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Optimizing Hepatitis C Virus (HCV) Treatment in a US Colocated HCV/Opioid Agonist Therapy Program

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Open Forum Infectious Diseases

MAJOR ARTICLE

Optimizing Hepatitis C Virus (HCV) Treatment in a US Colocated HCV/Opioid Agonist Therapy Program

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Background. A minority of patients with opioid use disorder are treated for hepatitis C virus infection (HCV). While colocated HCV and opioid agonist therapy (OAT) along with harm reduction can facilitate prevention and cascade to cure, there are few real-world examples of such embedded care models in the United States in the direct-acting antiviral (DAA) era.

Methods. We conducted a retrospective chart review to determine sustained virologic response (SVR) and reinfection rates during the first 5-year period of DAA availability among individuals tested and treated on-site at Rhode Island's only nonprofit methadone maintenance program.

Results. Of 275 who initiated DAAs, the mean age (range) was 43 (22–71) years, 34.5% were female, 57.5% had genotype 1a, 23.3% had cirrhosis, and 92% were Medicaid recipients. SVR was 85.0% (232/273), while modified intent-to-treat SVR was 93.2% (232/249); 17 patients did not achieve SVR, 2 awaited SVR 12 weeks post-end-of-treatment, and 24 were lost to follow-up. Thirty reinfections were identified over 375.5 person-years of follow-up (rate, 7.99/100 person-years). The median time to first reinfection (interquartile range) was 128 (85.25–202.5) days. Before July 1, 2018, 72 patients accessed DAAs over 3.7 years; after Medicaid DAA restrictions were lifted, 109 patients accessed DAAs over 1.3 years. The Prior Authorization (PA) process requires many steps, differing across 11 RI insurers, taking 45–120 minutes per patient.

Conclusions. DAA treatment was effective among a marginalized population in an urban colocated OAT/HCV program. Removing DAA restrictions facilitates treatment initiation. The PA process remains a modifiable barrier to expanding capacity in the United States.

Keywords. colocated care; direct-acting antivirals (DAAs); hepatitis C virus infection (HCV); opioid agonist therapy (OAT); people who inject drugs (PWID).

To achieve hepatitis C virus infection (HCV) elimination, a greater proportion of people who inject drugs (PWID) living with HCV need to be diagnosed, treated, and cured. PWID constitute the largest group of persons in the United States infected with HCV and account for most new infections [1]. PWID may be successfully treated with direct-acting antiviral (DAA) agents. Contemporary meta-analyses demonstrate high sustained virologic response (SVR) rates among PWID with or without opioid agonist therapy (OAT; methadone [μ-receptor full agonist] and buprenorphine [μ-receptor partial agonist]) [2, 3]. While national and international guidelines support HCV treatment scale-up for PWID, in the United States, a minority receive treatment.

Historically, HCV care has been delivered in specialist settings. Embedding HCV treatment into services utilized by PWID can facilitate access, as drug-involved populations may face stigma and difficulty navigating traditional health care environments. The advent of DAAs simplifies HCV therapy and enables prescription by a broad range of providers. Delivering all elements of care under 1 roof may be accomplished with colocated HCV and addiction care.

More than four out of five PWID predominantly inject opioids, making HCV treatment integration at OAT programs essential [4]. OAT, the key treatment for opioid use disorder (OUD), reduces illicit opioid use, withdrawal symptoms, and opioid-related morbidity and mortality [5]. OAT facilitates HCV screening, treatment initiation and SVR, and reduces incidence and reinfection [4, 6–8]. Administering DAAs in conjunction with OAT and high-coverage needle syringe programs (NSPs) establishes the optimal preventive strategy [5, 9–11].

Rhode Island (RI), ranked 10th in the nation for overdose deaths, reported 26 000 individuals with OUD in 2016 [12, 13]. A 2014 study conducted before considering the opioid crisis estimated 16 768 HCV-infected Rhode Islanders [14]. The work presented was developed given concerns that referral to off-site subspecialty care was failing a vulnerable population.

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METHODS

Study Design

We conducted a retrospective chart review of all patients treated on-site for HCV from November 1, 2014, to October 31, 2019, at CODAC Behavioral Health Inc. (CODAC), RI's only nonprofit methadone maintenance program (MMP). CODAC runs 9 geographically dispersed sites providing OAT to >2500 patients. The largest, in Providence, serves 1000 patients daily, a disenfranchised population with high rates of homelessness, poverty, and frequent incarceration. Included in this review were patients (1) on OAT at 1 of CODAC's 8 community sites (the ninth, a prison/jail, was excluded because patients receive HCV care in corrections) and (2) attending at least 1 HCV visit at CODAC Providence. Patients were not financially compensated for care, nor were they contacted for data collection purposes. The University of RI's Institutional Review Board approved this research.

Colocated Care Model

CODAC Providence's HCV Clinic started on May 1, 2014, with a part-time addiction, HIV, and viral hepatitis–trained internal medicine physician, an addiction and viral hepatitis–trained nurse, and a phlebotomist. CODAC Providence uses SMART Software for methadone dispensing, with paper charts for HCV care. For the first 4 years, CODAC Providence offered HCV antibody testing; with a reactive result, blood was drawn for HCV RNA. On May 1, 2018, CODAC Providence began universal, opt-out, serum HCV antibody screening with reflexive RNA and genotype upon entry into OAT care, with annual rescreening for HCV-uninfected patients (Figure 1). Phlebotomy also included testing for HIV, hepatitis A virus (HAV), and hepatitis B virus (HBV) serologies, liver panel, complete blood count, creatinine, prothrombin time/international normalized ratio, and rapid plasma reagin plus urine gonorrhea and chlamydia.

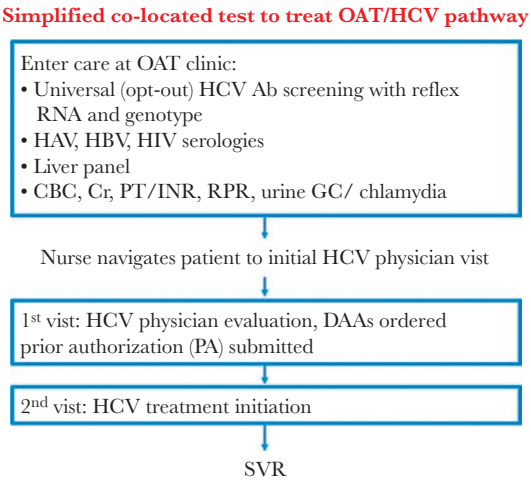

Figure 1. Simplified colocated test to treat OAT/HCV pathway.

The nurse navigates HCV-infected patients to an on-site HCV physician visit, provides viral hepatitis and harm reduction (HR) education, refers to NSP, supplies naloxone, and coordinates clinic flow. The initial physician visit includes a full medical history and physical exam, as many patients do not have primary care providers, along with viral hepatitis, HIV, polysubstance use, and prevention counseling. If history, physical exam, aspartate transaminase (AST)-to-platelet ratio index (APRI) and Fibrosis-4 (FIB-4) yield discordant results, Fibrosure (LabCorp, Research Triangle Park, NorthCarolina) is ordered. DAAs are prescribed at visit completion (unless selection is influenced by Fibrosure result). The physician provides care for HIV, HBV, other sexually transmitted infections, and cirrhosis, prescribes HIV pre-exposure prophylaxis (PrEP), and addresses urgent medical concerns. She attempts to link patients with primary care given that CODAC is not an ambulatory care center but a federally licensed MMP, organizationally and physically separate from mainstream health care [15]. For women of childbearing potential, the physician provides preconception counseling, recommends planned pregnancies and avoidance during DAA therapy, and assists with contraception. Patients with cirrhosis are referred to off-site ultrasound for hepatocellular carcinoma (HCC) and esophageal variceal surveillance (albeit few make these appointments) with on-site serum alpha-fetoprotein biannually. On-site HAV and HBV vaccination began in December 2018.

Patients are accommodated through scheduled and walk-in visits and may remain in care no matter the number of late or missed visits. HCV treatment is universal, except for those with a short life expectancy unable to be remediated by DAAs. For patients without stable housing, DAA pharmacy deliveries are accepted and stored on-site. With their approval, patients are put "on hold" at the methadone window; a nurse sees a SMART alert to "hold" the dose until conferring with the HCV nurse. The nurse then reminds the patient of an HCV-related appointment and/or phlebotomy. Patients are encouraged to bring in injecting partners for simultaneous treatment. Deliveries of DAAs are provided for patients who are hospitalized or incarcerated midtreatment.

In July 2018, a pharmacist joined the team to lead the DAA Prior Authorization (PA) process. Prescribing DAAs requires completing and faxing a PA form, plus supporting laboratory results, to each patient's insurer. There are 11 distinct RI insurers, each with different PA requirements and a unique PA form. The documentation and approval process takes 45 to 120 minutes per patient. PAs require repeat blood tests—HCV RNA and genotype within 90 days even for patients with documented viremia for years and recent genotyping, prescribed pan-genotypic regimens—and myriad administrative elements (phone calls, peer-to-peer discourse, responding to denials). Each payer dictates a preferred pharmacy, some mail order only, and a preferred DAA formulary. The pharmacist also obtains

medication lists, assists with drug–drug interactions, calls in approved prescriptions, coordinates with numerous pharmacies to expedite DAA acquisition, ensure that refills are obtained on time as DAAs are dispensed monthly, supports adherence, and maintains the clinic database.

The second visit is treatment initiation, held once the payer approves DAAs, typically within 3 weeks. For women of childbearing potential, urine pregnancy testing is performed to ensure a negative result. The first DAA dose is witnessed. Snacks are supplied to patients who contend with food insecurity and cannot eat before DAAs that require food. Individualized plans are developed regarding when patients will take DAAs, storage, refills, and HR. During treatment, patients may see the nurse or doctor with questions 5 days per week. Given the substantial prevalence of ongoing injection and polysubstance use, the staff recommends that patients see the physician or nurse at week 2 for discussing adherence, liver panel to gauge biochemical response, and HCV RNA. Liver panel and HCV RNA are checked at end of treatment (EOT) and post-treatment week 12, with additional laboratory monitoring and check-ins for patients with medical risk. SVR visits focus on next health steps, prioritizing tobacco cessation. Prompt retreatment is offered following reinfection. Reinfection visits afford opportunity to evaluate for other infectious consequences of injection drug use (IDU), PrEP, and OAT dose evaluation.

Medicaid DAA Restrictions

Until July 1, 2018, RI Medicaid restricted DAAs to patients with Meta-Analysis of Histologic Data in Viral Hepatitis (METAVIR) fibrosis stage F3 or F4; either no drug/alcohol use for 6 months or current addiction treatment; specialist physician to prescribe DAAs; and, if HIV-infected, confirmation of antiretroviral therapy or HIV RNA suppression [16]. On July 1, 2018, RI's DAA Medicaid Restrictions were lifted under threat of lawsuit [17].

Variables

We conducted a chart review to obtain baseline characteristics for treated patients (age, gender, payer), clinical measures (HCV genotype, HIV coinfection, HBV coinfection, cirrhosis, HCC), SVR, and reinfection. We included treatment initiation and reinfection data from November 1, 2014 (the first date we could access DAAs) through October 31, 2019, and SVR data through February 29, 2020. A patient is characterized as having cirrhosis if they fulfill any of the following: (1) liver biopsy with METAVIR stage 4 fibrosis; (2) presence or history of any of the following: ascites, spontaneous bacterial peritonitis (SBP), esophageal varices, hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome; (3) presence of 2 or more of the following: (a) Fibrosure >0.75, (b) FIB-4 >3.25, (c) APRI >2, (d) platelets <140 000/mL, (e) transient elastography >12.5 kPa, (f) imaging revealing signs of portal hypertension (spleen size >13 cm, portal flow mean velocity <12 cm/sec, portal vein mean diameter >13 mm). Decompensated cirrhosis was defined as presence or history of ascites, SBP, esophageal varices, hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, or HCC.

The primary outcome, SVR, was defined as undetectable HCV RNA 12 weeks post-EOT or at the first follow-up time point beyond the SVR date for patients missing this blood draw. SVR was marked as missing when SVR could not be confirmed 12 weeks post-EOT or in subsequent follow-up. HCV reinfection was defined as the presence of detectable HCV RNA following undetectable HCV RNA 12 weeks after EOT or genotype switch.

Ninety-four patients were treated through a research study providing sofosbuvir/velpatasvir (SOF/VEL). Other patients were prescribed SOF/VEL or a combination of the following medications consistent with society guidelines [18] and those accessible through each payer at the time of initial HCV encounter: simeprevir, sofosbuvir, daclatasvir, sofosbuvir/ledipasvir, elbasvir/grazoprevir, SOF/VEL, SOF/VEL/voxilaprevir, glecaprevir/pibrentasvir, and ribavirin.

Data were systematically abstracted from clinical charts, de-identified, and entered into an electronic database in a standardized process. Three authors performed data extraction, database entry, and cross-checking. Statistical analyses were performed using Excel, version 2016 (Microsoft). To ensure data accuracy, the expert clinician team member randomly verified collected data. Discrepancies were addressed through team discourse. Data were recoded as necessary.

Data Analysis

We descriptively examined patient baseline characteristics using counts and percentages for categorical variables. The continuous variable age was grouped into age range categories. We evaluated differences in continuous variables using 2-tailed *t* tests and assessed differences in binary categorical variables using the pooled z-test statistic for differences in proportions. We applied the .05 alpha level for assessing statistical significance.

The numerator for the intention-to-treat (ITT) SVR calculation was the number of patients with undetectable HCV VL 12 weeks post-EOT or at the first follow-up time point past this scheduled SVR date. The denominator consisted of all patients with an available SVR result (achieving or not achieving), excluded patients not yet due for SVR and patients still on treatment at the end of data collection, but included patients starting treatment and lost to follow-up (LTFU) after initiating DAAs and reaching SVR.

The modified ITT (mITT) SVR numerator was calculated as the number of patients with undetectable HCV viral load 12 weeks post-EOT or at the first follow-up time point past this scheduled SVR date. The denominator consisted of all patients

with available SVR results. The patients initiating treatment and LTFU were excluded from the denominator, as were patients not yet due for SVR and patients still on treatment. In the analysis of patients who did and did not achieve SVR, age and gender differences were compared with a 2-tailed *t* test and pooled z-test, respectively.

Reinfection rate was calculated as the number of reinfections divided by the at-risk person time between EOT and end of data collection for patients who were not reinfected, or the assumed date of reinfection for reinfected patients, defined as the midpoint between EOT and the first follow-up date with detectable HCV RNA [19, 20]. The following sensitivity analyses were carried out: At-risk person time was calculated as time between SVR date and the first follow-up date with detectable HCV RNA, and at-risk person time was calculated as time between SVR date and the midpoint between the SVR date and the first follow-up date with detectable HCV RNA [19, 20]. Median time to the first reinfection and interquartile range (IQR) were calculated and reported in days. In the analysis of patients who achieved SVR and were reinfected, comparisons of patients who were and were not reinfected were conducted to assess age and gender differences using a 2-tailed *t* test and pooled z-test, respectively.

RESULTS

Baseline Characteristics of DAA-Treated Patients

From May 1, 2014, to October 31, 2019, 426 patients underwent initial HCV physician evaluation. Of these, 275 (64.6%) initiated DAAs, with a mean age (range) of 43 (22–71) years, 34.5% female, and 57.5% genotype 1a (Table 1). Sixty-four (23.3%) had cirrhosis at presentation; of these, 7 (2.5%) presented with decompensated cirrhosis. Most patients, 92%, were Medicaid recipients, under the following Medicaid plans: 53.1% Neighborhood Health, 26.9% United Health, 16.9% RI Medicaid, 4.7% Tufts Health, 0.4% Mass Health.

One patient presenting with cirrhosis was diagnosed with HCC shortly after initial HCV evaluation and achieved SVR and long-term remission. A second patient presenting with cirrhosis was diagnosed with HCV-associated intrahepatic cholangiocarcinoma shortly after achieving SVR and died from this malignancy. A third presenting with cirrhosis was diagnosed with HCC 6 months post-SVR. For this patient, Medicaid denied the prescription for an optimal regimen, approving only a shortened treatment course. The patient did not achieve SVR with this first DAA regimen despite reporting perfect adherence. He was then promptly prescribed and Medicaid-approved for a second treatment course with an extended regimen. He achieved SVR following retreatment, then subsequently developed HCC and died.

SVR

Of the 275 patients who initiated DAAs, 2 were still awaiting SVR at the end of data collection (Figure 2). Of the 273 patients who were 12 weeks or more post-EOT, 232 patients had an undetectable HCV VL 12 weeks post-EOT or at the first follow-up time point past their scheduled SVR date. The ITT SVR was 85.0% (232/273). Twenty-four patients were LTFU, meaning they were missing SVR results 12 weeks or more post-EOT. Seventeen patients did not achieve SVR. The mITT SVR was 93.2% (232/249).

There was a difference in mean age between patients who did and did not achieve SVR (difference, 6.6 years; 95% CI, 1.8 to 11.9; $P < .01$). Patients achieving SVR were older, with a mean age (range) of 44 (22–71) years; for patients not achieving SVR, the mean age (range) was 37 (23–55) years. No gender differences were found between patients who did and did not achieve SVR (difference of proportions, 2%; 95% CI, –1.3% to 1.3%; $P = .4$).

Table 1. Demographics and Clinical Characteristics of 275 HCV-Infected Patients on OAT Treated for HCV

Characteristics	Total Treated (n = 275)
Age, y	No. (%)
21–30	46 (16.7)
31–40	91 (33.1)
41–50	53 (19.3)
51–60	54 (19.6)
61–70	30 (10.9)
71–80	1 (0.4)
Gender	
F	95 (34.5)
M	180 (65.5)
HCV genotype	
1a	158 (57.5)
1b	16 (5.8)
2	17 (6.2)
3	61 (22.2)
4	18 (6.5)
6	1 (0.4)
Mixed	4 (1.5)
Other liver disease	
HIV/HCV	4 (1.5)
HBV/HCV	4 (1.5)
Cirrhosis	64 (23.3)
Compensated	57 (20.7)
Decompensated	7 (2.5)
Insurance	
Public	270 (98.2)
Medicaid	253 (92.0)
Medicare	17 (6.2)
Private	5 (1.8)

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; OAT, opioid agonist therapy.

Reinfection

Of 275 patients initiating DAAs, 30 reinfections occurred over 375.5 person years of follow-up, for a reinfection rate of 7.99 (95% CI, 5.1 to 10.8) per 100 person-years. The median time to first reinfection was 128 days, with an IQR from 85.25 to 202.5 days. Sensitivity analyses conducted to determine

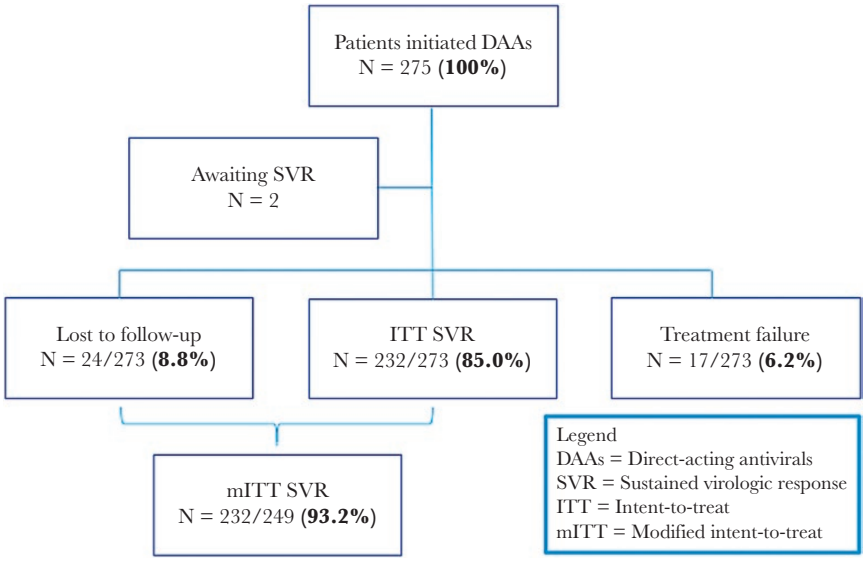

Figure 2. DAA treatment outcomes.

whether the reinfection rate would differ under alternate definitions of date of reinfection revealed nearly identical results (not shown).

There was a difference in mean age between those who were and were not reinfected (difference, 4.9 years; 95% CI, −9.1 to −0.6; $P < .01$). Reinfected patients were younger, with a mean age (range) of 39 (25–56) years; for patients not reinfected, the mean age (range) was 44 (22–71) years. No gender differences were found between those who were and were not reinfected.

Treatment and Medicaid Restrictions

Seventy-two patients initiated DAAs under Medicaid restrictions (November 1, 2014–June 30, 2018), with mean age of 55 (30–71 years), 26.4% female, and 69.4% having cirrhosis (Table 2). From July 1, 2018, to October 31, 2019, 109 patients initiated DAAs, with a mean age (range) of 39 (22–65) years, 38.5% female, and 9.2% having cirrhosis. This analysis excludes 94 patients treated through a study providing DAAs. There was a difference in mean age between those initiating treatment before and after lifting restrictions (difference, 15.8 years; 95% CI,

Table 2. Characteristics of Patients Initiating DAAs Before and After Lifting Medicaid DAA Restrictions

	Initiated DAAs November 2014–June 2018	Initiated DAAs July 2018–October 2019	Difference of Means,[b] *P*
Age, y	n = 72,[a] No. (%)	n = 109,[a] No. (%)	
21–30	1 (1.4)	26 (23.9)	<.001
31–40	7 (7.7)	42 (38.5)	
41–50	14 (14.4)	20 (18.2)	
51–60	26 (26.1)	17 (15.6)	
61–70	23 (23.9)	4 (3.7)	
71–80	1 (1.4)	–	
Gender			
F	19 (26.4)	44 (38.5)	.064
M	53 (73.6)	67 (61.5)	
Cirrhosis	50 (69.4)	10 (9.2)	<.001
Compensated	44 (61.1)	9 (8.3)	
Decompensated	6 (8.3)	1 (0.9)	
Insurance			
Public	69 (95.8)	107 (98.2)	
Medicaid	56 (77.8)	106 (97.2)	
Medicare	13 (18.1)	1 (0.9)	
Private	3 (4.2)	2 (1.8)	

Abbreviation: DAA, direct-acting antiviral agent.

[a]Excludes 94 patients treated in a study using sofosbuvir/velpatasvir.

[b]*P* values represent difference of means between the pre- and post-Medicaid restriction removal groups.

12.6 to 19; $P < .001$). With restrictions, most treated patients were >50 (67.3%), while once restrictions ended, a fifth (19.8%) were >50. There was a difference in the proportion with cirrhosis between those initiating DAAs before and after removing restrictions (difference, −59.3%; $P < .001$). With restrictions, 72 patients accessed DAAs over 3.7 years; without restrictions, 109 patients accessed DAAs over 1.3 years.

DISCUSSION

Our findings show that people who initiated DAAs in an urban MMP achieved high levels of SVR. This outcome in a real-world setting demonstrates how effective HCV clinical management can be for a marginalized US population on OAT without access to ideal multidisciplinary care—without on-site primary or psychiatric care, common among US MMPs. Our approach incorporating colocated HCV and OAT treatment, HR, flexible health care delivery, and universal "test to treat" delivered in a resource-limited setting can inform models of service delivery.

Our SVR rate (85%) is comparable to those from studies of DAAs in similar populations. A systematic review and meta-analysis of international DAA treatment outcomes reports SVR of 87.4% among people with recent IDU and 90.7% among those receiving OAT [2]. An even more recent prospective, open-label, observational trial at an HR organization in Washington DC reports SVR of 82% among 100 patients with OUD and ongoing IDU treated with SOF/VEL and offered concurrent buprenorphine initiation [21]. Two US retrospective evaluations of real-world colocated care reported SVR rates of 85% among 300 homeless-experienced individuals in Boston, Massachusetts, treated at a Federally Qualified Health Center providing integrated primary care and among 75 patients treated at a New Haven, Connecticut, not-for-profit addiction treatment program providing OAT with on-site primary and psychiatric care [19, 22].

Another success of this "real-world" cohort was the low proportion loss to follow-up and patients evaluable for SVR (8.8% of the ITT population). Engagement following DAA therapy is necessary for determining SVR, managing cirrhosis, ongoing HR, routine testing for reinfection, and prompt retreatment [23]. Colocated OAT can improve retention in HCV care [22]. This may signify the HCV team's experience in OUD, may reflect patients' possible lack of a medical home, and/or may be a consequence of patients being pharmacologically wedded to OAT.

The SVR rate and low proportion lost to follow-up in the absence of robust colocated ambulatory services could also reflect the support and organization built into other aspects of MMP care. MMPs are tightly structured, complex environments [15]. Following a physician assessment, patients ingest a daily methadone dose under direct nursing observation. Results of toxicology screens and compliance with behavioral parameters dictate the number of carry-home doses, which reduce the frequency of clinic attendance. This infrastructure may be leveraged for HCV care, which is important given the high HCV prevalence at MMPs and failure of off-site referral (Figure 3) [24]. Comfortable, compassionate care can be provided by staff cognizant of and working to ameliorate

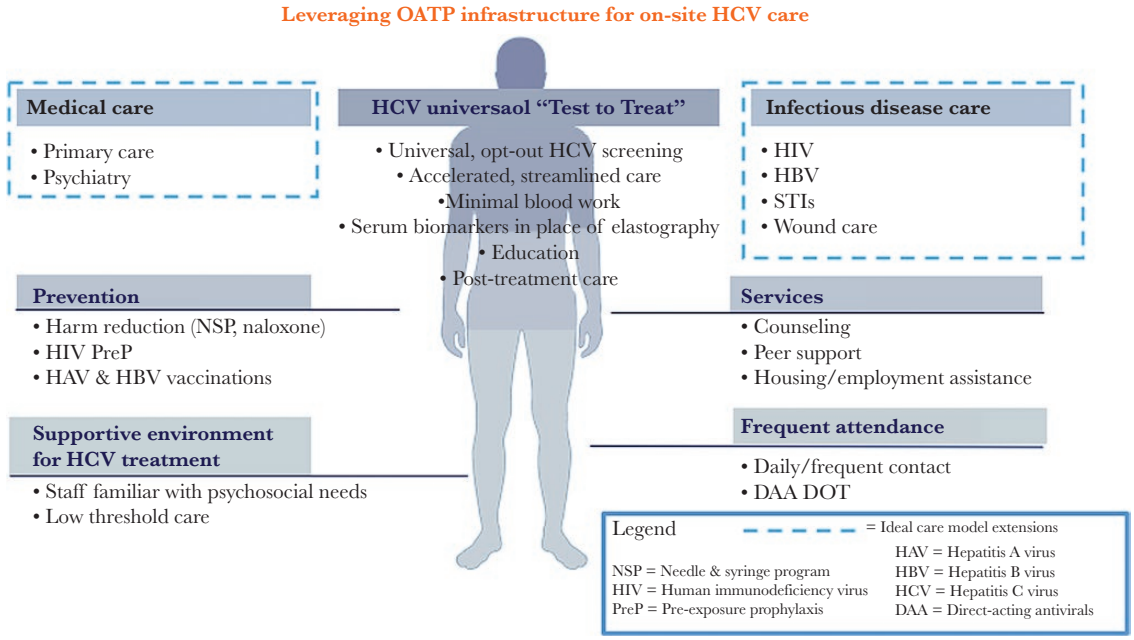

Figure 3. Leveraging MMP infrastructure for on-site HCV care.

the hardships faced by clients contending with OUD. Nursing services, peer support, mental health care and housing assistance may be offered. Regular contact presents opportunity for everyday support and time for development of therapeutic relationships.

Conversely, there are problems with MMPs. Methadone is the most common form of OAT in the United States [25]. The US federal 1974 Narcotic Addict Treatment Act mandated that patients attend a federally licensed clinic for methadone maintenance [15]. This created an MMP system outside of mainstream health care, in which medical standards of care are not always fully incorporated, care beyond dispensing methadone may be limited, and patients are ghettoized with patients with the same diagnosis [15].

The reinfection rate observed in this study is similar to that of other cohorts of PWID on OAT in the DAA era with ongoing IDU. Data are limited on reinfection rates among patients on OAT post-DAA therapy in the United States. Among a New York cohort of PWID on OAT, incidence of reinfection was 7.4 per 100 person-years among those reporting ongoing IDU [6]. In a recent meta-analysis, the reinfection rate was 5.9 per 100 person-years among PWID receiving OAT with recent drug use [26]. Near Rhode Island, among a homeless population in Boston, Massachusetts, the reinfection rate was 13.1 per 100 person-years [19].

CODAC Providence is situated in a hotspot of drug activity and overdose. NSP is available nearby but not on-site. Mounting fentanyl and methamphetamine use may contribute to more frequent injecting behavior. While OAT curtails opioid use, it does not hinder use of stimulants, benzodiazepines, or alcohol, and its efficacy can be compromised by use of these substances. An insufficient number of RI providers prescribing DAAs to drug-involved populations and slow scale-up of HCV treatment may also contribute to reinfection.

The timing of this evaluation highlights the impact of removing DAA restrictions. At program inception, we prioritized older patients, those at risk for advanced fibrosis, and those who were better able to access DAAs under fibrosis restrictions [27]. We were unable to treat HCV before progression to advanced fibrosis—typically in younger patients, often the transmitting population. The remaining US DAA restrictions should be abolished.

Adding a pharmacist to our team, along with ending DAA restrictions, supported treating more people in the year after restrictions ended than in the 4 years prior. The time- and labor-intensive PA processes remain a modifiable barrier to expanding treatment capacity as we aim for test to treat with same-day DAA initiation. It is time to eliminate the DAA PA process. Without the PA process, or with a simplified PA process, the pharmacist could undertake more clinical responsibilities such as treatment initiation visits, adherence support, and follow-up coordination and ultimately help expand treatment capacity.

The Veterans Administration (VA) is the largest provider of HCV care in the United States. Their successful elimination strategy includes pharmacist-led HCV management, an approach utilized globally. By 2017, one-fourth of VA DAA prescriptions were initiated by a network of 200 pharmacists [28]. Enabling community pharmacists—highly educated, underutilized health care workers—to prescribe DAAs with physician collaboration for patients with advanced liver disease is another key strategy to expand US treatment capacity.

This study has several limitations. It is from a single institution, retrospective, and limited to data collected within the context of routine clinical care. We lack a viral hepatitis surveillance system. We do not have data on the total number of patients screened and diagnosed with HCV. We only had staff to enter detailed data for patients prescribed DAAs. While delays in obtaining SVR testing were common, we did not record the date of actual SVR. We do not have data on the untreated population, nor on patient-level factors possibly associated with lack of SVR or reinfection, such as ongoing substance use and polysubstance use, mean OAT dose, or housing status. To strengthen respect and trust, we do not collect data on ongoing substance use, nor do we access the methadone clinic electronic health record (EHR), which contains this information. We work to develop system-level enhancements to overcome individual baseline characteristics. Most patients receive methadone maintenance, with a small minority prescribed buprenorphine/naloxone (Medicaid patients could not access buprenorphine until 2016); we do not have data on the exact percentage.

CONCLUSIONS

DAA treatment is effective among patients with OUD receiving colocated HCV care in a US resource-limited inner-city MMP. "One-stop shopping" with simplified pretreatment assessment and serum biomarkers to stage fibrosis accelerates the path to cure. Eliminating the PA process and remaining state DAA restrictions will expedite treatment initiation following diagnosis to reduce viremic time and incidence.

How can we incorporate HCV management into over 1600 US MMPs [29]? Financial challenges are a limiting factor. US health insurance and payment systems poorly reimburse HCV outpatient care. Models that improve the business case for HCV management without income from procedural billing for endoscopy, colonoscopy and radiology are needed to achieve financial sustainability at MMPs. Extending state and federal support for OUD to support HCV care would help. Virtual colocation via telemedicine can aid in HCV treatment rollout. Telemedicine imports HCV management into locales convenient for and familiar to patients, but lacking HCV expertise, infrastructure, and resources [30].

Determining the essential components of colocated OAT/HCV care to optimize outcomes requires additional study. To mitigate the syndemic of HCV and addiction, alternative payment and financing sources must be identified. Methadone must become more accessible across a range of clinical settings including primary care and community pharmacies, while the full spectrum of HCV services should be offered on-site at OAT programs via a holistic, patient-centered approach that best meets the needs of drug-involved populations.

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