Preventive Medicine Reports 32 (2023) 102138

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Clinician barriers, perceptions, and practices in treating patients with hepatitis C virus and substance use disorder in the United States

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ARTICLE INFO

Keywords:
HCV
Direct-acting antivirals
Survey
SUD
Medicaid

ABSTRACT

The likelihood of clinicians prescribing direct-acting antiviral (DAA) therapy for patients with chronic hepatitis C virus (HCV) and substance use disorder (SUD) was assessed via a survey emailed throughout the United States to clinicians (physicians and advanced practice providers) in gastroenterology, hepatology, and infectious disease specialties. Clinicians' perceived barriers and preparedness and actions associated with current and future DAA prescribing practices of HCV-infected patients with SUD were assessed. Of 846 clinicians presumably receiving the survey, 96 completed and returned it. Exploratory factor analyses of perceived barriers indicated a highly reliable (Cronbach alpha = 0.89) model with five factors: HCV stigma and knowledge, prior authorization requirements, and patient- clinician-, and system-related barriers. In multivariable analyses, after controlling for covariates, patient-related barriers ($P < 0.01$) and prior authorization requirements ($P < 0.01$) were *negatively* associated with the likelihood of prescribing DAAs. Exploratory factor analyses of clinician preparedness and actions indicated a highly reliable (Cronbach alpha = 0.75) model with three factors: beliefs and comfort level; action; and perceived limitations. Clinician beliefs and comfort levels were negatively associated with the likelihood of prescribing DAAs ($P = 0.01$). Composite scores of barriers ($P < 0.01$) and clinician preparedness and actions ($P < 0.05$) were also negatively associated with the intent to prescribe DAAs.

Conclusion: These findings underscore the importance of addressing patient-related barriers and prior authorization requirements—significant problematic barriers—and improving clinicians' beliefs (e.g., medication-assisted therapy should be prescribed before DAAs) and comfort levels for treating patients with HCV and SUD to enhance treatment access for patients with both HCV and SUD.

1. Introduction

Hepatitis C virus (HCV) is the most frequently reported blood-borne infection in the United States (US) and a leading cause of liver-related morbidity, liver cancer, liver transplantation, and mortality (Ditah et al., 2014). Treatment of HCV has greatly improved since the introduction of direct-acting antivirals (DAAs), which show therapeutic efficacy in >95 % of patients across the four major HCV genotypes and have limited adverse effects (Falade-Nwulia et al., 2017; Webster et al., 2015). In 2013, when DAAs were introduced to treat and cure HCV, the World Health Organization responded by calling for the elimination of viral hepatitis by 2030 (World Health Organization WHO, 2017). However, in the US, HCV treatment rates have been declining since their peak in 2015 and we are only about halfway to the expected rate needed

Abbreviations: DAA, direct-acting antiviral; GHAPP, Gastroenterology & Hepatology Advanced Practice Providers; HCV, hepatitis C virus; PWID, persons who inject drugs; SUD, substance use disorder; US, United States.

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https://doi.org/10.1016/j.pmedr.2023.102138
Received 9 August 2022; Received in revised form 19 December 2022; Accepted 10 February 2023
Available online 13 February 2023
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in 2020 to enable reaching the goal of the World Health Organization, leaving more patients that need to be treated (Centers for Disease Control and Prevention, 2021). With less than a decade remaining to reach the goal, HCV remains one of the top causes of chronic liver disease worldwide (Paik et al., 2020).

The reasons for suboptimal treatment uptake are multifactorial and include an increase in HCV infections resulting from the opioid crisis, poor linkage to care for individuals diagnosed with HCV, insurance barriers (e.g., Medicaid prior authorization requirement), sobriety requirements, and the COVID-19 pandemic (Ko et al., 2019; Liang and Ward, 2018; Centers for Disease Control and Prevention, 2017). These impediments are especially prevalent among poor and underserved populations (Jain et al., 2019; Park et al., 2021). There are other multilevel issues related to clinicians, patients, and the health system structure that have led to low HCV treatment rates (Malespin et al., 2019; Grebely et al., 2017). In a previous study by our group, individuals with HCV and substance use disorder (SUD) were 47 % less likely to receive DAAs compared with individuals with HCV but without SUD among Florida Medicaid beneficiaries (Park et al., 2021) despite evidence from several clinical trials supporting treatment with DAAs for persons who inject drugs (PWID) among those receiving current opioid agonist therapy (Simoncini et al., 2021; Trooskin et al., 2020).

Despite the importance of advancing understanding regarding the barriers to DAA treatment and the urgent need to implement innovative interventions to reach the global health goal of eliminating hepatitis by 2030, little is known about clinician experiences in treating HCV-infected patients with SUD in the DAA era. Thus, we developed a survey to assess clinician self-reported barriers, perceptions, and practices for treating HCV-infected patients with SUD and the associations of these barriers, perceptions, and practices with the willingness of clinicians to prescribe DAA treatment for patients with HCV and SUD.

2. Methods

2.1. Sampling and recruitment strategies

Using a modified Dillman approach (Dillman et al., 2014), we sampled US clinicians in gastroenterology, hepatology, and infectious disease specialties using two sampling strategies. First, we recruited a group composed primarily of physicians but that also included advanced practice providers (i.e., nurse practitioners and physicians assistants), using a list created with a search of the publicly available websites of study sites participating in the HCV-TARGET (Hepatitis C Therapeutic Registry and Research Network) and PRIORITIZE (a pragmatic, randomized controlled trial of oral antivirals for the treatment of chronic hepatitis C) studies (National Library of Medicine U.S., 2020; National Library of Medicine U.S., 2021). Second, to recruit a nationally representative group of advanced practice providers, we used three non-overlapping, proprietary lists owned by the Gastroenterology & Hepatology Advanced Practice Providers (GHAPP) organization drawn from their membership, subscribers, and hepatology specialists. GHAPP is a not-for-profit organization dedicated to educating and providing support resources for the professional advancement of advanced practice providers who treat patients with gastrointestinal disorders and chronic liver disease (Gastroenterology and Hepatology Advanced Practice Providers GHAPP, 2020).

We sent recruitment emails on March 25, 2021, to persons participating in the HCV-TARGET and PRIORITIZE studies, informing them of the present study and providing them with a link to the online questionnaire using REDCap. The listserv manager of GHAPP sent recruitment emails via Mailchimp to the GHAPP sample on June 9, 2021. For both recruitment samples, we contacted nonrespondents up to two additional times between April 13 and July 7, 2021, using REDCap and Mailchimp. HCV-Target and PRIORITIZE participants were offered a $25 electronic Amazon gift card on completion of the survey; GHAPP participants, a $10 electronic Amazon gift card. To ensure we had a sufficient sample size to conduct exploratory factor analysis, we set an *a priori* minimum of 95 respondents (5 respondents per item) for our model with the largest number of items. The University of Florida, Gainesville, Institutional Review Board approved this study (IRB201702880). After being informed of the purpose of the study, clinicians provided consent by completing and submitting the questionnaire.

2.2. Questionnaire instrument

Our team members developed the questionnaire instrument by identifying relevant items from the peer-reviewed literature. Our team reviewed and revised the original instrument containing 63 questions. We pilot tested the revised version containing 56 questions in a convenience sample of 20 hepatology clinicians. The final instrument, which included 2 adaptive response questions, 14 demographic characteristics questions, 43 assessment questions, and an option to leave an open-ended comment is provided in the **Appendix**. Responses to the assessment questions were collected using three Likert-type scales with five anchors each: (1) extremely unlikely to extremely likely, (2) never to always, and (3) strongly disagree to strongly agree. The assessment questions included three concepts: (1) current (n = 5) and anticipated future (n = 5) experiences with prescribing DAAs for HCV-infected patients with SUD, (2) perceived barriers to providing HCV treatment (n = 21), and (3) prescribers' preparedness and actions in treating HCV-infected patients with SUD (n = 12). The questionnaire used an adaptive strategy to guide participants. The first question asked if the participant treated patients with HCV and SUD. A response of *no* resulted in the participant progressing to the demographic characteristics questions without answering any assessment questions. A response of *yes* resulted in a follow-up question asking if the participant prescribed DAAs for patients with HCV and SUD. If the participants responded *yes* to the follow-up question, they were given all assessment and demographic characteristics questions, whereas if the participants responded *no*, they were given all questions except those five questions regarding current experiences.

3. Statistical analysis

Statistical analyses were conducted using R, version 3.6.3, in R Studio, version 1.2.5033. We conducted two exploratory factor analyses using varimax rotation of the correlation matrices. The first factor analysis included 19 items assessing barriers to prescribing DAAs. Barrier questions (n = 2) about non-Medicaid insurance requirements and open-ended "other" barriers were not included in this model. The second factor analysis included 12 items assessing prescriber preparedness and actions. The data obtained from both the HCV-TARGET and PRIORITIZE sample and the GHAPP sample were analyzed together. To determine the number of eigenvalues >1 and to generate scree plots, we used analyses of the correlation matrices. We then forced the number of factors using the principal axis method. We determined which items loaded on which factors by identifying high loadings (>|0.3|) and logical groupings among the factor patterns (Pett et al., 2003). Composite scores for each model and for each model's factors were created separately by averaging the relevant item scores. The internal consistencies of the composite and factor scores were measured using Cronbach α, with an acceptable internal consistency set a priori as $\alpha \geq 0.6$.

We then used multivariable linear regression to examine the association of prescriber-reported likelihood of prescribing DAAs using a 5-point Likert-type scale with (1) the composite and factor scores of each scale (i.e., barriers; and preparedness and actions scales) separately, and (2) the composite score for the two scales (i.e., barriers along with preparedness and actions scales) controlling for statistically significant clinician characteristics in univariate analyses. Significance was set a priori as $\alpha \leq 0.05$.

4. Results

4.1. Participant characteristics

Of 846 clinicians sent recruitment emails and presumably having received the survey invitation, 96 completed and submitted the survey (response rate of 11.3 %). The sample of clinicians comprised physicians (34.4 %), nurse practitioners (36.5 %), and physician assistants (28.1 %) (Table 1). Most clinicians self-reported being white (71.9 %) and female (70.8 %) and indicated that their specialty was hepatology (55.2 %). The clinicians were evenly distributed among the four regions of the country. The percentage of clinicians who treated 10–50 unique patients with HCV in the previous year was 46.9 %, and 40.7 % treated > 50 unique patients. The highest proportion of clinicians (55.2 %) worked in an academic setting, followed by clinicians who worked in a group setting (40.6 %).

4.2. Likelihood level for prescribing DAAs to patients with HCV and SUD

Overall, current DAA prescribing likelihood was high (mean likelihood score = 4.45, SD = 0.78; 1 = extremely unlikely to 5 = extremely likely) (Table 2). In their current practice, 56 % of clinicians were extremely likely to prescribe DAAs to patients with HCV and SUD, and 38 % were likely to prescribe DAAs to this population. In total, 64 % of clinicians reported that they were likely or extremely likely to prescribe DAAs for PWID with HCV and SUD, and 97 % were likely or extremely likely to prescribe DAAs to treat former PWID who had initiated medication-assisted treatment. In addition, 83 % of clinicians reported that they were likely or extremely likely to prescribe DAAs to treat patients with alcohol use disorder, and 96 % were likely or extremely likely to prescribe DAAs to treat patients with a history of alcohol use disorder who had been alcohol-free for 1 month. The overall mean prescribing likelihoods as well as the proportions for likelihoods of prescribing across the varied conditions in the ensuing 6 months were similar to those of current practice. Most clinicians reported that with regard to treating patients with HCV, COVID-19 had affected their practice from not at all to moderately (Table 1).

4.3. Exploratory factor and regression analyses of barriers

Factor analysis of the 19 barrier items resulted in six eigenvalues >1. The scree plot of the eigenvalues suggested one to five factors. We generated models with two to five factors based on the scree plot and eigenvalues. The five-factor model was deemed the most logical (Table 3): patient-related barriers (seven items), HCV stigma and knowledge (two items), prior authorization requirements (four items), clinician-related barriers (two items), and system-related barriers (four items). Item scores and factor loadings are presented in Table 3. Reliability estimates for the barriers to prescribing DAAs were high (composite Cronbach α = 0.89; factor Cronbach α range = 0.77–0.83), and the composite mean score was moderately low (mean = 2.40; 1 = Never to 5 = Always), indicating an overall moderately low perceived frequency of the barriers. Among the factors, patient-related barriers (mean = 2.62) were the most highly endorsed barriers, followed by HCV stigma and knowledge (mean = 2.56) and prior authorization requirements (mean = 2.32).

Using multivariable regression, we examined the ability of the five factors from the barriers model to explain clinician likelihood for prescribing DAAs, after controlling for significant covariates (medical specialty, number of HCV patients in the previous 12 months). The regression model containing the barrier model factor scores explained 41.3 % of the variation in clinician-reported DAA prescribing likelihoods (Table 4). Patient-related barriers (P < 0.001) and prior authorization requirements (P = 0.001) were significant negative predictors of clinician likelihood to prescribe DAAs for patients with HCV and SUD, whereas HCV stigma and knowledge (P = 0.028) and system-related

Table 1
Demographic and clinical characteristics of study participants (N = 96).

Clinician Characteristic (n = 96)	Frequency (%)
Medical Specialty	
Gastroenterology	35 (36.5)
Hepatology	53 (55.2)
Infectious Disease	5 (5.2)
Primary Care	1 (1.0)
Other	2 (2.1)
Ethnicity and Race	
White American	69 (71.9)
Asian/Pacific Islander	11 (11.5)
Black/African	7 (7.3)
Hispanic or Latino	2 (2.1)
Native American/American Indian	0 (0)
Other**	7 (7.3)
Gender	
Female	68 (70.8)
Male	25 (26.0)
Prefer not to answer	2 (2.1)
Unknown	1 (1.0)
Age, years	
<30	4 (4.2)
31–40	36 (37.5)
41–50	24 (25.0)
51–60	23 (24.0)
>60	6 (6.3)
Prefer not to answer	2 (2.1)
Unknown	1 (1.0)
Practice type	
Academic	53 (55.2)
Group	39 (40.6)
Solo	3 (3.1)
Other	1 (1.0)
Health Profession	
Nurse practitioner	35 (36.5)
Physician	33 (34.4)
Physician assistant	27 (28.1)
Other	1 (1.0)
How many years have you seen HCV-infected patients in your practice?	11 ± 8*
How many patients with HCV have you treated in the last 12 months?	
<10	12 (12.5)
10–50	45 (46.9)
51–100	21 (21.9)
>100	18 (18.8)
US Region	
South	26 (27.1)
Midwest	24 (25.0)
West	23 (24.0)
Northeast	22 (22.9)
Unknown	1 (1.0)
Approximately what percent of your HCV-infected patients had/have SUD?	
<10	16 (16.7)
10–25	21 (21.9)
26–50	22 (22.9)
51–74	20 (20.8)
>75	15 (15.6)
Unknown	2 (2.1)
To what extent has your practice been affected by COVID-19 in treating patients with HCV?	
To a great extent	3 (3.1)
To a large extent	9 (9.4)
To a moderate extent	33 (34.4)
To a small extent	39 (40.6)
Not at all	10 (10.4)
Unknown	2 (2.1)

Abbreviations: HCV, hepatitis C virus; SUD, substance use disorder; US, United States.
*Data represent mean ± standard deviation.
**_Other_ included multiple races, prefer not to answer, other, and unknown.

Table 2
Likelihood of prescribing direct-acting antivirals to treat HCV-infected patients with SUD.

Condition	Likelihood score, mean (SD)[a]	Extremely unlikely (%)	Unlikely (%)	Neither unlikely nor likely (%)	Likely (%)	Extremely likely (%)
In your current practice, how likely are you to prescribe DAAs to treat patients with HCV infection and SUDs? (n = 96)	4.45 (0.78)	1.0	3.1	2.1	37.5	56.3
PWID with or without needle exchange (n = 96)	3.79 (1.26)	3.1	19.8	13.5	21.9	41.7
Former PWID but who initiated medication-assisted treatment (e.g., buprenorphine) (n = 96)	4.67 (0.54)	0.0	0.0	3.1	27.1	70.0
Persons with alcohol use disorder (n = 96)	4.24 (0.93)	0.0	8.3	8.3	34.4	49.0
Persons with history of alcohol use disorder who have been alcohol-free for 1 month (n = 96)	4.68 (0.55)	0.0	0.0	4.2	24.0	71.9
In the next 6 months, how likely are you to prescribe DAAs to treat patients with HCV and SUD? (n = 94)	4.46 (0.83)	1.1	2.1	8.5	26.6	61.7
PWID with or without needle exchange (n = 96)	3.81 (1.19)	1.0	18.8	18.8	20.8	40.6
Former PWID who initiated substitution therapy (n = 95)	4.60 (0.61)	0.0	1.1	3.2	30.5	65.3
Persons with alcohol use disorder (n = 95)	4.25 (0.94)	0.0	9.5	6.3	33.7	50.5
Persons with history of alcohol abuse who have been alcohol-free for a certain period of time (n = 95)	4.74 (0.44)	0.0	0.0	0.0	26.3	73.7

Abbreviations: DAA, direct-acting antiviral; HCV, hepatitis C virus; PWID, persons who inject drugs; SUD, substance use disorder.
[a] Measured on a 5-point Likert-type scale (1 = extremely unlikely, 2 = unlikely, 3 = neither unlikely nor likely, 4 = likely, 5 = extremely likely).

barriers (P = 0.011) were significant positive predictors. The model containing the composite barrier score explained 22.6 % of the variation in clinician-reported willingness to prescribe DAAs, with the composite score (P < 0.001) being a significant negative predictor of clinician likelihood to prescribe DAAs for patients with HCV and SUD.

4.4. Exploratory factor and regression analyses of prescriber preparedness and actions

Factor analysis using the varimax rotation of 12 prescriber preparedness and actions items resulted in four eigenvalues > 1. The scree plot of the eigenvalues suggested two to five factors. Based on the scree plot and eigenvalues, we generated models with two to four factors. The three-factor model was deemed the most logical (Table 5): clinician beliefs and comfort level (6 items), clinician referral action (2 items), and clinician perceived training limitations (4 items). Item scores and factor loadings are presented in Table 5. Reliability estimates for the prescriber preparedness and actions items for prescribing DAAs were good (composite Cronbach α = 0.75; factor Cronbach α range = 0.61–0.81), and the composite mean score was 2.55 (1 = strongly disagree to 5 = strongly agree), indicating an overall moderately low level of perceived preparedness and actions. Among the factors, clinician referral actions (mean = 3.33) was the most highly endorsed as affecting clinician treatment of HCV-infected patients with SUD, followed by clinician perceived training limitations (mean = 2.92) and beliefs and comfort level (mean = 2.05).

Using multivariable regression, we examined the ability of the three factor scores from the model of the prescriber preparedness and actions items to explain clinician likelihood of DAA prescribing, after controlling for significant covariates. The regression model containing factor scores explained 23.3 % of the variation in clinician-reported likelihoods of prescribing DAAs (Table 6). Among the factors, the clinician beliefs and comfort level factor (P = 0.010) was a significant negative predictor of clinician likelihood to prescribe DAAs for patients with HCV and SUD. The model containing the composite preparedness and actions score explained 22.9 % of the variation in clinician-reported DAA prescribing likelihood, with the composite score (P < 0.001) being a significant negative predictor of clinician willingness to prescribe DAAs for patients with HCV and SUD.

4.5. Multivariable regression analysis of barriers and prescriber preparedness and actions combined

Using multivariable regression, we examined the ability of the composite barriers and composite preparedness and actions scores to predict clinician-reported likelihood of prescribing DAAs for patients with HCV and SUD, after controlling for significant covariates. The regression model containing the composite scores from the two models explained 29.1 % of the variation in clinician-reported likelihood of prescribing DAAs (Table 7). Both composite scores (P = 0.008 and P = 0.012) were significant negative predictors of prescribing DAAs for patients with HCV and SUD.

5. Discussion

Our findings suggested that the barriers that prevented, delayed, or interfered with DAA treatment for patients with HCV and SUD were multidimensional, with patient-related barriers (e.g., failure to keep appointments, patient continued to use substance) perceived by treating clinicians as the most problematic, followed by prior authorization requirements (e.g., laboratory results, requirement for patient to be drug- or alcohol-free), and system-related barriers (e.g., lack of insurance, prior authorization refusals). However, clinician beliefs and comfort levels (e.g., believing a patient with SUD should be receiving medication-assisted therapy before initiating HCV treatment; difficulty engaging with patients who continually fail drug tests) were associated with lower likelihoods of prescribing DAAs for patients with HCV and SUD.

The findings in the present study regarding barriers are consistent with what has been described in the literature in recent years. Failure of patients with HCV infection to attend multiple appointments is a barrier to HCV care that has been previously reported from both patient and clinician perspectives (Heard et al., 2021; Paisi et al., 2022; Litwin et al., 2019; von Aesch et al., 2021). Social and health circumstances (e.g., need to secure food, lack of transportation, concomitant mental or physical condition, and SUD) are competing priorities that may prevent patients from complying with HCV care (Paisi et al., 2022, Litwin et al., 2019, Zhang et al., 2020; Amoako et al., 2021). Clinician concerns about treatment adherence and reinfection have been found in previous studies to be persistent barriers to treating patients with HCV and SUD (von Aesch et al., 2021; Asher et al., 2016; Marshall et al., 2020; Winnock et al., 2013), but the clinicians surveyed in the present study identified patient risk of reinfection as being a less problematic barrier than patient lack of motivation and adherence.

Prior authorization required by payers to approve prescription of DAAs is a time-consuming process that continues to hamper access to medications by the marginalized subpopulation of patients infected with HCV (Duryea et al., 2020). Not surprisingly; the clinicians surveyed in this study deemed it as the second most problematic barrier for prescribing DAAs to patients with SUD. Evidence suggests that US

Table 3
Mean scores, factor loadings, and reliability estimates of barrier items (N = 96).

Factors and Items	Frequency score[a]		Factor loading	Cronbach α
	Mean	SD		
Factor 1: Patient-related barriers (7 items)	2.62	0.65	NA	0.83
Lack of motivation and adherence	2.96	0.88	0.79	
Patient with unmet social and physical needs (e.g., social support, nutrition, and housing)	3.00	0.91	0.53	
Failure to keep appointments	3.23	0.80	0.53	
Patient declined treatment	2.04	0.86	0.46	
Patient risk of reinfection	2.16	1.01	0.58	
Patient psychiatric disorder (e.g., depression)	2.31	0.98	0.51	
Patient continued substance abuse (alcohol or drug)	2.64	1.02	0.56	
Factor 2: HCV stigma and knowledge (patient knowledge and perceptions of HCV) (2 items)	2.56	1.01	NA	0.83
Stigma associated with HCV infection	2.26	1.00	0.95	
Lack of knowledge of HCV and its treatment	2.86	1.18	0.71	
Factor 3: PA Requirements (4 items)	2.32	0.97	NA	0.79
Consultation with a specialist required or specialist required	1.97	1.19	0.78	
Laboratory results required (e.g., HCV RNA level, fibrosis staging, genotype)	2.45	1.40	0.68	
Requirements for patient to be drug-free or alcohol-free	2.45	1.28	0.56	
CD-4 cell counts for patients with HIV co-infection	2.40	1.01	0.48	
Factor 4: Clinician-related barriers for working with patients with SUD (2 items)	1.97	0.87	NA	0.80
Lack of capacity and proper training for treating patients with SUD	1.85	1.01	0.72	
Difficulty establishing relationships with patients with SUD	2.08	0.90	0.69	
Factor 5: System-related barriers (4 items)	2.26	0.77	NA	0.77
High out-of-pocket medication costs	2.46	1.10	0.50	
Lack of health insurance	2.46	0.97	0.66	
Lack of office infrastructure to submit PA forms	1.64	0.90	0.45	
PA refusal	2.48	1.04	0.61	
Composite score (19 items)	**2.40**	**0.60**	**NA**	**0.89**

Abbreviations: HCV, hepatitis C virus; NA, not relevant; PA, prior authorization; SD, standard deviation; SUD, substance use disorder.

[a] Measured on a 5-point Likert-type scale (1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = always). Higher mean numbers indicate more barriers.

Table 4
Multivariable regression analysis of the likelihood of prescribing direct-acting antivirals to treat HCV-infected patients with SUD, using five factors and a composite score of barrier items (n = 94).

Model	Coefficient estimate	SE	P-values
Linear regression model using 5 factors*			
Factor 1: Patient-related barriers	−0.479	0.130	<0.001
Factor 2: HCV stigma and knowledge (patient knowledge and perceptions of HCV)	0.155	0.069	0.028
Factor 3: PA Requirements	−0.291	0.088	0.001
Factor 4: Clinician-related barriers associated with working with patients with SUD	−0.180	0.096	0.065
Factor 5: System-related barriers	0.309	0.119	0.011
Covariates			
Medical Specialty	0.098	0.093	0.296
No. of patients with HCV treated in the last 12 months	0.219	0.078	0.006
Linear regression model using composite score**			
Composite score	−0.522	0.126	<0.001
Covariates			
Medical Specialty	0.097	0.103	0.353
Patients with HCV treated in the last 12 months	0.158	0.0864	0.063

Abbreviations: HCV, hepatitis C virus; PA, prior authorization; SE, standard error; SUD, substance use disorder.

n = 94 (Owing to missing responses, 2 patients were excluded from the analysis).

*F = 8.649, df = 7 and 86; $p < 0.001$, $R^2 = 0.4131$, and adjusted $R^2 = 0.3654$.

**F = 8.747, df = 3 and 90, $p < 0.001$, $R^2 = 0.2257$, and adjusted $R^2 = 0.1999$.

physicians spend an average of 45–120 min per patient and an average of 14.9 h per week to complete the prior authorization process, which entails the submission of information that is not supported by scientific evidence (Duryea et al., 2020). Most of our surveyed clinicians were experienced HCV providers who had treated a fair number of patients with HCV in the past year. It is important to note that these experienced providers were presumably comfortable with HCV treatment and patients with HCV and SUD; but their practices were still limited by barriers such as prior authorization policy. Other countries, such as Australia and Canada, have experienced increasing trends in DAA initiation after the removal of restrictions based on the specialty of the clinician, fibrosis stage, and ongoing SUD (Simoncini et al., 2021; Marshall et al., 2020). In the US; as of June 2022 many states had removed fibrosis restrictions and specialist requirements while some states continue to require that prescriptions be written in consultation with a specialst or allow providers to prescribe after completing training courses (Harvard Law School Center for Health Law and Policy Intervention, 2022). These changes in the requirements for HCV specialist care will accelerate expansion of HCV treatment access as primary care providers at the forefront of patient contact can become providers of HCV care (Wang et al., 2022).

Similarly, many states dropped restrictions on sobriety after this study was conducted, while some states still require screening and counseling regarding substance use concurrent with HCV treatment (Harvard Law School Center for Health Law and Policy Intervention, 2022). However, there is also evidence suggesting that, in general, clinicians involved in HCV care have little experience working with people with SUD, which often leads to distorted beliefs about the adherence capacity of these patients (Trooskin et al., 2020; Jatt et al., 2021) and unfounded concerns of reinfection (Trooskin et al., 2020). These beliefs may be derived from stigmatization and discrimination (Simoncini et al., 2021; Trooskin et al., 2020; Jatt et al., 2021; Higashi et al., 2020). The lack of experience and the discomfort among clinicians were reflected in our findings. The clinician belief that a patient with SUD should be receiving medication-assisted therapy before initiating HCV treatment and the clinician concern that it is difficult to engage with patients who continually fail drug tests were associated with clinicians being less likely to prescribe DAAs for patients with HCV and SUD. Continuing education and training in SUDs are needed to improve clinician understanding, knowledge, and comfort level for treating patients with HCV and SUD.

Although clinician perceived limitations were not associated with the reported likelihood of prescribing DAAs to patients with HCV and SUD in the present study, it is important to underscore that clinicians reported a lack of knowledge on the availability of drug treatment facilities or support services for people with SUD. This “silo effect” has been previously reported and refers to the lack of integration of services and interdisciplinary collaboration when caring for patients with HCV and SUD (Trooskin et al., 2020).

Considering the persistence of these barriers among clinicians, it may be time to consider moving our complex health care system toward a more holistic, community-based approach for treating patients with HCV infection and SUD (Trooskin et al., 2020; Paisi et al., 2022; Litwin et al., 2019; von Aesch et al., 2021; Marshall et al., 2020). Indeed, some countries have implemented this approach and show improved access to

Table 5
Mean scores, factor loadings, and reliability estimates of clinician preparedness and actions (n = 95).

Factors and Items	Agreement score[a]		Factor loading	Cronbach α
	Mean	SD		
Factor 1: Clinician beliefs and comfort level (6 items)	2.05	0.58	NA	0.76
SUDs are a behavioral problem, not a disease.	2.06	0.97	0.61	NA
Treating HCV-infected patients with SUD is not effective.	1.58	0.66	0.68	
Patients with SUD should be on medication-assisted therapy (e.g., buprenorphine) before being treated for HCV to minimize the risk of HCV reinfection.	2.75	0.98	0.64	
I am comfortable treating HCV-infected patients with SUD respectfully and without bias. [reverse coded]	1.68	0.64	0.33	
I find it difficult to treat patients who use alcohol sporadically although they do not qualify for addiction therapy.	1.98	0.93	0.46	
I find it difficult to engage with patients who continuously fail to pass drug tests.	2.22	0.91	0.53	
Factor 2: Clinician referral actions (2 items)	3.33	0.87	NA	0.81
I connect patients with HCV infection and SUD to resources for social support.	3.53	0.87	0.90	NA
I refer HCV-infected patients with SUD to addiction specialists or drug treatment facilities.	3.14	1.02	0.77	
Factor 3: Clinician perceived training limitations (4 items)	2.92	0.75	NA	0.61
I need more training in the treatment of HCV-infected patients with SUD.	2.66	1.14	0.46	NA
I want to learn more about the best practices to treat patients with HCV who are addicted to non-opioid substances.	3.42	1.15	0.48	
I want to refer patients to addiction specialists or drug treatment facilities, but it is not covered by their insurance.	3.00	1.04	0.45	
I want to refer patients to addiction specialists or drug treatment facilities, but I cannot because I don't know what is available.	2.60	1.10	0.67	
Composite score (12 items)	**2.55**	**0.50**	**NA**	**0.75**

Abbreviations: HCV, hepatitis C virus; NA, not available; SD, standard deviation, SUD, substance use disorder. [a] Measured on a 5-point Likert-type scale (1 = strongly disagree, 2 = disagree, 3 = neither disagree nor agree, 4 = agree, 5 = strongly agree). Higher mean numbers indicate higher agreement.

HCV treatment and overall outcomes (Trooskin et al., 2020; von Aesch et al., 2021; Marshall et al., 2020). To overcome these barriers, we suggest several strategies including allowing non-specialist care providers the ability to prescribe treatment, co-locating screening, diagnosis, and treatment services for HCV at SUD treatment centers, and integrating HCV/SUD care delivered by a multidisciplinary team with case management services (Ho et al., 2015; Moussalli et al., 2010).

Clinicians reported that when a patient felt stigmatized or showed a lack of knowledge about HCV, the clinician was more likely to prescribe DAAs. This finding is in contrast to the majority of results assessing infectious disease stigma that indicate that stigma may lead patients to fail to seek treatment (Dolezal and Lyons, 2017). The discrepancy in findings may be because the clinicians in the present study were considering patients who had already connected to care rather than patients who had failed to seek care. The implication, then, is that enabling and stewarding a connection with care for this population may lead to a high likelihood of treatment. Also, we think that clinicians who understand patients' stigma as a potential barrier to HCV treatment were more likely to overcome stigma as a barrier for the patients under their care.

Despite the aforementioned concerns, a high proportion of the clinicians surveyed in the present study expressed willingness to treat patients experiencing SUD. Before DAAs became available, a Canadian study reported that <20 % of HCV clinicians were likely to provide treatment to current PWID using a needle exchange program, and 90 % of HCV clinicians were likely to provide treatment to former PWID (Myles et al., 2011). In the present study, 64 % of the surveyed clinicians were likely to provide DAA treatment to current PWID, and 97 % to former PWID. The increases in the willingness to treat PWID may be attributable to the higher sustained virologic response rates achieved with DAAs compared with interferon-containing treatments among PWID (Grebely et al., 2015; Dore et al., 2016; Lalezari et al., 2015; Grebely et al., 2018; Butner et al., 2017; Ottman et al., 2019). This finding is also consistent with that of studies conducted by Marshall et al. (Marshall et al., 2020; Higashi et al., 2020) in which surveyed clinicians expressed a moral responsibility to do "the right thing" when treating patients with HCV infection and SUD.

Table 6
Multivariable regression analysis of the likelihood of prescribing direct-acting antivirals to treat HCV-infected patients with substance use disorder, using three factors and a composite score of clinician preparedness and action items (n = 93).

Model	Coefficient estimate	SE	p-value
Linear regression model using 3 factors*			
Factor 1: Clinician beliefs and comfort level	−0.392	0.150	0.010
Factor 2: Clinician actions	−0.065	0.089	0.469
Factor 3: Clinician perceived training limitations	−0.191	0.119	0.111
Covariates			
Medical Specialty	0.038	0.111	0.733
Patients with HCV treated in the last 12 months	0.131	0.087	0.134
Linear regression model using composite score**			
Composite Score	−0.653	0.160	<0.001
Covariates			
Medical Specialty	0.053	0.105	0.617
Patients with HCV treated in the last 12 months	0.135	0.085	0.117

Abbreviations: HCV, hepatitis C virus; SE, standard error.
n = 93 (Owing to missing responses, 3 patients were excluded from the analysis).
*F = 5.299, df = 5 and 87, $p < 0.001$, $R^2 = 0.2334$, and adjusted $R^2 = 0.1894$.
**F = 8.832, df = 3 and 89, $p < 0.001$, $R^2 = 0.2294$, and adjusted $R^2 = 0.2034$.

Table 7
Multivariable regression analysis using composite score of barriers model and clinician preparedness and actions model to predict likelihood of prescribing direct-acting antivirals to treat HCV-infected patients with substance use disorder (n = 92).

Model	Coefficient estimate	SE	p-value
Barriers model composite score	−0.372	0.137	0.008
Clinician preparedness and actions model composite score	−0.443	0.173	0.012
Covariates			
Medical Specialty	0.036	0.102	0.725
Patients with HCV treated in the last 12 months	0.157	0.083	0.062

Abbreviations: HCV, hepatitis C virus; SE, standard error.
n = 92 (Owing to missing responses, 4 patients were excluded from the analysis).
**F = 8.924, df = 4 and 87, $p < 0.001$, $R^2 = 0.2909$, and Adjusted $R^2 = 0.2583$.

Although most clinicians responded that the COVID-19 pandemic had affected their practices in treating patients with HCV moderately to not at all, several previous studies have reported that during the pandemic, HCV antibody testing volume decreased, ribonucleic acid–-positive results fell, and prescriptions for HCV treatment were reduced compared with previous years (Kaufman et al., 2021).

The present study has several strengths. We evaluated barriers and perceptions of a nationwide sample of gastroenterology and hepatology clinicians regarding DAA treatment for patients with both HCV and SUD. Our investigation included the development of conceptual frameworks of those barriers and perceptions that are useful in describing clinicians' DAA prescribing choices. Such an investigation is also part of the validation of the instrument used in this study, which showed good face validity, and the reliability of the factors was good. The present survey study contributes to the urgent need to advance the understanding of clinician perceptions and barriers to treating patients with both HCV and SUD. Findings from this study may be used as a basis for future planning and development of interventions to improve DAA treatment access among patients with HCV and SUD. For example, educational programs for patients and clinicians should focus more on patient-related barriers.

6. Limitations

First, the generalizability of our findings may be limited because a large proportion of the clinicians surveyed were affiliated with academic institutions. Second, our findings were representative of a convenience sample of US clinicians; it is possible that clinicians who were highly involved in HCV-related care selectively completed the survey, resulting in a nonresponse bias, as participation was voluntary. Response bias inherent to survey design also cannot be excluded. Third, the response rate was lower than desired, although it was not unusually low for this type of data collection in this population (Tinsley et al., 2013) and our a priori required sample size was successfully met. Fourth, we assessed clinician self-report of barriers, beliefs, and practice, which may or may not correlate with real-life practices.

7. Conclusion

Findings from this survey study indicated that clinicians engaging in HCV care perceived patient-related barriers (e.g., failure to keep appointments) and prior authorization requirements to be significant problematic barriers to treating patients with HCV and SUD. The findings also underscore the importance of clinicians' beliefs and comfort levels toward patients with HCV and SUD in the reported likelihood of prescribing DAAs. Despite such challenges, this study highlighted the willingness of HCV clinicians to provide DAA treatment to current or former PWID infected with HCV. Multidimensional strategies providing regularly updated education regarding SUDs to health care professionals offering HCV care and adoption of multidisciplinary teams with case management services coupled with less restrictive prior authorization requirements would enhance treatment access among PWID.

Funding

This work was funded by the National Institute on Drug Abuse (K01DA045618) and the National Institute on Alcohol Abuse and Alcoholism (U24AA022002). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Research reported in this publication was supported in part by the National Institute on Drug Abuse of the National Institutes of Health (NIH) under award number K01DA045618 (to HP). RLC was supported by the National Institute on Alcohol Abuse and Alcoholism under award number U24AA022002. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. The other authors declare that there is no conflict of interest regarding the publication of this article.

Data availability

Data will be made available on request.

Acknowledgements

We extend our gratitude to the Gastroenterology & Hepatology Advanced Practice Provider (GHAPP) association for providing access for the purpose of recruitment to Advanced Practice Providers who are members or subscribers of GHAPP, and to Gayle Cooper, the GHAPP listerv manager, who coordinated the sending of recruitment letters on behalf of GHAPP.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2023.102138.

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