MAJOR ARTICLE



Adherence to Hepatitis C Therapy in a Shelter-Based Education and Treatment Model Among Persons Experiencing Homelessness

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Background. Medication adherence is a common reason for treatment deferment in persons experiencing homelessness. We evaluated adherence to hepatitis C virus (HCV) therapy following HCV education in a shelter-based care model.

Methods. Prospective study conducted at 4 homeless shelters in Minneapolis, Minnesota and San Francisco, California from November 2018 to January 2021. Sixty-three patients underwent HCV education and treatment. Multivariable modeling evaluated factors associated with (1) medication and (2) overall (composite score of medication, laboratory, and clinic visit) adherence.

Results. Median age was 56 years; 73% of participants were male, 43% were Black, 52% had psychiatric illness, and 81% used illicit drugs and 60% used alcohol in the past year. Following education, 52% were extremely confident in their ability to be adherent to HCV therapy. Medication adherence by patient and provider report was 88% and 48%, respectively, and 81% achieved HCV cure. Active alcohol use was associated with less confidence in medication adherence (43% vs 78%, P = .04). Older age was positively (coefficient = 0.3) associated with overall adherence to HCV treatment whereas prior therapy was associated with both medication (odds ratio, 0.08) and overall treatment (coefficient = -0.87) nonadherence.

Conclusions. Despite imperfect adherence, sustained virologic response rates were still high. Expanding opportunities to treat persons experiencing homelessness in a structured and supportive setting is critical to HCV elimination efforts.

Keywords. DAA therapy; health disparity; substance abuse; sustained virologic response; vulnerable populations.

Hepatitis C virus (HCV) in the United States disproportionately affects individuals experiencing homelessness with prevalence rates ranging from 7.5% to 52.2% [1]. Despite the substantial need and the availability of highly effective direct-acting antivirals (DAAs), HCV-infected homeless populations continue to be significantly undertreated [2, 3]. Medication adherence is a major concern in this vulnerable population, which experiences higher rates of mental health disorders and substance use disorders. Additionally, homeless populations face considerable challenges due to unstable residence, competing priorities, and lack of transportation and insurance coverage, among other concerns [3–5]. For many providers, medication adherence is a major concern when considering initiating HCV treatment for patients experiencing homelessness.

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As illustrated by a study assessing hepatology and primary care providers' perceived barriers to HCV treatment, 33% identified being homeless as a significant barrier to treatment and 25% felt homelessness was a barrier to adherence to DAA therapy [6]. Additionally, a survey of HCV providers found that the most common perceived barrier to DAA adherence was homelessness (65%) [7]. During the formative work for this study, homeless shelter providers and staff also raised concerns about adherence and reported current drug or alcohol use, mental health disorders, and safe medication storage (either through losing their belongings or theft) as potential barriers to medication adherence [4, 5].

Despite these concerns, several studies have demonstrated that patients experiencing homelessness can achieve high adherence rates while on DAA therapy. Successful programs have found innovative ways to provide HCV care within their targeted community. In a study utilizing a community-based treatment approach and adherence assessments through weekly calls from an HCV care coordinator, 78% of patients reported no missed doses while on DAA therapy [8]. A second study utilized the use of an on-site intensive specialty pharmacy (ON-ISP). In this retrospective study evaluating ON-ISP effectiveness compared to off-site specialty pharmacy when

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treating vulnerable populations accessing a safety-net hospital, patients enrolled in ON-ISP achieved 92% adherence rates compared to 87% for those using off-site specialty pharmacies [9]. Despite these successes, significant challenges remain for homeless patients to access and undergo successful HCV treatment.

For instance, a study looking at race disparities in sustained virologic response (SVR) rates found that African American patients had lower rates of SVR. When adjusting for homelessness, substance abuse, and mental health disorders among the African American cohort (N = 306), only homelessness affected SVR rates (adjusted odds ratio [OR], 0.39 [95% confidence interval {CI}, .19-.81]) [10]. This study highlights the need for ongoing research directed toward understanding ways to deliver high-quality and equitable HCV care to individuals experiencing homelessness. Through previous efforts we have confirmed that formalized HCV education can improve general knowledge of HCV and attendance to liver specialty clinics [11]. To our knowledge there have been no studies assessing how standardized pretreatment education coupled with on-site treatment can impact medication adherence among patients accessing homeless shelters.

From our initial research evaluating the feasibility of establishing standardized HCV screening and treatment within homeless shelters, we demonstrated that homeless shelter clients prioritize their health and are willing to engage in medical care if given the opportunity [4, 5]. Both shelter clients and shelter providers felt that with proper HCV education and infrastructure in place, people staying in homeless shelters would be engaged in treatment [4]. Unfortunately, we also determined that HCV knowledge among those experiencing homeless remained low and many were not aware of the new DAA therapies and their improved tolerabilities and outcomes. Therefore, a change in the HCV treatment narrative was deemed critical to improving HCV treatment uptake within homeless shelters [5]. We aimed to evaluate patients' confidence in their ability to be adherent to medication following completion of a comprehensive and standardized HCV education within a shelter setting. Additional study aims were to evaluate adherence to HCV therapy and patient-level factors that may have impacted adherence to HCV therapy.

MATERIALS AND METHODS

Study Population and Study Design

This prospective study was conducted by a multidisciplinary team at 4 large homeless shelters (2 in San Francisco, California, and 2 in Minneapolis, Minnesota) from 1 August 2018 to 30 January 2021. The homeless shelters provided supportive services on a daily basis to >300 residents in San Francisco and between 170 and 350 residents in Minneapolis. The services provided include housing, meals, and case management, and some level of medical care ranging from basic triage to specialist consultation.

Following informed consent, adults 18 years of age and older seeking shelter services and who were either treatment naive or had not received prior HCV treatment within the prior 12 weeks were enrolled. In addition, HCV-positive homeless clients who accessed low-threshold temporary shelters and safety-net liver specialty care were also recruited. Patients with significant medical or psychiatric conditions that prevented participation in the study were excluded.

Study Procedures

Clients who agreed to HCV testing and who met study eligibility criteria were enrolled, completed a questionnaire, and underwent point-of-care HCV testing (OraQuick HCV Rapid Antibody Test, OraSure Technology, Bethlehem, Pennsylvania). Participants who tested negative for HCV antibody were provided information about HCV and its prevention [12, 13].

Those who tested positive for HCV antibody received a confirmatory HCV RNA test and underwent a standardized, 30-minute HCV education. This in-person, comprehensive education was delivered using a PowerPoint slide format and was led by a designated care team member (RN, PharmD, or advanced practice provider). In addition, a preeducation and posteducation questionnaire [14, 15] was completed and information on HCV risk factors and HCV awareness was captured. The questionnaires were self-administered, and research staff were available to address any questions. Standard of care HCV therapy was offered to all participants with detectable HCV RNA that was primarily on-site at the shelters or through coordination with their primary care, liver specialty care, or addiction services. If needed, the study team assisted participants in obtaining insurance and facilitated linkage to primary care services. In San Francisco, a designated HCV nurse coordinator managed patients on treatment within the shelters in collaboration with shelter clinic providers, primary care providers, or safety-net liver specialty clinic. In Minneapolis, a PharmD embedded within shelter clinics managed patients on treatment in collaboration with shelter clinic staff and the safety-net liver specialty clinic. Patients were followed throughout therapy and completed laboratory tests and questionnaires at end of treatment and at 12 weeks following completion of therapy (SVR). Clinical data including bloodwork, imaging, and medical history were collected from the participants' medical record. A \$25 incentive was given for HCV testing and a total of \$75 was given following HCV education and completion of HCV therapy including SVR bloodwork. For this analysis, only participants who completed HCV education and underwent HCV therapy were included.

Patient Consent Statement

Institutional review board approvals were obtained for this study from the University of California, San Francisco and the Hennepin Healthcare Human Subjects Research Committee, and all participants provided written consent.

Assessment of Clinical Variables and Adherence to HCV Treatment

Active HCV infection was confirmed with detectable HCV RNA, and response to therapy was evaluated by HCV RNA testing at the end of therapy and at SVR time points.

Nonprescription drug use, alcohol consumption, and receipt of substance use therapy before treatment at the end treatment and SVR time point were assessed by self-report. Alcohol consumption was captured at baseline and at the end of HCV treatment. Alcohol consumption was categorized as (1) none or minimal (<1 drink per month); (2) moderate (more than none or minimal, but no more than 4 drinks/day or 14 drinks/week in men and no more than 3 drinks/day or 7 drinks/week in women); (3) heavy (>4 drinks/day for men, >3 drinks/day for women, or binge drinking [\geq 5 drinks for men or \geq 4 drinks for women, on the same occasion]) [16].

Following receipt of education, patient responses to the following 3 questions were captured: (1) Can you take your hepatitis C antiviral medication once a day, exactly as directed, without ever missing a dose? (2) Can you keep all of your doctor visits without ever missing an appointment? and (3) Can you take your medications correctly even if you are using drugs or alcohol? Responses to the questions were recorded as follows: "not confident," "slightly confident," "moderately confident," or "extremely confident." Patient-reported confidence in adherence to HCV therapy following education was categorized as "extremely confident" response to all 3 questions (yes/no).

Adherence to HCV treatment was captured by both patient report and provider documentation. Adherence to HCV therapy was determined by medication adherence, adherence to scheduled clinic visits, and recommended laboratory testing. Adherence to HCV medication was defined as taking medication daily for correct duration of therapy (yes/no) and was collected through provider documentation in medical records. Provider-documented measures of adherence captured from medical records included patient interview during clinic visits, pill count, or use of pharmacy refills. A composite score for overall adherence to HCV therapy (ranging from 0 to 3) was then calculated by summing the scores of medication adherence (yes/no = 1/0), clinic visit adherence (yes/no = 1/0), and laboratory testing adherence (yes/no = 1/0).

Statistical Analysis

Descriptive analyses of cohort characteristics were performed to obtain frequency (%) for categorical variables and median (interquartile range) or mean (standard deviation) for continuous variables. Patient characteristics by report of confidence in adherence to HCV therapy were compared using Mann-Whitney test for continuous variables, and χ^2 test or Fisher exact test as appropriate for categorical variables. Univariable and multivariable regression modeling was used to evaluate factors associated with primary outcome measure of medication adherence and secondary outcome of overall adherence to HCV therapy from an a priori–compiled list. Multivariable models included variables with *P* value <.05 and controlled for age, sex, history of psychiatric illness, and illicit drug use or alcohol use within the past 12 months. All analyses were performed in Stata 15 statistical software (StataCorp, College Station, Texas).

RESULTS

Participants

Between 1 August 2018 and 30 January 2021, 107 HCV antibody–positive patients with detectable HCV RNA experiencing homelessness received HCV education, and 63 patients underwent DAA therapy through 4 homeless shelters located in San Francisco, California and Minneapolis, Minnesota. The majority of patients were male with a median age of 56 and either African American/Black (43%) or non-Hispanic White (41%). Three-quarters of the participants achieved a high school education or less. The vast majority had used illicit drugs within the past 12 months (81%) and more than half of respondents reported moderate to heavy/binge alcohol use. More than half of the patients had a history of psychiatric illness (Table 1).

Patient Confidence in Adherence to HCV Therapy Following Receipt of Standardized HCV Education

Overall, following HCV education and prior to receipt of therapy, 81% of patients expressed extreme confidence in their ability to adhere to HCV medication as prescribed compared to 71% pre-HCV education. Extreme confidence in keeping doctor's visits also increased from preeducation (56%) to posteducation (68%). There was a significant improvement in confidence to adhere to HCV therapy score post-HCV education compared to preeducation (mean score, 1.9 ± 1.2 vs 2.2 ± 1.0 ; P = .006). Table 2 summarizes patient characteristics overall and by reports of extreme confidence in adherence to therapy following HCV education. A higher proportion of those who were extremely confident (vs those who were not) were uninsured and a lower proportion reported active alcohol use within the prior 12 months (P = .04). A higher proportion of those who reported lack of extreme confidence in adherence to HCV treatment reported heavy alcohol use or binge drinking compared to those who with extreme confidence in adherence to HCV treatment (53% vs 24%, respectively). Other patient and clinically related factors did not significantly differ between groups.

Adherence and Access to Medication

Following completion of therapy, 88% of patients reported completing the entire course of medication and 25% reported no

Table 1. Characteristics of Patients Who Initiated Hepatitis C Virus Therapy

Characteristics	Total (N = 63ª)
	10(a) (N = 03)
Age, y Median	50
	56
Range	28-82
IQR	49–62 73
Male sex, %	/3
Race/ethnicity, % Non-Hispanic White	41
Black/African American	41
Hispanic	5
Native American Multiple	3
	95
Born in the United States, % Education, %	95
,	24
Less than high school	44
High school	
More than high school	32
Insurance status, % Public insurance	07
	87
Private insurance	3
Uninsured	5
Has a health care provider, %	89
History of prior HCV testing, %	79
History of substance use therapy, % (n = 62)	61 14
History of prior HCV treatment, %	
Illicit drug use within the prior 12 mo, %	81
Injection drug use ever, %	68
Alcohol use in the prior 12 mo, % None/minimal	07
	37
Moderate	25
Heavy/binge	38
HIV coinfection, %	5
History of psychiatric illness, % (n = 62)	52
Employment status, %	
Employed	14
	40
Retired/disabled	37
	10
Any employment in past year	17

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range.

^aUnless otherwise specified.

missed doses with a mean of 4.2 missed doses overall. In contrast, medication adherence during therapy by provider report was low at 48%. With respect to prescribed duration of therapy, overall 46 patients (69.7%) completed the duration of the medication as prescribed. Figure 1 shows the treatment duration, Figure 2 the number of missed doses by patient report categorized by type of medication, and Figure 3 the number of missed doses by provider report categorized by type of medication. Complete medication adherence with no missed doses by patient report or provider documentation (42% vs 35% or 56% vs 29%, respectively) or prescribed length of therapy (51% vs 29%) was higher with glecaprevir-pibrentasvir compared with sofosbuvir-velpatasvir. When assessing how medication was stored while on treatment, 30% reported keeping medications on their person, 26% kept medications in the shelter, 33% stored medication in a personal locker, and 10% of patients accessed medication at their substance use treatment facility. Overall, 86.4% of the patients achieved per-protocol SVR after therapy, and 81.0% achieved SVR on intention-to-treat (ITT) analysis.

Factors Associated With Medication Adherence by Provider Documentation and Overall Adherence to HCV Therapy

The rate of overall adherence to HCV therapy (ie, combination of adherence to medication, clinic visits, and laboratory tests) was 38%. On univariable analysis (Table 3), prior receipt of HCV treatment was negatively associated with both medication adherence (OR, 0.11; P = .04) and overall adherence to HCV treatment (coefficient [Coef.] = -0.83; P = .03). In addition, having insurance was negatively associated with overall adherence to HCV treatment (Coef. = -1.06; P = .03), while older age was positively associated with overall adherence to HCV treatment (Coef. = 0.27; P = .02). When evaluating the relationship between shelter use or length of stay and adherence, having regular access to shelter on a nightly basis was positively associated with overall adherence to HCV treatment, but this did not reach statistical significance (P = .06). Illicit drug or alcohol use in the past 12 months or having a history of psychiatric illness was also not associated with patient adherence.

On multivariable analysis that included age, sex, use of illicit drugs or alcohol within the prior 12 months, and history of psychiatric illness, older age (Coef. = 0.30 per decade [95% CI, .04–.57]; P = .03) was positively associated with overall adherence. Prior HCV treatment was negatively associated with both medication (OR, 0.08; P = .046) and overall adherence (Coef. = -0.87 [95% CI, -1.61 to -.11]; P = .03) (Table 4).

DISCUSSION

Medication adherence is a major barrier to achieving HCV cure with DAA therapy and is often cited as a concern when considering initiation of HCV treatment in homeless populations [5, 7, 8, 17]. The considerable effects of nonadherence on SVR rates were described in a pooled analysis of clinical trials utilizing glecaprevir-pibrentasvir, where ITT SVR rates decreased to 87% in nonadherent participants compared to 98% in those who were adherent [18]. Additionally, this study noted that most patients who did not achieve SVR discontinued treatment early [18]. Knowing the significant HCV health disparities present among vulnerable populations, a better understanding of ways to improve adherence in these difficult-to-engage groups is critical to HCV elimination efforts. In this study, we showed the positive impact of our integrated treatment model on confidence in adherence to medication and monitoring during treatment. More than 80% of HCV-infected patients accessing homeless shelters in our

Table 2. Patient-Reported Confidence in Adherence to Hepatitis C Therapy Following Receipt of Hepatitis C Education

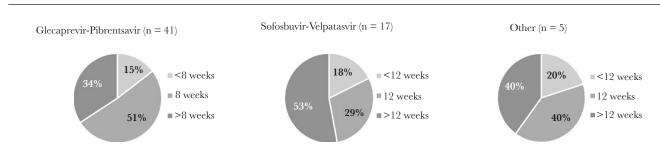
Characteristics	Overall (N = 63 ^a)	Extremely Confident in Adherence to HCVTherapy (n = 33)	Not Extremely Confident in Adherence to HCV Therapy (n = 30)	<i>P</i> Value
Age, y				.2
Mean	55	53	57	
Range	28–82	28–82	35–74	
SD	11.23	13.00	8.80	
Sex, %				1.0
Male	73	73	73	
Female	27	27	27	
Race/ethnicity, %				.7
Black/African American	43	36	50	
White	41	42	40	
Native American	3	3	3	
Hispanic	6	9	3	
Multiple	6	9	3	
English preferred language, %	97	94	100	.2
Insurance status, %				.049
Insured	90	82	100	
Uninsured	8	15	0	
Don't know	2	3	0	
History of psychiatric illness, % (n = 62)	52	52	52	1.0
Illicit drug use within prior 12 mo, %	81	85	77	.4
Alcohol use within the prior 12 mo, %	60	48	73	.04
Alcohol use amount within the prior 12 mo, %				.053
None/minimal	37	42	30	
Moderate	25	33	17	
Heavy/binge	38	24	53	
Has a health care provider, % (n = 62)	85	84	87	1.0
History of prior HCV testing, %	79	82	77	.8
History of substance use therapy, $\%$ (n = 62)	61	63	60	1.0
History of prior HCV treatment, %	14	12	17	.7
Coinfected with HIV, %	6	9	3	.6
Shelter site, %				.6
San Francisco	67	70	63	
Minneapolis	33	30	37	

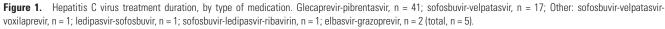
Bold value is statistically significant with P value <.05.

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus.

^aUnless otherwise specified.

study, a significant proportion of whom had active intravenous drug use and/or psychiatric illness, reported moderate or higher confidence in treatment adherence following education and were able to achieve HCV cure. In previous studies, medication adherence has been associated with improved SVR. For example, in one study of homeless patients treated with DAA therapy, 86.1% of those who missed between 1 and 7 doses achieved SVR whereas only 55.6% of those





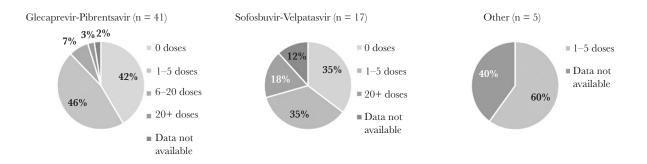


Figure 2. Number of missed doses of medication, by patient report.

missing >7 or an unknown number of missed doses achieved SVR [8]. Similarly, the majority of patients in our study reported ≤4 missed doses. Moreover, a low proportion (12%) of patients in our study reported they did not complete the entire course of treatment. While the self-reported adherence was similar to other studies [8], in using stringent criteria to define adherence as taking medication daily for correct duration of therapy by provider documentation, the medication adherence rate was 47.6%. Interestingly, complete adherence to medication dosing and duration by self-report or provider documentation was higher with the 8-week treatment regimen despite greater pill burden than the single-pill 12-week regimen, suggesting a potential influence of treatment duration on adherence. Notably, the providerreported adherence rate in our study was lower than other studies where a combination of patient self-report and pharmacy refill monitoring was used to define adherence [9]. Prior analysis of this study population showed that adherence to HCV therapy was one of the factors associated with SVR on ITT analysis [19]. Despite this, the SVR rate in our study (>80%) was relatively similar to that reported in other studies [18].

We found that older age was a positive predictor for overall adherence to HCV therapy but not medication adherence. In categorizing age, those aged \geq 50 years were more likely to achieve overall adherence than younger patients. This finding is similar to other studies assessing HCV compliance [20, 21] but not necessarily in patients experiencing homelessness, where some have not shown a relationship between age and improved HCV treatment outcomes [8]. Older patients are more concerned about their health in studies of chronic conditions [22], and are more likely to have other comorbidities requiring

medication use [22]. However, in our population of persons experiencing homelessness, the number of medical comorbidities among younger and older patients was similar; 37.8% of those aged \geq 50 years had 2 or more comorbidities compared to 38.9% in those aged <50 years. On the other hand, a higher proportion of younger patients had psychiatric illness (72.2% vs 42.4%; P = .05) which may have adversely influenced adherence to HCV therapy [8]. Interestingly, prior receipt of HCV treatment was negatively associated with both medication and overall adherence in our study. This was a unique finding that has not been reported in previous studies. In a pooled analysis of adherence to glecaprevir-pibrentasvir, no relationship was found between prior receipt of DAA-based or interferon-based therapy and adherence to DAA retreatment [18]. However, these studies were not confined to vulnerable populations where adherence issues, rather than virologic nonresponse, may have played a greater role in the prior treatment failure.

Alcohol use negatively impacts adherence to HCV therapy. In a study of 2091 HCV patients, use of any alcohol was the only baseline characteristic associated with medication nonadherence (OR, 2.38 [95% CI, 1.13–5.01]; P = .02) [21], and in another study of HCV-infected people who inject drugs, heavy alcohol use was similarly associated with >2 times higher odds of medication nonadherence [20]. However, in our study, despite lower self-reported confidence in adherence to HCV therapy, heavy alcohol use was not an independent predictor of either medication or overall treatment adherence. This suggests that self-reported confidence in adherence to therapy among individuals with heavy alcohol use who experience homelessness may not be a reliable measure of actual adherence to HCV



Figure 3. Number of missed doses of medication, by provider report.

Table 3. Univariable Analysis of Factors Associated With Medication Adherence and Overall Adherence to Hepatitis C Therapy

Characteristic	Medication Adherence				Overall Adherence			
	No.	OR	(95% CI)	<i>P</i> Value	No.	Coefficient	(95% CI)	<i>P</i> Value*
Age per decade	63	1.28	(.81–20.03)	.3	63	0.27	(.04–.51)	.02
Sex	63			1.0	63			1.0
Male		Ref.	(.32-2.95)			Ref.	(62 to.61)	
Female		0.97				0.31		
Race/ethnicity	63				63			
Non-Hispanic White		Ref.				Ref.		
Black/African American		0.69	(.23-2.02)	.5		0.004	(59 to 1.28)	1.0
Hispanic		0.86	(.10-7.04)	.9		0.12	(–1.05 to 1.28)	.8
Native American		NA	NA	NA		-0.88	(-2.48 to .71)	.3
Multiple		0.86	(.10-7.04)	.9		-0.63	(–1.80 to .53)	.3
Born in the United States					63	-1.23	(-2.47 to .004)	.051
Education	63				63			
Less than high school		Ref.				Ref.		.9
High school		1.5	(.42–5.35)	.5		0.06	(64 to .75)	1.0
More than high school		1.5	(.39–5.81)	.6		-0.00	(74 to .74)	
Has insurance					62	-1.06	(-2.04 to09)	.03
Has a health care provider	62	1.12	(.27-4.62)	.9	62	-0.04	(76 to .68)	.9
History of prior HCV testing	63	0.73	(.21-2.48)	.6	63	-0.03	(70 to .65)	.9
History of prior HCV treatment	63	0.11	(.01–.92)	.04	63	-0.83	(–1.58 to –.09)	.03
History of substance use therapy	62	0.47	(.16–1.31)	.2	62	0.0005	(26 to .26)	1.0
Illicit drug use within the prior 12 mo	63	0.59	(.16–2.10)	.4	63	-0.22	(91 to .47)	.5
Injection drug use ever	63	0.87	(.30-2.51)	.8	63	-0.11	(70 to .48)	.7
Alcohol use in the prior 12 mo	63				63			
None/minimal		Ref.				Ref.		
Moderate		2.17	(.59–7.99)	.3		0.30	(40 to 1.01)	.4
Heavy		0.93	(.29–2.95)	.9		0.14	(49 to .77)	.7
HIV coinfection	63	1.11	(.15-8.39)	.9	63	-0.08	(-1.20 to 1.03)	.9
History of psychiatric illness	63	0.94	(.35–2.53)	.9	63	-0.15	(70 to .39)	.6
Employment status	63				63			
Employed		Ref.				Ref.		
Unemployed		0.74	(.16–3.41)	.7		0.40	(44 to 1.25)	0.3
Retired/disabled		0.73	(.16–3.45)	.7		0.27	(59 to 1.13)	.5
Incarcerated		0.40	(.05–3.42)	.4		0.11	(-1.04 to 1.26)	.9
Spent every night in shelter while on treat- ment	41	0.90	(.71–1.15)	.4	41	0.71	(04 to 1.46)	.06
Changed shelters during treatment	42	0.91	(.72–1.14)	.4	42	0.32	(63 to 1.28)	.5
Extended shelter stay during treatment	42	1.00	(0.87–1.15)	1.0	42	-0.75	(-1.61 to .11)	.1
Patient confidence in adherence to treatment	63	2.34	(.85–6.46)	.1	63	0.11	(43 to .66)	.7

*P value <.05 bolded.

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; HIV, human immunodeficiency virus; NA, not applicable; OR, odds ratio.

treatment. As alcohol use is associated with increased liver disease progression and adverse outcome in the setting of HCV, reliance on patient-reported confidence in adherence may potentially lead to withholding treatment and increasing disparities among patients with alcohol abuse who would most benefit from HCV cure. These findings also suggest that providing tailored interventions including formal education to enhance confidence in those with active alcohol abuse could further improve this subpopulation's engagement in HCV care.

This study had several limitations. First, the use of pill counts was not standardized throughout the sites. However, this was not feasible given the heterogeneity around medication storage and how patients were followed on treatment. Second, our definition of medication adherence as being 100% compliant with medication dosing by provider report is more stringent than in other studies assessing adherence [8, 9, 17, 18]. Thus, the reported adherence rates are more conservative than prior studies but reflect complete adherence to medication. Finally, although we utilized 2 distinct geographical locations in an effort to demonstrate transferability of our models to different sites, these findings may not be generalizable to all homeless populations, especially those outside large urban centers.

Factor	Me	dication Adherence (r	= 62)	Overall Adherence (n = 62)		
	OR	(95% CI)	<i>P</i> Value	Coefficient	(95% CI)	PValue*
Age per decade	1.33	(.72-2.42)	.4	0.30	(.04–.57)	.03
Sex					(44 to .79)	.6
Male	Ref.			Ref.		
Female	1.58	(.43–5.83)	.5	0.17		
History of prior HCV treatment	0.08	(.0196)	.046	-0.87	(-1.61 to11)	.03
Use of illicit drugs within the prior 12 mo	0.52	(.11-2.44)	.4	-0.29	(97 to38)	.4
Alcohol use within the prior 12 mo						
None/minimal	Ref.			Ref.		
Moderate	4.47	(.78-25.54)	.1	0.36	(37 to 1.10)	.3
Heavy/binge	0.79	(.20-3.15)	.7	0.06	(57 to .69)	.8
History of psychiatric illness	1.30	(.36-4.68)	.7	0.35	(25 to .94)	.2
Patient has insurance				-0.99	(–1.98 to .003)	.051

*P value <.05 bolded.

Abbreviations: CI, confidence interval; HCV, hepatitis C virus.

^aAdjusted for age, sex, alcohol use, illicit drug use, and history of psychiatric illness.

Despite the challenges faced when treating HCV in persons experiencing homelessness, our study underscores that when provided with adequate support infrastructure, this highly vulnerable population can be effectively treated despite imperfect adherence. Indeed, we have previously shown that nearly all (>95%) of these patients felt supported and reported favorable views of their provider and a high level of treatment satisfaction. Optimization of care delivery and expanding opportunity to treat persons experiencing homelessness, including those with substance use and psychiatric illness, are therefore critical to reduction in HCV-related disparity in this population.

Notes

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References

 Edlin BR, Eckhardt BJ, Shu MA, et al. Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology 2015; 62:1353–63.

- Beck KR, Kim N, Khalili M. Sofosbuvir-containing regimens for chronic hepatitis C are successful in the safety-net population: a real-world experience. Dig Dis Sci 2016; 61:3602–8.
- Khalili M, Wong RJ. Underserved does not mean undeserved: unfurling the HCV care in the safety net. Dig Dis Sci 2018; 63:3250–2.
- Fokuo JK, Masson CL, Anderson A, et al. Recommendations for implementing hepatitis C virus care in homeless shelters: the stakeholder perspective. Hepatol Commun 2020; 4:646–56.
- Masson CL, Fokuo JK, Anderson A, et al. Clients' perceptions of barriers and facilitators to implementing hepatitis C virus care in homeless shelters. BMC Infect Dis 2020; 20:386.
- Rogal SS, McCarthy R, Reid A, et al. Primary care and hepatology providerperceived barriers to and facilitators of hepatitis C treatment candidacy and adherence. Dig Dis Sci 2017; 62:1933–43.
- 7. Zhang G, Patel K, Moghe A, et al. Provider perceptions of hepatitis C treatment adherence and initiation. Dig Dis Sci **2020**; 65:1324–33.
- Beiser ME, Smith K, Ingemi M, et al. Hepatitis C treatment outcomes among homeless-experienced individuals at a community health centre in Boston. Int J Drug Policy 2019; 72:129–37.
- 9. Tran AN, Sachdev R, Fricker ZP, et al. Intensive pharmacy care improves outcomes of hepatitis C treatment in a vulnerable patient population at a safety-net hospital. Dig Dis Sci **2018**; 63:3241–9.
- Benhammou JN, Dong TS, May FP, et al. Race affects SVR12 in a large and ethnically diverse hepatitis C-infected patient population following treatment with direct-acting antivirals: analysis of a single-center Department of Veterans Affairs cohort. Pharmacol Res Perspect 2018; 6:e00379.
- Surjadi M, Torruellas C, Ayala C, et al. Formal patient education improves patient knowledge of hepatitis C in vulnerable populations. Dig Dis Sci 2011; 56:213–9.
- 12. Centers for Disease Control and Prevention. Hepatitis C—general information. https://www.cdc.gov/hepatitis/hcv/pdfs/hepcgeneralfactsheet.pdf. Accessed 15 February 2021.
- Centers for Disease Control and Prevention. Hepatitis C and injection drug use. https://www.cdc.gov/hepatitis/hcv/pdfs/factsheet-pwid.pdf. Accessed 15 February 2021.
- Balfour L, Kowal J, Corace KM, et al. Increasing public awareness about hepatitis C: development and validation of the brief hepatitis C knowledge scale. Scand J Caring Sci 2009; 23:801–8.
- Fife BL, Wright ER. The dimensionality of stigma: a comparison of its impact on the self of persons with HIV/AIDS and cancer. J Health Soc Behav 2000; 41:50–67.
- National Institute on Alcohol Abuse and Alcoholism. What are the different drinking levels? https://www.rethinkingdrinking.niaaa.nih.gov/how-much-is-too-much/ is-your-drinking-pattern-risky/Drinking-Levels.aspx. Accessed 15 February 2021.
- Akiyama MJ, Norton BL, Arnsten JH, et al. Intensive models of hepatitis C care for people who inject drugs receiving opioid agonist therapy: a randomized controlled trial. Ann Intern Med 2019; 170:594–603.

- Brown A, Welzel TM, Conway B, et al. Adherence to pan-genotypic glecaprevir/ pibrentasvir and efficacy in HCV-infected patients: a pooled analysis of clinical trials. Liver Int 2020; 40:778–86.
- Khalili M, Powell J, Park H, et al. Shelter-based integrated model is effective in scaling up hepatitis C testing and treatment in homeless clients in two large urban settings. Hepatol Commun 2021. In press.
- Brown RS Jr, Buti M, Rodrigues L, et al. Glecaprevir/pibrentasvir for 8 weeks in treatment-naïve patients with chronic HCV genotypes 1-6 and compensated cirrhosis: The EXPEDITION-8 trial. J Hepatol 2020; 72:441–9.
- 21. Chehl N, Maheshwari A, Yoo H, et al. HCV compliance and treatment success rates are higher with DAAs in structured HCV clinics compared to general hepatology clinics. Medicine (Baltimore) **2019**; 98:e16242.
- 22. Townsend K, Petersen T, Gordon LA, et al. Effect of HIV co-infection on adherence to a 12-week regimen of hepatitis C virus therapy with ledipasvir and sofosbuvir. AIDS **2016**; 30:261–6.
- Kim S, Powell J, Naugle J, et al. Patient-reported experiences with direct acting antiviral therapy in an integrated model of hepatitis C care in homeless shelters. J Viral Hepat 2021; 28:1488–90.