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Research Paper

Treatment of Hepatitis C virus among people who inject drugs at a syringe service program during the COVID-19 response: The potential role of telehealth, medications for opioid use disorder and minimal demands on patients

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A R T I C L E   I N F O

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A B S T R A C T

Background: Healthcare delivery was disrupted during the COVID-19 pandemic, requiring minimized in-person contact between patients and clinicians. During the pandemic, people with opioid use disorder (OUD) were not only at elevated risk for COVID-19, but had markedly reduced access to treatment for OUD, Hepatitis C virus (HCV) and HIV due to recommended decreased in-person visits.

Methods: From March 15-June 15, 2020 at the syringe services program (SSP) in New Haven, Connecticut, USA, a differentiated care model evolved with reduced clinical demands on people who inject drugs (PWID) to ensure screening and treatment for HCV, HIV and OUD, with a focus on HCV treatment. This model involved a single, bundled screening, evaluation, testing (SET) and monitoring strategy for all three conditions, minimal in-person visits, followed by tele-health communication between patients, outreach workers and clinicians. In-person visits occurred only during induction onto methadone and phlebotomy at baseline and phlebotomy 12 weeks post-treatment for HCV to measure sustained virological response (SVR). Patients received supportive texts/calls from outreach workers and clinicians.

Results: Overall, 66 actively injecting PWID, all with OUD, underwent bundled laboratory screening; 35 had chronic HCV infection. Participants were 40 years (mean), mostly white (N = 18) men (N = 28) and 12 were unstably housed. Two were lost to follow-up and 2 were incarcerated, leaving 31 who started pan-genotypic direct-acting antivirals (DAAs). The mean time from referral to initial phlebotomy and initiation of DAAs was 6.9 and 9.9 days, respectively. Fourteen additional patients were newly started on buprenorphine and 6 started on methadone; three and four, respectively, were on treatment at baseline. Overall, 29 (93.5%) PWID who initiated DAAs achieved SVR; among unstably housed persons the SVR was 83.3%.

Conclusions: In response to COVID-19, an innovative differentiated care model for PWID at an SSP evolved that included successful co-treatment for HCV, HIV and OUD using a client-centered approach that reduces treatment demands on patients yet supports ongoing access to evidence-based treatments.

I N T R O D U C T I O N

The COVID-19 pandemic markedly disrupted healthcare service delivery as healthcare providers rapidly shifted to telehealth and reduced or eliminated in-person clinical encounters. This transformation, however, had the potential to markedly reduce access to treatment services, especially in circumstances that have traditionally required “in-person” visits, or markedly delay delivery of needed services.

People who inject drugs (PWID), especially those with opioid use disorder (OUD), were disproportionately impacted by COVID-19 (Vaslyeva, Smyrnov, Stratthed & Friedman, 2020). Not only are people with OUD at 10-fold elevated risk of acquiring COVID-19 relative to others (Wang, Kaelber, Xu & Volkow, 2020), they often have complex medical and psychiatric needs, including treatment for chronic conditions like HIV, HCV, OUD and depression (Altice, Kamarulzaman, Soriano, Schechter & Friedman, 2010). Low access to necessary treatment...
services for OUD, COVID-19 and other infectious diseases also elevates mortality risk (Farhoudian et al., 2020).

Healthcare delivery changes due to COVID-19 greatly reduced HCV testing and identification (Sperring, Ruiz-Mercado & Schechter-Perkins, 2020). Early in the COVID-19 pandemic, screening for and treatment of HCV infection markedly decreased relative to the previous year (Kauffman et al., 2021), potentially leaving PWID with undiagnosed and/or untreated disease.

HCV treatment has traditionally called for several in-person clinical assessments before prescribing treatment, including antibody testing, confirmatory HCV RNA testing to confirm chronic HCV infection, clinical staging (e.g., Fibroscan) and in-person laboratory monitoring during treatment. The availability of extremely safe, pan-genotypic direct-acting antivirals (DAAs) and laboratory testing that reflexively assesses a number of scenarios depending on the preliminary results, has allowed for the potential to transform care (Zignego, Monti & Gragnani, 2018). As proof of concept, the MinMon study (a recent AIDS Clinical Trials Group (ACTG), international and multisite study of 400 patients) reduced clinical assessment to baseline and SVR laboratory testing (Fibroscan was optional); they were able to achieve high (95%) SVR rates in patients without decompensated cirrhosis (Solomon et al., 2020). This approach also enables expansion of the pool of HCV treaters and promotes treatment delivery in a broader range of venues. Many clinicians, however, perceive that PWID will not adhere to recommended treatment and therefore impose a number of additional clinical assessment to assure treatment completion (Asher et al., 2016), despite findings from the SIMPLIFY study (Grebely et al., 2018) and others that show PWID, in general (Mazhnaya et al., 2017), and even those on MOUD (Dore et al., 2016; Norton, Akiyama, Zamor & Litwin, 2018), have SVR rates that exceed 90% (though these studies did not reduce in-person demands on patients). The extent to which HCV treatment outcomes are optimized in patients who newly initiate MOUD is not known.

Simplified HCV treatment algorithms are advocated by the AASLD/IDSA to target treatment naïve adults without or with compensated cirrhosis to facilitate shortcourse treatments with limited staging and monitoring (Ghany, Morgan & panel, 2020). HCV treatment guidelines currently recommend pan-genotypic, direct acting antiviral (DAAs) medications (e.g. glecaprevir (300 mg)/pibrentasvir (120 mg) for 8 weeks (GLE/PB-8 W) or sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks (SOF/VEL-12 -W)) for treatment-naïve patients (Ghany et al., 2020; Zignego et al., 2018). The previously mentioned MinMon study suggested that 12 weeks of daily SOF/VEL with minimal monitoring can achieve high SVR rates; however, only 3% of participants were PWID and treatment using MOUD was not addressed (Solomon et al., 2020).

Access to MOUD for PWID was also impacted by COVID-19 restrictions. Prior to the pandemic, MOUD induction required in-person visits, laboratory and urine drug testing (UDT) and required counseling visits. Emergency regulations for MOUD emerged in late March 2020 from the Substance Abuse and Mental Health Services Agency (SAMHSA) and the Drug Enforcement Agency (DEA) that reduced demands on patients and clinicians for the treatment of OUD by eliminating in-person exams and UDT for patients initiating buprenorphine and allowing increasing amounts of take-home dosing for methadone and buprenorphine in stabilized patients; however, methadone required in-person visits. Telehealth counseling was introduced in April of 2020 and reimbursement guidance followed soon thereafter (Substance Abuse & Mental Health Services Administration, 2020). Despite the relaxation of guidelines, many treatment programs either did not accept new patients or did so less often, reducing access to MOUD (Joudrey et al., 2021).

Initiation of medications for both HCV and OUD in PWID, however, still became significantly more challenging during COVID-19 due to patient and clinic factors, thus requiring a differentiated model of care. Differentiated care models have emerged as “client-centered approaches” to optimize HIV care for specialized subpopulations, and have been applied to HCV treatment in PWID, especially in the context of co-treatment of HCV and OUD (Norton et al., 2018). Where “in-person” services were eliminated or markedly reduced during COVID-19, we describe an innovative model of treating HCV and OUD (and HIV for those co-infected) that exemplifies the differentiated care model.

Methods

Study setting

New Haven, Connecticut is an urban, mid-size city that is the 7th poorest city for its size in the United States and has among the highest levels of HIV, HCV and OUD in PWID. Connecticut was among the first states profoundly impacted by COVID-19, having peaked in terms of the number of cases and hospitalizations in April 2020 (Price et al., 2020). Connecticut is a Medicaid Early Expansion State, and allows all FDA-approved DAAs to patients with chronic HCV. It was also the first state to remove all treatment restrictions (e.g., sobriety, fibrosis, type of clinician, etc.). The New Haven Syringe Service Program (NHSSP), legally operational since 1989, provides low-demand services at a fixed location (“storefront”), through home delivery using a minivan and through a 40-foot mobile medical clinic (MMC) that provides a number of acute and episodic services (Altice, Springer, Buitrago, Hunt & Friedland, 2003; Gibson et al., 2017; Liebman, Path Lamberti & Altice, 2002; Morano et al., 2014; Morano, Gibson & Altice, 2013), including buprenorphine induction and maintenance (Schwarz, Bruce, Ball, Herme & Altice, 2009, 2012). In response to COVID-19, the NHSSP expanded its home delivery program to provide syringes and outreach services in the field, with increased reliance on telephone communication. In-person point-of-care rapid testing for HIV and HCV, however, was markedly curtailed and in-person testing was mostly restricted to diagnostic centers that were able to maintain social distancing protocols. The storefront hours were reduced and procedures were revised to order supplies by phone and deliverables were made directly to patients in the field using physical distancing protocols. The MMC ceased in-person visits and clinicians shifted immediately to telehealth to provide medical services; telehealth involved telemedicine for those with broadband and phone calls for those without it. NHSSP services generally include syringe and paraphernalia exchange and distribution, overdose education and naloxone distribution, fentanyl test strips, safe “crack” use apparatus, direct prescription (buprenorphine) or linkage (methadone) to MOUD, HIV pre-exposure prophylaxis (PrEP), and screening and treatment for HIV, HCV, tuberculosis and STIs. To ensure linkage to healthcare services, outreach workers served as the interface between clients and clinicians and orchestrated screening, evaluation and treatment (SET) services.

Study sample

Between March 15, 2020 and June 15, 2020, clients who accessed the NHSSP services were verbally screened for OUD by outreach workers. Those interested in HCV screening or treatment were referred by the MMC clinician to a local clinical laboratory where phlebotomy could safely be performed. Overall, 66 adults with insurance who were injecting opioids followed through with testing (number assessed not known). Only people with insurance (all had public insurance) were referred for testing (89% of MMC clients have public insurance); few SSP clients in Connecticut do not have insurance to cover HCV treatment.

Differentiated care model procedures

Before COVID, patients were generally screened for HCV and often required 1–2 visits to the clinician in person to evaluate them and initiate treatment. Clinicians often opted to see the patient after 7 days to assess for adverse side effects and assess adherence. A repeated assessment often occurred at week 4. They were often seen at the end of treatment and underwent laboratory testing and again 12 weeks later to assess SVR.
The differentiated care model that evolved for SSP clients is depicted in Fig. 1. The model involved integrated screening, evaluation, treatment (SET) and minimal monitoring for OUD, HCV, and HIV. Screening for OUD involved using a single-item screening question (SISQ) (Wakeman, 2020), followed by diagnosis confirmation using the Rapid Opioid Dependence Scale (RODS) (Wickersham, Azar, Cannon, Altice & Springer, 2015). Laboratory testing for OUD involved only UDT and phlebotomy screened and evaluated patients for HCV and HIV. All patients were screened for chronic HBV and women underwent urine beta-HCG testing for pregnancy, collected at the same time as UDT. In general, there were three elements of the differentiated care model during COVID: 1) laboratory testing that included screening and partial evaluation using bundled testing with reflex testing; 2) two in-person visits only for laboratory assessments; and 3) optional counseling that was delivered using tele-health (phone or video). Those who screened positive for HIV antibody underwent further evaluation with reflex testing for HIV RNA, followed by HCV genotype and FIB-4 assessment of hepatic fibrosis. Those screening positive for HIV underwent reflex HIV-1 RNA quantification and CD4 testing. A clinician at the NHSSP (MMC) reviewed these findings with the patient, completed the evaluation by phone to ensure no contraindications, and developed a care plan. Those with chronic HCV were offered the choice of once daily SOF/VEL for 12 weeks or three pills daily of GLE/PIB for 8 weeks. Decision for the regimen was based on potential pharmacokinetic drug interactions and patient preferences for pill burden and treatment duration. Due to Medicaid regulations, only 4 weeks of medications were provided before medications were renewed. Medications could be delivered to the client’s home, a pharmacy or to our storefront if the patient expressed housing instability and the outreach workers could make home deliveries. All buprenorphine prescriptions were sent to the patient's preferred pharmacy. No scheduled or monitoring procedures were in place, aside for SVR testing 12 weeks after treatment completion, but outreach workers communicated with clients by phone and when delivering sterile syringes.

Treatment for OUD for those not already prescribed MOUD included same-day home induction with buprenorphine using the “BUP Home Induction®” app, a free online “app” developed at Yale University. Those preferring methadone maintenance therapy received same-day expedited initiation of methadone at a nearby addiction treatment clinic that required an initial onsite visit with same-day treatment initiation (Madden et al., 2018). Patients prescribed buprenorphine received a prescription for 7 days, followed by monthly prescriptions thereafter without any in-person visits or required urine drug testing. Methadone supervision varied per client based on treatment program regulations.

Patients with HIV were counseled about medication adherence if they were not virologically suppressed. For those who were not adherent to their antiretroviral therapy (ART), their medications were renewed for 90 days with delivery options similar to those for DAAs. No in-person visits were made, but patients were offered in-person visits if they had an adverse side effect.

**Chart review**

To assess the quality, implementation and clinical outcomes of this differentiated care model, we conducted a retrospective chart review approximately one month after phlebotomy to determine presence of an SVR. A standardized template for HCV management was housed in EPIC, the electronic medical record for the MMC. It was queried for: age, sex, race, housing status (as described by outreach workers who agreed to make home delivery of medications for those with unstable housing), recent drug injection (past 30 days), presence of opioid use disorder, prior HCV and HIV treatment status, HCV genotype, FIB-4 Score, HCV RNA and HIV RNA level, and treatment regimen (SOF/VEL 12 week or GLE/PIB 8 week). In addition, the following values were also queried as important outcome measures: type of MOUD initiated (Buprenorphine maintenance treatment (BMT) continuously, Methadone maintenance treatment (MMT) continuously, and newly started BMT and MMT, or no MOUD), maximum MOUD dose, HIV status, and SVR. Deidentified data were compiled into a table using Excel without patient identifiers.

**Analyses**

The efficacy outcome for the differentiated care model is SVR for the 31 patients who initiated treatment with DAAs. Implementation out-
comes include numbers who were co-treated using MOUD as well as time from referral to phlebotomy for the initial assessment and time to receipt of DAAs (i.e., treatment initiation).

**Ethical oversight**

This study was reviewed by the Institutional Review Board at Yale University who exempted it from requiring full approval.

**Results**

**HCV viral suppression**

Among the 35 patients with chronic HCV, 31 initiated HCV treatment. Two were lost to follow-up and 2 were incarcerated, leaving 31 individuals with confirmed chronic HCV whose characteristics are presented in Table 1. In general, these 31 patients were mostly white (51.6%) men (77.4%) in their late 30s (range: 22–59 years) and most (77.4%) were actively injecting drugs (the remainder were smoking or sniffing opioids and/or cocaine); 12 (38.7%) were described as unstably housed. Among the 7 patients with HIV, all were on ART and 6 initiated DAAs; prior to initiating treatment, 2 of these 6 HIV patients were not virally suppressed. At baseline, all had HIV-1 RNA levels under 400 copies/mL and 4 of the 6 had HIV-1 RNA levels <20 copies/mL. When SVR was assessed for HCV treatment, all six patients with HIV had HIV-1 RNA levels <20 copies/mL.

HCV genotype 1 was most prevalent (67.7%) and the mean HCV RNA level was 160,223 IU/mL (log₁₀=4.98). None had a FIB-4 score of greater than 1.25 (indicating no cirrhosis). Patients were offered one pill per day for 12 weeks (SOF/VEL) or 3 pills per day for 8 weeks (GLE/PIB) with 24 (77.4%) selecting SOF/VEL. Overall, 29 (93.5%) PWID who initiated DAAs achieved sustained virological response (SVR); it was 83.3% among the subset of 12 who were unstably housed and initiated treatment (Table 2).

**Implementation outcomes**

A number of implementation outcomes were observed during the low demand differentiated care model. First, the mean time to phlebotomy from referral for treatment by the outreach worker to the clinician was 6.9 days, ranging from 0 to 22 days. On average, it required an additional 4.1 days before medications were ordered and was overall 9.9 (range: 1–35) days before treatment was delivered to the patient for initiation. During this time, communication was either by texting or by telephone, depending on patient preference. Medication delivery was provided in 4-week allocations, meaning that there were 3 deliveries for SOF/VEL and 2 for GLE/PIB. Overall, 23 (74.2%) patients received all of their 4-week prescribed medication allocations, including 17 of 24 patients on SOF/VEL and 6 of 7 on GLE/PIB. For the 5 patients on SOF/VEL who received only 2 of their 3 prescriptions, 4 achieved SVR and of the 2 who received only 1 prescription, one of them achieved SVR.

**Medication for opioid use disorder outcomes**

For the 31 patients with OUD, 6 were already on MOUD (4 on methadone and 2 on buprenorphine). Importantly, 14 additional patients (12 of the SOF/VEL and 2 of the GLE/PIB) were successfully initiated on BMT and 6 (5 of the SOF/VEL and 1 of the GLE/PIB) were initiated on MMT (in person induction), resulting in 26 of the 31 patients being treated with MOUD by completion of HCV treatment (83.9%).

**HIV treatment outcomes**

All six of the patients with HIV achieved maximal viral suppression (HIV-1 RNA <20 copies/mL) 12 weeks after the completion of HCV treatment; 2 of these had detectable HIV-1 RNA levels before starting HCV treatment.

**Discussion**

The COVID-19 pandemic necessitated adaptations in clinical service delivery that substantiated a differentiated care model that successfully led to timely treatment of HCV and OUD in PWID. In response to COVID-19 and to address health disparities, we implemented a simplified treatment algorithm with minimal in-person visits administered through a SSP during the early months of the COVID pandemic. In this group of PWID that often experiences suboptimal access to consistent medical care, our patients at the SSP successfully achieved 93.5% sustained virological response (SVR); 83.3% among the subset who were unstably housed. These are in line with the findings from the SIMPLIFY study which found high (94%) SVR rates in PWID with high rates of active drug use and unstable housing (Grebelly et al., 2018). The MinMon study also demonstrated that non-PWID could achieve high SVR rates (93.5%) with minimal monitoring, but both these studies were done in the pre-COVID era and within a traditional clinic trials context where participants were provided financial incentives and substantial monitoring.

Our findings support real-world, successful simplified service delivery for both HCV and OUD in a non-traditional venue. Added value for HIV care was also observed, perhaps because of the added contribution

Table 1

| Characteristics of participants who initiated treatment for HCV (N = 31). | TotalN = 31 (%) | SOF/VEL (12 W)N = 24 (77.4%) | GLE/PIB (8 W)N = 7 (22.6%) |
|---|---|---|---|
| Mean age (S.D.), years | 39.9 (9.9) | | |
| Sex | | | |
| Male | 24 (77.4) | 19 (79.2) | 5 (71.4) |
| Female | 7 (22.6) | 5 (20.8) | 2 (28.6) |
| Race/ethnicity | | | |
| Black | 8 (25.8) | 5 (20.8) | 3 (42.9) |
| Hispanic | 7 (22.6) | 6 (25.0) | 1 (14.3) |
| White | 16 (51.6) | 13 (54.2) | 3 (42.9) |
| Injected drugs past 30 days | | | |
| Unstably housed | 12 (38.7) | 8 (33.3) | 4 (57.1) |
| HIV-infected (all on ART) | 6 (19.4) | 4 (16.7) | 2 (28.6) |
| HIV-1 RNA <400 copies/mL | 6 (19.4) | 4 (16.7) | 2 (28.6) |
| HIV-1 RNA <20 copies/mL | 4 (12.9) | 3 (12.5) | 1 (14.3) |
| HCV genotype | | | |
| 1 | 21 (67.7) | 17 (70.8) | 4 (57.1) |
| 2 | 7 (22.6) | 5 (20.8) | 2 (28.6) |
| 3 | 3 (9.7) | 2 (8.3) | 1 (14.3) |
| HCV treatment naive | 27 (87.1) | 22 (91.7) | 5 (71.4) |
of MOUD, which has been documented to improve HIV treatment outcomes along the HIV care continuum (Low et al., 2016; Mazhnaya et al., 2018). This differentiated care model may be pertinent to future service delivery even after COVID case rates decrease and patients can resume in-person visits. This is especially crucial for individuals who may not be able to maintain steady access to regular in-person monitoring due to various socioeconomic or structural factors (e.g., housing instability, lack of health insurance, stigmatization by the healthcare system) and confirms that the can be successfully treated for HCV and achieve high SVR rates. These findings also provide reassurance for clinicians who are concerned about non-adherence even in the absence of enhanced in-person monitoring. Here, findings suggest that by placing minimal demands on PWID with HCV that patients can be able to manage their care adequately. A study in Ukraine found that by reducing demands on patient receiving methadone by giving patients take-home dosing to over 85% of patients, retention outcomes improved and mortality did not increase (Meteliuk et al., 2021). Clinicians often perceive that results from clinical trials do not reflect outcomes in real-world settings and findings here confirm high SVR rates that are similar to those found in clinical trials.

In addition, MOUD treatment was also initiated with limited clinician monitoring. Aside from the in-person induction for MMT, which continued to be required by regulation during the public health emergency caused by COVID-19, patients had minimal physical contact with MOUD providers. In the case of buprenorphine, there were no in-person contacts and for methadone, there were initial in-person induction and stabilization visits that were required, but such patients could be transitioned early to take-home dosing when deemed clinically stable. Counseling and social support was provided through SSP outreach workers and when needed, via telehealth (mostly by telephone). Thus, physical distancing guidelines were implemented while maintaining appropriate care for their OUD. This suggests that reduced demands on patients treated with MOUD is feasible. As many of the relaxed regulations that allowed for this low-contact care (including allowing the use of telemedicine for MOUD) may be removed with the expiration of the public health emergency, it is critical to consider whether or not maintaining these policy changes may ensure improved care moving forward. Moreover, such a model could be considered for other prevention methods like prescribing pre-exposure prophylaxis (PrEP) to prevent HIV infection.

These findings have significant implications for public policy. While the low-demand model of care as a whole was designed in response to the COVID-19 pandemic, its success suggests that providing this low-contact care could allow for improved individual health, but also for HCV micro-elimination efforts that involve HCV treatment as prevention in PWID (Zelenev, Li, Mazhnaya, Basu & Altice, 2018, 2021). In order to achieve micro-elimination, it is crucial to focus on people actively injecting drugs as they are the main contributors to ongoing transmission.

Over a third (N = 12) of those treated in this sample were unstably housed, but most (N = 10; 83.3%) of this group were able to achieve SVR. Our initial results support the hypothesis that low-contact HCV treatment can achieve results in populations that are less easily reached or less likely to receive treatment. This is a critical finding, as PWID are also among the most likely to further transmit HCV to others (Page, Morris, Hahn, Maher & Prins, 2013).

Despite these important findings, this study is not without limitations, including the small sample size in this observational study, the limited amount of data that was collected as a clinical case series (e.g., insufficient data on the number of texts or calls that were made), and its location at a single site within the longest-standing SSP in the U.S. that has evolved to include a number of clinical and preventive services. In the future, more extensive studies are needed to establish the extent of contact necessary to maintain optimal care for PWID and to assess patient satisfaction. This observational study, in a setting where telehealth was primarily provided via telephone rather than using broadband, was sufficient to engage patients. In other sites where there is reliance on telemedicine, further challenges may emerge in implementation elsewhere where broadband access is limited (e.g., rural settings). In other settings, reimbursement for telemedicine often requires broadband and videoconferencing capabilities, but the need to ensure health equity to PWID at SSP sites necessitated a human rights over a reimbursement-driven approach where standard phones rather than smartphones can be used. Last, none of the patients in this series presented with cirrhosis. Future investigations will require further differentiation into whether patients with cirrhosis have decompensated disease, but inquiry can be obtained verbally by asking key clinical questions to assess for bleeding varices, ascites or pedal edema.

**Conclusion**

This study adds to the literature by providing proof-of-concept in a real-world setting that PWID at SSPs can be successfully treated for HCV in the absence of in-person visits. This observational study yielded promising outcomes for both HCV and OUD treatment that highlight the successful development of an integrated care model during the COVID-19 pandemic. This integrated model, involved simplified screening, reflex bundling for evaluation, and low demand treatment. Future studies might include implementation science trials of differentiated care models for HCV treatment delivery to PWID using lessons learned during the COVID-19 pandemic.
Declarations of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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