Enhancing Linkage to Hepatitis C Virus Treatment Following Pregnancy in Women Identified During Perinatal Care

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Amid the current US opioid crisis, hepatitis C virus (HCV) infection rates continue to rise in young adults, including among pregnant women, yet few studies describe linkage to care and treatment in pregnant or postpartum women with HCV infection. We used electronic health record data to estimate HCV treatment rates for postpartum women before (January 2014-September 2016) and during (October 2016-March 2018) implementation of a maternal–infant HCV linkage program in combination with a multidisciplinary clinic to colocate mother and infant care. Using Poisson regression models, we compared HCV treatment initiation rates, adjusting for demographics, substance use, and treatment. From January 2014 through March 2018, 343 women who were HCV seropositive delivered at our institution. Of these, 95% completed HCV nucleic acid testing and 255 women had chronic HCV infection. Mean age was 30 years, 96% were publicly insured, and 94% had documented substance use. HCV treatment initiation increased from 28/164 (17.1%) women with chronic HCV infection in the preintervention period to 16/66 (24.2%) with the linkage-only intervention and 13/25 (52.0%) with the linkage intervention and colocated care. Adjusted analyses demonstrated that women delivering during the intervention period initiated HCV treatment at 2.40 times (95% confidence interval [CI], 1.10-5.25; linkage only) and 3.36 times (95% CI, 1.57-7.17; linkage and colocated care) the rate of women delivering preintervention. Women on buprenorphine had higher HCV treatment initiation rates compared with those on methadone (rate ratio, 2.10; 95% CI, 1.05-4.21). *Conclusion:* HCV linkage to care and treatment rates improved in the setting of mother–infant linkage and colocated care interventions. Perinatal care may represent a critical venue to identify, link, and treat women for HCV infection to improve their own health and prevent transmission to subsequent pregnancies. (*Hepatology Communications* 2021;5:1543-1554).

The current opioid overdose crisis in the United States primarily affects young adults under age 40, half of whom are women of reproductive age.[1,2] In association with increasing rates of injection drug use, hepatitis C virus (HCV) infection incidence continues to rise in the United States. Between 1999 and 2014, the number of pregnant women with diagnosed opioid use disorder (OUD) quadrupled from 1.5 to 6.5 per 1,000 delivery hospitalizations,[3] and the number of deliveries affected by hepatitis C rose 5-fold over the same period to 29,000 affected deliveries in 2015.[4,5]

Until this year, the Centers for Disease Control and Prevention (CDC) recommended HCV testing during pregnancy only in women at high risk for HCV. These women are those identified with injection drug

Abbreviations: BMC, Boston Medical Center; CDC, Centers for Disease Control and Prevention; CI, confidence interval; DAA, direct-acting antiviral; EHR, electronic health record; HCV, hepatitis C virus; HIV, human immunodeficiency virus; OUD, opioid use disorder; RR, rate ratio; SOFAR, Supporting Our Families through Addiction and Recovery; SVR, sustained virologic response.

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use; certain medical conditions, such as human immunodeficiency virus (HIV); unregulated tattoos; or a known exposure[6]; yet, as in HIV, data demonstrate that risk-based testing alone fails to identify HCV infections and halt transmission.[7-10] The CDC recently responded with new guidance, consistent with 2018 guidance from national infectious diseases and liver societies,[11] to recommend universal prenatal HCV testing.[12] This change should help identify more women with undiagnosed HCV infection but also requires infrastructure to link identified women to HCV care and treatment. Although direct-acting antivirals (DAAs) have revolutionized HCV care with cure rates >95% in virtually all populations, only an estimated 37% of the 4.3 million individuals infected with HCV in the United States had been treated as of 2018.[13] DAAs are not currently approved by the US Food and Drug Administration for use during pregnancy because data remain limited in this population. Clinical trials are ongoing to test DAA safety and efficacy, and treatment during pregnancy may be a possibility in the future.[14,15] Currently, women can be linked to HCV care for treatment after pregnancy and cessation of breastfeeding.

Linkage to HCV treatment from perinatal care could be a powerful strategy to enhance care continuum follow-up for both women and their infants as women could be motivated to take charge of their family's health at that time.[16,17] Linking new mothers to care could improve not only their own health through seeking cure but also follow-up for their HCV-exposed infant and prevent vertical transmission in future pregnancies. Few studies describe HCV referral and treatment practices in women diagnosed with HCV during pregnancy,[5,17-21] and only one describes HCV treatment in the DAA era, with improved treatment rates for a limited number of postpartum women compared to the general population.[20]

In October 2016 at Boston Medical Center (BMC), an urban academic medical center serving a medically underserved population, we implemented a maternal–infant HCV care linkage program alongside a multidisciplinary program to colocate maternal and infant primary and specialty care for women and families affected by substance use. The objective of this study was to compare linkage rates to HCV cure for women before and after implementation of these programs.

Participants and Methods

MATERNAL–INFANT LINKAGE TO CARE PROGRAM

The BMC is the largest safety-net hospital and prenatal care provider for women with substance use in New England. Approximately 120 women with OUD and 75 women with chronic HCV infection deliver annually at BMC. In October 2016, the pediatrics department initiated consultation from pediatric infectious diseases for any postpartum woman with identified HCV antibody positivity. The consultation, which continues to date, involves (1) nurse practitioner or physician review of the mother's medical chart, (2) maternal education on HCV treatment

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and transmission, and (3) active linkage to an HCV care clinician (any specialty, per maternal preference) for herself, if applicable, and to the pediatric infectious diseases program for follow-up of her exposed infant. The consulting team also works to link fathers to care, depending on privacy and availability. The active linkage involves maternal and infant appointment scheduling, appointment reminder calls or texts, and in-person reminders, if possible, during pediatric infectious diseases, primary care, or addiction care visits at BMC. HCV treatment occurs in both primary care and specialty clinics within the BMC health system, and multiple primary care clinics at BMC integrate HCV and addiction medicine care. Massachusetts removed restrictions to HCV state Medicaid treatment policies in August 2016 and since then has not restricted HCV treatment by fibrosis stage, abstinence criteria, or provider specialty.[22]

MULTIDISCIPLINARY COLOCATED CARE CLINIC

In July 2017, in response to the many BMC families affected by addiction and limited success with engagement of postpartum women back to primary, HCV, or other specialty care for themselves or their infants,[17,23] the pediatric department initiated a multidisciplinary clinic to colocate postpartum maternal and infant care, the Supporting Our Families through Addiction and Recovery (SOFAR) program.[24] This program combines under one roof intensive medical and sociobehavioral support to families experiencing addiction, including infant primary care, developmental and behavioral pediatrics, infectious diseases, psychiatric and addiction care for mothers, social work, case management, and peer navigation support. The colocated care is designed to minimize the number of postpartum appointments mothers have for both themselves and their infants to maximize follow-up for the entire family. The program began in July 2017 and is open to all infants born with prenatal substance-use exposure followed at BMC. The program is designed for both maternal and infant care but continues to follow the infants if the mother seeks care elsewhere.

Both initiatives required departmental commitment and hospital funding to support a specialized nurse practitioner for the HCV nursery consult and a part-time program coordinator for SOFAR. For both interventions, lead pediatricians helped with program design and staff education for the nursery, neonatal intensive care, and pediatrics units about the respective programs and how to place consults to initiate each.

DATA COLLECTION

In this single-center retrospective cohort study, we analyzed data for all women identified as HCV antibody positive by electronic health record (EHR) laboratory data who delivered a live birth at BMC from January 2014 to March 2018. This time period allowed evaluation of deliveries for 2 years before the intervention but still during the DAA era. We collected laboratory and medication data, problem lists, social history data fields, demographics, and visit data through the EHR-based BMC Clinical Data Warehouse through June 2019. This allowed at least 15 months follow-up after delivery as HCV treatment is not recommended concurrent with pregnancy or breastfeeding. We also reviewed pediatric infectious diseases consults conducted for perinatal HCV consultation during the intervention period to ensure inclusion of women who may have had HCV testing performed outside the BMC EHR. Finally, in October 2020, we manually reviewed charts of women who were prescribed DAAs but did not have laboratory evidence of cure by June 2019 to better determine cure rate and adequacy of DAA prescription as a linkage marker.

CATEGORIZATION OF OUD

We combined the following three data sources to categorize substance use: the EHR problem list (International Classification of Disease, Ninth or Tenth Revision [mapped to Tenth Revision] codes for diagnosed opioid [F11], cannabis [F12], sedative, hypnotic, or anxiolytic [F13], cocaine [F14], other stimulant [F15], hallucinogen [F16], inhalant [F18], or other substance [F19] abuse or dependence); social history section (templated choices and free text of clinician-recorded individual substances); and medication list (presence of methadone, buprenorphine, or buprenorphine/naloxone). We included substance use occurring before or during pregnancy up through delivery and recorded the medication prescribed closest to delivery. We defined substance use as a categorical variable as

opioid use alone (without unprescribed stimulant use), opioid and unprescribed stimulant use together, other substance use, or no substance use identified.

OUTCOME DEFINITIONS

We used descriptive statistics to characterize the sample and the HCV care cascade, including mean time from delivery to the first recorded HCV treatment prescription. We defined the HCV care cascade as follows: (1) positive HCV antibody testing (any time before delivery); (2) HCV nucleic acid (RNA) testing completed to test for chronic HCV infection; (3) detectable HCV RNA before or during pregnancy, without interim negative HCV RNA testing (through either spontaneous clearance or HCV treatment); (4) HCV genotype testing completed; (5) HCV treatment initiation, evidenced by prescription order in the EHR for a DAA; and (6) HCV cure (sustained virologic response [SVR]), meaning undetectable HCV RNA ≥12 weeks after treatment completion.

We defined treatment initiation as our primary outcome as it confirms linkage to HCV care, which was the objective of the maternal HCV linkage program.

INCLUSION CRITERIA

For the linkage to cure analysis, we included only women with current chronic HCV infection because women who have cleared virus spontaneously do not require treatment. For women with more than one eligible pregnancy, we included only the most recent pregnancy so as not to count the second pregnancy toward time she may have linked and to better capture care behavior since more recent DAA approvals and availability.

STATISTICAL ANALYSIS

We summed person time between delivery and either HCV treatment initiation (primary outcome) or loss to follow-up (censoring event) for each woman by quarter. For the analysis, we included only women who were viremic at pregnancy start or during pregnancy and who had at least one follow-up care visit after delivery within our institution in infectious diseases, gastroenterology, addiction medicine, or primary care. We restricted the sample in this way to focus on women who continued to seek care at BMC after delivery as it was more likely we would accurately capture their follow-up and less likely they would be treated for HCV at an outside institution. Each woman contributed person time (during which she was eligible to be treated) from the latest of her delivery date or July 1, 2016, when Massachusetts Medicaid HCV treatment restrictions were removed, until the earliest date of (1) treatment start date, if treated, or (2) last visit date at BMC before the end of the study (June 2019). Intervention group served as the primary predictor as follows: those who delivered preintervention, those who received an HCV consult only (linkage), and those who received both an HCV linkage consult and participated in the mother–baby multidisciplinary clinic (linkage and SOFAR/colocated care).

We used Poisson models to estimate and compare HCV treatment initiation rates for women delivering before and after intervention. Univariable models evaluated the following covariates that clinically we expected to affect HCV treatment rates: age (continuous), race/ethnicity, substance use (categorical variable described above encompassing problem list, medication, and social history data), opioid agonist medication at delivery (methadone, buprenorphine, or none), and smoking status at delivery. We did not include insurance status or language spoken as covariates due to the predominance of Medicaid insurance and English as a primary language (Table 1). In the final adjusted models, we included age *a priori* and all variables with $P < 0.1$ in univariable analyses. Opioid agonist treatment was strongly associated with substance use category at delivery, so separate multivariable models included either substance use or opioid agonist treatment to evaluate effects of each. All analyses were performed in SAS, version 9.4 (Cary, NC).

This study was approved by the Boston University Medical Campus Institutional Review Board as exempt research as it involved chart review only.

Results

The cohort included 343 women who were HCV seropositive and who delivered at BMC from January 2014 through March 2018. Of these, 255 women had known HCV viremia either during or after pregnancy and were included in the analysis. The distribution of characteristics was similar before and during intervention periods. The majority of women had substance

TABLE 1. DEMOGRAPHICS AND CLINICAL INFORMATION FOR WOMEN INFECTED WITH HCV AND DELIVERING BEFORE AND DURING IMPLEMENTATION OF A MATERNAL–INFANT LINKAGE PROGRAM WITH OR WITHOUT COLOCATED MATERNAL–INFANT CARE IN THE SOFAR CLINIC*

		Intervention Period	
Variable	Preintervention n = 164 (%)†	Linkage n = 66 (%)†	Linkage + SOFAR n = 25 (%)†
Age at delivery, years as mean (SD, range)	29.8 (4.8, 20-40)	29.8 (4.9, 20-40)	30.8 (4.4, 24-39)
Race/ethnicity			
Black non-Hispanic	20 (12.2)	6 (9.1)	0
Hispanic or Latino	11 (6.7)	5 (7.6)	1 (4.0)
White non-Hispanic	127 (77.4)	52 (79.8)	23 (92.0)
Other‡	1 (0.6)	0	0
Declined/unknown	5 (2.9)	3 (4.6)	1 (4.0)
Primary language spoken			
English	158 (96.9)	64 (97.0)	25 (100.0)
Other	5 (3.1)	2 (2.2)	0
Insurance type			
Medicaid	155 (94.5)	65 (98.5)	24 (96.0)
Commercial	5 (3.0)	0	0
Free care or other	2 (1.2)	0	0
Missing/unknown	2 (1.2)	1 (1.5)	1 (4.0)
Marital status			
Single	143 (87.7)	58 (87.9)	19 (76.0)
Married	10 (6.1)	3 (4.6)	3 (12.0)
Previously married	7 (4.3)	4 (6.1)	3 (12.0)
Other/unknown	4 (2.4)	1 (1.5)	0
Tobacco use, at delivery			
Current	107 (65.2)	43 (65.2)	20 (80.0)
Prior	19 (11.6)	11 (16.7)	5 (20.0)
Never	14 (8.5)	11 (16.7)	0
Unknown	24 (14.6)	1 (1.5)	0
Any identified substance use			
Yes	155 (94.5)	59 (89.4)	25 (100)
No	9 (5.5)	7 (10.6)	0
Diagnosed substance abuse or dependence, by ICD-9/10 code§			
Any	132 (80.5)	54 (81.8)	24 (96.0)
Opioid	89 (54.3)	32 (48.5)	22 (88.0)
Cocaine, amphetamines, or methamphetamines	24 (14.6)	4 (6.1)	4 (16.0)
Cannabis	1 (0.6)	0	1 (4.0)
Other‖	92 (56.1)	42 (63.6)	21 (84.0)
Drug use recorded in social history			
Any	96 (58.5)	36 (54.6)	17 (68.0)
Any documented intravenous drug use	84 (51.2)	34 (51.5)	16 (64.0)
Cocaine, amphetamines, or methamphetamines	42 (25.6)	18 (27.3)	10 (40.0)
Heroin or fentanyl	81 (49.4)	34 (51.5)	16 (64.0)
Other opioids	11 (6.7)	3 (4.6)	2 (8.0)
Marijuana	24 (14.6)	3 (4.6)	3 (12.0)
Other¶	24 (14.6)	3 (4.6)	3 (12.0)
Medication for OUD, at delivery			
None	32 (19.5)	14 (21.2)	5 (20.0)

TABLE 1. *Continued*

Variable	Preintervention n = 164 (%)†	Intervention Period: Linkage n = 66 (%)†	Intervention Period: Linkage + SOFAR n = 25 (%)†
Methadone	85 (51.8)	31 (47.0)	11 (44.0)
Buprenorphine#	47 (28.7)	21 (31.8)	19 (36.0)
Combined substance use categorization**			
Opioid use alone	93 (56.7)	37 (56.1)	12 (48.0)
Opioid and nonprescribed stimulant use	58 (35.4)	19 (28.8)	13 (52.0)
Other substance use only	4 (2.4)	3 (4.6)	0
None	9 (5.5)	7 (10.6)	0
HCV-treating physician specialty††			
Primary care/addiction medicine	14 (50.0)	10 (62.5)	9 (69.2)
Gastroenterology	9 (32.1)	3 (18.8)	2 (15.4)
Infectious diseases	5 (17.9)	3 (18.8)	2 (15.4)

*Before implementation was January 2014-September 2016; during implementation was October 2016-March 2018.
†n (%) unless otherwise indicated.
‡Asian, American Indian, Alaska Native, or Pacific Islander.
§As recorded in the maternal problem list, not mutually exclusive categories.
||Sedatives, hypnotics, hallucinogens, inhalants, or other psychoactive substances.
¶Benzodiazepine, barbiturate, LSD, MDMA, marijuana, or psilocybin.
#Buprenorphine alone or combination buprenorphine/naloxone.
**Incorporates data from each category above (ICD-9/10 codes, social history, and medications for OUD).
††Percentages are out of the 28 women in the preintervention period and 28 in the intervention period who had HCV treatment initiation.
Abbreviations: ICD-9/10, International Classification of Diseases, Ninth or Tenth Revision; LSD, lysergic acid diethylamide; MDMA, 3,4-methyl enedioxy methamphetamine.

use documented in the problem list, medication list or social history section (155/164 [94.5%] of women who delivered pre-intervention, 59/66 (89.4%) in linkage alone and 25/25 (100%) in linkage plus SOFAR) had substance use documented in the problem list, medication list, or social history section. Opioid use alone was most common, in 93/164 (56.7%) women before and 49/91 (53.8%) women during the intervention period. Concurrent opioid and unprescribed stimulant (cocaine, amphetamine, or methamphetamine) use was also frequently reported, particularly among individuals in the linkage plus SOFAR group (52.0%), and approximately half had documented injection drug use in each group (Table 1). At delivery, 132/164 (80.5%) women before and 72 (79.1%) women during the intervention were prescribed opioid agonist therapy, with more women on methadone (85/164 [51.8%] before and 42/91 [46.1%] during intervention) compared with buprenorphine (47/164 [28.7%] vs. 30/91 [33.0%], respectively).

HCV CARE CASCADE

Across both periods, 95% of women who were seropositive had RNA testing completed, and 74% of women who were seropositive were diagnosed with chronic HCV infection (Fig. 1). Sixteen women (6.3%) were likely (previous negative HCV testing) and 45/255 (17.6%) women were possibly (no previous laboratories documented) newly diagnosed with chronic HCV infection during pregnancy. The majority of women who were viremic (75.0% preintervention, 83.3% who received the linkage intervention only, and 92.0% with the linkage intervention and SOFAR) had genotype testing completed, and 28 (17.1%) women who were viremic before intervention, 16 (24.2%) with the linkage intervention only, and 13 (52.0%) with the linkage intervention and SOFAR had evidence of HCV treatment initiation (Fig. 1). By October 2020, 24/28 (85.7%) women preintervention, 13/16 (81.2%) women with the linkage intervention, and 9/13 (69.2%) women with the intervention and SOFAR who were prescribed therapy had evidence of cure (SVR). Chart review revealed that those who did not achieve SVR either never started treatment (2 women before and 2 women during the intervention, including 1 who spontaneously cleared during a 6-month delay between prescription order and representation to care) or were lost to follow-up before SVR laboratories were obtained (2 preintervention and 5 during the intervention). Preintervention,

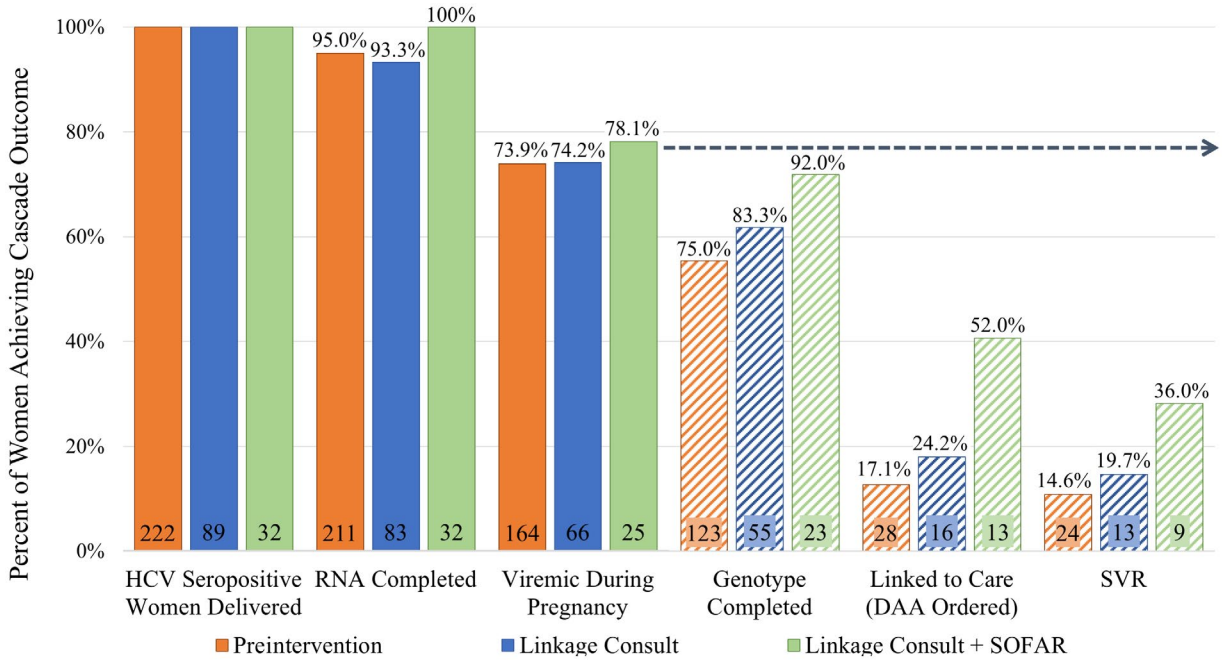

FIG. 1. HCV cascade to cure, preintervention period (January 2014-September 2016) and during the intervention period (October 2016-March 2018), by intervention received. Number of women achieving each HCV care cascade outcome, by intervention period and intervention type. Numbers at base of bars indicate total number (n). Percentages for the first three columns (solid bars) are per total women delivered who were HCV seropositive; percentages for the last three columns (dashed bars) are per those with evidence of HCV viremia during pregnancy, as indicated by the arrow. Linkage indicates linkage intervention exposure only; Linkage + SOFAR indicates women exposed to both the linkage and colocated care interventions.

primary care or addiction clinicians wrote 50% of DAA prescriptions, and during the intervention this increased to 19/29 (65.5%) of prescriptions (Table 1).

SUBGROUP WITH CONTINUED FOLLOW-UP CARE AT BMC

In the cohort of women with BMC follow-up postpregnancy, characteristics were similar before and during intervention periods, with two exceptions. Buprenorphine treatment for OUD was more common during the intervention period (44.0% linkage group, 33.3% linkage plus SOFAR group vs. 27.0% preintervention group) as methadone maintenance therapy became less frequent (40.0% during linkage intervention, 45.5% in linkage plus SOFAR vs. 57.1% preintervention) (Table 2). Women who delivered preintervention also had an overall longer BMC follow-up observed (mean, 593 vs. 326 days) because of the greater observation time in the study with a specified end date. Mean time between delivery and HCV treatment initiation decreased from 336 (SD, 228) days for women delivering preintervention to 247 (SD, 100; linkage alone) and 243 (SD, 183; linkage plus SOFAR) days for women delivering during the intervention period. Of the 70 women who were not treated, 38 (54.3%) were still in care during the last study year. For those lost to follow-up before the end of the study (n = 32), mean time in care postpartum was 331 (SD, 201; range, 26-743) days.

REGRESSION ANALYSIS

In univariate analysis, women received HCV treatment in the linkage group at 3.23 times (95% confidence interval [CI], 1.54-6.76) and in the linkage plus SOFAR group at 3.26 times (95% CI, 1.60-7.04) the rate of women preintervention (Table 3). Buprenorphine compared with methadone opioid agonist therapy and opioid use alone compared with opioid and unprescribed stimulant use were also associated with increased treatment rates. In the model adjusted for substance use, delivery during intervention compared with the preintervention period was

TABLE 2. CHARACTERISTICS OF WOMEN WITH HCV INFECTION (VIREMIA) WHO DELIVERED AT BMC JANUARY 2014-MARCH 2018 WITH CONTINUED FOLLOW-UP POSTPARTUM WITHIN THE HEALTH SYSTEM THROUGH AT LEAST JULY 2016

		Intervention Period*	
Variable	Preintervention* n = 63 (%)†	Linkage n = 25 (%)†	Linkage + SOFAR n = 24 (%)†
Age in years, mean (range)	30.1 (20-40)	29.8 (20-38)	30.9 (24-39)
Age (years)			
<25	5 (7.9)	2 (8.0)	2 (8.3)
25-35	47 (74.6)	17 (68.0)	17 (70.8)
≥35	11 (17.5)	6 (24.0)	5 (20.8)
Race/ethnicity			
White non-Hispanic	48 (76.2)	22 (88.0)	22 (91.7)
Other	15 (23.8)	3 (12.0)	2 (8.3)
Current tobacco use‡			
Yes	43 (68.2)	17 (68.0)	18 (75.0)
No	20 (31.8)	8 (32.0)	6 (25.0)
Substance use‡			
Opioid use only	30 (47.6)	18 (59.2)	11 (45.8)
Opioid and nonprescribed stimulant use	31 (49.2)	5 (20.0)	13 (54.2)
Other or none	2 (3.2)	2 (8.0)	0
Opioid agonist medication‡			
None	10 (15.9)	4 (16.0)	5 (20.8)
Buprenorphine	17 (27.0)	11 (44.0)	8 (33.3)
Methadone	36 (57.1)	10 (40.0)	11 (45.8)
Mean follow-up time, days§ (SD)	593(362)	326 (188)	327 (196)

*Preintervention period, January 2014-September 2016; intervention period, October 2016-March 2018.
†n (%) unless otherwise indicated.
‡At time of delivery, as noted in the social history section, problem list, or medication list.
§Follow-up time denotes days from delivery through first of either HCV treatment or last recorded BMC primary/addiction care, gastroenterology, or infectious diseases visit completed.

associated with an increased treatment rate (rate ratio [RR], 2.87; 95% CI, 1.34-6.18 for the linkage group; RR, 3.89; 95% CI, 1.83-8.26 for the linkage plus SOFAR group). Results were similar after adjusting for opioid agonist therapy rather than substance use (Table 3), and buprenorphine prescription at delivery was also associated with increased HCV treatment compared to methadone (RR, 2.10; 95% CI, 1.05-4.21).

Discussion

We describe a linkage intervention and a multidisciplinary clinic colocating mother and infant care to identify peripartum women eligible for HCV treatment postdelivery and engage them in HCV care and treatment after pregnancy and breastfeeding. Adjusting for follow-up time, age, substance use, and opioid agonist treatment, HCV treatment initiation increased for women delivering after intervention implementation. For women who continued to seek care at our institution postpregnancy, those delivering during the linkage intervention had over 2 times the rate of HCV treatment initiation and women exposed to both the linkage intervention and colocated care had over 3 times the rate of HCV treatment initiation compared with women delivering preintervention.

This is among the first studies to examine HCV treatment rates and linkage to care interventions in women identified during pregnancy. Nearly all women who were seropositive had HCV RNA testing, aided by reflex testing implementation (all positive-HCV antibody testing is automatically reflexed to RNA and genotype testing) initiated in August 2016. Approximately 75% of women who were HCV

TABLE 3. HCV TREATMENT INITIATION RATES IN WOMEN WITH HCV INFECTION (VIREMIA) WHO DELIVERED AT BMC JANUARY 2014-MARCH 2018 WITH CONTINUED FOLLOW-UP POSTPARTUM WITHIN THE HEALTH SYSTEM THROUGH AT LEAST JULY 2016

Variable	Treated (n = 42)*	Not Treated (n = 70)*	Unadjusted Rate Ratio† (95% CI)	Adjusted Rate Ratio‡ (95% CI)	Adjusted Rate Ratio§ (95% CI)
Intervention period					
Preintervention	17 (27.0)	46 (73.0)	Ref.	Ref.	Ref.
Linkage	13 (52.0)	12 (48.0)	**3.23 (1.54, 6.76)**	**2.87 (1.34, 6.18)**	**2.40 (1.10, 5.25)**
Linkage + SOFAR	12 (50.0)	12 (50.0)	**3.26 (1.60, 7.04)**	**3.89 (1.83, 8.26)**	**3.36 (1.57, 7.17)**
Age in years, mean, (SD; range)	29.3 (4.1; 20-36)	30.8 (4.6; 21-40)	0.93 (0.87, 1.01)	0.92 (0.86, 0.99)	0.92 (0.86, 0.99)
Race/ethnicity					
White non-Hispanic	36 (39.1)	56 (60.9)	1.49 (0.63, 3.55)	—	—
Other	6 (30.0)	14 (70.0)	Ref.	—	—
Current tobacco use‖					
Nonsmoker	11 (32.4)	23 (67.6)	Ref.	—	—
Smoker	31 (39.7)	47 (60.3)	1.36 (0.68, 2.71)		
Substance use‖					
Opioid use only	28 (47.5)	31 (52.5)	Ref.	Ref.	—
Opioid and nonprescribed stimulant use	13 (26.5)	36 (73.5)	**0.46 (0.23, 0.89)**	0.56 (0.28, 1.12)	—
Other	1 (25.0)	1 (75.0)	0.40 (0.05, 2.92)	0.32 (0.04, 2.44)	—
None	0 (0)	0 (0)	—	—	—
Opioid agonist medication‖					
Buprenorphine	20 (55.6)	16 (44.4)	**2.71 (1.40, 5.23)**	—	**2.10 (1.05, 4.21)**
Methadone	17 (29.8)	40 (70.2)	Ref.	—	Ref.
None	5 (26.3)	14 (76.7)	0.85 (0.31, 2.33)	—	0.80 (0.29, 2.19)

*Data show n (%) unless otherwise indicated.
†CIs that do not overlap the null value of RR = 1 are shown in bold.
‡Adjusted for age *a priori* and all variables with $P < 0.1$ in unadjusted analysis, excluding opioid agonist medication at delivery.
§Adjusted for age *a priori* and all variables with $P < 0.1$ in unadjusted analysis, excluding substance use at delivery.
‖At the time of delivery, as noted in social history, problem list, or medication list.
Abbreviation: Ref., reference.

seropositive in this study had ongoing viremia, consistent with the literature-reported spontaneous acute clearance rate (26%) and with very few women having received treatment before delivery.[25] With recent CDC guidelines to screen all women during each pregnancy, infrastructure must be created to link women identified to have chronic HCV infection to HCV cure after delivery. Increasing HCV treatment rates for women identified during pregnancy imparts benefits not just to the women treated as it can also prevent vertical transmission in any future pregnancies and horizontal transmission with further risk behavior.

This study has several limitations. Data are limited by availability through a single medical center; treatment received elsewhere is not captured. However, we restricted the primary analysis cohort to individuals continuing to receive primary or HCV-treating specialty care at our institution to minimize bias introduced from missing data for women treated elsewhere. This restricts our study to a population with continued care-seeking behaviors and therefore may be less generalizable; however, it allows for more accurate person-time measurement and more accurate comparisons between the selected groups. As a retrospective study with a historic control group, findings may be confounded by time-related variables, such as new drug approvals, increased state Medicaid treatment eligibility criteria, other linkage initiatives, and improved provider education over the study period. To minimize these time-related confounding effects, we analyzed women in all groups by quarter over the same calendar time starting from July 2016 when Massachusetts removed Medicaid HCV treatment restrictions. We also restricted our population to

women "in care" to avoid biasing the preintervention population estimates by assuming all women were still in care at BMC years after delivery.

At least 98% of women in this study were insured at delivery and likely had continued health insurance postpartum.[26] We realize this is not the case in all countries or US states and limits generalizability. Initiatives to enroll participants in health insurance coverage postpartum could be coupled with these interventions to improve both HCV and general health care for women and families. Treatment during pregnancy could be an option in the future, or treatment immediately postpartum for women who do not breastfeed (depending on duration of postpartum coverage) could be an option to capture women with limited insurance options postpartum. Our institution plans to pilot an obstetrician-led program for obstetric and family medicine clinicians to treat HCV during an extended 12-month postpartum and recovery care model to further reduce linkage to care barriers.

The limited number of women in each intervention group with continued BMC follow-up and overlap between the linkage program and colocated care clinic limited our ability to isolate the effects of either intervention from the other. A few women were discharged before the linkage consultation, which may have biased results toward the null hypothesis, but we did not exclude these women as the linkage intervention extended to touchpoints with women during pediatric and colocated care appointments. We also cannot isolate whether the intervention itself or the overall interaction with prenatal care during a period of treatment availability accounted for the results. Either explanation, however, highlights perinatal care as an effective venue to screen women with HCV and link them to cure. Finally, we were unable to ascertain the reasons women declined or delayed HCV treatment. In clinical practice, we observe the competing priorities of maintaining recovery and caring for infants in the postpartum period in addition to transportation and other logistic hurdles. The active linkage and colocated care interventions in this study aimed to decrease the hurdle of finding a treating provider and of attending additional appointments. They were successful for many but not all women in this study, and research to understand additional barriers to HCV treatment for postpartum women and solutions to overcome them is needed.

Treatment initiation rates and time to treatment initiation (mean was 8 months during the intervention period) were equal to or higher than literature-reported rates in most observational and linkage studies (excluding those offering direct treatment in the same clinic).[27-29] Given lower breastfeeding rates in this population,[30] other factors, such as insurance prior authorizations (and their required laboratory work-up) and delays in obtaining appointments, likely influenced observed delays in treatment, but most women who initiated treatment did so <1 year postdelivery. SVR rates were relatively high as well, although subject to loss to follow-up, similar to rates observed in real-world demonstration studies.[27,28] Chart review did not reveal evidence of treatment failure in those patients, but we cannot be certain; further studies into treatment adherence are warranted in this population.

Over 90% of women infected with HCV in this study had chart evidence of current or prior opioid use or misuse. These results are consistent with recent CDC data indicating that the majority of pregnant women with HCV infection have diagnosed OUD.[4] Buprenorphine treatment and absence of polysubstance use were associated with increased treatment rates, and a high percentage of women were treated in primary care with integrated addiction medicine programs (64% during the intervention). Demonstration studies reveal high HCV treatment efficacy in populations who inject drugs, particularly when treatment is offered in the same location they receive other care or services.[31-34] However, HCV treatment is not universally offered in OUD treatment programs, and many states continue to restrict the use of HCV treatments for individuals with ongoing or recent substance use. Although most states have made great strides in reducing barriers to HCV treatment, 27 state Medicaid programs still maintain restrictions by disease stage, concurrent substance use, or provider specialty.[22] These restrictions pose significant obstacles to HCV elimination, particularly in women of reproductive age who are likely to have recent substance use and are unlikely to have significant liver disease. In order to translate universal prenatal HCV testing recommendations into treatment as prevention and progress toward HCV elimination, reproductive age women must have access to HCV cure.

Linking women to HCV cure is just one step in the HCV continuum of care and must be coupled with addiction management during pregnancy,

postpartum treatment programs, and recovery support for the majority of women with coexisting substance use. Colocating care for HCV and substance use treatment is effective,[31,33,34] and combining this with infant care could prove an even stronger intervention for this population. Furthermore, work to link fathers to both HCV and addiction care can help improve health for the entire family and decrease the likelihood of reinfection. The World Health Organization (WHO) 2030 HCV global elimination targets include ensuring 80% of eligible individuals are treated to help meet a 90% reduction in incidence and 65% reduction in liver mortality.[35] Following the role testing and treatment of pregnant women has played in the HIV epidemic, screening pregnant women for HCV, engaging them in care, treating them to prevent exposure in subsequent pregnancies, and diagnosing and curing infected infants could be key measures to help achieve these goals. Our findings provide evidence that a program beginning in prenatal care and extending to a postpartum multidisciplinary program can successfully increase treatment initiation rates in women with HCV infection initiating HCV treatment. This intervention provides a framework on which health systems can build prenatal HCV testing to advance toward WHO HCV elimination goals.

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