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Failure to Test and Identify Perinatally Infected Children Born to Hepatitis C-Positive Women

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Summary:

A considerable number of HCV-positive women are giving birth, and most of their children are not being adequately tested for perinatal HCV. As a result, most chronically infected children are not identified and, therefore, unable to be linked to specialty care.

Abstract

Background: Vertical transmission of hepatitis C virus (HCV) is the most common route of pediatric HCV infection. Approximately 5% percent of children born to HCV-positive mothers develop chronic infection. Recommendations employ risk-based HCV testing of pregnant women, and screening children at a young age. This study assesses testing rates of children born to HCV-positive mothers in a major US city with a high burden of HCV infection.

Methods: HCV surveillance data reported to the Philadelphia Department of Public Health (PDPH) are housed in the Hepatitis Registry. Additional tests, including negative results, were retrospectively collected. HCV data were matched with 2011-2013 birth certificates of children ≥20 months to identify HCV-positive mothers and screened children. The observed perinatal HCV seropositivity rate was compared to the expected rate (5%).

Results: 8,119 females (12-54 years) were HCV-positive and in the Hepatitis Registry. Of these, 500 (5%) had delivered ≥1 child, accounting for 537 (1%) of the 55,623 children born in Philadelphia during the study period. Eighty-four (16%) of these children had HCV testing; four (1% of the total) were Confirmed cases. Twenty-four additional children are expected to have chronic HCV infection, but were not identified by 20 months of age.

Conclusion: These findings illustrate that a significant number of women giving birth in Philadelphia are HCV-positive and that most of their at-risk children remain untested. To successfully identify all HCV-infected children and integrate them into HCV-specific care, practices for HCV screening of pregnant women and their children should be improved.

Background

Vertical transmission (mother to infant) is the primary route of hepatitis C virus (HCV) infection in children. An estimated 40,000 children are born annually to HCV-positive women, resulting in up to 4,000 new perinatally infected children each year. [1-3] As the HCV infection rate among young people continues to increase as a result of the rise in injection drug use (IDU), a concomitant increase in the number perinatally infected children may be expected.[2, 4, 5] Pediatric HCV can impact cognitive development and the overall health of children, and may lead to more severe adverse outcomes including cirrhosis, hepatocellular carcinoma, and liver failure.[6-9]

The mechanism and risk-factors of vertical transmission are poorly understood, however extended exposure to maternal blood, elevated HCV viremia during pregnancy, and coinfection with human immunodeficiency virus (HIV) are shown to increase the risk of transmission.[10-14] While some infants spontaneously clear HCV infection before 18 months of age, the proportion of children who develop chronic infection after vertical transmission from HCV-positive/HIV-negative mothers is thought to be approximately 5%, though study results range from 1 – 11%.[10, 12-14]

Prenatal screening for HCV is not routine, in part because there are no proven clinical interventions that prevent or minimize vertical transmission, including elective caesarian section and treatments which are not approved for use during pregnancy (ribavirin is contraindicated and direct acting antivirals (DAA's) are not approved).[1, 11, 14, 15] While the American

Congress of Obstetricians and Gynecologists (ACOG) recommends HCV screening for pregnant women who have risk factors such as a history of injection drug use (IDU) and/or HIV infection, many patients remain unidentified using risk-based testing criteria.[3, 16] Failure to capture all HCV-infected pregnant women through risk-based screening has driven other countries, including Australia in 2013, to adopt universal prenatal HCV screening.[17, 18]

Since pediatric cases of disease are often asymptomatic, all children born to HCV-infected women should be tested to rule out vertical transmission.[19] Current guidelines from the American Association for the Study of Liver Disease (AASLD) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recommend that children born to HCV-infected women be tested for anti-HCV antibody (HCV-Ab) after 18 months of age; screening before this age is less reliable due to the possible presence of maternal antibodies. Any positive HCV-Ab result should be followed by a HCV ribonucleic acid (RNA) testto confirm that the child is infected.[19, 20] HCV RNA tests may also be performed after two months of age, with retesting after an additional two months, or performed one-time after 12 months of age.[21] Multiple tests may be needed because viral titers can fluctuate in the first year of life, though testing for HCV RNA earlier may assuage parental anxiety.[20]

Children who test positive for HCV RNA should be evaluated by a pediatric HCV specialist and considered for treatment (interferon-α and ribavirin are currently approved for children three years of age and older).[20] Treating HCV infection during childhood can prevent liver damage caused by long-term chronic HCV infection, has the advantage of improved adherence with parental supervision, and can limit secondary transmission that may occur as a result of risk

behaviors initiated during adolescence. However, adverse consequences of the current pediatric treatment regimen should be considered and may lead physicians to warehouse patients for improved regimens in the pipeline. [7, 20, 22, 23] While DAA's have not yet been approved for use in children, they are more tolerable and more effective in curing HCV infection in adults and will likely become available for children within a few years.[22]

The public health impact of perinatal HCV infection remains largely unexplored. In both Australia and Europe, studies have been conducted to assess effects of HCV in pregnant women, policies on perinatal HCV screening, and vertical transmission risks.[1, 14, 24-26] A 2012 analysis of National Health and Nutrition Examination Survey (NHANES) data found that only 4.9% of expected perinatally HCV infected children were identified in the United States (U.S.), and medical record review of the pediatric HCV cases in Florida revealed that less than 2% of known cases had received follow-up care.[27] Given the uncertain generalizability of NHANES estimates when used to approximate populations at high risk for HCV, the 2012 study likely underestimates the true burden of perinatal HCV infections. [1-3, 27] This study uses population-based surveillance data to estimate both the scale of perinatal exposures and the success of current testing recommendations for children born to HCV-positive women

Methods

Data Sources

All positive HCV-Ab, HCV RNA, and HCV genotype laboratory tests, and all negative HCV RNA tests results, performed on Philadelphia residents are routinely reportable to the

Philadelphia Department of Public Health (PDPH). They are stored in an electronic Hepatitis Registry and de-duplicated to the person level. For this study, additional negative HCV laboratory test results from 2011 – 2015 were obtained from major commercial laboratories and hospital systems in the Philadelphia region. Women with positive HCV-Ab, HCV RNA, and/or HCV genotype were included as HCV-positive, and those with a negative HCV RNA result were considered HCV-negative.

PDPH receives birth certificates for all births occurring within Philadelphia or to a Philadelphia resident. For this study, birth certificates were limited to children who were born to a Philadelphia resident during January 2011 – July 2013 and were at least 20 months of age (study period is January 2011-February 2015). This age restriction allowed at least two months for HCV testing to be performed and results to be reported to PDPH following the American Academy of Pediatrics' recommended 18 month well visit. Additional demographic and contact information for children included in the study was obtained from the Philadelphia Immunization Registry, a database housing all vaccinations performed in Philadelphia.

Data Matches

All matching methodology in this study utilized name and date of birth comparisons using the 'spedis' function in SAS Version 9.3® (SAS Institute, Cary, NC). Address information and manual review were used to verify matches.

To measure the number of children born to HCV-positive women, 2011-2013 birth records were matched to the Hepatitis Registry. The match yielded women who were HCV-positive and gave

birth during the time period. After the initial match, children listed as deceased or adopted on the birth certificate were excluded from the analysis due to the limitations to assessing the HCV testing they received.

Children born to HCV-positive mothers were subsequently matched to the Hepatitis Registry to assess whether they had been tested for HCV according to current guidelines. The final dataset was then matched to the Immunization Registry to obtain recent contact information. Children who were no longer Philadelphia residents were excluded from the analysis, since their HCV laboratory results would not be reported to PDPH.

Case Definitions

Children with an HCV-Ab test performed after 18 months of age or an RNA test performed after 12 months were adequately tested according to current guidelines, and were defined as Confirmed Perinatal cases if the result was positive.[21] Children who received one positive HCV-Ab test before 18 months, or one positive HCV RNA test before 12 months and no follow-up tests after an additional two months were inadequately tested and defined as Probable Perinatal cases. Children with a positive HCV-Ab test and a negative HCV RNA test after 12 months were defined as Uninfected. An infant with no test results was considered untested. Those children who were tested, but whose testing did not follow AASLD/NASPGHAN guidelines were considered inadequately tested.

Analysis

The expected number of Confirmed Perinatal cases in Philadelphia was calculated by applying the predicted proportion of children with perinatal HCV born to HCV-positive/HIV- negative women (5%) to the number of HCV-positive women who gave birth. Since mothers' HIV status was unknown in this study, the more conservative HIV-negative vertical transmission estimate was used. The number of undiagnosed children with perinatal HCV infection was calculated by subtracting the number of Confirmed Perinatal cases from the expected number of cases. Given that ~ 30% of HCV-Ab positive women who lack a reported HCV RNA test may be HCV RNA-negative, a lower limit of perinatally infected children was calculated using 70% of the HCV RNA-unknown women.

Maternal demographic and clinical information, including race/ethnicity, marital status, education history, insurance, and child gender was extracted from the birth certificates. Univariate analysis was used to compare demographic and testing information for mothers who gave birth during 2011-2013 and matched with the HCV Registry (known HCV-positive) to those who did not match or had a negative RNA (unknown HCV infection status or HCV-uninfected). Variables found to be associated with HCV positivity in univariate analyses (with $p<0.20$) were included in an initial multivariate model. The final model was adjusted for potential confounding and variables were retained via backwards selection using likelihood ratio tests significant at p-value<0.05. All odds ratios were weighted for hospital of birth to adjust for geographic and provider-specific variations. All analyses were conducted using SAS.

Institutional Review Board

This study was reviewed and approved by the Philadelphia Department of Public Health (PDPH) Institutional Review Board.

Results

From January 1st, 2011- July 1st, 2013, Philadelphia residents gave birth to 55,623 children (Figure 1). The maternal age at birth ranged from 13 - 54 years (Table 1). The Hepatitis Registry contained 8,119 women in the same age range with a positive HCV infection status (Figure 1). Date of first laboratory report for these women ranged from 1998 to the study period. The original match between these data sources yielded 568 children born to HCV-positive women, of whom 5.5% (N=31) had died or moved at the time of analysis, and were subsequently excluded (Figure 1). The final match indicated that 4.6% (N=500) of women in the Hepatitis Registry gave birth to 537 children during the study period (Table 1, Figure 1), 57% of whom had no known HCV RNA result.

Births during the study period to women who were not HCV-positive were significantly different than the 1% (537/55,623) of births to mothers who were HCV-positive. In both univariate and multivariate models, births to HCV-positive mothers had higher adjusted odds of being to white, older, less educated, publically insured, and unmarried women than to mothers without a positive HCV test result (Table 1). Retention of multiple births (sequential or non-singleton) by mothers did not significantly change the results of these analyses (data not shown). Of the births to mothers known to be HCV-positive, 20.3% (n=109) had received an HCV test during their

pregnancy, though testing in pregnancy had no effect on the likelihood of their child being tested for HCV (data not shown).

At the time of this analysis, PDPH had received an HCV test result for 84 children (16%) who were born to HCV-positive women in the Registry (Figure 1, Table 1, Figure 2). Of these, 38 (45%) were adequately tested and four (5%) were identified as Confirmed Perinatal cases (all HCV-Ab and HCV RNA positive) (Figure 2). An additional four children were identified as Probable Perinatal cases (all tested HCV-Ab positive before six months of age with no follow-up testing) that will require further testing to confirm infection. Two of the Confirmed Perinatal children were born to women with no reported RNA result, three were born to mothers who were not tested for HCV during pregnancy, and one to a woman who was reported for the first time after childbirth (data not shown). There were 34 adequately tested children classified as Uninfected, including four with HCV-Ab positive and HCV RNA-negative test results after 18 months of age who are thought to have spontaneously cleared the infection.

Using the 5% vertical transmission rate, an estimated 27 children of the 537 births to HCV-positive mothers are expected to be chronically infected with HCV (Figure 1). Given that four (15%) are Confirmed Perinatal children, 23 (85%) children remain unidentified and may be living with chronic HCV infection (Figure 1). The lower limit for the estimate of children perinatally infected with HCV is 22 (4%), which would leave 18 (82%) of children unidentified.

Discussion

This study demonstrates that a notable number of HCV-positive women are giving birth in a major US city, and the majority of their children, 84% (N=181 per year), are not being adequately tested for HCV infection. As a result, most chronically infected children are unidentified and therefore unable to be linked to specialty care. These findings support the 2012 analysis that highlighted a nationwide failure to identify HCV Ab-positive children.[27] The delay in identifying pediatric HCV infections can elevate a child's risk of developing adverse health consequences of prolonged infection, increase secondary transmission, and result in higher health care costs.[7, 23]

HCV-positive mothers in this study show evidence of being socioeconomically disadvantaged: more likely unmarried, less educated, and publicly insured than mothers without a reported HCV positive result. Infected mothers were also nearly eight times as likely to be white, an observation that correlates with the nationwide increase in HCV infection among young non-Hispanic white injection drug users.[4] Barriers to HCV-specific care within this population have been well identified and include a lack of knowledge about the severity of the infection, inadequate insurance coverage, limited access to HCV care, and ineligibility for treatment.[28, 29] As a result of these barriers and the limits of risk-based testing, it is likely that there are many more HCV-infected mothers in Philadelphia who have not yet been identified.[16, 30] While there are currently no interventions that can prevent a woman with HCV from perinatally transmitting to her children, screening pregnant women for HCV infection is critical to ensuring that exposed children are tested for HCV infection. Prenatal care also provides an opportunity to identify HCV infected women not regularly engaged in the healthcare system.

There are multiple explanations for the considerable gap in the testing of children born to HCV-positive women. First, screening of pregnant women for HCV is not routine in prenatal care and HCV-related risk factors may not be regularly ascertained; thus opportunities for an active dialogue between infected mothers and their healthcare providers are missed. Indeed, there is a need for increased physician education about HCV infection in general, including prevention, early detection, and current therapies.[30, 31] Secondly, women may be unaware of the severity and transmissibility of their HCV infection and therefore not disclose their status to their obstetrician. Education about the importance of HCV-related medical care for mother and child must be effectively communicated to women at all points of care. Third, pediatricians may not be alerted to a mother's HCV infection status from the obstetrician, birthing hospital, or mother, therefore preventing adequate testing from being initiated.[19, 20] Further, pediatricians may be waiting until a later age to test children for HCV, however children in this study born in 2011 were tested at statistically the same rate as those born in 2013 (data not shown). Lastly, many pediatricians may be unaware or skeptical of the guidelines for testing children exposed to HCV. This study showed that even when performed, testing often did not adhere to current guidelines.. Wide-spread education of pediatricians on the adequate testing recommendations and a review of the national guidelines may be warranted. Without improved communication between primary care providers, obstetricians, pediatricians, and HCV-infected mothers, children are likely to remain untested.

This study has a few limitations. Surveillance-based research relies on the reporting of laboratory test results. While additional data were obtained to more accurately assess HCV testing among

both mothers and children, it is likely that some missing data still exists. Another limitation is the absence of maternal HIV status in this study. Since HCV-HIV co-infection increases the risk of perinatal transmission, our analysis likely underestimates the number of children perinatally infected with HCV during the study period. It is also likely that there are women infected with HCV who were unreported to PDPH or who remain untested as evidenced by children identified in this study with no PDPH record of maternal infection (data not shown). Inclusion of these women would further increase the number of potential children with perinatal HCV infection. Given the wide range of published perinatal transmission rates resulting from differences in study design and populations,[10] it is possible that the true expected number of HCV-infected children may differ from study estimates. Finally, the up to 30% of HCV-positive mothers with unknown RNA status may include some women who would have tested HCV RNA-negative. Inclusion of HCV Ab-positive mothers with unknown RNA status was important because many high-risk groups may only be tested in environments where HCV RNA testing is not offered, such as methadone clinics and drug rehabilitation facilities. Two of the Confirmed Perinatal cases were born to women with unknown RNA status and the perinatal transmission estimate adjusted for HCV RNA-negative mothers was still noteworthy.

It is important for both patients and providers to be aware of the risks of vertical HCV transmission, and to understand the steps required to identify children perinatally infected with HCV. This study showed that a notable number of births are occurring to HCV-positive women but that a gap exists in testing of perinatally-exposed children. As a part of standard healthcare, women should be encouraged to communicate their HCV infection statuses to relevant providers. In addition, healthcare providers of mother and child must communicate with each other and

adequately test every child who is exposed to HCV. Identifying children with perinatal HCV infection and introducing them to specialty care and eventual treatment and cure is imperative to their comprehensive wellbeing. Further efforts should ascertain the reasons for the gap in testing of children born to women with HCV infection and guide future research and policy discussions surrounding the care of HCV-infected women and their children.

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References

1. Cottrell EB, Chou R, Wasson N, Rahman B, Guise JM. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med **2013** Jan 15;158(2):109-13.
2. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med **2006** May 16;144(10):705-14.
3. Prasad MR, Honegger JR. Hepatitis C virus in pregnancy. Am J Perinatol **2013** Feb;30(2):149-59.
4. Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged </=30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. MMWR Morb Mortal Wkly Rep **2015** May 8;64(17):453-8.
5. Suryaprasad AG, White JZ, Xu F, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. Clin Infect Dis **2014** Nov 15;59(10):1411-9.
6. Rodrigue JR, Balistreri W, Haber B, et al. Impact of hepatitis C virus infection on children and their caregivers: quality of life, cognitive, and emotional outcomes. J Pediatr Gastroenterol Nutr **2009** Mar;48(3):341-7.
7. Rumbo C, Fawaz RL, Emre SH, et al. Hepatitis C in children: a quaternary referral center perspective. J Pediatr Gastroenterol Nutr **2006** Aug;43(2):209-16.
8. Nydegger A, Srivastava A, Wake M, Smith AL, Hardikar W. Health-related quality of life in children with hepatitis C acquired in the first year of life. J Gastroenterol Hepatol **2008** Feb;23(2):226-30.

9. Robinson JL, Doucette K. The natural history of hepatitis C virus infection acquired during childhood. Liver Int **2012** Feb;32(2):258-70.

10. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. Clin Infect Dis **2014** Sep 15;59(6):765-73.

11. Wen JW, Haber BA. Maternal-fetal transmission of hepatitis C infection: what is so special about babies? J Pediatr Gastroenterol Nutr **2014** Mar;58(3):278-82.

12. Dal Molin G, D'Agaro P, Ansaldi F, et al. Mother-to-infant transmission of hepatitis C virus: rate of infection and assessment of viral load and IgM anti-HCV as risk factors. J Med Virol **2002** Jun;67(2):137-42.

13. Mast EE, Hwang LY, Seto DS, et al. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. J Infect Dis **2005** Dec 1;192(11):1880-9.

14. European Paediatric Hepatitis C Virus Network. A significant sex--but not elective cesarean section--effect on mother-to-child transmission of hepatitis C virus infection. J Infect Dis **2005** Dec 1;192(11):1872-9.

15. Roberts SS, Miller RK, Jones JK, et al. The Ribavirin Pregnancy Registry: Findings after 5 years of enrollment, 2003-2009. Birth Defects Res A Clin Mol Teratol **2010** Jul;88(7):551-9.

16. Smith BD, Yartel AK, Krauskopf K, et al. Hepatitis C virus antibody positivity and predictors among previously undiagnosed adult primary care outpatients: cross-sectional analysis of a multisite retrospective cohort study. Clin Infect Dis **2015** Apr 15;60(8):1145-52.

17. El-Kamary SS, Hashem M, Saleh DA, et al. Reliability of risk-based screening for hepatitis C virus infection among pregnant women in Egypt. J Infect **2015** May;70(5):512-9.

18. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Management of Hepatitis C in Pregnancy, RANZCOG Clinical Guideline. Melbourne: RANZCOG, **2013**.

19. AASLD/IDSA/IAS–USA. HCV testing and linkage to care. Recommendations for testing, managing, and treating hepatitis C; http://www.hcvguidelines.org/full-report/hcv-testing-and-linkage-care. Available at: Accessed April 24, 2015.

20. Mack CL, Gonzalez-Peralta RP, Gupta N, et al. NASPGHAN practice guidelines: Diagnosis and management of hepatitis C infection in infants, children, and adolescents. J Pediatr Gastroenterol Nutr **2012** Jun;54(6):838-55.

21. NIH Consensus Statement on Management of Hepatitis C: 2002. NIH Consens State Sci Statements **2002** Jun 10-12;19(3):1-46.

22. Lee CK, Jonas MM. Treating HCV infection in children. Clinical Liver Disease **2015**;5(1):14-6.

23. Wirth S. Current treatment options and response rates in children with chronic hepatitis C. World J Gastroenterol **2012** Jan 14;18(2):99-104.

24. Pembrey L, Newell ML, Tovo PA. European paediatric hepatitis C virus network. Antenatal hepatitis C virus screening and management of infected women and their children: policies in Europe. Eur J Pediatr **1999** Oct;158(10):842-6.

25. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 86: Viral hepatitis in pregnancy. Obstet Gynecol. 2007/10/02 ed Vol. 110, **2007**:941-56.

26. Wilson E, Beckmann M. Antenatal screening for hepatitis C: Universal or risk factor based? Aust N Z J Obstet Gynaecol **2015** Aug;55(4):318-22.

27. Delgado-Borrego A, Smith L, Jonas MM, et al. Expected and actual case ascertainment and treatment rates for children infected with hepatitis C in Florida and the United States: epidemiologic evidence from statewide and nationwide surveys. J Pediatr **2012** Nov;161(5):915-21.

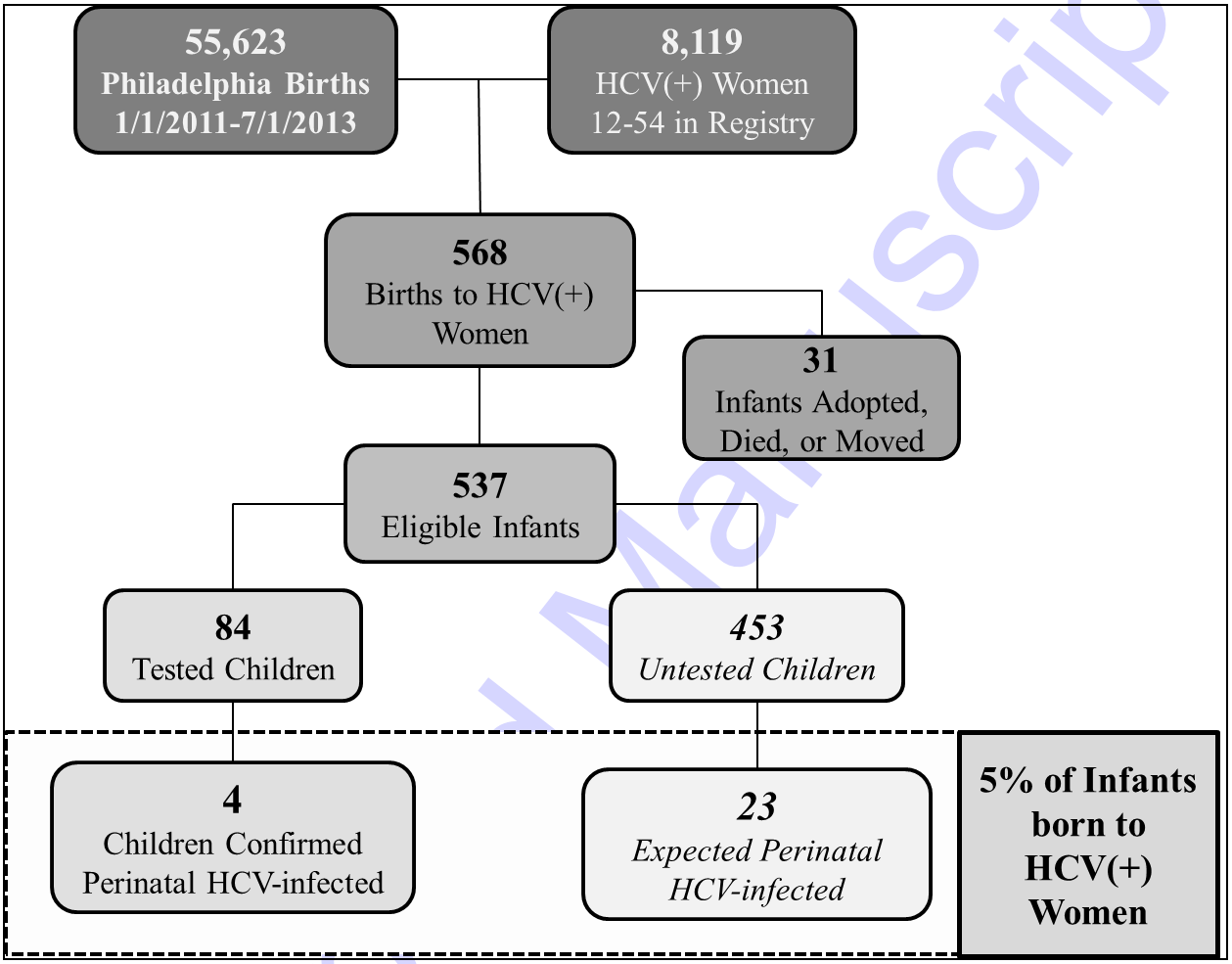
28. Swan D, Long J, Carr O, et al. Barriers to and facilitators of hepatitis C testing, management, and treatment among current and former injecting drug users: a qualitative exploration. AIDS Patient Care STDS **2010** Dec;24(12):753-62.

29. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001-2008. Hepatology **2012** Jun;55(6):1652-61.

30. Mitchell AE, Colvin HM, Palmer Beasley R. Institute of Medicine recommendations for the prevention and control of hepatitis B and C. Hepatology **2010** Mar;51(3):729-33.

31. Coughlin SS. "Test, Listen, Cure" (TLC) Hepatitis C Community Awareness Campaign. JMIR Res Protoc **2015**;4(1):e13.

Figure 1: Case identification of HCV-Positive women who gave birth in Philadelphia in the study period, subsequent testing on their children, and observed and expected outcomes.



*HCV: Hepatitis C virus

Table 1: Comparison of births to HCV-positive and all other mothers from January 2011-July 2013 in Philadelphia. Please note percentages may not sum to 100 due to rounding.

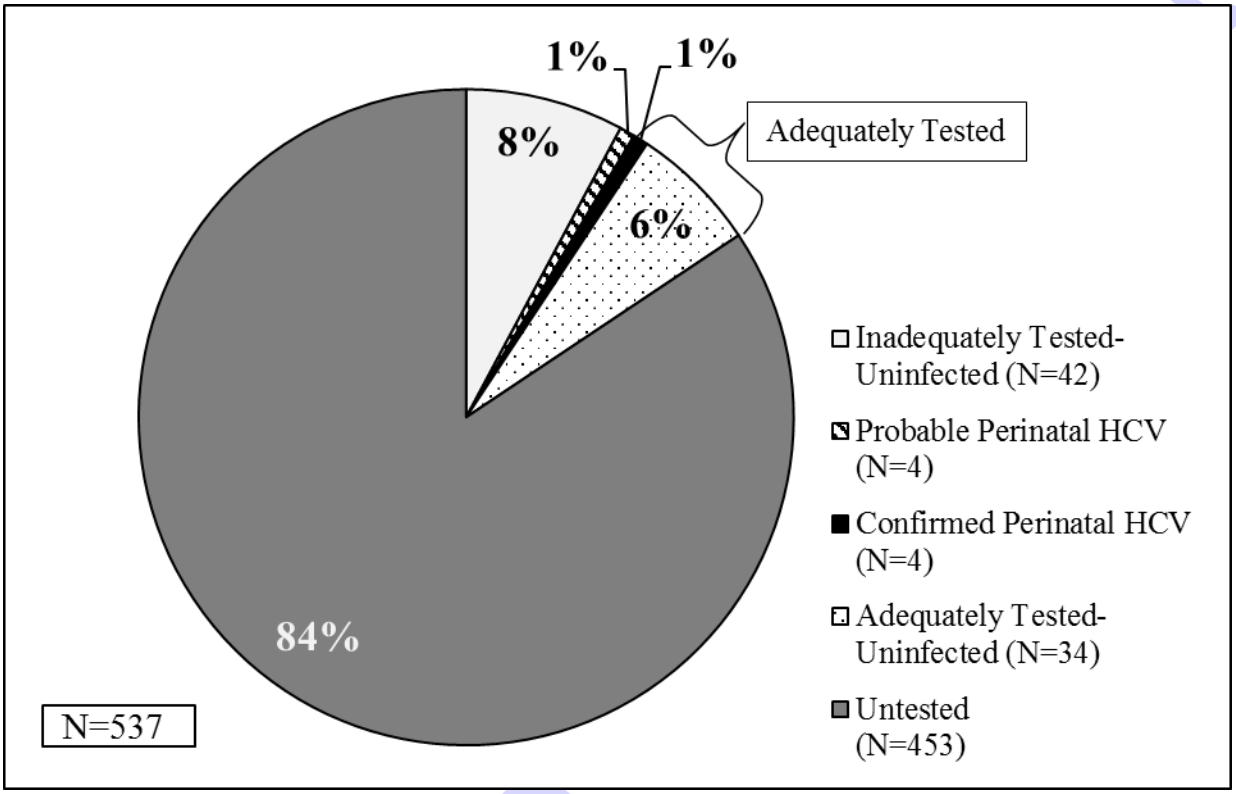
	Mother HCV-Positive in Hepatitis Registry		**Univariate Analysis**		**Multivariate Analysis**	
	No (n=55,086) N (%)	**Yes (n=537) N (%)**	***AOR (95% CI)***	***P-value***	**AOR (95% CI)**	***P-value***
Median Age(years)	27 (13 - 54)	29 (16 - 47)	---	---	---	---
Age Group						
12-19 years	6237 (11)	24 (5)	1.0 (Referent)		1.0 (Referent)	
20-27 years	23263 (42)	209 (39)	2.7 (2.1 -3.4)		3.6 (2.8 – 4.6)	
28-35 years	18497 (34)	224 (42)	3.9 (3.1 - 4.9)	*<0.0001*	7.9 (6.1 – 10.2)	*<0.0001*
36-45 years	7014(13)	79 (15)	3.7 (2.9 -4.8)		8.8 (6.7 – 11.5)	
45 years +	56 (<1)	1 (<1)	12.5 (5.9 -26.1)		53.6 (25.0 – 114.6)	
Unknown	19 (<1)	0 (0)	---		---	
Race/Ethnicity						

NH Black	25582 (46)	141 (27)	1.0 (Referent)		1.0 (Referent)	
NH White	13890 (25)	293 (55)	3.6 (3.3 - 4.0)		7.8 (7.0 – 8.6)	
Hispanic	9756 (18)	69 (13)	1.2 (1.0 -1.4)	*<0.0001*	1.2 (1.0 - 1.4)	*<0.0001*
Asian	3474 (6)	7 (1)	0.4 (0.3 -0.6)		0.8 (0.5 – 1.1)	
Other	1396(3)	11 (2)	1.7 (1.3 -2.2)		2.2 (1.7 - 3.0)	
Unknown	988 (2)	16 (3)	---		---	
Insurance						
Private	18865 (34)	95 (18)	1.0 (Referent)		1.0 (Referent)	
Self-Pay	2111 (4)	10 (2)	0.8 (0.6 -1.1)		0.9 (0.6 - 1.2)	
Public	29794 (54)	362 (67)	2.1 (1.9 - 2.3)	*<0.0001*	2.1 (1.9 – 2.4)	*<0.0001*
Other	2224 (4)	35 (7)	2.5 (2.1 – 3.0)		2.8 (2.3 - 3.4)	
Unknown	2097 (4)	35 (7)	---		---	
Married						
Yes	19632 (36)	100 (19)	1.0 (Referent)	*<0.0001*	1.0 (Referent)	*<0.0001*
No	35395 (64)	436 (81)	2.3 (2.1 – 2.5)		2.9 (2.5 -3.2)	
Unknown	60 (<1)	1 (<1)	---		---	

Education						
< High school	11192 (20)	158 (29)	1.0 (Referent)	*<0.0001*	1.0 (Referent)	*<0.0001*
High school	27954 (51)	308 (57)	0.8 (0.7 – 0.8)		0.6 (0.5 - 0.7)	
Higher Degree	15079 (27)	58 (11)	0.3 (0.2 - 0.3)		0.2 (0.2 - 0.3)	
Unknown	874 (2)	13 (2)	---		---	
Infant Gender						
Male	28136 (51)	255 (48)	1.0 (Referent)	*0.2878*	---	---
Female	26945 (49)	282 (53)	1.0 (1.0 - 1.1)			

*HCV: Hepatitis C virus; AOR: Adjusted Odds Ratio; NH: Non-Hispanic

Figure 2. Hepatitis C testing and testing results for children born to HCV-positive women and the testing adequacy according to AASLD and NASPGHAN national guidelines.



*HCV: Hepatitis C virus; AASLD: American Association for the Study of Liver Disease ; NASPGHAN: the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

Legend

Inadequately Tested-Uninfected (N=42)

Probable Perinatal HCV (N=4)

Confirmed Perinatal HCV (N=4)

Adequately Tested-Uninfected (N=34)

Untested (N=453)