DISCLOSURES

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Upon successful completion of this activity 1 contact hour will be awarded

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CONFLICT OF INTEREST

Paulina Deming is on an advisory committee for Gilead.

None of the other planners or presenters of this CE activity have any relevant financial relationships with any commercial entities pertaining to this activity.

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UNM HEALTH SCIENCES CENTER

Project ECHO HCV:

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

Figure 1 Percentage of all admissions to substance abuse treatment centers attributed to the injection of any opioid, prescription opioid analgesics, heroin, and all other drugs, by year—United States, 2004–2014

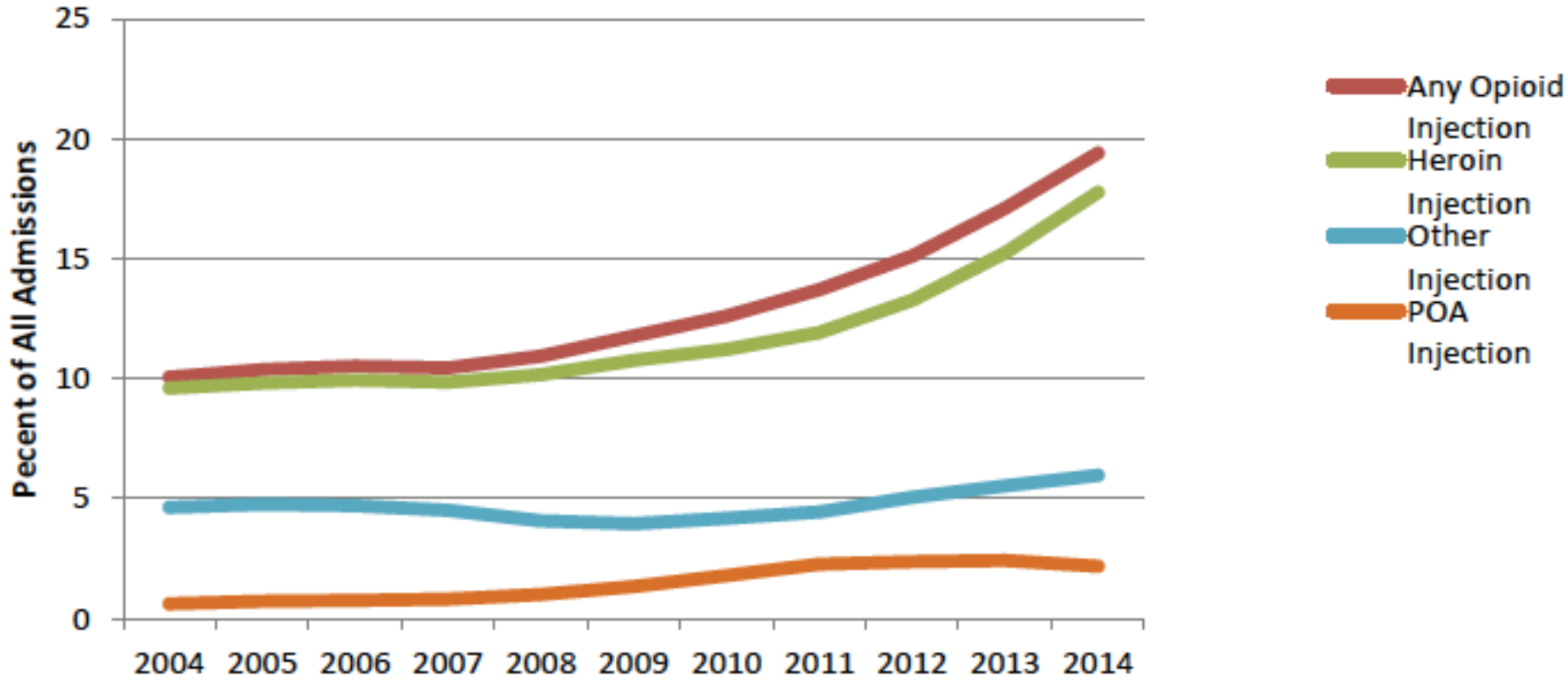


Figure 2. Percentage of all admissions to substance abuse treatment centers attributed to the injection of any opioid, by year and age — United States, 2004–2014

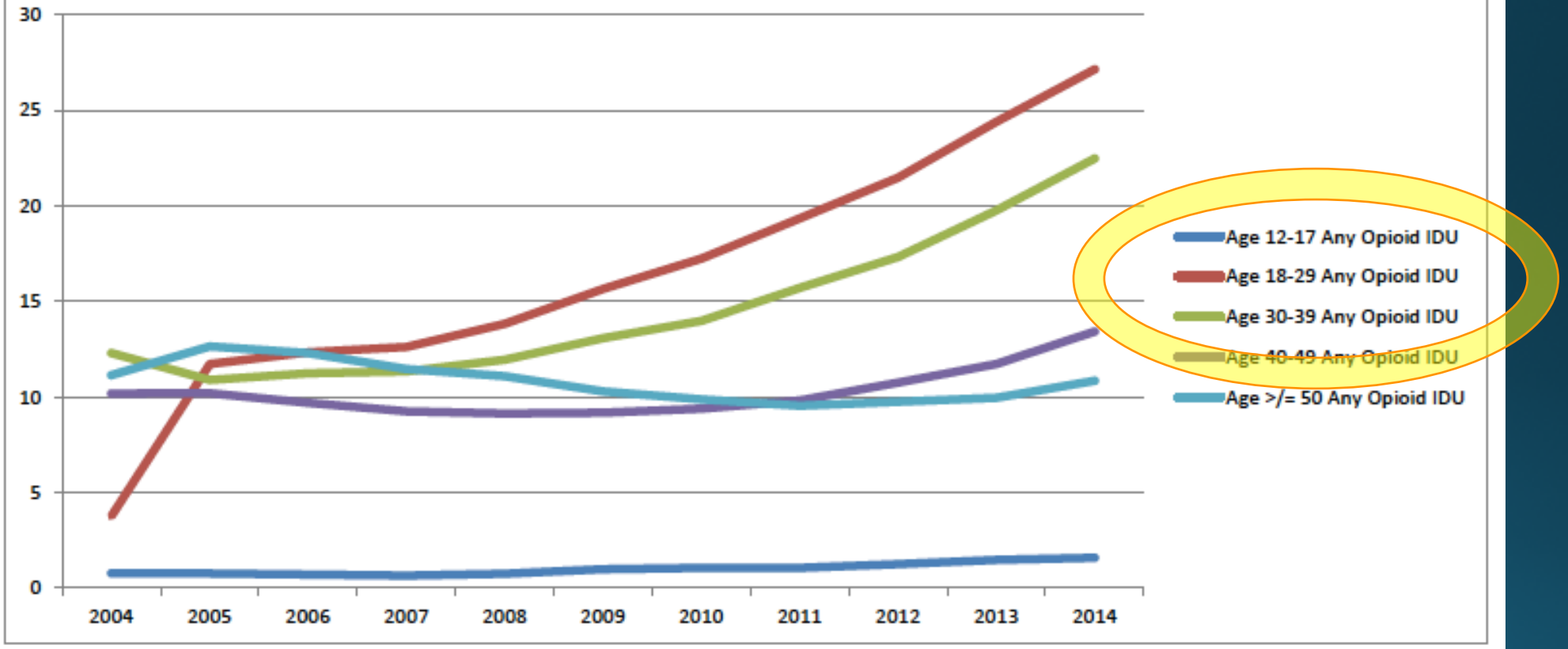


Figure 3. Percentage of all admissions to substance abuse treatment centers attributed to the injection of any opioid, by year and sex — United States, 2004–2014

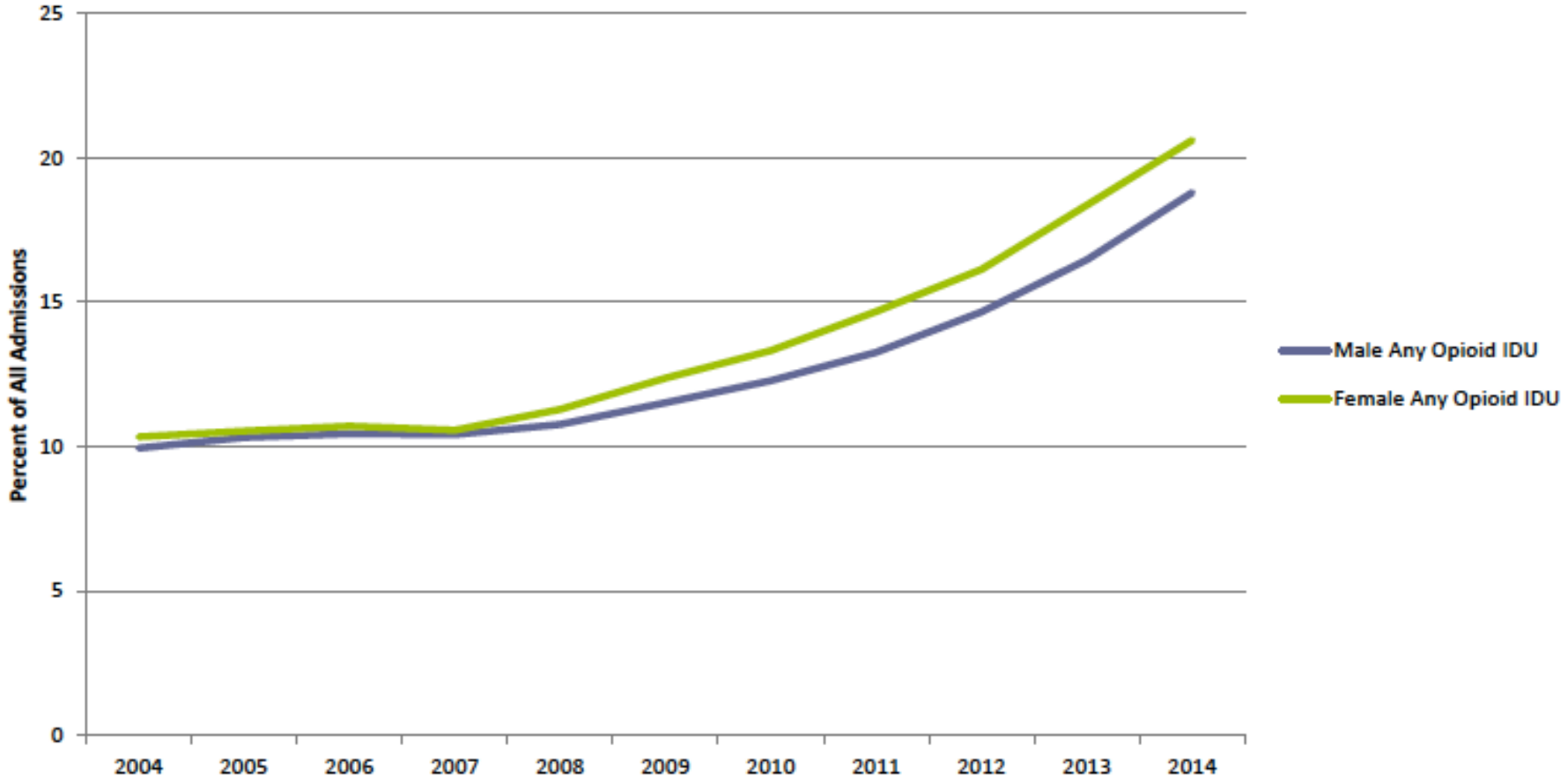


Figure 4. Percentage of all admissions to substance abuse treatment centers attributed to the injection of any opioid, by year and race/ethnicity — United States, 2004–2014

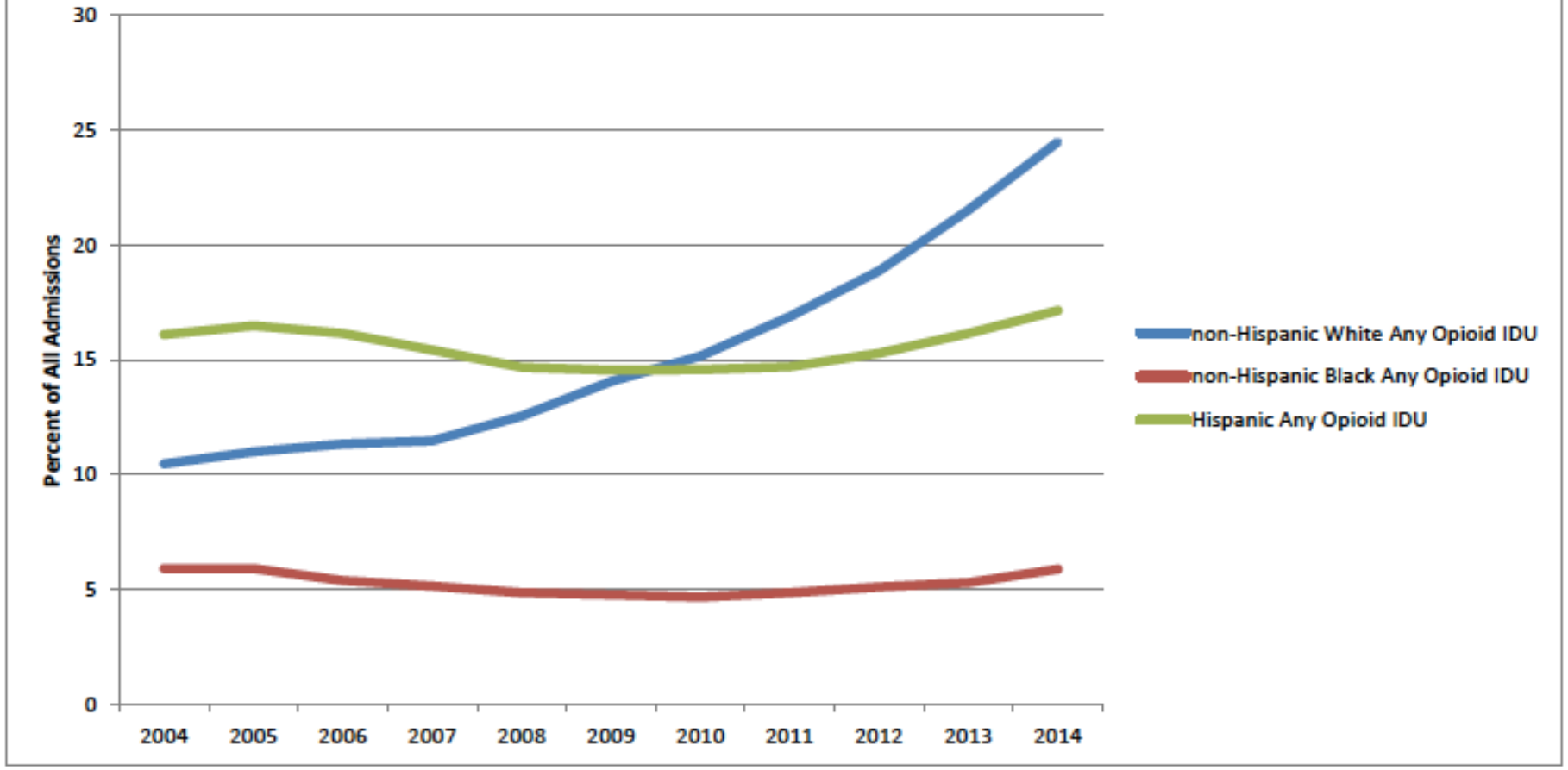
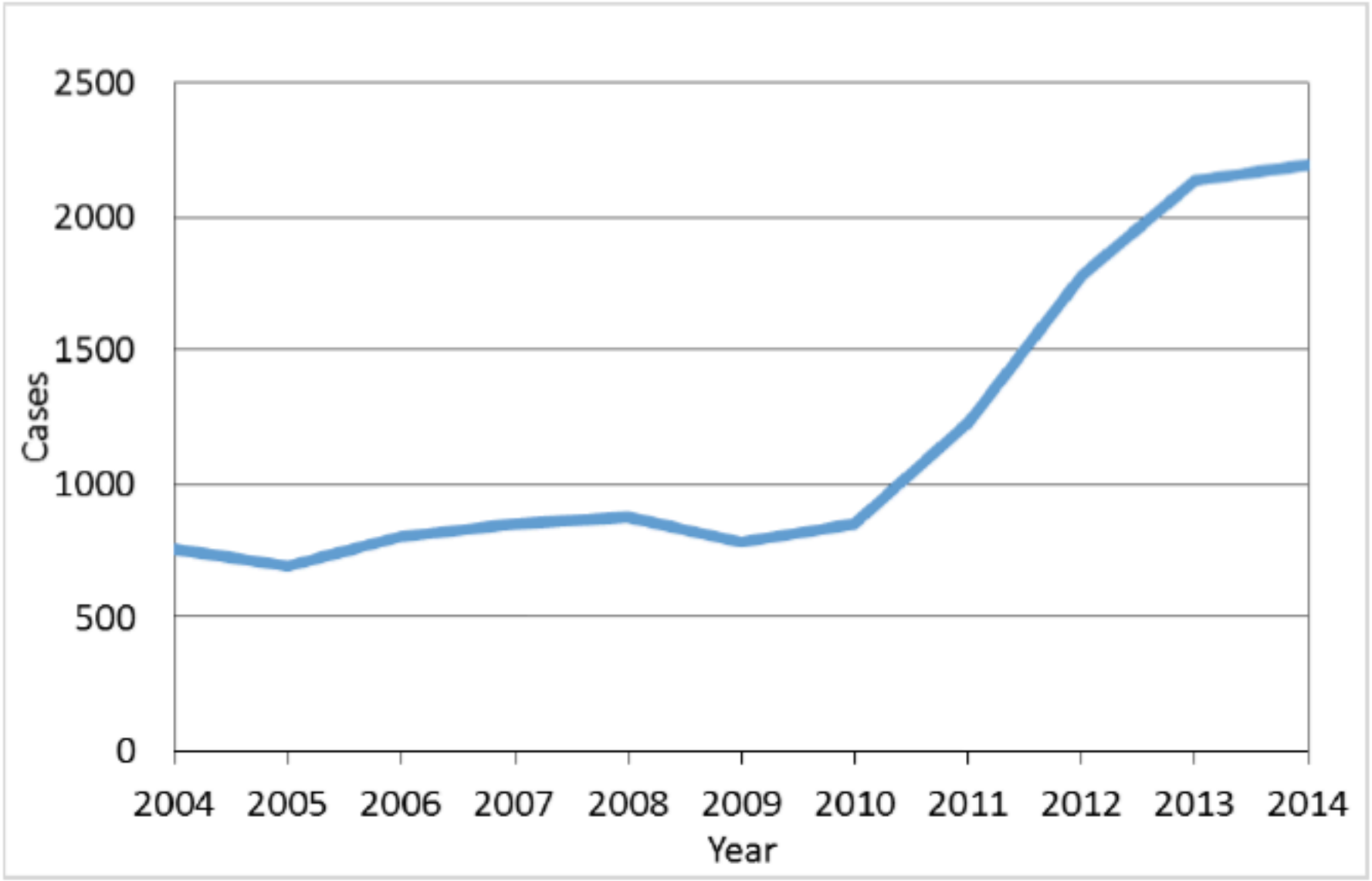


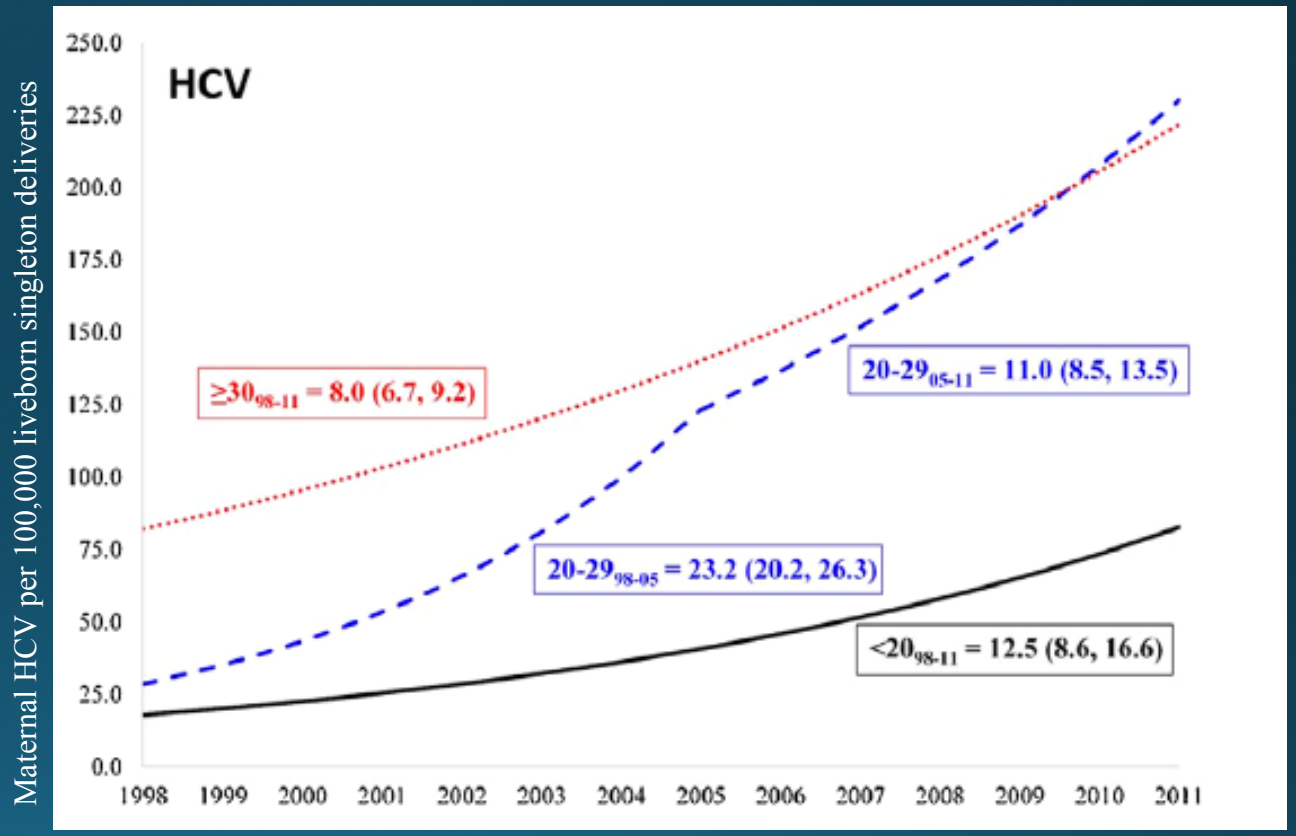
Figure 5 Reported cases of acute hepatitis C virus infection by year, United States, 2004-2014, NNDSS*



*National Notifiable Disease Surveillance System

U.S. Temporal Trends in the Rate of HIV, HBV, and HCV During Pregnancy, 1998-2011

- Inpatient hospitalizations for all liveborn singleton deliveries in the US between 1998 and 2011 from Nationwide Inpatient Sample.
- Annual average of 4,473 cases of maternal HCV.
- Maternal HCV rate was 118.6 per 100,000 deliveries, but higher for:
  - drug users (3,931.2),
  - HIV-positive mothers (2,764.9),
  - alcohol abusers (2,222.1),
  - tobacco users (965.7),
  - Women on Medicare/Medicaid (213.8)
- A ~5X increase in HCV/100,000 pregnancy: from 42.0 in 1998 to 210 in 2011.
- 50% to 75% decreased odds of HCV in racial/ethnic minority women compared to Non-Hispanic Whites.



Values expressed in boxes are the annual percent changes (95% CI). <20 years (solid black line); 20–29 years (dashed blue line); 30 years (dotted red line).

Salemi et al., J Med Vir 2016

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

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)
- 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;] IDU mediated by PBMC infection[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

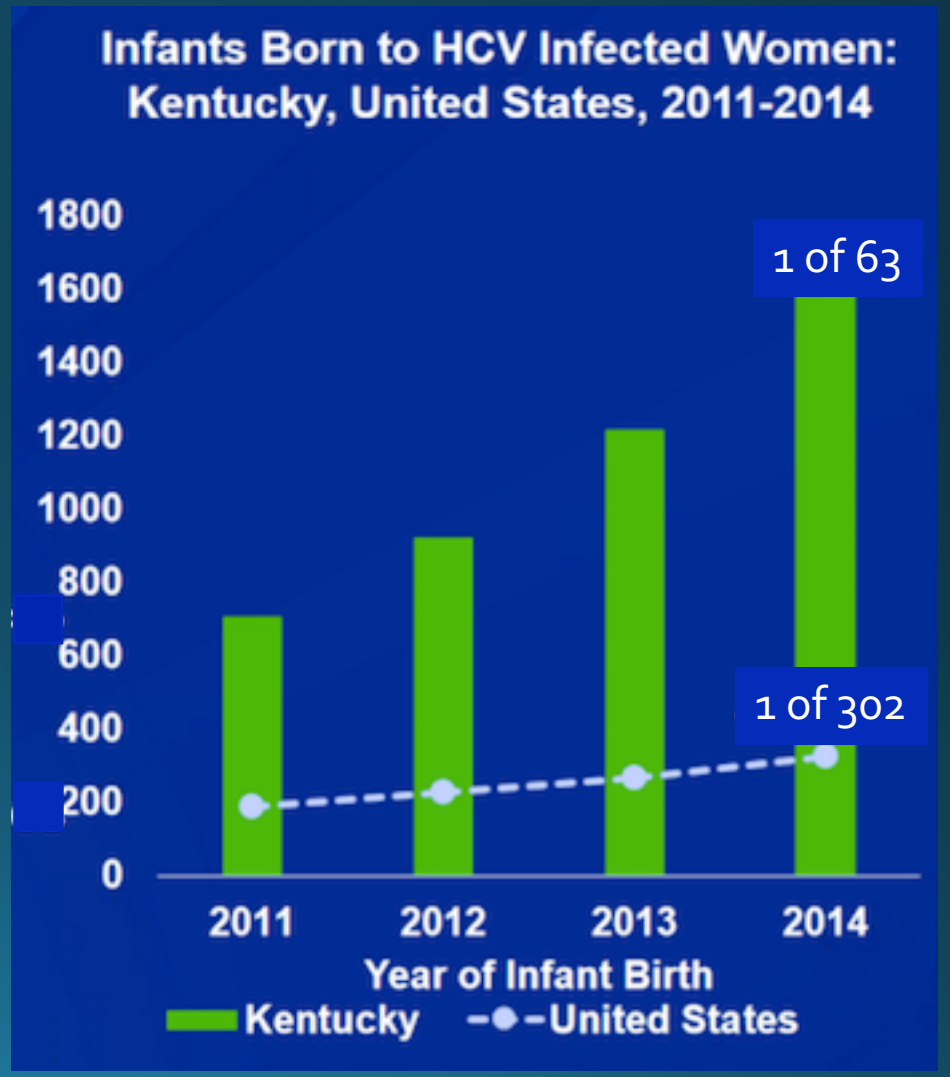
HCV in infants

- Passive transfer of antibody (anti-HCV) with 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 children diagnosed as uninfected lose maternal antibodies by 12 months of age[5]
- In addition to circulating HCV viremia, the presence of HCV antibodies at ≥18 months of age has been used as a surrogate measure of infection[5].

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

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

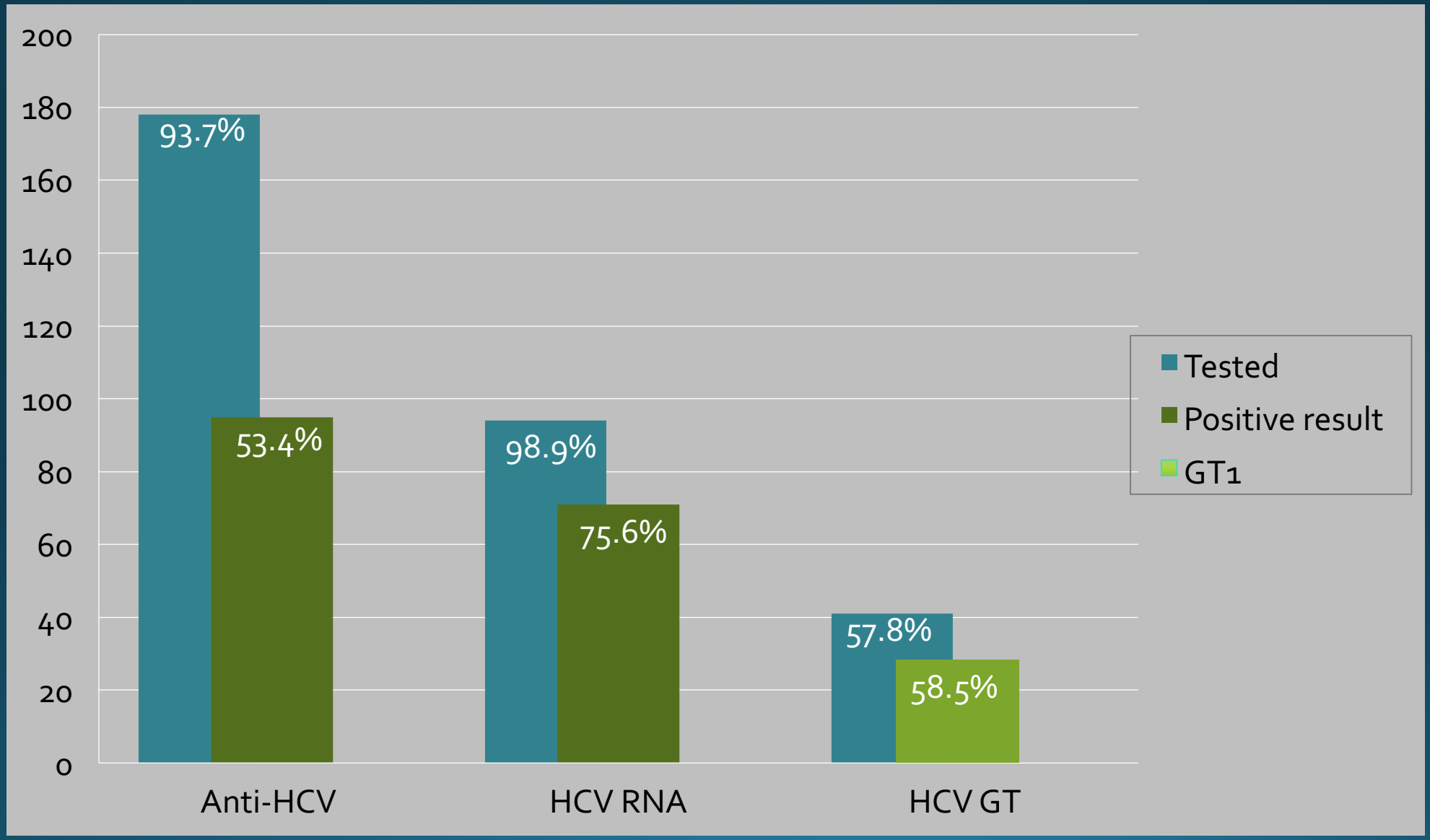
	National	Kentucky
HCV detection in women of childbearing age	22% increase From 139 to 169/100,000	213% increase from 275 to 862/ 100,000
HCV testing in children ages ≤2 years	14% increase From 310 to 353/100,000	151% increase from 403 to 1,011/100,000
% of infants born to HCV+ women	68% increase From 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

HCV testing in pregnant women on OAT pharmacotherapy at Milagro Clinic at UNM*

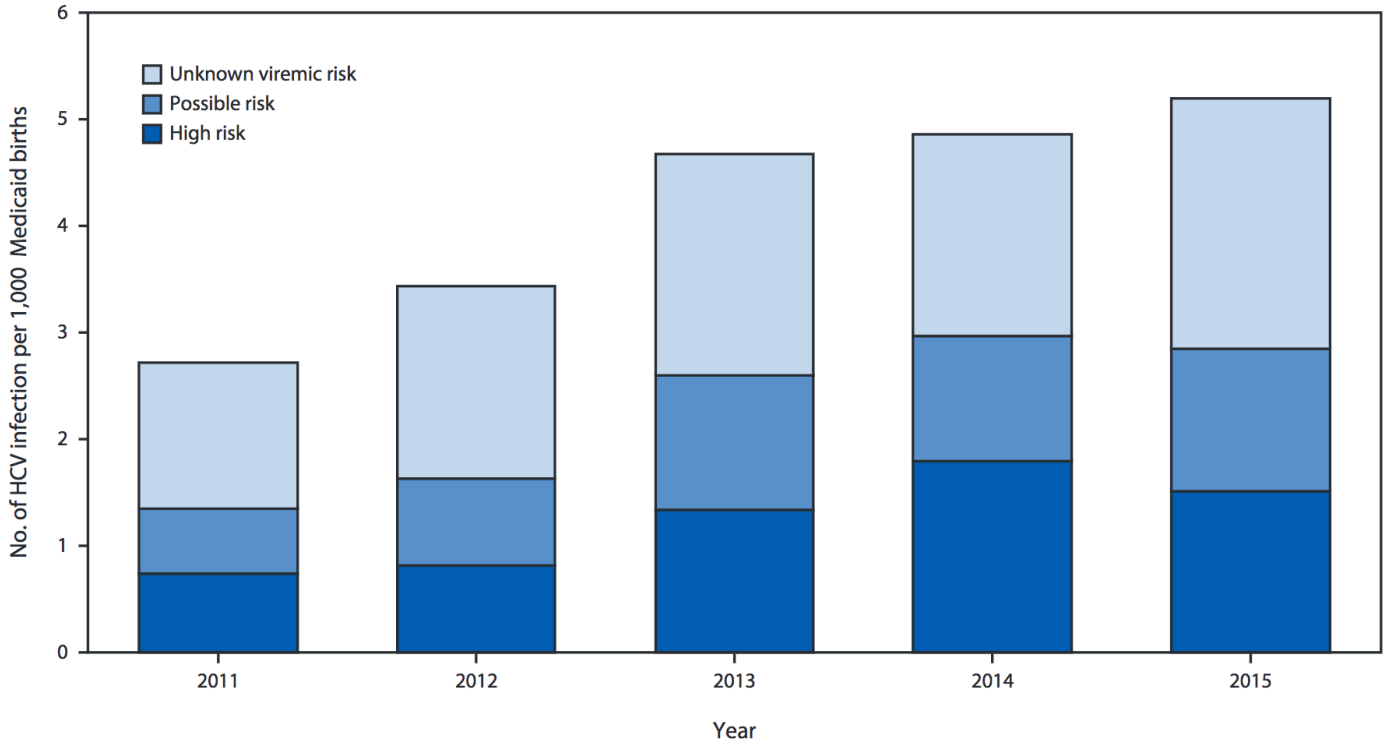


Page et al, Mat&Child Health J 2016

… and in Wisconsin

- 81% increase in HCV detection in 15–44 year olds (45.7 to 82.6/ 100,000)
- 43% women
- 93% increase in HCV in pregnancies (2.7 to 5.2 per 1,000) (= to 1/368 to 1/192)
- Among 183 infants born to HCV+ women with evidence HCV, 34% received recommended HCV testing.

FIGURE 2. Proportion of pregnant Medicaid recipients with evidence of hepatitis C virus (HCV) infection before delivery, by risk category* — Wisconsin Medicaid data and the Wisconsin Electronic Disease Surveillance System, Wisconsin, 2011–2015



* Unknown viremic risk = anti-HCV antibody-positive, but no viremia (RNA) results available; Possible risk = evidence of viremia before pregnancy, but no RNA results during pregnancy; High risk = evidence of viremia (RNA-positive) during pregnancy.

Watts et al., MMWR Oct 2017

HCV in pregnant women in OAT programs: "cascade" 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%	na
Krans et al, 2016	Pittsburgh, PA: Magee Womens Hosp; 2009-2012	791	611 (77.2%)	369 (60.4%)	153 (25%)		77.2% referred; 24.9% attended; 1.6% 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

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

- Mothers:
  - Cholestasis (6.3% vs. 0%)
  - Pre-term delivery (24.5% vs. 14.9%)
- Neonatal
  - Birthweight <2500 g (32.9% vs. 17.1%)*
  - Lower gestational age (37.9 vs. 38.4 wks)*
  - Neonatal abstinence syndrome (88.4% vs. 36.4%)

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 (%).

Berkley et al., Obstetic Gyn 2008; *controlling for methadone and tobacco

Conclusions

- HCV is increasing in many groups including women of childbearing age with risk exposures, 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.

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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  - John Ward, MD

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