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Indian Country ECHO

HCV in Pregnant Women: how the opioid crisis is changing the landscape

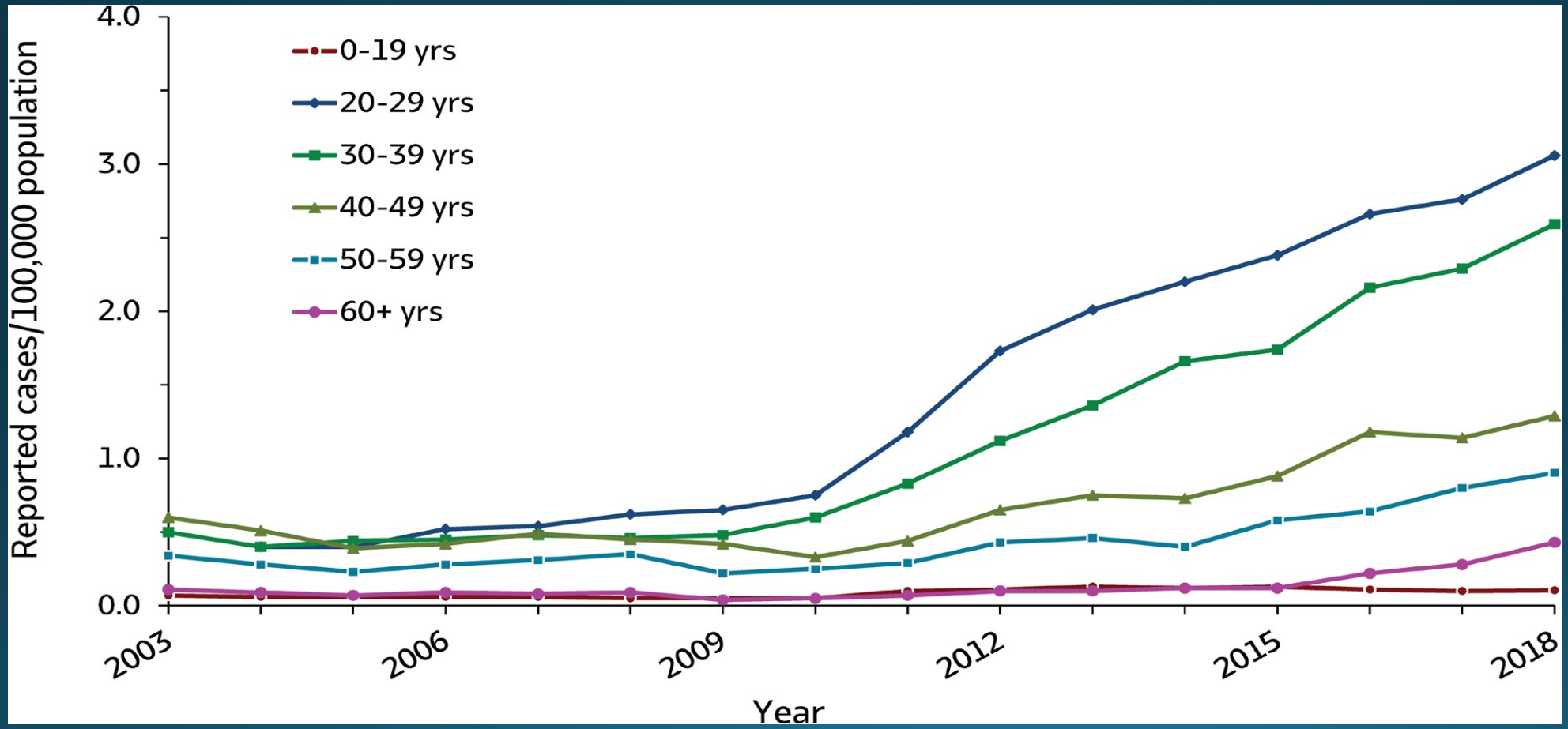
No Disclosures

- I have no financial relationships with commercial entities producing healthcare related products and/or services

Objectives

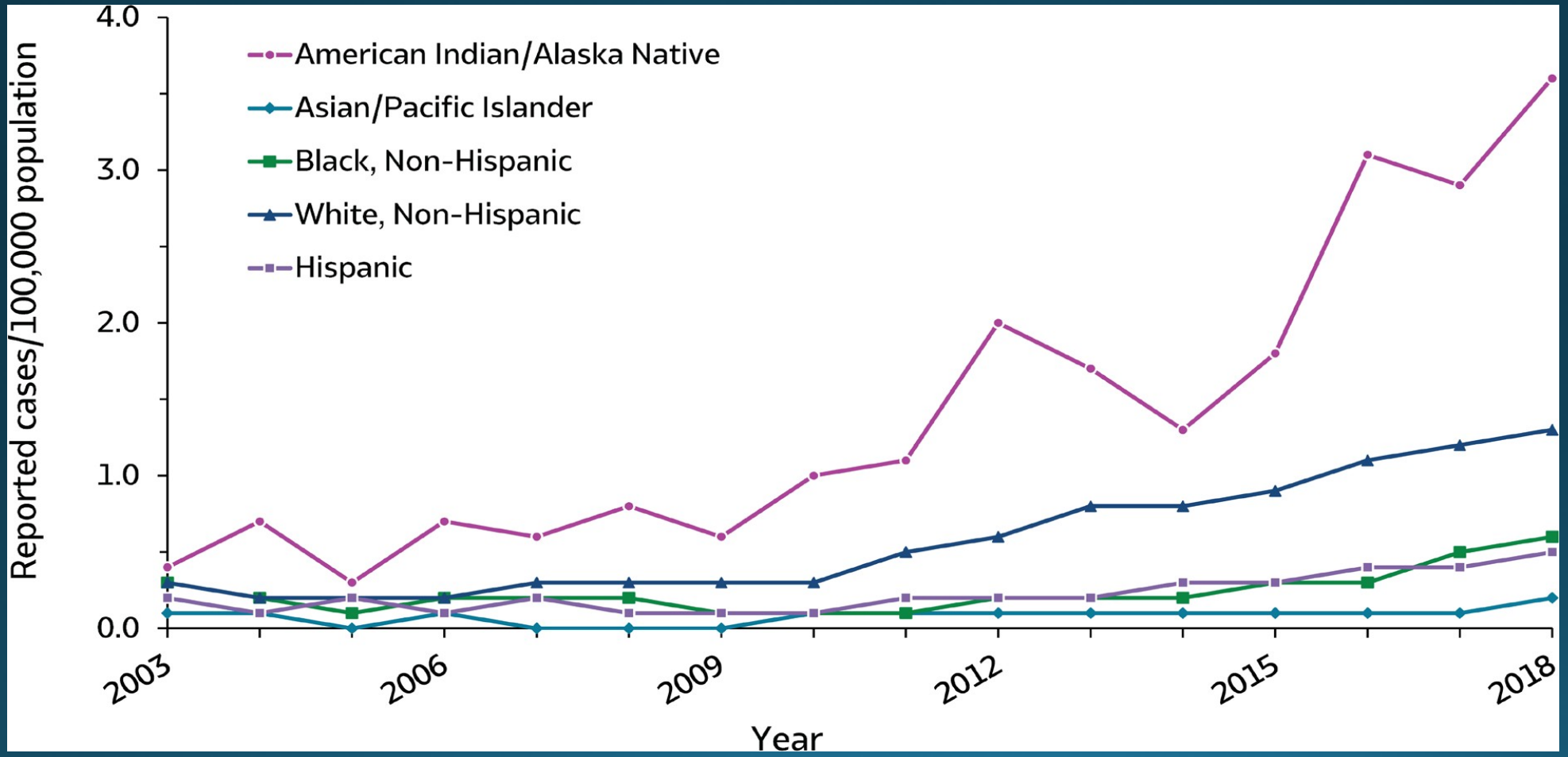
- Describe overall HCV infection trajectory in the U.S.
- Describe trends seen in HCV infection among pregnant women women and children
- Review Cascade of Care results of women and children with HCV exposure
- Review factors associated (or not) with perinatal transmission of HCV'
- Review recommendations for obstetric care providers for pregnant and parturient women with HCV

Figure 1 Rates of reported acute hepatitis C, by age group — United States, 2002–2018



Source: CDC, National Notifiable Diseases Surveillance System.

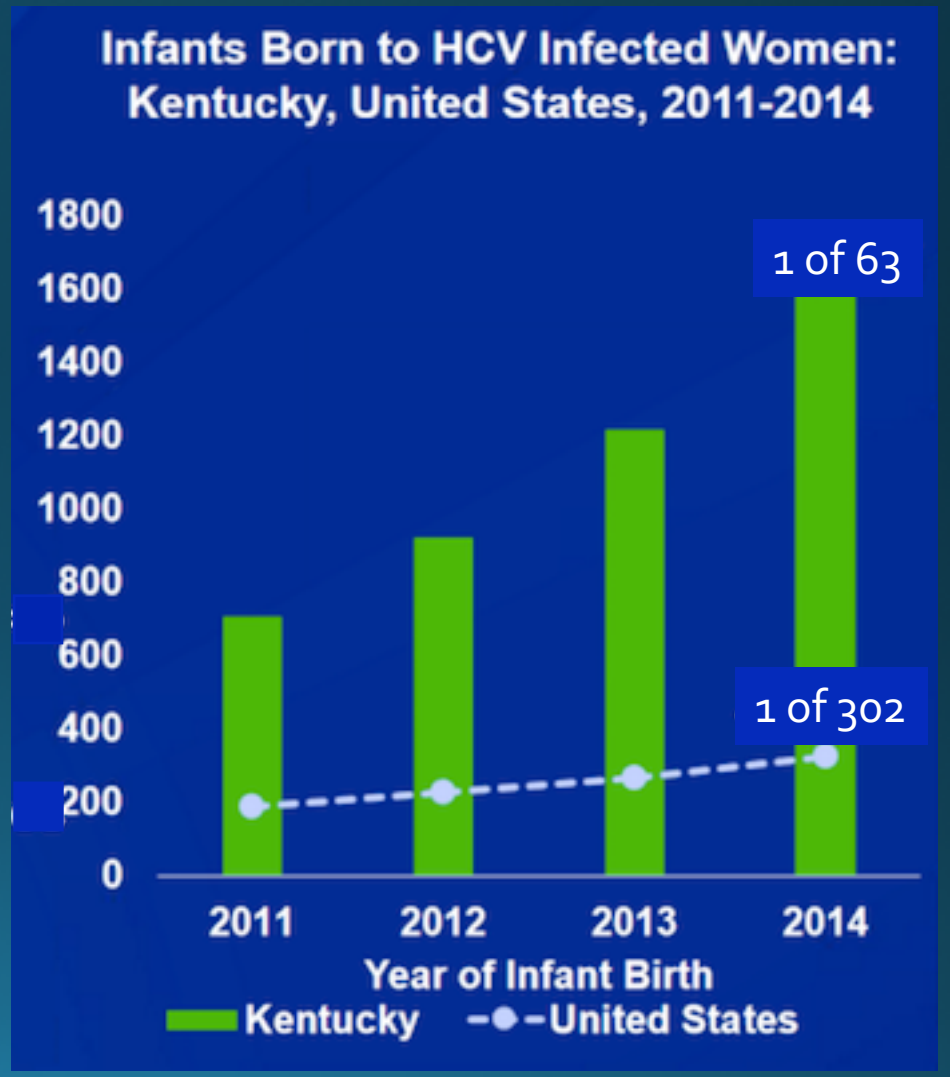
Figure 2. Rates of reported acute hepatitis C, by race/ethnicity — United States, 2002–2018



Source: CDC, National Notifiable Diseases Surveillance System.

HCV detection in women and testing in children 2011-2014[1]

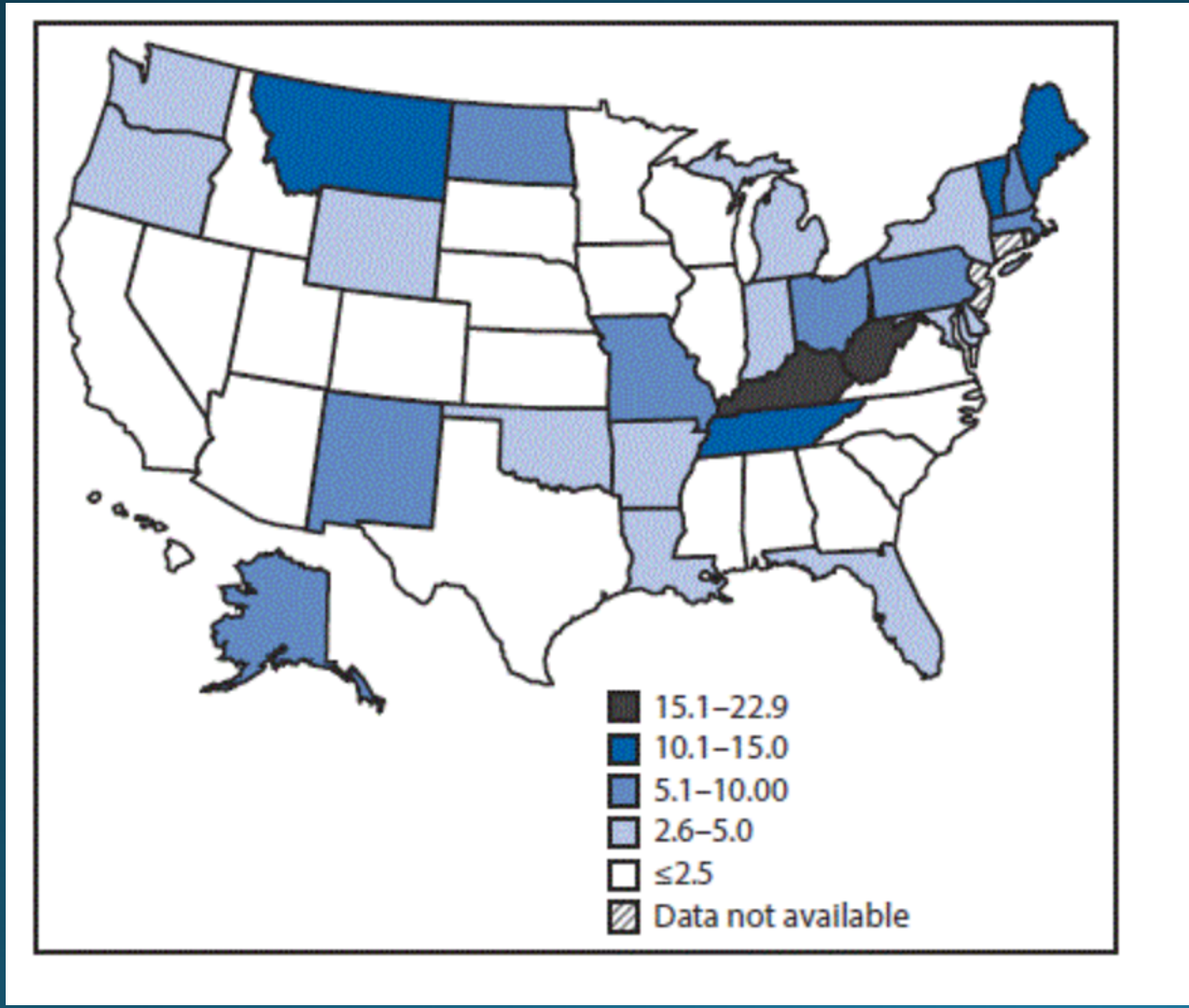
	National	Kentucky
HCV detection in women of childbearing age	22% increase From 139 to 169/100,000	213% increase from 275 to 862/ 100,000
HCV testing in children ages ≤2 years	14% increase From 310 to 353/100,000	151% increase from 403 to 1,011/100,000
% of infants born to HCV+ women	68% increase From 1/536 (0.19%) to 1/302 (0.32%)	124% increase from 1/142 (0.71%) to 1/63 (1.59%)



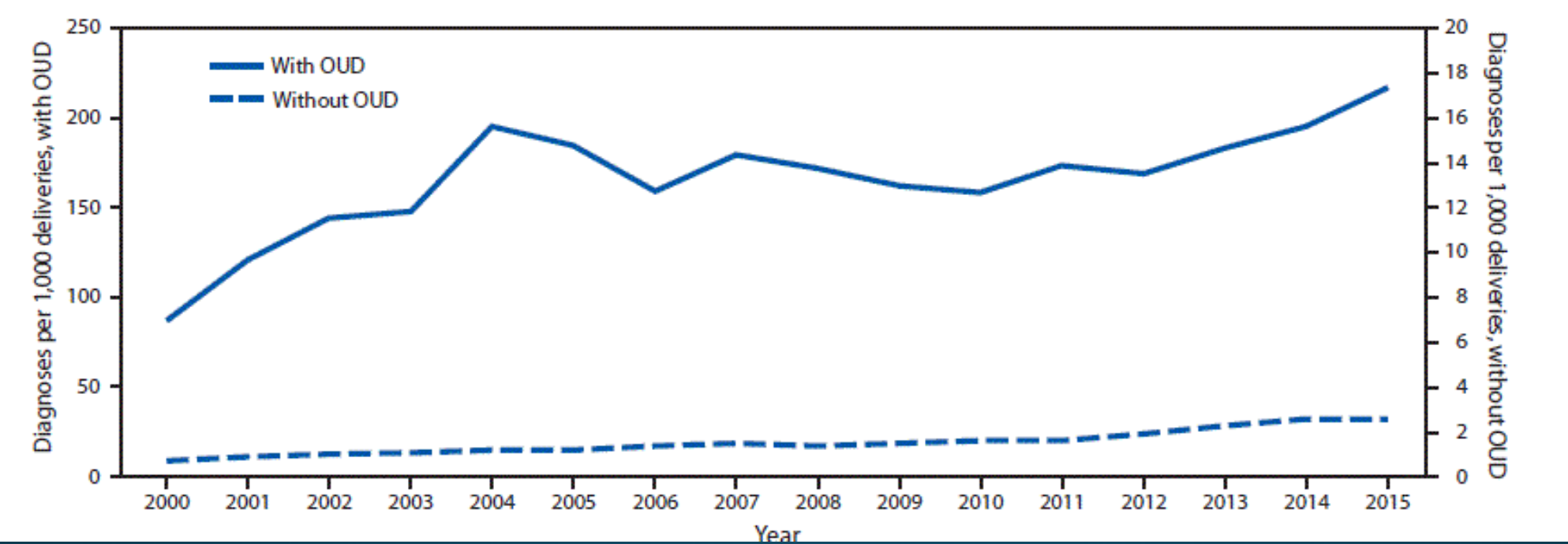
*HCV testing (anti-HCV or RNA in population served by Quest Diagnostics;

1.Koneru et al, MMWR 2016

During 2009–2014, HCV infection at delivery among pregnant women from states reporting HCV on the birth certificate increased 89%, from 1.8 to 3.4 per 1,000 live births.



Patrick et al., HCV Infection Among Women Giving Birth — Tennessee and United States, 2009–2014
MMWR 2017



- The national rate of HCV infection among women giving birth increased >400%, from 0.8 to 4.1 / 1,000 deliveries.
- Among women with OUD, rates of HCV infection increased 148%, from 87.4 to 216.9 /1,000 deliveries

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 68 / No. 39
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National Trends in Hepatitis C Infection by Opioid Use Disorder Status Among Pregnant Women at Delivery Hospitalization — United States, 2000–2015

Jean Y. Ko, PhD[1]; Sarah C. Haight, MPH[1]; Sarah F. Schillie, MD[2]; Michele K. Bohm, MPH[3]; Patricia M. Dietz, DrPH[2]

Diagnosis* of HCV (and OUD) was more likely in women:

- **Aged 24-34 years vs. ≥35 years :** OR = 1.2 (95% CI 1.0- 1.4)
  - Both HCV and OUD: OR = 1.8 (95% CI: 1.4–2.3).
- **Publicly insured vs. Private**: OR = 5.5 (95% CI 4.7–6.4)
  - Both HCV and OUD (OR = 9.9, 95% CI 7.8–12.6).
- **Native American vs. non-Hispanic Blacks** (OR 5.0, 95% CI 2.9–8.7)
  - And OUD: OR = 5.9 (95% CI = 4.0–8.8)
  - But Non-Hispanic Whites vs. Blacks more likely to have HCV and OUD: OR = 5.9 (95% CI 4.0–8.8).
- **Lower median income** (<$42,000 vs ≥$68,000):OR 2.5 (95% CI 2.0–3.0)
  - Both HCV and OUD: OR 2.5 (95% CI 1.8–3.4).

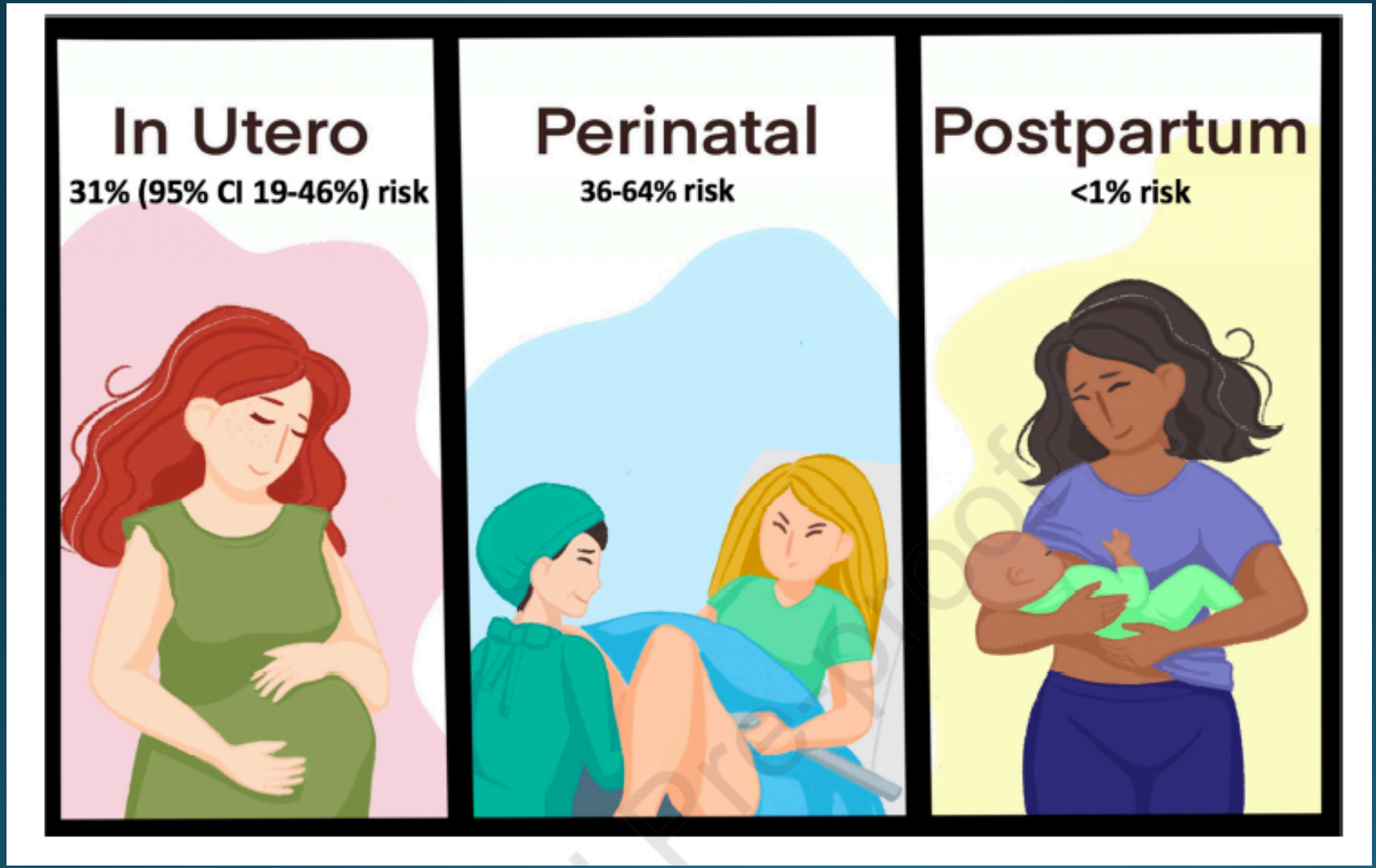
*At delivery

Perinatal transmission of HCV

- Transmission from HCV RNA+ mothers[1] (pooled risk)
  - HCV mono-infected: 5.8% (95%CI: 4.2%, 7.8%)
  - HCV/HIV co-infected: 10.8% (95%CI: 7.6%, 15.3%; AOR 2.56 (95%CI: 1.5, 4.5)
    - Lower risk of MTCT if HCV/HIV+ women are on ART (small observational samples: 3.6[0] 0-7%)
- Factors associated with increased risk of transmission
  - Viremia <6 log: 3.9%
  - Viremia ≥ 6 log: 14.3% ; OR 4.0 (95% CI 1.3, 12.4)[2]
  - Prolonged membrane rupture (>6 hrs): aOR 9.3 (95%CI 1.5, 180)[3*]
- Not associated with increased risk:
  - Breastfeeding[2#,] Internal fetal monitoring[2*], Cesarean vs. vaginal delivery[2^], Mothers age, parity, and HCV genotype[1;] Current/past injection drug use[4,5]
- **There is no current recommendation to prevent MTC HCV transmission**

1. Benova et al, (*SR and MA*) CID 2014; 2. Delotte J Mat-Fetal & Neonatal Med 2014; 3. Cottrell (SR and MA) Annals IM 2013 [# N=14 w/high heterogeneity;*2 studies; ^ small N w/conflicting results]; 4. Resti et al., JID 2002; 5. Azzari et al, J Med Vir 2008

Maternal to Child Transmission of HCV can occur during pregnancy (in utero) but is more commonly thought to occur in the peri-partum time period



(Mok et al. 2005),

A tale of two cohorts: the "Irish" and the "German" Anti-D cohorts:

- Rh negative women infected by HCV-contaminated anti-D immunoglobulin during 1970s
- Irish cohort (1977-79): 863 exposed; 682 (79%) infected women followed; 302 (45%) spontaneously cleared;
  - Median age at infection 28 years (range 17-44)
  - BABIES with chronic HCV: 3/380 chronic mothers =0.79%[1]
- German cohort (1978-79): 2867 exposed; 1980 (69%) followed; 883 (48%) spontaneously cleared; (66% of icteric women SC)
  - Median age at infection 24 years (range: 16-34)
  - BABIES with HCV: 3/132 chronic HCV mothers =2.27%[2]

1. Power et al, Lancet 1995; 2. Meisel et al., Lancet 1995

HCV in infants

- **Current recommendations is to test children for anti-HCV at ≥ 18 months of age (prior to which many may become lost to follow up.**
- Passive transfer of anti-HCV w/gradual loss by 18 months by majority (many by 12 mo.)[1]
- Clearance of viremia among children with transient RNA positivity occurs at the median age of 15 months. [2,3.]
- 95% of uninfected children lose maternal antibodies by 12 mo. [5]
- In addition to circulating HCV RNA, the presence of anti-HCV at ≥18 mo. has been used as a surrogate measure of infection[5].
- Can postpone testing for HCV RNA until age 3, as Rx is now approved

1. Yeung et al., Hepatology 2001; 2.Pembrey et al., CID 2005; 3. Polywka et al., J Med Virol 2006; 4. England et al., Acta Ped 2005; 5. Resti et al., Dig Liv Dis 2003

Hepatitis C Virus Screening Among Children Exposed During Pregnancy (Univ Pittsburg Medical Center)

- Between 2006 and 2014, 1043 (1.2%) HCV-infected pregnant women delivered, and HCV prevalence increased by 60%.
- **68% of pregnant women with HCV had opioid use disorder (OUD) (vs. 1% of HCV negative women)**
- Among 1025 HCV-exposed infants, 323 (31%) received well-child services, and among these, only 96 (30%) were screened for HCV.

Chappell et al., Pediatrics 2018

HCV in pregnant women in OAT programs: "cascade of care" outcomes

Author	Setting	N	Anti-HCV screened N (%)	anti-HCV +	HCV RNA test	HCV RNA +	Post-partum referral
Page et al, 2017	ABQ, NM: Milagro Clinic 2012-2015	190	178 (97%)	95 (53.4%)	94 (98.9%)	75.6%	*Not available*
Krans et al, 2016	Pittsburgh, PA: Magee Womens Hosp; 2009-2012	791	611 (77.2%)	369 (60.4%)	153 (25%)	*Not reported*	77.2% referred; 24.9% attended; 1.6% initiated Tx
Berkley et al., 2008	ABQ, NM. Milagro Clinic 2000-2006	371	300 (85%)	159 (53%)	26 (16%)	16 (61.5%)	5.5% referred; 1.9% of neonates referred

Hepatitis C Virus Screening Among Children Exposed During Pregnancy (Univ Pittsburg Medical Center)

- Among 1025 HCV-exposed infants - 323 (31%) received well-child services, and among these, only 96 (30%) were screened for HCV.
- Of 96 children 73 (76%) received an optimal initial HCV screening test.
- Suboptimal HCV screening evaluations for the remaining 23 children resulted because 11 (48%) anti-HCV tests were sent before 18 months of age and 12 (52%) HCV PCR tests were sent after 18 months of age

Chappell et al., Pediatrics 2018

Other complications and outcomes in HCV+ mothers and infants vs. HCV-neg

- Mothers:
  - Cholestasis (6.3% vs. 0%)
  - Pre-term delivery (24.5% vs. 14.9%)
- Neonatal
  - Birthweight <2500 g (32.9% vs. 17.1%)[1]
  - Lower gestational age (<37 weeks) [1, 2.]
  - Require NICU care[2]
  - Neonatal abstinence syndrome (88.4% vs. 36.4%)[1]

Table 3. Neonatal Outcomes and Complications

	Hepatitis C+ (n=159)	Hepatitis C– (n=141)	*P*
Birth weight (g)	2,803.6±623	2,942.9±581	.047
Birth weight less than 2,500 g	54 (32.9)	26 (17.1)	.002, .06*
Apgar score			
1 min	7.7±1.5	7.6±1.6	.57
5 min	8.8±0.8	8.7±1.0	.47
Gestational age at delivery	37.92±2.8	38.44±2.6	.09
NICU admissions	33 (20.8)	17 (12.1)	.045, .20*
IUFD	1 (0.01)	1 (0.01)	1.00
Withdrawal-methadone wean	95 (88.4)	33 (36.4)	<.0001

NICU, neonatal intensive care unit; IUFD, intrauterine fetal death.
Data are mean±standard deviation or n (%).

1Berkley et al., Obstetic Gyn 2008; 1. Chappell et al, Pediatrics 2019)

DAA treatment for pregnant women

- Recommended: for women of reproductive age with known HCV infection, antiviral therapy is recommended before considering pregnancy, whenever practical and feasible, to reduce risk of HCV transmission to future offspring.
- *Previously AASLD/IDSA recommended to avoid treatment – but now:*
- Despite the lack of a recommendation**, treatment can be considered during pregnancy on an individual basis after a patient-physician discussion about the potential risks and benefits.**
  - Safety data is limited (mostly animal studies), but reassuring
  - Trials underway

AASLD/IDSA: www. HCVguidelines.org

Conclusions

- HCV is increasing in many groups including women of childbearing age , and there are increasing N/% of infants born to HCV+ mothers
- Vertical transmission is the leading cause of childhood HCV infection
- No intervention has been clearly demonstrated to reduce the risk for mother-to-infant HCV transmission. Some may increase
- Identification of effective management strategies to reduce risk for transmission is an important clinical and public health concern
- Many gaps in follow up of women and children.
- Treatment of opioid use disorder should include screening and referral for related conditions such as HCV infection.

Society for Maternal Fetal Medicine recommendations for obstetric care providers

1) Screen women who are at increased risk for HCV by testing for anti-HCV at first prenatal visit. If anti-HCV negative, repeat later in pregnancy in women with persistent or new risk factors for HCV (eg, new or ongoing use of injected or intranasal illicit drugs) (GRADE 1B).
2) Screen HCV infected pregnant women for other sexually transmitted infections (GRADE 1B).
3) Counsel HCV infected women to abstain from alcohol (Best Practice).
4) HCV direct-acting antiviral treatment should be deferred to post-partum period (not currently approved during pregnancy (GRADE 1C), or only in the setting of a clinical trial.
5) If invasive prenatal diagnostic testing is requested, women be counseled that data on the risk of vertical transmission are reassuring but limited; amniocentesis is recommended over chorionic villus sampling given the lack of data on the latter (GRADE 2C).
6) Recommend against cesarean delivery solely for the indication of HCV (GRADE 1B).
7) Avoid internal fetal monitoring, prolonged rupture of membranes, and episiotomy in managing labor in HCV–positive women (GRADE 1B).
8) Do NOT discourage breast-feeding based on a HCV infection (GRADE 1A).

Society for Maternal-Fetal Medicine Am J Obt&Gyn 2017

Recommendations to fill gaps in care and knowledge

- Improve early identification of HCV-infected women of childbearing age, link-treat-cure, and avoid HCV infection during pregnancy, and prevent mother-to-child transmission
- Consider strategies and policies to increase HCV detection among women of childbearing age.
- Improve follow up care and monitoring of both mothers and children.
- All of these require more and better data.

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