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Perinatal Transmission of Hepatitis C Virus: Defining the Cascade of Care

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Abstract

Objectives: The US National Viral Hepatitis Action Plan calls for major efforts to expand Hepatitis C Virus (HCV) diagnosis and treatment; prenatal care settings are potential venues for expanding HCV testing. We aimed to characterize the HCV diagnostic cascade for women and infants and to investigate factors associated with linkage and follow-up.

Study design: We used electronic health records for a 10-year cohort of 879 women with opioid use disorder from an obstetric clinic serving women with substance use disorders.

Results: Altogether, 744 women (85%) were screened for HCV; 510 (68%) were seropositive, of whom 369 (72%) had nucleic acid testing performed and of these 261 (71%) were viremic. Of 404 infants born to HCV seropositive women, 273 (68%) were tested at least once for HCV, 180 (45%) completed the American Academy of Pediatrics-recommended perinatal HCV screening, and 5 (2.8%) were diagnosed with HCV infection and linked to care. More recent delivery date (2014–2015) was associated with maternal linkage to care (adjusted odds ratio [aOR] 2.5, 95% confidence interval [CI] 1.4–4.7). Maternal HIV co-infection (aOR 9.0, 95% CI: 1.1–72.8) and

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methadone maintenance therapy, compared with buprenorphine (aOR 1.5, 95% CI: 0.9–2.5), were associated with higher rates of infant HCV testing.

Conclusions: HCV prevalence among pregnant women with opioid use is high, and infant HCV screening is imperfect. Programmatic changes to improve both mother and infant follow-up may help bridge identified gaps in the cascade to cure.

Keywords

Vertical Transmission; Prenatal Screening; Linkage to Care; Pediatric Hepatitis C

The US Department of Health and Human Services National Viral Hepatitis Action Plan details goals to prevent new Hepatitis C Virus (HCV) infections, including elimination of mother-to-infant transmission(1). However, amid rising HCV incidence, especially among young adults aged 20–39 years, eliminating transmission, including perinatal, requires strategies to expand HCV testing and linkage to care(2–4).

Prenatal care settings are candidate venues for expanding HCV screening in the United States, as they often represent the primary point of contact for young women and the healthcare system(5). HCV treatment is not currently recommended during pregnancy, and proven methods for preventing perinatal transmission of HCV are lacking(6,7). However, a woman identified as HCV-infected can link to care for disease staging and treatment following pregnancy, with potential to both cure herself and prevent infant HCV exposure during future pregnancies. Further, identifying a pregnant woman with HCV alerts providers to appropriately evaluate her child for HCV infection.

It is important to understand the outcomes associated with HCV testing in prenatal care settings to inform guidance. We utilized registry data and electronic health records (EHR) of one of the largest obstetric programs for women with substance use disorder in the United States to characterize the HCV care cascade among women and their infants.

Methods:

Boston Medical Center (BMC) Project “Recovery, Empowerment, Social Services, Prenatal care, Education, Community and Treatment” (RESPECT) is a multidisciplinary program that cares for pregnant women with substance use disorders. The clinic provides on-site support from psychiatry, social work, nursing, and lactation in conjunction with obstetric providers who specialize in treating women in various stages of recovery and prescribing medications for opioid use disorder.

Data collection:

The RESPECT program data registry includes demographic characteristics, medical history, and pregnancy and birth outcomes abstracted from chart review of women enrolled in RESPECT. Maternal substance use is determined by third trimester reported tobacco use and urine toxicology screens compared with chart evidence of prescribed opioids and opioid agonists at delivery. Zip codes are geocoded into distance from medical center to home zip code geometric center and dichotomized to within or outside the subway system. The EHR

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was retrospectively queried to add HCV-related laboratory results (HCV Antibody (Ab), nucleic acid (RNA) tests, and genotypes, and HIV and hepatitis B virus testing).

Patients:

We included all women with a diagnosis of opioid use disorder who delivered a live birth at BMC between 1/1/2006 and 12/31/2015. For the HCV cascade and the multivariable analysis, we included only the most recent pregnancy to not double-count women, and only infants at least 18 months old at study end to allow adequate follow-up time for infant HCV screening. Given very few transmission events, our sub-analysis of factors associated with vertical transmission of HCV includes all infants regardless of birth order or age at study end.

HCV cascade of care outcomes:

The primary outcome was follow-up along the HCV care cascade. We defined key points as follows.

The proportion assessed for HCV infection by documented history of HCV diagnosis in the EHR problem list, prior positive anti-HCV, or testing for anti-HCV or HCV RNA during pregnancy (40 weeks prior to delivery date up to 4 days post-partum); of those assessed for HCV, the proportion with reactive anti-HCV (seropositive) by documented history or result in EHR; of seropositive women, the proportion with HCV RNA testing during pregnancy; the proportion with positive HCV RNA testing during pregnancy (viremic); and of viremic women, the proportion who were linked to HCV care.

We defined linkage to HCV care as documentation of HCV genotype in the EHR during pregnancy through study end. We chose genotype as our proxy for linkage because genotype is a consistent marker for initiation of further diagnostic evaluation for HCV(8).

To delineate the infant cascade, we used the American Academy of Pediatrics (AAP) Redbook guidelines, which recommend HCV testing for all infants born to HCV seropositive mothers, regardless of maternal HCV RNA status (consistent with other published guidelines)(9– 12). We define infant diagnostic cascade outcomes as follows. The proportion born to HCV seropositive mothers with at least one anti-HCV or RNA test result in the EHR (but not necessarily complete, appropriate testing for perinatal HCV); the proportion with complete followup, defined as meeting 1 of 4 conditions: 1) confirmed diagnosis of HCV infection by two positive HCV RNA tests at least one month apart, 2) confirmed diagnosis of HCV by reactive HCV Ab at age 18 months or greater, or 3) confirmed exclusion of HCV infection by two negative HCV RNA tests at least one month apart, or 4) by negative anti-HCV at any age; of infants with complete follow-up, proportion diagnosed as HCV-infected; and among HCV-infected infants, proportion linked to HCV care, determined by manual chart review confirmation of visits for chronic HCV follow-up at BMC.

Institutional practice was to schedule all infants for HCV follow-up with pediatric infectious diseases at BMC; however, infants may ultimately have completed screening at alternate locations. A dedicated pediatric infectious diseases nurse at BMC routinely makes multiple

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attempts to reschedule infants with missed appointments, and documents relevant communications with non-BMC providers who may screen infants for HCV. We compared follow-up rates between infants with and without primary care at BMC to account for infants expected to have laboratory data accessible through the EHR. We also completed chart review of a random subset of 50 infants without complete HCV screening at BMC to categorize whether those infants were truly unscreened. We reviewed charts for notes documenting confirmed HCV testing performed outside the EHR (confirmed screening), notes indicating outside provider intention to screen (likely screening), ≥2 missed appointments for HCV screening without later re-engagement in care (loss to follow-up), or confirmed primary care at BMC without HCV testing completed through study end (confirmed unscreened). For infants in the latter categories, their mothers' records were also checked for evidence of false positive HCV testing during pregnancy.

We used a survival analysis to display time until clearance of maternal anti-HCV for infants ultimately screening negative for HCV to inform whether earlier testing schedules might be possible. Given several month gaps between repeat anti-HCV testing in clinical practice, we calculated for each infant the midpoint between last positive and first negative anti-HCV as an estimate of predicted time of anti-HCV clearance.

Statistical analyses

We compared demographic characteristics and co-morbidities in HCV seropositive women with seronegative women using *t* tests for continuous and χ^2 test for categorical variables. Employing multivariable logistic regression, we modeled HCV viremic mothers' odds of linking to HCV care adjusting for confounders including: maternal age, race, distance from medical center, HIV, psychiatric diagnoses, tobacco and un-prescribed drug use (opioids, benzodiazepines, cocaine, amphetamines, or barbiturates), and opioid agonist therapy at delivery.

We next modeled predictors of infant diagnostic completion using maternal demographic characteristics, co-morbidities, and maternal HCV viremia. Multivariable regression utilized factors predicting complete follow-up in univariate analysis with an effect size of at least 30%. Finally, we described characteristics of HCV-infected infants.

All data analysis was performed using SAS version 9.4 (Cary, North Carolina). Institutional Review Board Approval was obtained from Boston Medical Center.

Results:

Of 879 women with opioid use disorder included in the analysis, 744 (85%) were assessed for HCV infection by review of known HCV infection in the problem list or laboratory testing, and 510 (68% of those assessed) were anti-HCV positive (Figure 1). Compared to those without HCV, seropositive women were more likely to be white non-Hispanic ($P < .001$) and have comorbid HIV infection ($P = .006$) and tobacco use during pregnancy ($P < .01$) (Table 1). Seropositive women were also more likely to be prescribed opioid agonist therapy at delivery ($P < .001$) but had similar rates of illicit or un-prescribed drug use during

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pregnancy (39% vs 36%, $P = 0.35$). All women were hepatitis B surface antigen negative (data not shown); the number of prenatal visits was the same for both groups.

HCV care cascade:

Of 510 HCV seropositive women, 369 (72%) had HCV RNA testing completed during pregnancy (Figure 1), of whom 261 (71%) had detectable HCV RNA, corresponding to a chronic HCV prevalence estimate among women with opioid disorder at this clinic of at least 30% (261/879). Of the 261 viremic mothers, 107 (41%) were linked to HCV care at BMC after pregnancy. If we assume that 68% of untested women were seropositive as well and that 71% of these women and of seropositive women without RNA testing were viremic, then the clinic chronic HCV prevalence would be 48% and linkage to care only 25%.

In multivariable logistic regression analysis, only calendar year of delivery was significantly associated with linkage to HCV care (Table 2). Those who delivered in 2014–2015 were more likely than those who delivered in 2006–2013 to link to care (adjusted odds ratio [aOR] 2.5, 95% confidence interval [CI] 1.4–4.7). No other variables significantly predicted linkage.

Among 404 infants included in the cascade (those born to HCV seropositive mothers and at least 18 months of age at study end), 273 (68%) had evidence of at least one HCV laboratory result, but only 180 (45%) had complete evaluation for perinatal HCV acquisition (Figure 1). Among the 180 screened, five transmission events occurred (2.8%), and all five infants were linked to care with pediatric infectious diseases specialists for follow-up of chronic HCV. Of 163 infants with initial positive anti-HCV testing followed by a later negative anti-HCV, 50 (31%) were seronegative by 12 months of age and none had positive anti-HCV later than 14 months of age (Figure 2; available at www.jpeds.com). Estimating for each infant average age between last positive and first negative anti-HCV, 70% of infants had a predicted negative anti-HCV by 12 months of age, 85% by 15 months, and 99% by 18 months.

In assessing infant follow-up care, we found 234/404 infants (58%) had at least one completed visit with pediatric infectious diseases specialists at BMC. Of those, 169/234 (72%) completed diagnostic testing for HCV. Furthermore, of 120 infants (30%) who received primary care at BMC, 97/120 (81%) had complete HCV screening (data not shown).

Chart review of 50 infants without complete HCV screening at BMC demonstrated 6 (12%) definitely and 12 (24%) likely completed screening elsewhere given documented communication about HCV follow-up with their primary care pediatrician. Five (10%) were confirmed unscreened despite primary care at BMC, and 23 (46%) appeared lost to follow-up given missed appointments for screening. One infant died, and three had mothers later proven HCV seronegative (false positive screening during pregnancy). Extrapolating to all 224 infants without complete follow-up, if 56% (125/224) were truly unscreened, this predicts a more conservative estimate of 125/404 (31%) exposed infants lost to follow-up and 69% screened (data not shown).

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In multivariable logistic regression, maternal HIV co-infection was associated with increased odds of infant HCV diagnostic follow-up completion, aOR 9.0 (95% CI: 1.1–72.8) (Table III). Maternal methadone maintenance therapy compared with buprenorphine at delivery also increased odds of complete infant screening in univariate analysis (OR 1.8, 95% CI: 1.12.8), but not in the adjusted model (aOR 1.5, 95% CI: 0.9–2.5). No other factors significantly predicted completion of follow-up screening, although higher odds were observed with maternal HCV viremia (aOR 1.3, 95% CI: 0.9–2.1), tobacco use (aOR 1.8 95% CI 0.9–3.6), and female infant sex (aOR 1.5, 95% CI 1.0–2.3).

Infants diagnosed with HCV:

Twelve children were diagnosed with chronic HCV. Only 5 were included in cascade outcomes because the others were either younger than 18 months at study end or excluded for having a younger sibling in the cohort. Ten infected infants (83%) were female, 11 (92%) were born full-term. All mothers were receiving opioid agonist therapy at delivery; 10/12 (83%) on methadone and 2 (17%) on buprenorphine. Of dyads in whom mother and infant had HCV genotypes, all infant genotypes matched their mothers': four dyads with genotype 1 and two with genotype 3 infection. All women who transmitted HCV infection to their infants were seropositive, but one had negative RNA testing early in pregnancy and no further testing during the study period (data not shown).

Discussion:

Our analysis demonstrates that even a prenatal care program specifically serving women with substance use disorders, and therefore at high-risk for HCV infection, assessed most, but not all, women for HCV. This demonstrates areas for improvement in evaluation of viremia, linkage to care and infant follow-up. Ultimately, 41% of women identified as HCV viremic were ever linked to HCV care and 45–69% of HCV-exposed infants had complete diagnostic testing for HCV transmission. The National Academies of Sciences, Engineering and Medicine concluded that HCV can be eliminated as a public health threat and laid out goals for reaching elimination in the United States by 2030(13). Achieving these goals requires efforts to identify and link HCV-infected patients to care, especially those under 40 years old, who are most likely to transmit(1). Obstetric care provides a prime opportunity to identify women – and infants – at risk for HCV to test and link to care. Although linkage programs would provide economic value and likely be cost-effective, establishing adequate "wrap-around" services to bridge HCV infected women and their infants to care and treatment remains a major challenge(14).

We found women who delivered in more recent years had greater linkage to HCV care. This trend may reflect motivation for treatment in the new era of effective and tolerable antivirals with >90% cure rates. However, prospective studies in this prenatal clinic may also contribute to increased testing and linkage, demonstrating a potential confounder but also a model of collaboration to improve the HCV care cascade.

Infants of women engaged in longitudinal chronic care for HIV and methadone maintenance therapy had higher univariate odds of completing infant screening. Smaller sample size, especially among HIV co-infected women, and correlation between variables limited our

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ability to observe statistical significance in the multivariable analysis and created large confidence intervals, however effect sizes were large. These factors were not associated with women linking to their own HCV care. Perhaps not surprising, this provides insight into effective design of programs intended to improve infant follow-up. Combining infant programs with chronic care for women could maximize infant HCV follow-up *and* provide needed services to women.

Infant HCV screening guidelines differ in recommendations to obtain HCV RNA testing(9–12). Infants with complete screening in this study include those with two negative HCV RNA tests prior to 18 months. If a guideline recommending only anti-HCV testing had been used by our institution, and some of these infants were lost to follow-up prior to completing the 18-month anti-HCV our screening rate could have been lower. Nearly two-thirds of infants completed at least one HCV diagnostic test, suggesting a single-step algorithm that does not require sequential testing could improve infant diagnosis. The utility of obtaining a second RNA after an initial negative RNA performed at older than two months is uncertain, and its added value should be further assessed. Likewise, many infants lose maternal anti-HCV prior to 18 months, and an earlier recommended age to test could minimize the risk of loss to follow-up and better capture and diagnose infants(15). Our imputation assumes maternal anti-HCV loss exactly at the midpoint between last positive and first negative anti-HCV, and a large prospective study testing anti-HCV at varying intervals would be required.

RESPECT is a unique multidisciplinary prenatal care program, and the pediatric infectious diseases program at BMC has dedicated nursing staff regularly following missed visits with several attempts to reschedule, and this limits generalizability to other centers. However, our finding of low linkage to care for women is consistent with findings in comparable programs in New Mexico and Pittsburgh(16,17). We expect new diagnoses of HCV in community-based general obstetrics practices, without the referral infrastructure of RESPECT, will pose even greater challenges. Lower infant screening rates predicted by public health reporting data in previous studies support this concern(18–21). Delgado-et al compared expected population prevalence of HCV with positive HCV laboratory data reported in children and found that only 11.7% of predicted pediatric HCV cases were ascertained in Florida and 4.9% across the country in 2009(18). More recently, HCV diagnoses reported to public health departments matched with birth certificate data demonstrated only 16% of expected exposed infants had any HCV testing by 20 months of age in a Philadelphia study, and 34% completed appropriate testing in the Wisconsin Medicaid population(19,20). Finally, a large single center study in Pittsburgh also demonstrated only a 30% screening rate for perinatal HCV, even in infants followed for primary care within their hospital system(22).

An important limitation of our data is that only testing and visits that occurred at BMC were captured. To the extent women and infants followed at alternative sites, we underestimate HCV screening, diagnoses, and linkage. However, even with the more conservative estimate including infants likely tested elsewhere by chart review analysis, only 69% completed HCV screening. Although more optimistic than previously reported rates, this represents 31% of HCV vertical transmission missed.

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Foster care may alter the perinatal HCV screening cascade. Lack of medical history disclosure to foster parents poses potential for higher loss to follow-up. However, demographic differences and formal guidance for medical care of children in foster care could increase screening in this population(23). We attempted to adjust for this, but foster care is not well documented in the EHR, which limited our ability to analyze this variable. Prospective studies could better delineate this association.

In addition, we used HCV genotype as a proxy for linkage to care. Genotype has been used by other studies to measure HCV linkage and is known to have good sensitivity and specificity as a marker for entering HCV care(8,16,24). Using visit data can be misleading, as many provider types could offer HCV treatment, and not all visits to these providers are necessarily a visit focused on HCV.

Finally, we analyzed only the most recent pregnancy for each woman, which limited the sample size for infant analyses and ability to compare differences in linkage between initial and subsequent pregnancies. We did so to avoid double-counting women in the cascade and multivariable analyses. It is unclear if multiple births over time would affect linkage to HCV care, which requires further exploration in the future.

As we implement strategies to eliminate HCV as a public health threat, we must be mindful of the rising number of HCV infections among US women of reproductive age. Strategies to effectively screen and link women and their exposed infants to HCV care and treatment are essential, especially with direct acting antivirals now FDA-approved in children 12–17 years old and being studied as young as age 3(22). Our analysis characterizes the HCV care cascade among women in a high-risk prenatal population along with their exposed infants. We demonstrated a high yield venue for identifying and linking HCV-infected women to care and highlighted missed opportunities at each stage in the cascade to cure. Further research should address these gaps to improve progression through the HCV care cascade to achieve elimination goals.

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Abbreviations:

HCV	Hepatitis C Virus
aOR	adjusted Odds Ratio
CI	Confidence Interval

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BMC	Boston Medical Center
RESPECT	Project “Recovery, Empowerment, Social Services, Prenatal care, Education, Community and Treatment”
EHR	electronic health record
RNA	nucleic acid testing
anti-HCV	HCV Antibody
AAP	American Academy of Pediatrics
SD	Standard Deviation
HIV	Human Immunodeficiency Virus

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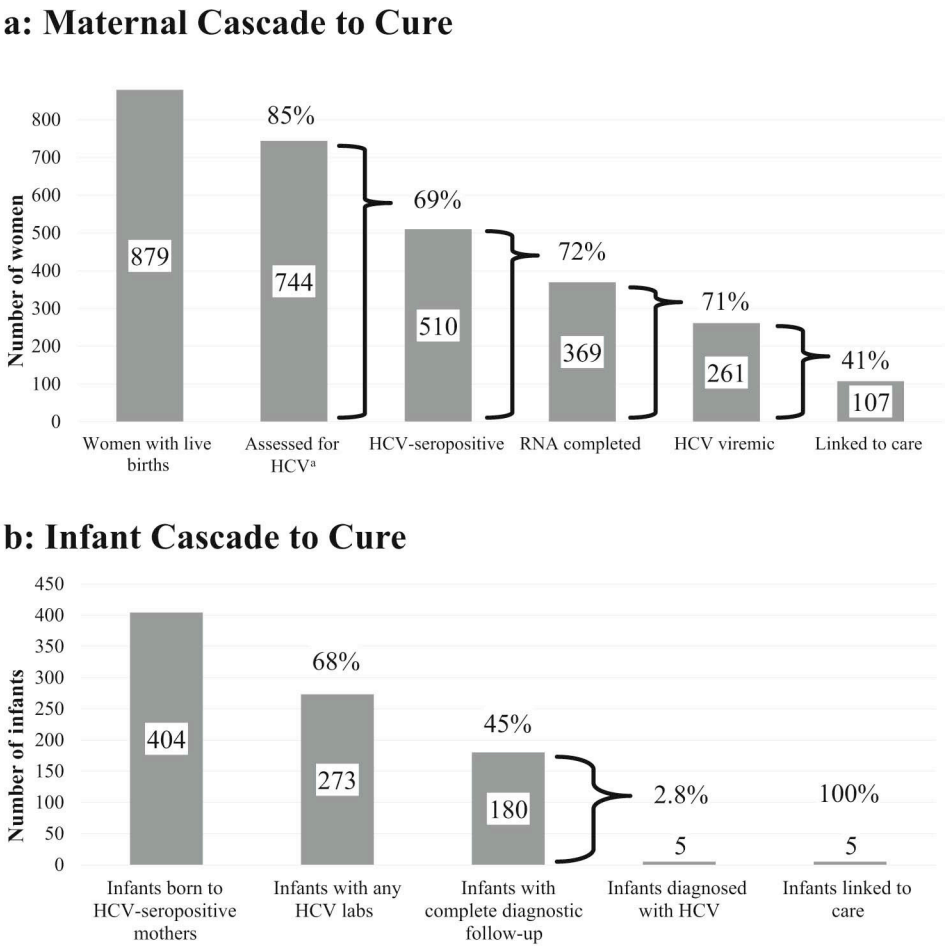

Figure 1 Legend:

[a] Assessed for HCV refers to history of HCV documented in EHR or completed HCV testing.

Visualization of HCV Cascade to Cure for women and their infants. 1a: The percentage values at the top of each bar are conditional. 1b: Percentages for columns 2–3 are of the 404 infants ≥18 months old at study end born to HCV-seropositive mothers. Columns 4–5 percentage values are conditional. Abbreviations: HCV hepatitis C virus, RNA ribonucleic acid, EHR electronic health record.

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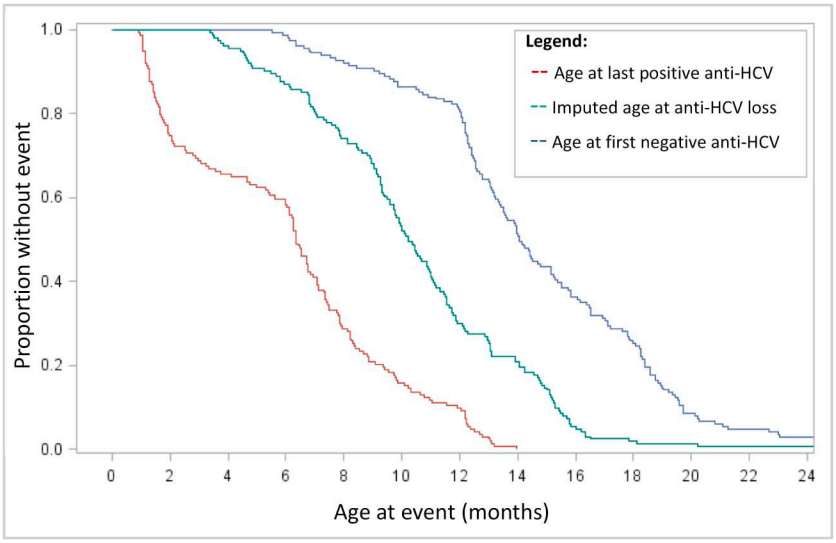

Figure 2 Legend (Online Only):
Kaplan-Meier survival curve of time to maternal HCV Ab clearance for all 163 infants who ever had an initial positive HCV Ab followed by a negative Ab at a later time point. Imputed age in months at antibody clearance is calculated from the midpoint between age at last positive HCV Ab and first negative HCV Ab testing. Abbreviations: HCV hepatitis C virus, Ab antibody.

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Table 1:

Demographic data for all women (for most recent pregnancy only)

Characteristic	HCV Negative (N=369) (42%)	HCV Seropositive[a] N=510 (58%)	*P* value
Age (mean [SD])	28.8 [5.6]	29.1 [5.2]	.31
Race			<.001
White non-Hispanic	246 (67)[b]	433 (85)	
Black non-Hispanic	72 (20)	22 (4)	
Hispanic	36 (10)	42 (8)	
Other or Declined	15 (4)	13 (3)	
Clinic Distance			.32
≥ 8 Miles	240 (65)	348 (68)	
< 8 Miles	129 (35)	162 (32)	
HIV	1 (0)	14 (3)	.006
Diabetes	8 (2)	17 (3)	.31
Psychiatric Diagnosis	171 (66)	341 (72)	.06
Tobacco Use	212 (72)	422 (87)	<.001
Opioid Agonist Therapy[c]	263 (78)	475 (95)	<.001
Methadone	111 (33)	327 (66)	<.001
Buprenorphine	147 (43)	148 (30)	
Illicit/un-prescribed drug use[d]	123 (36)	195 (39)	.35
Cocaine	47 (14)	79 (16)	.40
Opioids	70 (20)	127 (26)	.09
Benzodiazepines	13 (4)	47 (9)	.002
Prenatal Visits (mean [SD])	9.2 [5.4]	9.2 [5.3]	.98

Abbreviations: HCV, hepatitis c virus; SD, standard deviation; HIV, human immunodeficiency virus

[a] By positive HCV antibody, positive HCV nucleic acid, or by history of HCV in electronic health record.

[b] For variables with incomplete data, percentages shown are of those with complete data.

[c] First line indicates any agonist therapy versus none, second and third lines delineate which agonist therapy actively prescribed at time of delivery, with second *P* value indicating comparison between methadone and buprenorphine.

[d] Illicit/un-prescribed drug use within 30 days of delivery by urine toxicology screen that demonstrated either an illicit or un-prescribed substance as indicated. Categories are not mutually exclusive.

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Table 2:

Factors associated with HCV-infected (viremic) pregnant women linking to care, evidenced by presence of HCV genotype ordered during or after pregnancy.

Characteristic	Linked to Care N=107 (41%)	Not Linked to Care N=154 (59%)	Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Age:				
<25 years	26(45)	32(55)	0.9(0.4, 1.9)	0.8(0.3, 2.0)
25–35 years	59(38)	98(62)	0.7(0.3, 1.3)	0.6(0.3, 1.4)
≥35 years	22(48)	24(52)	Ref	Ref
Race				
White Non-Hispanic	86(39)	133(61)	0.6(0.3, 1.3)	0.9(0.4, 2.2)
Other	21(50)	21(50)	Ref	Ref
Clinic Distance[b]				
≥ 8 miles	72(39)	111(61)	0.8(0.5, 1.4)	0.7(0.4, 1.4)
< 8 miles	35(45)	43(55)	Ref	Ref
HIV	5(50)	5(50)	1.5(0.4, 5.2)	1.0(0.2, 4.6)
Psychiatric Diagnosis	66(38)	106(62)	0.7(0.4, 1.3)	0.6(0.3, 1.2)
Tobacco Use	94(42)	129(58)	2.1(0.8, 5.1)	2.1(0.8, 5.8)
Opioid Agonist Therapy				
Methadone	70(40)	103(60)	1.0(0.5, 1.7)	1.0(0.5, 1.8)
Buprenorphine	29(41)	41(59)	Ref	Ref
Illicit/un-prescribed drug use[c]	52(44)	65(56)	1.3(0.8, 2.1)	1.3(0.8, 2.4)
Delivery Date				
2014 – 2015	38(55)	31(45)	**2.2(1.2, 3.8)**	**2.5(1.4, 4.7)**
2006 – 2013	69(36)	123(64)	Ref	Ref

Abbreviations: HCV, hepatitis c virus; OR, odds ratio; CI, confidence interval; HIV, human immunodeficiency virus

[a]Multivariable analysis is adjusted for all variables shown in this table. Data was incomplete for 39 of the 261 viremic women, who were therefore excluded from the multivariable analysis.

[b]Indicates miles from Boston Medical Center by zip code centroid (8 miles is approximate edge of the subway system)

[c]Illicit or un-prescribed drug use within 30 days of delivery by urine toxicology screens

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Table 3:

Factors Associated with Completion of Infant Follow-Up Screening for HCV

Variable	Completed Follow-Up N=180(45%)	Lost to Follow Up N=224 (55%)	Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Infant Sex				
Female	80(48)[b]	87(52)	1.3(0.9, 2.0)	1.5(1.0, 2.3)
Male	85(41)	123(59)	Ref	Ref
Race				
White non-Hispanic	152(44)	196(56)	0.8(0.4, 1.4)	
Other	28(50)	28(50)	Ref	
Clinic Distance[c]				
≥ 8 miles	130(47)	145(53)	1.4(0.9, 2.2)	1.4(0.8, 2.2)
< 8 miles	50(39)	79(61)	Ref	Ref
Foster Care[d]	24(42)	33(58)	0.9(0.5, 1.6)	
Maternal HIV	10(91)	1(9)	**12.3(1.6, 97.3)**	**9.0(1.1, 72.8)**
Psychiatric Diagnosis	123(46)	142(54)	1.4(0.9, 2.1)	1.1(0.7, 1.9)
Tobacco Use	153(46)	181(54)	1.8(0.9, 3.5)	1.8(0.9, 3.6)
Illicit/Un-prescribed Drug Use[e]	71(45)	87(55)	1.0(0.7, 1.5)	
Opioid Agonist Therapy				
Methadone	125(49)	132(51)	**1.8(1.1, 2.8)**	1.5(0.9, 2.5)
Buprenorphine	40(35)	75(65)	Ref	Ref
Maternal HCV Viremia	101(49)	106(51)	1.4(1.0, 2.1)	1.3(0.9, 2.1)
Premature Delivery[f]	33(46)	38(54)	1.1(0.7, 1.9)	
Delivery Date				
2014–2015	16(52)	15(48)	1.4(0.7, 2.8)	1.5(0.7, 3.3)
2006–2013	164(44)	209(56)	Ref	Ref

Note: Odds of completing follow-up screening for HCV (as defined in methods) for infants who were at least 18 months of age at study end and born to an HCV seropositive mother.

Abbreviations: HCV, hepatitis c virus; OR, odds ratio; CI, confidence interval; HIV, human immunodeficiency virus

[a]Multivariable analysis adjusted for infant sex, distance from medical center, maternal HIV, presence of a psychiatric diagnosis, tobacco use, opioid agonist therapy, HCV viremia, and delivery date.

[b]Data listed as N (%) indicating row percentages of infants with a given variable (of those with full data for that variable) who did or did not complete follow-up screening. Data was missing for more than 20 (5%) infants for the variables foster care (158 missing), maternal psychiatric diagnosis (34), HIV (32), infant sex (29), and smoking (23).

[c]Indicates miles from Boston Medical Center by zip code centroid (8 miles is approximate edge of the subway system).

[d]Infant discharged to foster care at birth hospitalization discharge.

[e]Illicit or un-prescribed drug use within 30 days of delivery by urine toxicology screens.

[f]Gestational age <37 weeks at birth.