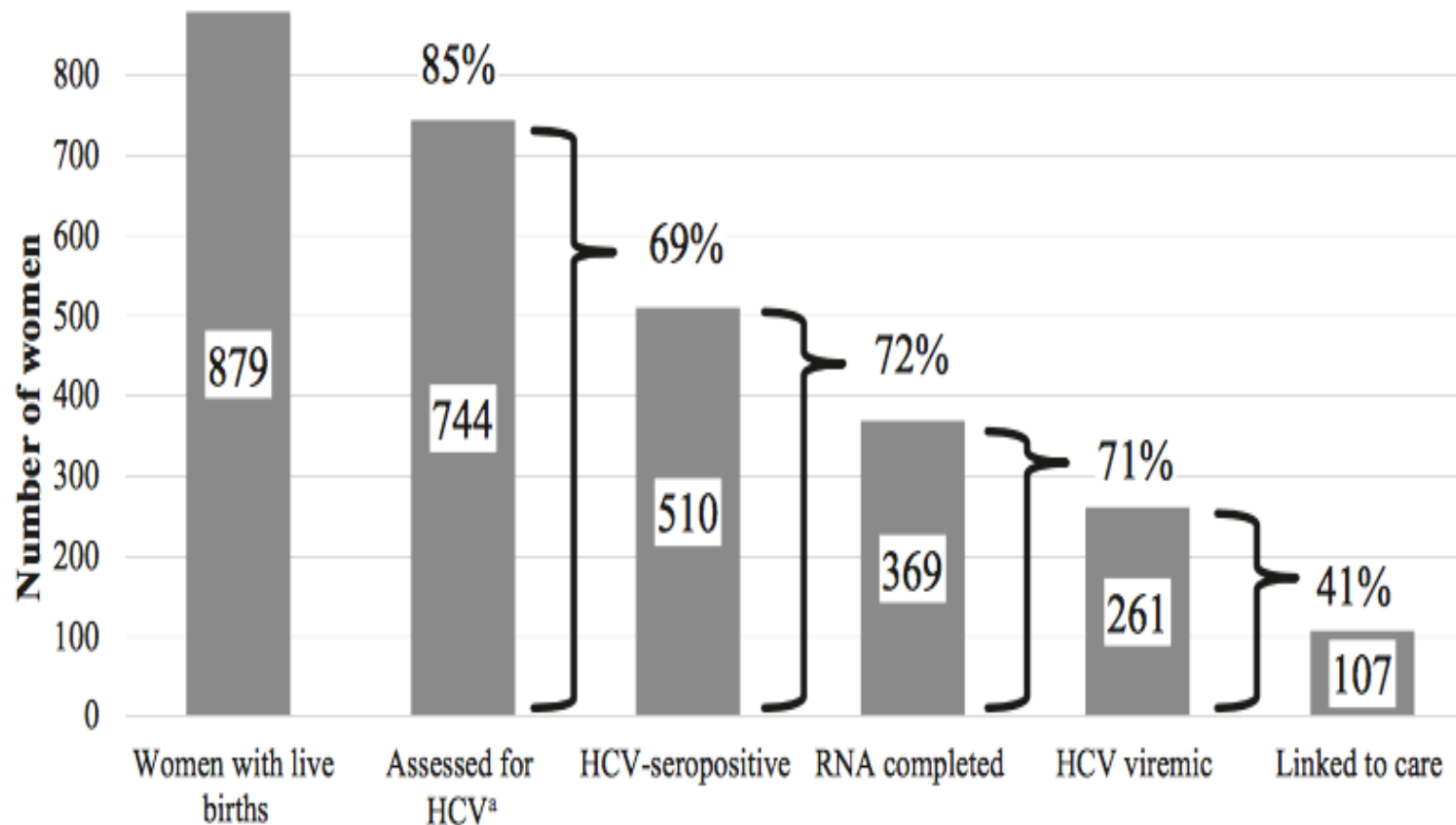
^a The ACOG website states that the organization is currently reviewing the CDC and USPSTF 2020 guidance, after which ACOG will issue updated guidance.²¹

Linkage to care

Proportion of Pregnant Women Who were AB Positive, RNA Positive, and were linked to HCV care Stratified by Time Period



Maternal cascade of care



- Percentage values at the top of each bar are conditional
- Assessed for HCV refers to history of HCV or completed HCV testing

Where we are?

- **DAAAs have revolutionized HCV treatment in adults, but currently there are not approved therapies for pregnant women**
- **A phase I clinical trial using ledipasvir/sofosbuvir in HCV infected pregnant women showed rapid achievement of undetectable HCV viral load and sustained virologic response without significant adverse events**
- **A phase I study with a pangenotypic DAA combination (sofosbuvir/velpatasvir) begun in October 2020 is expected to be completed by June 2023**

Where are we going?

- **Clinical trials hopefully will support the possibility of treatment during pregnancy, because this is a time that many women are engaged in health care services**
- **Treatment during pregnancy could be a key strategy to both decrease vertical transmission and eliminate maternal infection**
- **Pregnancy is still an opportune time to identify and to link women to care with the possibility of treatment after delivery to improve their own health care and decrease subsequent vertical transmission**



Where are we going?

**Elimination of hepatitis C in
children and adolescents**



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