Drug and Alcohol Dependence Reports 3 (2022) 100038

Contents lists available at ScienceDirect

Drug and Alcohol Dependence Reports

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

Development and pilot-testing of a hepatitis C reinfection prevention intervention for patients in treatment for hepatitis C infection

Adam Viera[a,g,*], Lauretta E. Grau[b], Jeffrey D. Fisher[c], Scott O. Farnum[d], Jeanette M. Tetrault[e], Greg Scott[f], Robert Heimer[b]

[a] Department of Social and Behavioral Sciences, Yale University School of Public Health, New Haven, CT, USA
[b] Department of Epidemiology of Microbial Diseases, Yale University School of Public Health, New Haven, CT, USA
[c] Department of Psychological Sciences and the Institute for Collaboration on Health, Intervention, and Policy (InCHIP), University of Connecticut, Storrs, CT USA
[d] APT Foundation, Inc, New Haven, CT USA
[e] Department of Internal Medicine and the Yale Addiction Medicine Program, Yale University School of Public Health, New Haven, CT, USA
[f] Department of Sociology, DePaul University, Chicago, IL USA
[g] Center for Interdisciplinary Research on AIDS, Yale University, New Haven, CT, USA

1. Introduction

Direct-acting antiviral (DAA) medications demonstrate almost universal, pangenotypic success in resolving hepatitis C virus (HCV) infection (Alavian et al., 2018; Falade-Nwulia et al., 2017; Graf et al., 2019). The benefits of successful treatment are undermined by HCV reinfection (Hellard et al., 2015; Midgard et al., 2016). Rates of HCV reinfection among people who inject drugs (PWID) range from 5% to 22% annually (Falade-Nwulia et al., 2018; Grebely et al., 2019; Hajarizadeh et al., 2020; Springer, 2019), suggesting that preventing HCV reinfection remains an overlooked step in the HCV care continuum (Falade-Nwulia and Sulkowski, 2017; Martinello et al., 2018).

Researchers have posited that HCV treatment can serve as a critical period for intervention to prevent future HCV reinfection (Grebely et al., 2019). Formative work by co-authors highlighted the need for education around the risk of HCV infection through sharing of syringes and other injection equipment (Heimer et al., 2002; Koester et al., 2003) and the importance of reinforcing risk reduction messaging (Grau et al., 2009) and bolstering self-efficacy in employing safer injection techniques (Grau et al., 2005). We used the Information-Motivation-Behavioral Skills (IMB) Model as the framework for developing a behavioral intervention for individuals starting HCV treatment to build knowledge, motivation, and self-efficacy to engage in safer injection practices and avoid HCV reinfection. Applications of the IMB Model have demonstrated that behavior change is related to knowledge of the problem and strategies to overcome it, motivation to engage in safer behavior, and belief one has the skills to change their behavior (Fisher et al., 2008; Fisher & Fisher, 1992; Fisher et al., 2003).

We report findings from a pilot study conducted at an opioid treatment program (OTP) that was curtailed due to the COVID-19 pandemic. We believe the data presented provide a guide for future efforts to reduce HCV reinfection risk among PWID.

2. Methods

The intervention was developed and piloted through a collaboration between the research team and an implementation team at the APT Foundation, one of the largest OTPs in Connecticut, with over 5,000 unique patients seen annually. Since 2015, it has provided onsite HCV treatment with high rates of HCV treatment completion and elimination of detectable virus (Butner et al., 2017).

2.1. Intervention structure

The intervention consisted of two sessions integrated into DAA treatment. The initial session used treatment-related phlebotomy to provide visual instruction on the essentials of safe injection. The second session, informed by the IMB Model, reinforced the first session's content.

2.2. First session: the 10-minute intervention (10-MI)

Treating the first session as a "teachable moment," content was tailored to what could be delivered during a 10 min phlebotomy session for DAA treatment. Intervention content was delivered by trained staff narrating the actions of the phlebotomist that protect against venipuncture-related adverse events. The session covered five key steps: (1) preparing a clean space for injection, (2) finding a vein, (3) getting the skin ready for injection, (4) registering the needle in the vein, and (5) cleaning up after injection.

2.3. Second session: the IMB intervention

The second session was designed as an hour-long, interactive group session, consistent with other group sessions offered by the APT Foundation. The IMB Intervention had four sequential components: (1) interactive review of information presented during the 10-MI; (2) discussion of

* Corresponding author.
E-mail address: adam.viera@yale.edu (A. Viera).

https://doi.org/10.1016/j.dadr.2022.100038
Received 13 October 2021; Received in revised form 4 February 2022; Accepted 7 March 2022

reasons and social supports motivating safer injection; (3) mock demonstration of safer injection; and (4) provision of harm reduction resources and information.

2.4. Development of intervention materials

We developed a plain-language script and facilitator's guide for both intervention sessions. The research team reviewed these materials and presented them to the implementation team for their feedback. Final materials (available in **supplement**) were approved by the Yale University IRB prior to use.

2.5. Participant recruitment and intervention delivery

All participants were patients starting treatment for HCV infection at the OTP. In addition to initiating HCV treatment, participants were eligible if they: (1) were over 18 years of age, (2) spoke English, and (3) provided informed consent. Receipt of medications for opioid use disorder was not a criterion for study inclusion. Patients starting HCV treatment were approached by members of the implementation team, who assessed interest in the study, obtained informed consent, and administered the baseline assessment. After four months of recruitment without incentives, participants were offered up to $60 for study participation: $10 each for the baseline, first intervention session, and first follow-up assessment, and $30 for the second follow-up assessment. No monetary incentive was offered for the second session, which served to meet substance use treatment group requirements.

After study enrollment, the 10-MI was delivered at approximately the fourth week of HCV treatment during a planned blood draw. Approximately two weeks later, participants were invited to attend the IMB intervention.

2.6. Data collection and analysis

Questionnaires were designed to determine if the intervention improved participants' competence to prevent HCV reinfection. The baseline assessment collected data on demographic characteristics, history of injection practices, and knowledge of HCV infection, safe injection, and syringe access. A subsequent survey (hereafter called the safer injection assessment) was administered at four time points during and after treatment; it assessed safer injection knowledge, motivation, intention, self-efficacy, and behaviors. After the IMB intervention, participants completed a satisfaction survey. All data collection instruments were self-administered, with intervention staff available to assist as needed.

Data were collected to identify intervention elements that could be feasibly, acceptably, and reliably implemented. We assessed recruitment feasibility by comparing the number of individuals starting HCV treatment to the number who agreed to participate in the study, noting common reasons for declining to participate. We assessed the feasibility of intervention engagement by charting the extent to which participants attended intervention sessions within the allotted time frame. We assessed retention feasibility by comparing the total number of participants enrolled in the study to the number who completed relevant benchmarks (i.e., session attendance, assessment completion). Finally, we assessed the feasibility of data collection by examining the percentage of complete responses for all data collection instruments.

2.7. Pilot coordination

We convened regular meetings of the research, implementation, and HCV treatment provider teams to assess their experiences recruiting participants and delivering the intervention according to the protocol. Consensus among all partners was obtained before major modifications of the protocol.

3. Results

We recruited 17 participants over a ten-month period (May 2019 – February 2020). Recruitment and follow-up ended when SARS-CoV-2 pandemic restrictions in Connecticut curtailed HCV treatment at the OTP.

3.1. Participant baseline characteristics

3.1.1. Description of study sample

Table 1 summarizes the 17 participants' characteristics. Participants were mostly male (70.6%). Most had completed a high level of education, with 41.2% reporting some level of college or technical school. The majority was unemployed (58.8%); of those who were employed, most were employed part-time (85.7%). All participants had public health insurance.

All but one participant (93.8%) had ever been arrested, half had been convicted of a felony, nearly a third (29.4%) were on parole or probation, and three (17.6%) were awaiting trial or some other court appearance. All participants reported a history of injection drug use, but only three (17.6%) reported injecting drugs in the month before study enrollment.

At baseline, all participants were aware of the hepatitis B vaccine; by contrast ten (58.8%) knew there was no such vaccine against HCV. All participants but one (94.1%) knew reinfection with HCV is possible after being cured. Few participants (11.8%) knew that protecting skin after injection can help prevent HCV infection. Few participants (17.6%) knew it is legal to carry syringes in Connecticut, and little more than half (58.8%) knew it is legal to buy syringes from a pharmacy without a prescription.

3.2. Implementation outcomes

3.2.1. Feasibility of recruitment and enrollment

During the study recruitment period, 17 of the 35 individuals who started HCV treatment at the APT Foundation consented to participate, yielding a 48.6% enrollment rate. Common reasons for declining participation were the initial lack of financial incentive and the time commitment involved in completing assessments. Recruitment efforts also lagged due to clinical staff turnover, which prevented OTP staff from contacting potential participants in a timely manner. In response, the protocol was amended to offer $60 for study participation broken down by session. Additionally, an intake nurse in the medical unit was trained to enroll participants. After these changes, the enrollment rate nearly doubled, from 35.0% before these changes to 66.7% afterwards.

3.2.2. Feasibility of intervention delivery

Three participants completed both intervention sessions. Another five completed only the first session. Two participants, recruited the month before study termination, could not receive the first session. The remaining seven participants were enrolled but did not participate in the intervention. (See **Fig. 1**) Lack of coordination between the implementation team and medical unit staff resulted in missed opportunities to conduct intervention sessions. Difficulties in coordinating participants' schedules and on-site logistics contributed to the low rate of delivering the second session. The research and implementation teams agreed to change the second session from a group session to a one-on-one session (using the same intervention materials). Following this change, the implementation team reported intervention delivery as more feasible.

3.2.4. Feasibility of data collection

Complete baseline data were collected from all participants. Initially, data collection was a challenge with safer injection assessments; only 3 of the first 6 participants completed scheduled assessments. Providing the implementation team additional training in administering assessments resulted in 5 of 7 returning completed assessments. Completion

Table 1
Participant Characteristics ($N = 17$).

Demographics	N (%) or Mean (SD)
Gender	
Female	5 (70.6%)
Male	12 (29.4%)
Age	41.9 (13.8)
Education	
8th grade or less	1 (5.9%)
Some high school	3 (17.6%)
High school graduate/GED	6 (35.3%)
Some college/technical school	7 (41.2%)
Employment	
Not employed	10 (58.8%)
Full-time	1 (5.9%)
Part-time	6 (35.3%)
Insurance	
Medicaid	13 (76.5%)
Medicare	2 (11.8%)
Medicaid & Medicare	2 (11.8%)
Arrested	15 (93.8%)
Felony Conviction	8 (50.0%)
Probation or Parole	5 (29.4%)
Awaiting Charges	3 (17.6%)
Past Month Alcohol Use	3 (18.5%)
Past Month Cocaine Use	4 (25.0%)
Past Month Methamphetamine Use	1 (5.9%)
Past Month Opioid Use	0 (0.0%)
Past Month Street Fentanyl Use	3 (18.8%)
Past Month Injection	3 (17.6%)
Knowledge	
Question	**Number (%) Correct**
HCV can cause liver cancer	15 (88.2%)
HIV is easier to spread than HCV	8 (47.1%)
You can prevent HCV spread by covering the skin where you just injected	2 (11.8%)
You can tell someone is infected with HCV by the way they look	16 (94.1%)
Drinking alcohol makes HCV worse	13 (76.5%)
There is a vaccine to prevent HCV infection	10 (58.8%)
There is a vaccine to prevent HBV infection	17 (100.0%)
Most people who get infected with HCV totally recover from it	9 (52.9%)
Most people who get infected with HBV totally recover from it	4 (23.5%)
You can get HCV from contaminated food	12 (70.6%)
HCV is easily spread by both sex and used needles	2 (11.8%)
Once you have been cured of HCV, it is impossible to get reinfected	16 (94.1%)
It is legal to buy syringes without a prescription in pharmacies in CT	10 (58.8%)
It is legal in CT to carry used syringes	3 (17.6%)
It is legal in CT to carry injection gear other than syringes*	3 (50.0%)

*Question was only asked of 6 participants before the form changed.

of the safer injection assessment increased to nearly 100% after providing this additional training and checking assessments for completion.

4. Discussion

The purpose of this study was to develop and pilot test a behavioral intervention to reduce HCV reinfection among individuals completing HCV treatment. Initial recruitment challenges included the lack of monetary incentive and interruptions in treatment initiation due to turnover of medical personnel. After offering a monetary incentive for study participation and expanded staff training, we observed a higher rate of recruitment.

Although participants were fairly knowledgeable about some aspects of viral hepatitis at baseline, most were ill-informed about transmission risks related to injecting drugs, the most likely route of HCV reinfection. This lack of knowledge is consistent with previous studies (Heimer et al., 2014; Heimer et al., 2002), demonstrating ongoing need for an intervention of the kind we developed.

Initial barriers to implementing the intervention included poor coordination between medical staff and the implementation team and difficulty in managing the logistics of convening group sessions. These barriers demonstrate that careful attention must be paid to balance the costs of implementing each intervention session with its benefits. Subsequent to adjustments in intervention protocol, implementation team members

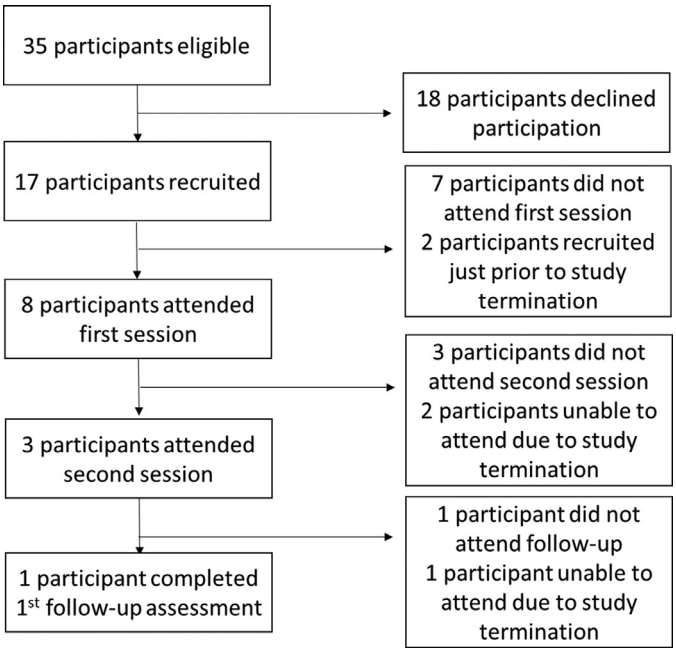

Fig. 1. CHIME Study Flow Diagram.

reported increased feasibility and acceptability of intervention activities. Future work will focus on more rigorous assessment of intervention feasibility, acceptability, and efficacy as well as the effect of limiting the intervention to a single session.

Assessing the feasibility of data collection has been critical in planning for a future clinical trial of the intervention. Completion of the safer injection assessment increased to nearly 100% after providing the implementation team with additional training and checking assessments for completion prior to the end of the session. Data collection could be improved further by creating a digitally automated version.

Although intervention development was fully completed, implementation challenges and the COVID-19 pandemic proved substantial barriers to a successful pilot. These considerations represent limitations of our findings. Participants reported low rates of recent injection drug use; future efforts will focus on recruiting participants at higher risk for HCV reinfection.

5. Conclusions

Formative work has produced a two-session behavioral intervention to prevent HCV reinfection delivered in tandem with DAA treatment for HCV infection. Baseline data, showing limited knowledge and poor application of safer injection practices, demonstrates the need for an intervention that increases safer injection knowledge, motivation, and self-efficacy. Our findings highlight the importance of staff training and coordination and reveal that conducting group sessions in an integrated OTP setting may not be feasible. Future work will focus on delivering intervention components virtually and rigorously demonstrating feasibility for the intervention to change knowledge, motivation, self-efficacy, intention, and behavior in ways that reduce HCV reinfection following curative treatment.

Role of funding source

This work was made possible through funding (Contract# IN-US-987-5293) from Gilead Sciences, Inc.

Contributors

AV developed the IMB intervention, trained the staff at the OTP to conduct the intervention, entered and analyzed the knowledge, feasibility and acceptability data, and drafted the manuscript. LEG directed the development of the 10-MI, participated in the design of the IMB session, reviewed all data collection instruments, and assisted with the implementation of the pilot. JDF supervised the design and development of the IMB session. SOF served as the liaison with the OTP staff and managed the processes of and bureaucratic work associated with pilot implementation. JMT supervised the interaction with the HCV treatment staff, helped identify OTP patients initiating HCV treatment, and reviewed all information pertaining to HCV prevention. GS collected the data that informed the 10-MI by providing film footage and still photographs of the injection practices of people who has not been trained through the 10-MI and piloted the 10-MI outside an HCV treatment setting with people who inject drugs in Chicago. RH oversaw the overall design of the intervention, obtained the funding, reviewed all study instruments, directed the training of the staff at the OTP, and led processes of revising the content and delivery of the intervention pilot. All authors participated in drafting and finalizing study instruments, discussing revisions to pilot content and delivery, and reviewed this manuscript.

Conflict of Interest

No conflict declared

Acknowledgments

Immense thanks to the APT Foundation team members who were instrumental in the development and implementation of the pilot intervention: Edin Bajraktarevic, Brian Bonilla, Heather Knox, and Dana Proto. Special thanks to our pilot participants.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dadr.2022.100038.

References

Alavian, S.M., Dolatimehr, F., Sharafi, H., Safi-Abadi, M., Rezaee-Zavareh, M.S., Bayatpour, M.E., Karimi-Sari, H., Mohazzab-Torabi, S., 2018. Treatment of HCV infection with direct-acting antiviral agents in patients with HIV/HCV co-infection: a systematic review. Hepat. Mon. 18 (12).

Butner, J.L., Gupta, N., Fabian, C., Henry, S., Shi, J.M., Tetrault, J.M., 2017. Onsite treatment of HCV infection with direct acting antivirals within an opioid treatment program. J. Subst. Abuse Treat. 75, 49–53. doi:10.1016/j.jsat.2016.12.014.

Falade-Nwulia, O., Suarez-Cuervo, C., Nelson, D.R., Fried, M.W., Segal, J.B., Sulkowski, M.S., 2017. Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review. Ann. Intern. Med. 166 (9), 637–648. doi:10.7326/m16-2575.

Falade-Nwulia, O., Sulkowski, M., 2017. The HCV care continuum does not end with cure: a call to arms for the prevention of reinfection. J. Hepatol. 66 (2), 267–269. doi:10.1016/j.jhep.2016.10.027.

Falade-Nwulia, O., Sulkowski, M.S., Merkow, A., Latkin, C., Mehta, S.H., 2018. Understanding and addressing hepatitis C reinfection in the oral direct-acting antiviral era. J. Viral Hepat. 25 (3), 220–227. doi:10.1111/jvh.12859.

Fisher, J.D., Amico, K.R., Fisher, W.A., Harman, J.J., 2008. The information-motivation-behavioral skills model of antiretroviral adherence and its applications. Curr. HIV/AIDS Rep. 5 (4), 193–203. doi:10.1007/s11904-008-0028-y.

Fisher, J.D., Fisher, W.A., 1992. Changing AIDS-risk behavior. Psychol. Bull. 111 (3), 455–474. doi:10.1037/0033-2909.111.3.455.

Fisher, W. A., Fisher, J. D., and Harman, J. (2003). The Information-Motivation-Behavioral Skills Model: A General Social Psychological Approach to Understanding and Promoting Health Behavior. In *Social Psychological Foundations of Health and Illness* (pp. 82-106). doi:10.1002/9780470753552.ch4.

Graf, C., Mücke, M.M., Dultz, G., Peiffer, K.-H., Kubesch, A., Ingiliz, P., Zeuzem, S., Herrmann, E., Vermehren, J., 2019. Efficacy of direct-acting antivirals for chronic hepatitis C virus infection in people who inject drugs or receive opioid substitution therapy: a systematic review and meta-analysis. Clin. Infect. Dis. 70 (11), 2355–2365. doi:10.1093/cid/ciz696.

Grau, L.E., Bluthenthal, R.N., Marshall, P., Singer, M., Heimer, R., 2005. Psychosocial and behavioral differences among drug injectors who use and do not use syringe exchange programs. AIDS Behav. 9 (4), 495–504. doi:10.1007/s10461-005-9020-3.

Grau, L.E., Green, T.C., Singer, M., Bluthenthal, R.N., Marshall, P.A., Heimer, R., 2009. Getting the message straight: effects of a brief hepatitis prevention intervention among injection drug users. [journal article]. Harm Reduct. J. 6 (1), 36. doi:10.1186/1477-7517-6-36.

Grebely, J., Hajarizadeh, B., Lazarus, J.V., Bruneau, J., Treloar, C., 2019. Elimination of hepatitis C virus infection among people who use drugs: ensuring equitable access to prevention, treatment, and care for all. Int. J. Drug Policy 72, 1–10. doi:10.1016/j.drugpo.2019.07.016.

Hajarizadeh, B., Cunningham, E.B., Valerio, H., Martinello, M., Law, M., Janjua, N.Z., Midgard, H., Dalgard, O., Dillon, J., Hickman, M., Bruneau, J., Dore, G.J., Grebely, J., 2020. Hepatitis C reinfection after successful antiviral treatment among people who inject drugs: a meta-analysis. J. Hepatol. 72 (4), 643–657. doi:10.1016/j.jhep.2019.11.012.

Heimer, R., Barbour, R., Palacios, W.R., Nichols, L.G., Grau, L.E., 2014. Associations between injection risk and community disadvantage among suburban injection drug users in southwestern Connecticut, USA. AIDS Behav. 18 (3), 452–463. doi:10.1007/s10461-013-0572-3.

Heimer, R., Clair, S., Grau, L.E., Bluthenthal, R.N., Marshall, P.A., Singer, M., 2002. Hepatitis-associated knowledge is low and risks are high among HIV-aware injection drug users in three US cities. Addiction 97 (10), 1277–1287. doi:10.1046/j.1360-0443.2002.t01-1-00211.x.

Hellard, M., McBryde, E., Sacks Davis, R., Rolls, D.A., Higgs, P., Aitken, C., Thompson, A., Doyle, J., Pattison, P., Robins, G., 2015. Hepatitis C transmission and treatment as prevention – The role of the injecting network. Int. J. Drug Policy 26 (10), 958–962. doi:10.1016/j.drugpo.2015.05.006.

Koester, S., Heimer, R., Barón, A.E., Glanz, J., Teng, W., 2003. RE: "Risk of Hepatitis C virus among young adult injection drug users who share injection equipment. Am. J. Epidemiol. 157 (4) 376-376.

Martinello, M., Dore, G.J., Matthews, G.V., Grebely, J., 2018. Strategies to reduce hepatitis C virus reinfection in people who inject drugs. Infect. Dis. Clin. North Am 32 (2), 371–393. doi:10.1016/j.idc.2018.02.003.

Midgard, H., Weir, A., Palmateer, N., Lo Re 3rd, V., Pineda, J.A., Macias, J., Dalgard, O, 2016. HCV epidemiology in high-risk groups and the risk of reinfection. J. Hepatol. 65 (1 Suppl), S33–s45. doi:10.1016/j.jhep.2016.07.012.

Springer, S.A., 2019. Hepatitis C virus reinfection rate among persons who use drugs and are maintained on medication treatment for opioid use disorder. Clin. Infect. Dis. doi:10.1093/cid/ciz695.