JAMA Internal Medicine | Original Investigation

Accessible Hepatitis C Care for People Who Inject Drugs
A Randomized Clinical Trial

Benjamin Eckhardt, MD; Pedro Mateu-Gelabert, PhD; Yesenia Aponte-Melendez, PhD; Chunki Fong, MS; Shashi Kapadia, MD; Melinda Smith, MA; Brian R. Edlin, MD; Kristen M. Marks, MD

IMPORTANCE To achieve hepatitis C elimination, treatment programs need to engage, treat, and cure people who inject drugs.

OBJECTIVE To compare a low-threshold, nonstigmatizing hepatitis C treatment program that was colocated at a syringe service program (accessible care) with facilitated referral to local clinicians through a patient navigation program (usual care).

DESIGN, SETTING, AND PARTICIPANTS This single-site randomized clinical trial was conducted at the Lower East Side Harm Reduction Center, a syringe service program in New York, New York, and included 167 participants who were hepatitis C virus RNA–positive and had injected drugs during the prior 90 days. Participants enrolled between July 2017 and March 2020. Data were analyzed after all patients completed 1 year of follow-up (after March 2021).

INTERVENTIONS Participants were randomized 1:1 to the accessible care or usual care arm.

MAIN OUTCOMES AND MEASURES The primary end point was achieving sustained virologic response within 12 months of enrollment.

RESULTS Among the 572 participants screened, 167 (mean [SD] age, 42.0 [10.6] years; 128 (77.6%) male, 36 (21.8%) female, and 1 (0.6) transgender individuals; 8 (4.8%) Black, 97 (58.5%) Hispanic, and 53 (32.1%) White individuals) met eligibility criteria and were enrolled, with 2 excluded postrandomization (n = 165). Baseline characteristics were similar between the 2 arms. In the intention-to-treat analysis, 55 of 82 participants (67.1%) in the accessible care arm and 19 of 83 participants (22.9%) in the usual care arm achieved a sustained virologic response ($P < .001$). Loss to follow-up (12.2% [accessible care] and 16.9% [usual care]; $P = .51$) was similar in the 2 arms. Of the participants who received therapy, 55 of 64 (85.9%) and 19 of 22 (86.3%) achieved a sustained virologic response in the accessible care and usual care arms, respectively ($P = .96$). Significantly more participants in the accessible care arm achieved all steps in the care cascade, with the greatest attrition in the usual care arm seen in referral to hepatitis C virus clinician and attending clinical visit.

CONCLUSIONS AND RELEVANCE In this randomized clinical trial, among people who inject drugs with hepatitis C infection, significantly higher rates of cure were achieved using the accessible care model that focused on low-threshold, colocated, destigmatized, and flexible hepatitis C care compared with facilitated referral. To achieve hepatitis C elimination, expansion of treatment programs that are specifically geared toward engaging people who inject drugs is paramount.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03214679

Visual Abstract
Editor's Note
Supplemental content

Author Affiliations: New York University School of Medicine, New York, New York (Eckhardt); City University of New York Graduate School of Public Health and Health Policy, New York (Mateu-Gelabert, Aponte-Melendez, Fong); Weill Cornell Medicine, New York, New York (Kapadia, Smith, Marks); National Development and Research Institute, New York, New York (Edlin); US Centers for Disease Control and Prevention, Atlanta, Georgia (Edlin).

Corresponding Author: Benjamin Eckhardt, MD, 462 First Ave, NBV 16S-5, New York, NY 10016 (benjamin.eckhardt@nyumc.org).

JAMA Intern Med. doi:10.1001/jamainternmed.2022.0170
Published online March 14, 2022.

Hepatitis C virus (HCV) is a major public health problem domestically and globally and is associated with substantial morbidity and mortality.[1-3] With the introduction of direct-acting antiviral (DAA) therapy considerable progress has been made in reducing the health effects of HCV. These new therapies have removed the most difficult aspects of prior interferon-based HCV therapy, including the need for injections, adverse effects, long duration of treatment, and adherence burden, and have substantially increased treatment efficacy, giving rise to international and national discussion about HCV elimination.[4,5]

Complicating HCV elimination efforts has been the high rates of HCV infections in people who inject drugs[6,7] and the poor health infrastructure and investment to care for this patient population. People who inject drugs represent most HCV cases in the US, where injection drug use is a reported risk factor in more than two-thirds of new HCV infections.[7-12] Obstacles for engaging people who inject drugs in HCV care include their competing priorities (eg, housing, food access, the need to stave off withdrawal), comorbid psychiatric illness, addiction, fear of stigma, and historically poor relations with health care clinicians.[13-16] Additionally, health care networks and insurance providers have created barriers to people who inject drugs accessing HCV care through requiring abstinence before initiating and reimbursing treatment.[17-20] These policies exist despite numerous studies demonstrating high rates of HCV cure in people who inject drugs[21] and low rates of reinfection[22] and modeling studies suggesting that treating people who inject drugs, even in the setting of moderate reinfection rates, has a large public health effect on elimination because of the prevention of continued viral transmission.[23]

Eliminating HCV is possible in the US, but the obstacles that limit people who inject drugs from receiving HCV treatment need to be overcome.[24,25] The onus lies on health care clinicians to develop and implement systems and strategies to make HCV treatment accessible to people who inject drugs. Integrating HCV care into settings where people who inject drugs frequent and/or feel accepted is one such intervention. Prior studies demonstrated effective integration of HCV treatment in community primary care clinics, mobile health units, correctional settings, and methadone maintenance.[26-29] Syringe service programs (SSPs) are potential sites for community-based treatment because of high levels of engagement with people who inject drugs. However, these community programs do not traditionally provide direct clinical services; therefore, they may not have the infrastructure to effectively treat HCV. Prior research that informing this model (accessible care model) demonstrated that integrating low-threshold HCV treatment at an SSP yielded high rates of cure among those treated, but this work lacked a comparison group.[30]

To assess the effectiveness of the accessible care model for HCV treatment in people who inject drugs within a harm reduction program in the US, we designed a single-site, unblinded, randomized clinical trial that compared accessible care intervention with usual care. Accessible care for people who inject drugs is a low-threshold care model designed specifically for people who inject drugs that is colocated within a community-based SSP with a goal of providing comfortable and flexible access to HCV care without the fear of the shame or stigma that people who inject drugs often experience in mainstream institutions.

Key Points

Question Is the accessible care model, which is characterized by low-threshold, nonstigmatizing care that is colocated in a syringe service program, better at curing people who inject drugs of hepatitis C virus (HCV) infection compared with facilitated referral?

Findings In this single-site randomized clinical trial of patients with HCV, 167 adults with recent injection drug use were enrolled. Sixty-seven percent of participants who received accessible care treatment vs 23% of those who received usual care (facilitated referral) achieved a hepatitis C virus cure (sustained virologic response), which was a significant difference.

Meaning The results of this randomized clinical trial suggest that the accessible care model provides a framework for developing treatment programs geared toward engaging, treating, and curing HCV infection in people who inject drugs.

Methods

Participants and Setting

Participants were recruited at various settings and sites around New York, New York, that people who inject drugs frequent and enrolled at 1 site, the Lower East Side Harm Reduction Center (LESHRC), from July 2017 through March 2020 (Supplement 1). The LESHRC site is a community-based, nonprofit organization whose mission is to reduce the spread of HIV/AIDS, HCV, and other drug-related harm among people who inject drugs and the community located in the Lower East Side in New York, New York. The site is a New York State Department of Health–authorized SSP that offers services, including injection equipment distribution, overdose prevention training and medication, on-site access to clinicians who provide treatment with buprenorphine, HIV and HCV screening, case management, and other harm reduction services.

Eligible participants were 18 years or older, spoke English or Spanish, had injected illicit drugs for at least 1 year, reported at least 1 illicit drug injection within the last 90 days, and had a detectable HCV RNA within the last 90 days. Pregnant women, individuals with advanced liver disease (decompensated cirrhosis or hepatocellular carcinoma), and those currently engaged in HCV treatment (defined as having at least 2 medical visits with a HCV treatment clinician during the last 6 months) were excluded. All participants provided written informed consent, and the study was conducted in accordance with Good Clinical Practice and the ethical principles that originated in the Declaration of Helsinki. The study was approved by the Weill Cornell Medicine and NYU School of Medicine institutional review boards.

Study Design

Prescreening occurred via telephone or at various locations around New York, New York, including the LESHRC. For patients who required an HCV antibody or HCV polymerase chain reaction (PCR) test, free walk-in phlebotomy services were available at the LESHRC. Neither HCV antibody nor HCV PCR testing were incentivized, and HCV PCR testing was billed to the individual's insurance. After providing written informed consent, enrolled participants underwent a baseline interview and were then randomized 1:1 to receive either accessible care or usual care. Participants randomized to the accessible care arm were connected to an on-site HCV treatment team comprising a study physician and study HCV care coordinator, whereas participants randomized to the usual care arm were connected with a separate, nonstudy, on-site HCV patient navigator.

Study Interventions

Accessible Care (Intervention)

The accessible care model is a low-threshold, nonstigmatizing model that features flexible appointment scheduling and a supportive harm reduction framework that works with clients to help them identify and pursue their own personal health goals without pressuring them to adopt or reject any specific behavior (such as engaging in drug treatment or attaining illicit drug abstinence). Study staff attempted to maintain a friendly, informal, and nonjudgmental atmosphere to reduce the stigma associated with health care. Accessible care participants received medical evaluations, follow-up, phlebotomy for laboratory testing, and care coordination at the LESHRC site. Flexible appointments and drop-ins were welcome and encouraged, with proactive outreach for missed visits. The cost of DAA therapy was covered by either the participant's insurance or through pharmaceutical drug assistance programs (for those ineligible for insurance). The on-site treatment team helped obtain medical insurance for participants who were eligible for insurance but not actively enrolled. Medications were prescribed in accordance with Infectious Diseases Society of American/American Association for the Study of Liver Diseases HCV management guidelines and accounted for insurance formulary preference.[31] Medications were delivered to the LESHRC, where participants decided their own dispensing schedule (eg, daily, weekly, or monthly). The HCV care coordinators provided on-site education and logistical, insurance, social, and adherence support. Additionally, all participants who were treated with DAA therapy were offered on-site reinfection prevention training that was adapted from a validated HCV prevention tool.[32]

Usual Care (Control)

Usual care participants were referred to the on-site HCV patient navigator, who was funded through the New York City Department of Health's Check Hep C Patient Navigation Program.[33] The Check Hep C program provides HCV RNA–positive individuals supportive services, connections to HCV care, accompaniment to medical appointments, adherence support, and medication access support at no cost. The HCV patient navigator for the usual care arm provided similar education and logistical, insurance, and social support as the care coordinator in the accessible care arm while working with participants to facilitate linkage and engage with care with an HCV treatment clinician at surrounding hospital-, clinic-, and/or harm reduction-based HCV treatment programs.

Study Assessment and Compensation

Research visits were conducted at baseline, 3 months, 6 months, 9 months, and 12 months. Participants underwent structured interviews eliciting sociodemographic characteristics, current and past injection and noninjection drug use, substance use disorder treatment, HIV and HCV risk behavior, health care utilization, and hepatitis C treatment linkage. Participants were compensated equally in both arms for partaking in the quarterly research visits through 12 months at $50 to $70 per visit. Participants were not compensated for engaging in clinical care or receiving HCV treatment; however, accessible care and usual care participants were compensated $40 for undergoing HCV PCR testing 12 weeks after completing treatment (for those who initiated treatment) and 12 months after enrollment (for all participants). Ribonucleic acid testing for reinfection testing was offered to all participants who achieved an HCV cure every 3 months after a sustained virologic response (SVR12) through study closure (June 30, 2021).

Study Outcomes

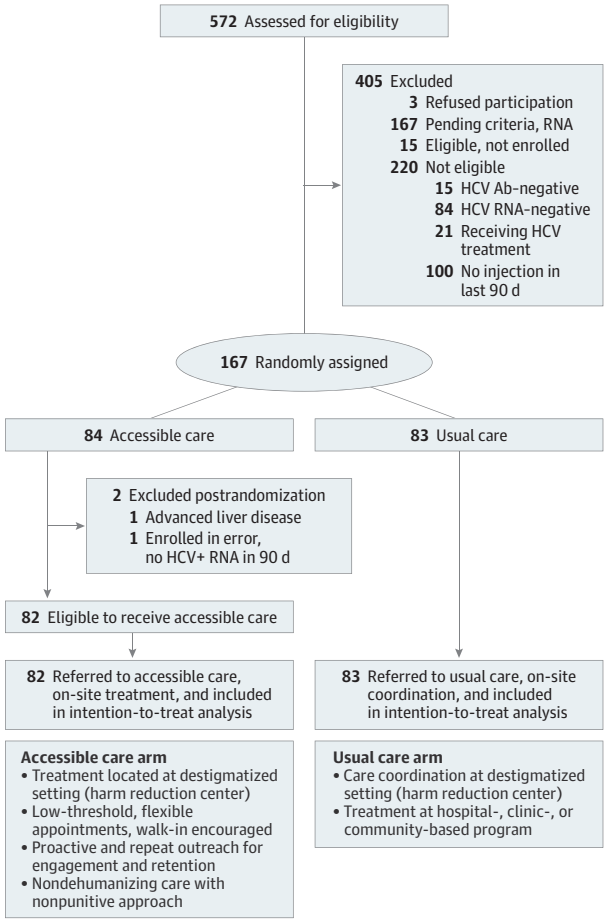
The primary outcome of the study was the percentage of participants who achieved an SVR12 with treatment within 12 months of study enrollment. Secondary outcomes included rates of reinfection and achievement of steps along the HCV treatment cascade. Patients who failed to complete at least 1 of the final 2 quarterly research visits (at 9 months and 12 months) were considered lost to follow-up unless they already had a confirmed SVR12. To be conservative, reinfection was assumed to have occurred on the day of the last documented negative hepatitis PCR test, and follow-up person-time was calculated from the date of SVR12. Attendance of clinical visit was defined as presenting to a single visit with an HCV clinician, and HCV treatment initiation was defined as physically receiving at least 1 dose of DAA therapy (with or without confirmed oral intake).

Statistical Analysis

A sample size of 300 was sought to be able to detect a statistically significant difference ($\alpha = .05$) if 66% of accessible care participants and 50% of usual care participants achieved SVR12 with 80% power. The baseline characteristics and outcomes of participants were reported as frequencies with percentages or means with standard deviations. Comparisons between the study arms were analyzed with use of the χ^2, Fisher exact, or Wilcoxon ranked sum tests when appropriate.

All analyses were performed in the intention-to-treat population. The 95% CIs were obtained using a 2-sided *t* test, with a *P* value of .05 or less considered statistically significant. The subgroup analysis was computed comparing the percentage of participants who achieved an SVR12 between the 2 arms by calculating the relative risk ratio with 95% CIs, which were dis-

Figure 1. Consolidated Standards of Reporting Trials Diagram of Accessible Care Study Participants



HCV indicates hepatitis C virus.

played on a forest plot. Analysis was performed using SPSS, version 25 (IBM).

Results

Between July 2017 and March 2020, 572 individuals were screened for eligibility, with 405 (70.8%) excluded, most commonly for lack of HCV RNA confirmatory testing (167 [41.2%]), no injection drug use during the last 90 days (100 [24.7%]), or HCV RNA confirmation being negative (84 [20.7%]) (**Figure 1**). One hundred sixty-seven participants provided written informed consent, were enrolled, underwent the baseline interview, and were randomized. Recruitment was terminated early in March of 2020 because of the initial SARS-CoV-2 outbreak in New York, New York. Two participants were excluded postrandomization because of ineligibility (decompensated cirrhosis, no HCV RNA detected within 90 days). The remaining 165 participants (82 [49.7%] in the accessible care arm and 83 [50.3%] in the usual care arm) were included in the intention-to-treat analysis. Overall, the 2 arms were balanced regarding baseline characteristics (**Table 1**), with the only difference being a lower rate of recent incarceration (during the last 90 days) in the accessible care arm (2.4%) compared with the usual care arm (12.0%).

The percentage of participants achieving SVR12 within 1 year of study enrollment was significantly higher in the accessible care arm (67.1%) compared with the usual care arm (22.9%) (**Table 2**). This was not because of a difference in treatment response between the 2 arms, as the proportion of participants achieving SVR12 among those who initiated therapy were similar in the accessible care arm (85.9%) and the usual care arm (86.3%); rather, it was because of the earlier steps in the care cascade. The percentage of participants who advanced along the care cascade was significantly higher at each step for the accessible care arm compared with the usual care arm from participant-reported referral to a HCV clinician (92.7% vs 44.6%), attendance of the initial HCV clinical visit (86.6% vs 37.4%), completion of baseline laboratory testing (86.6% vs 31.3%), and treatment initiation (78.0% vs 26.5%) (**Figure 2**). A significantly higher percentage of participants in the accessible care arm attended a visit with an HCV clinician. Of the subset of patients in each arm that attended a visit with an HCV clinician, a significantly higher percentage of participants in the accessible care arm initiated therapy. No patient in either arm was denied treatment with DAA therapy by their insurance provider. A subgroup analysis showed a consistent trend of higher rates of SVR12 achievement in the accessible care arm compared with the usual care arm regardless of age, sex, race and ethnicity, homeless status, prior HCV treatment, and daily injection drug use (among others) (**Figure 3**). Overall loss to follow-up was similar between the 2 arms (12 of 82 [14.6%] in the accessible care arm and 14 of 83 [16.9%] in the usual care arm).

Sixty-four participants in the accessible care arm and 22 participants in the usual care arm initiated treatment. The DAAs prescribed included glecaprevir/pibrentasvir (46 [71.9%]), sofosbuvir/velpatasvir (8 [12.5%]), elbasvir/grazoprevir (5 [7.8%]), sofosbuvir/ledipasvir (3 [4.7%]), and sofosbuvir/velpatasvir/voxilaprevir (2 [3.1%]). Of the participants who initiated DAA therapy, only 3 participants (2 in the accessible care arm and 1 in the usual care arm) did not have testing results to evaluate for SVR12. Treatment failure occurred in a similar proportion of participants treated in each arm (7 of 64 [10.9%] in the accessible care arm and 2 of 22 [9.1%] in the usual care arm) (eFigure in Supplement 2). In addition to the participants who were cured with treatment, 6 participants cleared their HCV infection without treatment (4 in the accessible care arm and 2 in the usual care arm). Of the 55 participants in the accessible care arm who achieved SVR12, 4 were reinfected during 57.9 patients-years of follow-up for a reinfection rate of 6.9 per 100 patient-years (95% CI, 2.7-17.8).

Discussion

The results of this randomized clinical trial supported the efficacy of a low-threshold, destigmatized HCV treatment program that was colocated in an SSP. The accessible care intervention achieved superior HCV cure rates compared

Table 1. Baseline Characteristics of Study Participants

Characteristic	No. (%)		
	Overall (n = 165)	Accessible care (n = 82)	Usual care (n = 83)
Age, mean (SD), y	42.0 (10.6)	42.6 (10.7)	41.3 (10.6)
Age, y			
18-29	21 (12.7)	11 (13.4)	10 (12.0)
30-44	77 (46.7)	34 (41.5)	43 (51.8)
≥4	67 (40.6)	37 (45.1)	30 (36.1)
Gender			
Male	128 (77.6)	62 (75.6)	66 (79.5)
Female	36 (21.8)	19 (23.2)	17 (20.5)
Transgender	1 (0.6)	1 (1.2)	0
Race and ethnicity			
Hispanic	97 (58.8)	45 (54.9)	52 (62.7)
Non-Hispanic			
White	53 (32.1)	26 (31.7)	27 (32.5)
Black	8 (4.8)	7 (8.5)	1 (1.2)
Other[a]	7 (4.2)	4 (4.9)	3 (3.6)
Homeless (past 3 mo)	94 (57.3)	48 (58.5)	46 (56.1)
Health insurance			
Public	155 (93.9)	76 (92.7)	79 (95.2)
Other	5 (3.0)	1 (1.2)	4 (4.8)
None	5 (3.0)	5 (6.1)	0
Borough of resident			
Manhattan	96 (38.2)	34 (41.5)	29 (34.9)
Staten Island	3 (1.8)	1 (1.2)	2 (2.4)
Brooklyn	32 (19.4)	18 (22.0)	14 (16.9)
Bronx	48 (27.9)	20 (24.4)	26 (31.3)
Queens	17 (10.3)	8 (9.8)	9 (10.8)
Referral source			
LESHRC SSP (research site)	41 (24.8)	25 (30.5)	16 (19.3)
Outside SSP	36 (21.8)	17 (20.7)	19 (22.9)
Participant, peer, or recruiter	51 (30.9)	24 (29.3)	27 (32.5)
Other (outside research study, media, other)	37 (22.4)	16 (19.5)	21 (25.3)
Incarceration history			
Ever incarcerated	138 (83.6)	70 (85.4)	68 (81.9)
Recent incarceration (during last 90 d)[b]	12 (7.3)	2 (2.4)	10 (12.0)
HIV positive	12 (7.3)	6 (7.3)	6 (7.2)
Prior HCV treatment	18 (10.9)	10 (12.2)	8 (9.6)
Current medication for opioid use disorder[c]			
Methadone	106 (64.2)	52 (63.4)	54 (65.1)
Buprenorphine	10 (6.1)	6 (7.3)	4 (4.8)
No medication for opioid use disorder	50 (30.3)	24 (29.3)	26 (31.3)
Injection frequency during past 30 d			
Daily	65 (39.4)	33 (40.2)	32 (38.6)
Less than daily	100 (60.6)	49 (59.8)	51 (61.4)
Drugs used regularly (last 90 d)			
Heroin	79 (47.9)	36 (43.9)	43 (51.8)
Cocaine	46 (27.9)	24 (29.3)	22 (26.5)
Speedball	41 (24.8)	20 (24.4)	21 (25.3)
Other[d]	39 (23.6)	19 (23.2)	20 (24.1)
Attended SSP during past 90 d	133 (80.6)	69 (84.1)	64 (77.1)

Abbreviations: HCV, hepatitis C virus; LESHRC, Lower East Side Harm Reduction Center; SSP, syringe service program.

[a] Includes American Indian or Alaska Native, Asian, and Native Hawaiian or Pacific Islander individuals.

[b] Statistical difference between the 2 arms with $P < .05$.

[c] One participant was receiving methadone and buprenorphine treatment.

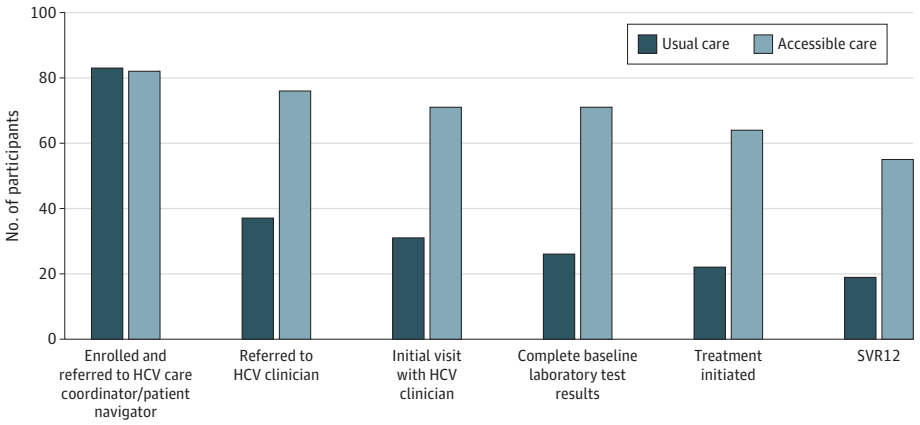
[d] Other drugs used regularly included crack, methamphetamine, prescription opioids, benzodiazepines, and fentanyl.

Table 2. Clinical Outcomes at 12 Months

Outcome	No. (%) [95% CI]		*P* value
	Accessible care (n = 82)	Usual care (n = 83)	
SVR12 (intention-to-treat)	55 (67.1) [55.8-77.0]	19 (22.9) [14.4-33.4]	<.001
SVR12 (of those initiating therapy)	55/64 (85.9) [75.0-93.3]	19/22 (86.3) [65.1-97.1]	.96
Lost to follow-up	12 (14.6) [7.8-24.2]	14 (16.9) [9.5-26.7]	.69

Abbreviation: SVR12, sustained virologic response at 12 months.

Figure 2. Hepatitis C Virus (HCV) Infection Treatment Cascade Comparing the Accessible Care Arm With Usual Care



	Of those enrolled, referred and attended initial visit	Of those who attended initial visit with HCV clinician, completed laboratory testing and initiated treatment	SVR12, %
Usual care	37	71	86
Accessible care	87	90	86
P	<.001	.01	.96

SVR12 indicates sustained virologic response at 12 months.

with a robust control of facilitated referral to local HCV clinicians. Despite perceptions of people who inject drugs as being difficult to engage in HCV treatment while actively injecting drugs, these findings indicate that when provided with HCV treatment that was tailored to their needs, people who inject drugs successfully engaged in treatment, and two-thirds achieved an HCV cure.

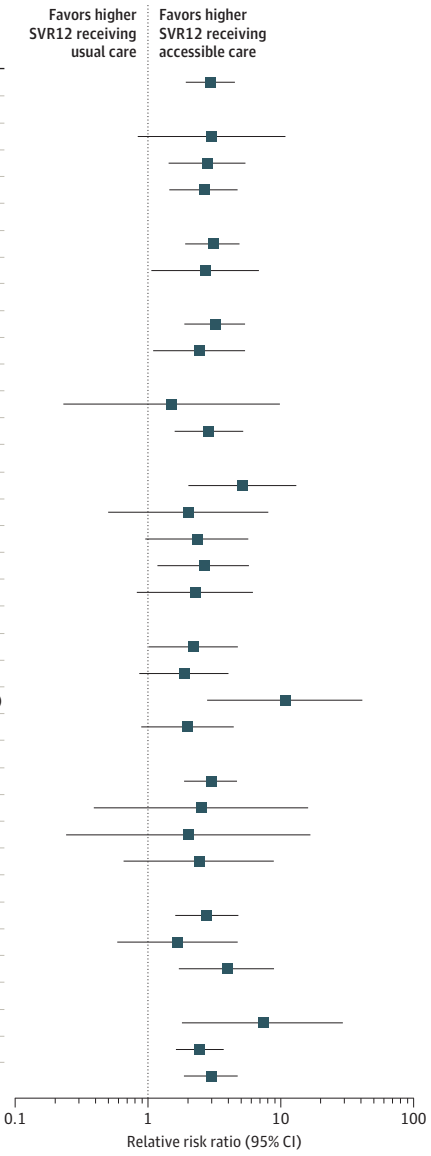
Roughly 3 times more participants achieved SVR12 in the accessible care arm than the usual care arm. All patients in both arms were referred to either an HCV care coordinator or HCV patient navigator; however, more participants in the accessible care arm were referred to and attended an HCV clinician visit, which led to more initiating therapy ultimately. This was true despite usual care arm use of a dedicated, city-funded HCV patient navigator embedded within the SSP, a resource that does not exist at most other programs. The rates of engagement, treatment, and cure in the usual care arm were similar to those seen in HCV treatment navigation programs geared toward people who inject drugs[34-36] and higher than rates seen in populations of people who inject drugs for whom navigation programs are less developed.[37,38] The higher SVR12 rates at 1 year in the accessible care arm benefited people with demographic characteristics or behaviors that may make engagement in medical care more challenging, such as participants who report recent homelessness and those with daily injection drug use. Validated adherence data were not collected as part of this study to determine the effect of missed doses or incomplete treatment courses on cure rates. However, the success of the accessible care intervention did not appear to stem from an improved effectiveness of the therapy itself. For participants who initiated treatment, the SVR12 rates in the accessible care arm (85.9%) and usual care arm (86.3%) were similar and consistent with the SVR12 rates reported in a meta-analysis of other treatment studies of participants who reported recent drug use.[21]

One unanticipated finding was that colocation of treatment within a SSP familiar to the participant did not appear to be essential to the success of the accessible care intervention. Although many existing clients from the SSP at the study site enrolled in the research study, three-quarters were not study site SSP clients, and many lived in other New York, New York boroughs. One explanation might be that the success of the program was less about increasing physical accessibility through colocation and more about providing a low-threshold, nonstigmatizing community environment where participants felt respected and comfortable. This demonstrates the potential of this model to reach additional individuals with HCV outside of an individual program's clientele.

In the greater context of HCV elimination, this randomized clinical trial had a few concerning findings. First, more

Figure 3. Comparison of Participant Characteristics With Sustained Virologic Response Rates at 12 Months (SVR12)

Subgroup	No. of participants/total No. of participants (SVR12%)	Relative risk ratio (95% CI)
Overall	74/165 (44.8)	2.93 (1.92-4.47)
Age, y		
18-29	9/21 (42.9)	3.00 (0.83-10.86)
30-44	27/77 (35.1)	2.78 (1.44-5.38)
≥45	38/67 (56.7)	2.62 (1.46-4.71)
Gender		
Male	58/128 (45.3)	3.05 (1.90-4.90)
Female	16/36 (44.4)	2.68 (1.07-6.76)
Race and ethnicity		
Hispanic	45/97 (46.4)	3.18 (1.88-5.38)
Non-Hispanic White	20/53 (37.7)	2.42 (1.10-5.34)
Non-Hispanic Black	6/8 (75.0)	NA
Non-Hispanic Other	3/7 (42.9)	1.50 (0.23-9.80)
Homeless (during past 3 mo)	40/94 (42.6)	2.88 (1.59-5.19)
Borough of resident		
Manhattan	28/63 (44.4)	5.12 (2.01-13.04)
Staten Island	2/3 (66.7)	2.00 (0.50-8.00)
Brooklyn	16/32 (50.0)	2.33 (0.96-5.68)
Bronx	18/46 (39.1)	2.60 (1.18-5.72)
Queens	9/17 (52.9)	2.25 (0.82-6.16)
Referral source		
LESHRC SSP	22/41 (53.7)	2.18 (1.00-4.72)
Outside SSP	16/36 (44.4)	1.86 (0.86-4.03)
Participant, peer, or recruiter referral	21/51 (41.2)	10.69 (2.77-41.20)
Outside research study referral	15/37 (40.5)	1.97 (0.88-4.39)
Incarceration		
Ever	65/138 (47.1)	2.98 (1.89-4.69)
During past 90 d	3/12 (25.0)	2.50 (0.39-16.05)
HIV-positive	3/12 (25.0)	2.00 (0.24-16.61)
Prior HCV treatment	8/18 (44.4)	2.40 (0.65-8.83)
Current medication for opioid use disorder		
Methadone	44/106 (41.5)	2.77 (1.61-4.77)
Buprenorphine	7/10 (70.0)	1.67 (0.59-4.73)
No medication for opioid use disorder	23/50 (46.0)	3.90 (1.72-8.86)
Injection frequency during past 30 d		
Daily	17/65 (26.2)	7.27 (1.81-29.29)
Less than daily	57/100 (57.0)	2.45 (1.62-3.69)
Attended SSP during past 90 d	63/133 (47.4)	2.97 (1.86-4.75)



HCV indicates hepatitis C virus; LESHRC, Lower East Side Harm Reduction Center; NA, not applicable; SSP, syringe service program.

than 70% of the untreated participants had regular engagement with substance use treatment, particularly methadone, at baseline. This suggests that there are missed opportunities for HCV treatment in substance use treatment programs, despite proven effectiveness.[28] A second concern is the 167 screened participants who were excluded from enrollment simply because of being unable to arrange HCV RNA confirmatory testing. Point-of-care HCV RNA testing was not available in the US at the time of this study but would help to mitigate loss to follow-up at the diagnosis stage. This point-of-care HCV RNA testing will become increasingly important in people who inject drugs who achieved HCV cure, providing them with regular longitudinal monitoring for reinfection.

Limitations

The study limitations to generalizability include that the study was conducted at a single site and in an urban environment with a high concentration of harm reduction services and minimal state HCV DAA prescribing restrictions. As observed in this trial, most patients were insured or eligible for insurance, and no participants had their insurance company deny treatment with HCV DAA therapy. This relatively easy access to insurance and HCV DAA therapy was a key component to the intervention being successful and is unfortunately not replicated across much of the US. Without expanded Medicaid eligibility and insurance providers covering treatment with HCV DAA therapy, high SVR12 rates for people who inject drugs cannot be achieved.

Conclusions

This randomized clinical trial suggests that hepatitis C elimination will not be possible without improvement in programs that focus on curing people who inject drugs of HCV. The accessible care model presented in this article potentially provides a framework for developing novel treatment programs nationally and internationally that are specifically geared toward engaging, treating, and curing HCV in people who inject drugs.

ARTICLE INFORMATION

Accepted for Publication: December 24, 2021.

Published Online: March 14, 2022. doi:10.1001/jamainternmed.2022.0170

Author Contributions: Dr Eckhardt had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Eckhardt, Mateu-Gelabert, Kapadia, Pai, Edlin, Marks.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Eckhardt, Edlin.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Eckhardt, Fong, Edlin.
Obtained funding: Edlin, Marks.
Administrative, technical, or material support: Eckhardt, Aponte-Melendez, Fong, Pai, Marks.
Supervision: Eckhardt, Mateu-Gelabert, Marks.

Conflict of Interest Disclosures: Dr Eckhardt reported grants from the National Institutes of Health (NIH) and Gilead during the conduct of the study. Dr Kapadia reported grants from Gilead Sciences Inc during the conduct of the study. Dr Pai reported grants from Gilead Sciences Inc and the National Institute on Drug Abuse (NIDA) during the conduct of the study as well as grants from Gilead Sciences Inc and NIDA outside the submitted work. Dr Edlin reported grants from NIH during the conduct of the study. Dr Marks reported grants from Gilead Sciences that were paid to Weill Cornell Medicine outside the submitted work. No other disclosures were reported.

Funding: This trial received funding from NIDA grant R01DA041298.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 3.

REFERENCES

1. Ly KN, Miniño AM, Liu SJ, et al. Deaths associated with hepatitis C virus infection among residents in 50 states and the District of Columbia, 2016-2017. *Clin Infect Dis*. 2020;71(5):1149-1160. doi:10.1093/cid/ciz976

2. Stanaway JD, Flaxman AD, Naghavi M, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. *Lancet*. 2016;388(10049):1081-1088. doi:10.1016/S0140-6736(16)30579-7

3. Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising mortality associated with hepatitis C virus in the United States, 2003-2013. *Clin Infect Dis*. 2016;62(10):1287-1288. doi:10.1093/cid/ciw111

4. World Health Organization. Global hepatitis report, 2017. Accessed July 27, 2021. https://www.who.int/publications/i/item/global-hepatitis-report-2017

5. Biden J. A proclamation on national Hepatitis Testing Day, 2021. Accessed July 21, 2021. https://www.whitehouse.gov/briefing-room/presidential-actions/2021/05/18/a-proclamation-on-national-hepatitis-testing-day-2021/

6. Zibbell JE, Asher AK, Patel RC, et al. Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004 to 2014. *Am J Public Health*. 2018;108(2):175-181. doi:10.2105/AJPH.2017.304132

7. Trickey A, Fraser H, Lim AG, et al. The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. *Lancet Gastroenterol Hepatol*. 2019;4(6):435-444. doi:10.1016/S2468-1253(19)30085-8

8. Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC recommendations for hepatitis C screening among adults—United States, 2020. *MMWR Recomm Rep*. 2020;69(2):1-17. doi:10.15585/mmwr.rr6902a1

9. Degenhardt L, Peacock A, Colledge S, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. *Lancet Glob Health*. 2017;5(12):e1192-e1207. doi:10.1016/S2214-109X(17)30375-3

10. Amon JJ, Garfein RS, Ahdieh-Grant L, et al. Prevalence of hepatitis C virus infection among injection drug users in the United States, 1994-2004. *Clin Infect Dis*. 2008;46(12):1852-1858. doi:10.1086/588297

11. Williams IT, Bell BP, Kuhnert W, Alter MJ. Incidence and transmission patterns of acute hepatitis C in the United States, 1982-2006. *Arch Intern Med*. 2011;171(3):242-248. doi:10.1001/archinternmed.2010.511

12. US Centers for Disease Control and Prevention. 2019 Viral hepatitis surveillance report. Accessed December 4, 2021. https://www.cdc.gov/hepatitis/statistics/SurveillanceRpts.htm.

13. Madden A, Hopwood M, Neale J, Treloar C. Beyond interferon side effects: what residual barriers exist to DAA hepatitis C treatment for people who inject drugs? *PLoS One*. 2018;13(11):e0207226. doi:10.1371/journal.pone.0207226

14. Zeremski M, Dimova RB, Zavala R, et al. Hepatitis C virus-related knowledge and willingness to receive treatment among patients on methadone maintenance. *J Addict Med*. 2014;8(4):249-257. doi:10.1097/ADM.0000000000000041

15. Fong C, Mateu-Gelabert P, Ciervo C, et al. Medical provider stigma experienced by people who use drugs (MPS-PWUD): development and validation of a scale among people who currently inject drugs in New York City. *Drug Alcohol Depend*. 2021;221:108589. doi:10.1016/j.drugalcdep.2021.108589

16. Biancarelli DL, Biello KB, Childs E, et al. Strategies used by people who inject drugs to avoid stigma in healthcare settings. *Drug Alcohol Depend*. 2019;198:80-86. doi:10.1016/j.drugalcdep.2019.01.037

17. Mehta SH, Genberg BL, Astemborski J, et al. Limited uptake of hepatitis C treatment among injection drug users. *J Community Health*. 2008;33(3):126-133. doi:10.1007/s10900-007-9083-3

18. Treloar C, Newland J, Rance J, Hopwood M. Uptake and delivery of hepatitis C treatment in opiate substitution treatment: perceptions of clients and health professionals. *J Viral Hepat*. 2010;17(12):839-844. doi:10.1111/j.1365-2893.2009.01250.x

19. Barua S, Greenwald R, Grebely J, Dore GJ, Swan T, Taylor LE. Restrictions for Medicaid reimbursement of sofosbuvir for the treatment of hepatitis C virus infection in the United States. *Ann Intern Med*. 2015;163(3):215-223. doi:10.7326/M15-0406

20. Sublette VA, Smith SK, George J, McCaffery K, Douglas MW. The hepatitis C treatment experience: patients' perceptions of the facilitators of and barriers to uptake, adherence and completion. *Psychol Health*. 2015;30(8):987-1004. doi:10.1080/08870446.2015.1012195

21. Hajarizadeh B, Cunningham EB, Reid H, Law M, Dore GJ, Grebely J. Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2018;3(11):754-767. doi:10.1016/S2468-1253(18)30304-2

22. Hajarizadeh B, Cunningham EB, Valerio H, et al. Hepatitis C reinfection after successful antiviral treatment among people who inject drugs: a meta-analysis. *J Hepatol*. 2020;72(4):643-657. doi:10.1016/j.jhep.2019.11.012

23. Martin NK, Vickerman P, Dore GJ, et al; STOP-HCV Consortium. Prioritization of HCV treatment in the direct-acting antiviral era: An economic evaluation. *J Hepatol*. 2016;65(1):17-25. doi:10.1016/j.jhep.2016.02.007

24. Edlin BR, Winkelstein ER. Can hepatitis C be eradicated in the United States? *Antiviral Res*. 2014;110:79-93. doi:10.1016/j.antiviral.2014.07.015

25. Committee on a National Strategy for the Elimination of Hepatitis B and C; Board on Population Health and Public Health Practice; Health and Medicine Division; National Academies of Sciences, Engineering and Medicine. *Eliminating the Public Health Problem of Hepatitis B and C in the United States: Phase One Report*. Buckley GJ, Strom BL, eds. National Academies Press; 2016. doi:10.17226/23407.

26. Wade AJ, Doyle JS, Gane E, et al. Outcomes of treatment for hepatitis c in primary care, compared to hospital-based care: A randomized, controlled trial in people who inject drugs. *Clin Infect Dis*. 2020;70(9):1900-1906. doi:10.1093/cid/ciz546

27. Chan J, Schwartz J, Kaba F, et al. Outcomes of hepatitis C virus treatment in the New York city jail

population: Successes and challenges facing scale up of care. *Open Forum Infect Dis*. 2020;7(7):ofaa263. doi:10.1093/ofid/ofaa263

28. Akiyama MJ, Norton BL, Arnsten JH, Agyemang L, Heo M, Litwin AH. Intensive models of hepatitis C care for people who inject drugs receiving opioid agonist therapy: a randomized controlled trial. *Ann Intern Med*. 2019;170(9):594-603. doi:10.7326/M18-1715

29. Lazarus JV, Øvrehus A, Demant J, Krohn-Dehli L, Weis N. The Copenhagen test and treat hepatitis C in a mobile clinic study: a protocol for an intervention study to enhance the HCV cascade of care for people who inject drugs (T'N'T HepC). *BMJ Open*. 2020;10(11):e039724. doi:10.1136/bmjopen-2020-039724

30. Eckhardt BJ, Scherer M, Winkelstein E, Marks K, Edlin BR. Hepatitis C treatment outcomes for people who inject drugs treated in an accessible care program located at a syringe service program. *Open Forum Infect Dis*. 2018;5(4):ofy048. doi:10.1093/ofid/ofy048

31. American Association for the Study of Liver Diseases–Infectious Diseases Society of America. Recommendations for testing, managing, and treating hepatitis C. Accessed August 16, 2016. http://www.hcvguidelines.org

32. Mateu-Gelabert P, Gwadz MV, Guarino H, et al. The staying safe intervention: training people who inject drugs in strategies to avoid injection-related HCV and HIV infection. *AIDS Educ Prev*. 2014;26(2):144-157. doi:10.1521/aeap.2014.26.2.144

33. Ford MM, Johnson N, Desai P, Rude E, Laraque F. From care to cure: demonstrating a model of clinical patient navigation for hepatitis C care and treatment in high-need patients. *Clin Infect Dis*. 2017;64(5):685-691. doi:10.1093/cid/ciw806

34. Falade-Nwulia O, Sacamano P, McCormick SD, et al. Individual and network factors associated with HCV treatment uptake among people who inject drugs. *Int J Drug Policy*. 2020;78:102714. doi:10.1016/j.drugpo.2020.102714

35. Morris MD, Mirzazadeh A, Evans JL, et al. Treatment cascade for hepatitis C virus in young adult people who inject drugs in San Francisco: Low number treated. *Drug Alcohol Depend*. 2019;198:133-135. doi:10.1016/j.drugalcdep.2019.02.008

36. New York City Department of Health and Mental Hygiene. Check Hep C patient navigation program final report 2018. Accessed November 16, 2021. https://hepfree.nyc/wp-content/uploads/2018/03/2018-Check-Hep-C-Patient-Navigation-Program-Report.pdf

37. Tsui JI, Miller CM, Scott JD, Corcoran MA, Dombrowski JC, Glick SN. Hepatitis C continuum of care and utilization of healthcare and harm reduction services among persons who inject drugs in Seattle. *Drug Alcohol Depend*. 2019;195:114-120. doi:10.1016/j.drugalcdep.2018.11.026

38. Socías ME, Ti L, Wood E, et al. Disparities in uptake of direct-acting antiviral therapy for hepatitis C among people who inject drugs in a Canadian setting. *Liver Int*. 2019;39(8):1400-1407. doi:10.1111/liv.14043