

# Best practices to increase engagement and retention in hepatitis C care among people who use drugs

## Question

What are the best practices to increase engagement and retention in hepatitis C care among people who use drugs?

## Key Take-Home Messages

- Chronic HCV infection can now be treated with direct-acting antivirals (DAAs), a drug regimen that can effectively cure HCV infection among all population groups, including people who use drugs (1).
- While the uptake of HCV treatment is higher in the DAA era compared to the interferon era (2–4), it is still at suboptimal levels (5).
- Overall, research suggests that integrating HCV care into other health care settings, as well as patient navigation or care coordination, can significantly improve linkage to HCV care and the uptake of DAA treatment (6).
- Numerous interventions have been developed to improve engagement and retention in HCV care specifically among people who use drugs, and can be classified into four different categories: integrated services and case management, contingency management, telemedicine, and peer-involvement and support (7). In addition, there are certain approaches such as task-shifting (delivery of HCV care by non-specialist physicians or nurses or peers rather than specialists) or micro-elimination (incrementally achieving national elimination through initiatives that eliminate HCV for defined segments of the population) that can be utilized across these four broad categories of interventions.

## Rapid Response: Evidence into Action

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- Contingency management (i.e. cash incentives) may have a positive impact on engagement and retention in care among people who use drugs (8–12).
- Telemedicine is one strategy used by integrated services that may facilitate engagement in the HCV care cascade among people who use drugs (13, 14).
- Peer involvement and support can be used to promote engagement in HCV care in various capacities: facilitating HCV testing (15), outreach and education (16), mentorship (9), and recruitment (17).
- Several studies found that co-locating treatment for HCV with treatment for opioid use disorders can improve retention in the HCV care cascade (18–20).
- For individuals co-infected with HIV/HCV, co-locating care had favourable outcomes for linkage to and engagement in the HCV care cascade (21, 22).

## ! The Issue and Why it's Important

Hepatitis C virus (HCV) is transmitted when the blood of an infected person comes into contact with the blood of an uninfected person (23). Approximately 25% of individuals spontaneously clear the virus after infection; however, the majority of individuals go on to develop chronic HCV infection (24, 25). With chronic HCV, healthy liver cells are destroyed and replaced with scar tissue in a process called fibrosis (24). Cirrhosis, scarring of nearly the entire liver, can occur if HCV goes untreated (24).

As HCV is a bloodborne pathogen, one way it can be spread is when equipment used for preparing, injecting, smoking or snorting drugs and other substances is shared (23, 24, 26). People who inject drugs are disproportionately impacted by HCV (27), and some estimates suggest that in Canada, up to 85% of new infections occur in this population (28, 29). One modelling study estimates that if the transmission risk of HCV due to needle and syringe sharing among people who inject drugs was removed, 79% of HCV infections in high-income countries would be averted (30).

When an individual contracts HCV, their progress through stages of medical care can be tracked on a continuum of care (31). Though there is no standardized care continuum for HCV, also referred to as the cascade of care (5), most studies report outcomes that can be grouped into three stages: testing, linkage to care, and treatment (5, 31). Successful completion of all steps results in cure rates of more than 95% (32) as individuals linked to care are treated with highly efficacious direct-acting antivirals (DAAs) (33), a regimen that has transformed HCV care in recent years (29, 34). People

## References

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5. Yousafzai MT, Bajis S, Alavi M, Grebely J, Dore GJ, Hajarizadeh B. Global cascade of care for chronic hepatitis C virus infection: A systematic review and meta-analysis. *Journal of Viral Hepatitis*. 2021;28(10):1340–54.

who have a negative or undetectable HCV RNA test result 12 weeks after the end of their treatment are considered to be cured (or to have achieved sustained virological response–SVR) (32). Previously, treatment for HCV was interferon-based: it was poorly tolerated, had the potential for many negative side effects, required injections over 24–48 weeks, and was associated with a lower likelihood of cure (1, 35). In comparison, DAAs are dosed once per day, taken for 8–12 weeks, have few side effects and a >95% cure rate (35), and it is a more feasible treatment option for people who inject drugs (35). CATIE’s official statement on HCV treatment efficacy among people who use drugs states that:

*“Treatment is highly effective at curing hepatitis C for all people, including people who use drugs. People who use drugs, including those who are on opioid agonist treatment, are just as likely to cure their hepatitis C with treatment as other populations who received treatment. People who use drugs should be offered hepatitis C treatment, regardless of whether they plan to continue, reduce or stop their use of substances.”* (1)

Canadian hepatitis C treatment guidelines now recommend that all people with chronic hepatitis C be considered for treatment, including people who use drugs (1, 36).

Achieving an SVR (i.e. cure, or clearance of the virus) as a result of DAAs reduces the risk of HCV-related morbidity and mortality, and decreases the risk of forward transmission at the individual and population levels (31). The efficacy of DAAs for people who use drugs has been examined in several studies (37). Graf *et al.* (2020) concluded that DAA treatment outcomes among people who inject drugs had rates of SVR comparable to those without a history of injecting drugs (38), and Hajarizadeh *et al.* (2018) found that response to DAA therapy was favourable among people with recent drug use, including those who inject (39).

Some real-world data demonstrate that uptake of DAAs is greater compared to treatment uptake in the interferon era (2–4), including among those co-infected with HIV (40). Furthermore, some studies also show that adherence to DAAs can be high (41, 42).

Despite this, uptake of DAAs among people who use drugs is suboptimal. One study in the U.S. with over 29,000 individuals newly diagnosed with HCV found that those with substance use disorders were significantly less likely to initiate DAA treatment (43). In Australia, in a sample of individuals from the Illicit Drug Reporting System (2018–2019) who regularly inject drugs, it was found that among those who self-reported a positive HCV RNA test (n=546), about 58% (n=316) achieved SVR (44). In Canada, the Phase 4 (2017–2019) Tracks survey of people who inject drugs (n=2,383) found that among those who were aware of their HCV infection (n=238), only 3.8% (n=9) were taking HCV treatment at the time of the survey (45, 46). Additionally, a systematic review from 2021 found that among

6. Cunningham EB, Wheeler A, Hajarizadeh B, French CE, Roche R, Marshall AD, et al. Interventions to enhance testing, linkage to care, and treatment initiation for hepatitis C virus infection: A systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology*. 2022;7(5):426–45.
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9. Ward KM, Falade-Nwulia O, Moon J, Sutcliffe CG, Brinkley S, Haselhuhn T, et al. A randomized controlled trial of cash incentives or peer support to increase HCV treatment for persons with HIV who use drugs: The CHAMPS study. *Open Forum Infectious Diseases*. 2019;6(4):ofz166.
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people who inject drugs, DAA treatment uptake was estimated at 40% in Canada, 37% in Australia, and 13% in the U.S. (5). More research is needed to fully understand how DAAs have impacted treatment uptake in people who use drugs and other high-risk populations (45).

Overall, engagement and retention in HCV care, core components of the HCV care cascade (7), are at suboptimal levels in Canada and in other high-income countries, evidenced by low DAA treatment uptake (5). Not only do low engagement and retention rates for HCV treatment and care contribute to negative health outcomes, they also drive forward transmission of the virus (45). This review discusses interventions that aim to increase engagement and retention in HCV care.

## What We Found

### Systematic and scoping reviews on the HCV cascade of care published since 2016

There is a very large body of literature investigating different types of interventions aimed at increasing engagement and retention in HCV care in general. For example, a recent systematic review by Cunningham *et al.* (2022) found that integrated care and patient navigation or care coordination significantly improved linkage to care and the uptake of DAA treatment (6). At the same time, there is research that is focused on identifying such interventions for people who use drugs specifically. We identified nine systematic reviews (7, 47–54) and one scoping review (55) published since 2016 that included interventions describing engagement and retention in HCV care, as well as other stages of the care cascade, specifically focused on people who use drugs. Each of these reviews is described briefly below, followed by a section that details the specific interventions with outcomes related to engagement and retention in HCV care.

Bajis *et al.* (2017) conducted a systematic review to evaluate the effectiveness of interventions to enhance HCV testing, linkage to care, and treatment uptake among people who inject drugs; 14 studies from high-income settings were included, though all were conducted in the interferon treatment era (47). Results indicated that integrated HCV care and case management services, where drug use and psychiatric services are delivered by a multidisciplinary team, enhanced HCV treatment uptake (47).

Vold *et al.* (2019) evaluated the impact of integrated models of care on the treatment of infectious diseases among people with substance use disorders (54). Vold *et al.* defined integrated models of care as a “comprehensive set of patient-centered health services that involve the care of chronic infectious disease as a part of coordinated services for people with substance use disorders” (54). Of the ten studies included in the systematic review, three addressed HCV; however,

11. Norton BL, Bachhuber MA, Singh R, Agyemang L, Arnsten JH, Cunningham CO, et al. Evaluation of contingency management as a strategy to improve HCV linkage to care and treatment in persons attending needle and syringe programs: A pilot study. *International Journal of Drug Policy*. 2019;69:1–7.
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15. Broad J, Mason K, Guyton M, Lettner B, Matelski J, Powis J. Peer outreach point-of-care testing as a bridge to hepatitis C care for people who inject drugs in Toronto, Canada. *International Journal of Drug Policy*. 2020;80:102755.

all three studies were conducted in the interferon treatment era (54). Findings across included studies were mixed on the impact of integrated care (54).

Sociás *et al.* (2019) assessed the impact that co-locating HCV and substance use services had on engagement in the HCV cascade of care among people who inject drugs (53). This systematic review included 44 studies, though only six were from the DAA era (56–61). Authors concluded that integrating HCV care with substance use services may improve engagement in the HCV care cascade among people who inject drugs (53).

Grebely *et al.* (2021) examined the association between opioid agonist therapy and HCV testing, treatment uptake, and treatment outcomes among people who inject drugs; eight studies examining HCV treatment uptake were included (48). Of these eight studies, four were conducted in the DAA era (48). Authors concluded that opioid agonist therapy can increase linkage to HCV care (42).

Ortiz-Paredes *et al.* (2022) identified interventions designed to improve DAA uptake among people who inject drugs and other population groups (51). Of the 39 studies, 37 focused on people who use drugs (51). Three groups of interventions were identified: interventions involving patients, providers, or the healthcare system (51). Interventions directed to patients included care coordination, accelerated DAA initiation, and patient education (51). Interventions involving providers included provider education, telemedicine, multidisciplinary teams, and general practitioner-led care (51). System-based interventions comprised DAA universal access policies and offering HCV services in healthcare and community settings (51). Most studies (30 of 39) described complex interventions, i.e. those with two or more strategies combined (51).

In their scoping review, Abdelwadoud *et al.* (2021) assessed the inclusion of eight different dimensions of patient-centred care in HCV treatment delivery to people who inject drugs in the DAA era (55). These eight dimensions are: access to care; coordination and integration of care; continuity and transition; physical comfort; information, education, and communication; emotional support; involvement of family and friends; and respect for individual patient preferences, perceived needs, and values (55). Authors included 36 studies from all three stages of the HCV care cascade (55). The analyzed studies incorporated the dimensions of patient-centred care using different approaches and strategies, however, none of them included all eight dimensions (55). The authors suggested more engagement of people who inject drugs and comprehensive involvement of their families and friends in HCV treatment journey, decisions, and outcomes (55).

Hashim *et al.* (2021) examined interventions addressing community-based assessment and treatment of HCV and substance use among people who are homeless (49). Of 39 included studies, only six

16. Conway A, Valerio H, Alavi M, Silk D, Treloar C, Hajarizadeh B, et al. A testing campaign intervention consisting of peer-facilitated engagement, point-of-care HCV RNA testing, and linkage to nurse support to enhance hepatitis C treatment uptake among people who inject drugs: The ETHOS Engage study. *Viruses*. 2022;14(7):16.
17. Falade-Nwulia O, Ward KM, McCormick S, Mehta SH, Pitts SR, Katz S, et al. Network-based recruitment of people who inject drugs for hepatitis C testing and linkage to care. *Journal of Viral Hepatitis*. 2020;27(7):663–70.
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19. Radley A, De Bruin M, Inglis SK, Donnan PT, Hapca A, Barclay ST, et al. Clinical effectiveness of pharmacist-led versus conventionally delivered antiviral treatment for hepatitis C virus in patients receiving opioid substitution therapy: A pragmatic, cluster-randomised trial. *The Lancet Gastroenterology & Hepatology*. 2020;5(9):809–18.

were conducted in the DAA era, in a high-income country, where more than 50% of the population was identified as people who use drugs (49). Authors concluded that people who are homeless are a vulnerable group with a risk of poor HCV-related health outcomes, and that there are few well-designed studies that assess interventions to improve their liver health (49).

Lazarus *et al.* (2022) reported on global micro-elimination efforts, a strategy that can be useful in driving engagement in HCV treatment and cure (50) by focusing on eliminating HCV in defined segments of the population (62). Target populations included incarcerated persons, people who inject drugs, people with bleeding disorders, people experiencing homelessness, and the general population (50). Of the 60 studies that were included, 29 were from peer-reviewed journals; of these, seven were among people who use or inject drugs (50). Across all included studies, those who adhered to the main components of micro-elimination (a clearly defined plan, time-bound targets, a multi-stakeholder process, and monitoring the outcomes) achieved statistically significant higher proportions of treatment initiation and SVR (50).

Oru *et al.* (2021) evaluated how decentralisation, integration of the HCV care cascade with harm reduction services, and task-shifting to non-specialists impacted outcomes across the HCV care continuum (52). Authors included 142 studies; close to one-third of the studies reported on linkage and/or treatment uptake (52). Authors found that treatment uptake among people who inject drugs was higher with full decentralization compared with partial or no decentralization, while task-shifting of care to non-specialist physicians or nurses rather than specialists (e.g. hepatologists) was associated with SVR rates similar to treatment delivered by specialists in general (52).

Schwarz *et al.* (2022) sought to evaluate the effectiveness of interventions on HCV linkage to care and adherence to treatment among people who inject drugs (7). Included studies had a comparative design and reported on primary outcomes for linkage to care and adherence; for studies examining linkage to care, this included visits and treatment initiation (7). Of the 14 studies identified, ten were focused on linkage to care; of these ten, nine were based in the DAA era in high-income settings (7). Authors found that studies could be grouped into four categories: contingency management, telemedicine, peer involvement, and integrated services and case management (7). The review concluded that integrated, people-centered approaches may improve engagement throughout the continuum of HCV care among people who inject drugs (7).

## Studies examining engagement and retention in HCV care

There is a large number of studies in the literature examining engagement and retention in HCV care. In this review we have

20. Bartlett SR, Wong S, Yu A, Pearce M, MacIsaac J, Nouch S, et al. The impact of current opioid agonist therapy on hepatitis C virus treatment initiation among people who use drugs from the direct-acting antiviral (DAA) era: A population-based study. *Clinical Infectious Diseases*. 2022;74(4):575–83.
21. Rizk C, Miceli J, Shiferaw B, Malinis M, Barakat L, Ogbuagu O, et al. Implementing a comprehensive HCV clinic within an HIV clinic: A model of care for HCV micro-elimination. *Open Forum Infectious Diseases*. 2019;14:14.
22. Falade-Nwulia O, Sutcliffe CG, Mehta SH, Moon J, Chander G, Keruly J, et al. Hepatitis C elimination in people with HIV is contingent on closing gaps in the HIV continuum. *Open Forum Infectious Diseases*. 2019;6(10):ofz426.
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24. CATIE. The epidemiology of hepatitis C in Canada. 2019. Available from: <https://www.catie.ca/the-epidemiology-of-hepatitis-c-in-canada-0> Accessed November 24, 2022.



included only a selected number of interventions with outcomes that focus on **visits (broadly defined as coming into contact with a care provider)** and **DAA treatment initiation**. The included studies are summarized in Table 1 and meet the following inclusion criteria:

- Full-text articles, published in a peer-reviewed journal (i.e. conference abstracts and posters, as well as published protocols, are excluded)
- Studies conducted in either Canada, the U.S., the UK, or Australia
- Studies where at least 50% of the participants had ever used/were currently using drugs

Additionally, studies with participants on different treatment regimens (e.g. some participants taking interferon-based treatment while others on DAAs) and without separate data analysis for the two groups were excluded.

The 26 studies in Table 1 are organized using the four intervention categories proposed by Schwarz *et al.* (2022), as these categories appear to reflect the general scope of interventions to improve engagement and retention in HCV care (7):

- contingency management (n=5),
- peer involvement and support (n=4),
- telemedicine (n=2), and
- integrated services and case management (n=15).

Several of the interventions across these categories utilize task-shifting, which is “...the rational redistribution of tasks to individuals within the healthcare team with fewer qualifications that conventionally were not within their scope of work” (63). As noted previously, Oru *et al.* (2021) found that generally, task-shifting of care to non-specialists was associated with SVR rates similar to treatment delivered by specialists (52). Several of the studies described in Table 1 utilized task-shifting as a strategy, such as Bartholomew *et al.* (2019) (64), which describes a comprehensive HCV treatment program developed at a clinic without specialist staff, and Radley *et al.* (2020), where pharmacists managed HCV care alongside opioid substitution therapy at a pharmacy (19). The four studies detailing peer involvement, also included in Table 1, are other examples of task-shifting (9, 15–17). Thus, even though task-shifting does not appear as a separate category in our classification of interventions, its principles are used across the identified broad categories.

As some studies included populations with HIV/HCV co-infection, Table 1 also reports the number of people living with HIV in the

25. Smith DJ, Jordan AE, Frank M, Hagan H. Spontaneous viral clearance of hepatitis C virus (HCV) infection among people who inject drugs (PWID) and HIV-positive men who have sex with men (HIV+ MSM): A systematic review and meta-analysis. *BMC Infectious Diseases*. 2016;16(1):1–13.
26. CATIE. Safer substance use and hepatitis C prevention. 2021. Available from: <https://www.catie.ca/hepatitis-c-an-in-depth-guide/safer-substance-use-and-hepatitis-c-prevention> Accessed February 2, 2023.
27. Public Health Agency of Canada. People living with hepatitis C: Canada, 2019. 2022. Available from: <https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/infographic-people-living-with-hepatitis-c/infographic-people-living-with-hepatitis-c.pdf> Accessed November 28, 2022.
28. Laniece Delaunay C, Maheu-Giroux M, Marathe G, Saeed S, Martel-Laferrriere V, Cooper CL, et al. Gaps in hepatitis C virus prevention and care for HIV-hepatitis C virus co-infected people who inject drugs in Canada. *International Journal of Drug Policy*. 2022;103:103627.
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study sample (9, 21, 22, 65, 66). The global prevalence of HCV among people living with HIV is observed to be higher compared to people living without HIV, especially among individuals who inject drugs (67, 68). Of note, one study among individuals co-infected with HIV and HCV (n=11), of whom 73% (n=8) were people who inject drugs, identified eight types of potential interventions to support HCV initiation; the highest ranked were multidisciplinary clinics, HCV awareness campaigns and patient education, nurse- or pharmacist-led care, and peer involvement and support (69).

For the purpose of brevity, here we only provide a brief description of two interventions for each of the four intervention categories. Detailed information about all included interventions can be found in Table 1.

### Contingency management

We identified five studies that examined contingency management interventions to improve engagement and retention in HCV care (8-12).

Examples:

Ward *et al.* (2019) conducted a randomized-controlled trial among people living with HIV/HCV co-infection and substance use disorder to evaluate if an intervention utilizing peer mentors and cash incentives impacted HCV treatment uptake and cure (9). The CHAMPS (Chronic Hepatitis C Management to Improve OutcomeS) study randomized individuals from an HIV outpatient clinic in Baltimore who had not engaged in co-located HCV care (n=144) to three treatment groups (9). Participants in usual care (n=36) were linked to an HCV provider and treated according to standard clinic protocol; participants in usual care plus cash incentives (n=54) were offered a cash incentive to reinforce visit attendance behaviours with a maximum collectible incentive totalling USD 220; and participants in usual care plus peer mentor support (n=54) had structured, face-to-face interactions with peers who were successfully treated for HIV and HCV (9). Of the 144 participants, 76% (n=110) initiated DAA treatment (9). Individuals randomized to peers (83%; n=45/54) or cash incentives (76%; n=41/54) had a higher initiation rate compared to usual care (67%; n=24/36), though these differences were not statistically significant (p=0.11) (9). The majority of the individuals who initiated treatment achieved SVR (91%; n=100/110) (9).

Lee *et al.* (2020) conducted a non-randomized trial to evaluate the effectiveness of a financial incentive program to improve appointment attendance at a hospital-based HCV treatment program in Boston serving many patients with substance use disorder (10). Individuals living with HIV were purposely excluded, as they were receiving specialty care (10). Authors implemented cash incentives at three different steps of the HCV care continuum: the initial visit, the follow-up visit, and a final visit to ascertain SVR three months

30. Trickey A, Fraser H, Lim AG, Peacock A, Colledge S, Walker JG, et al. The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: A modelling study. *The Lancet Gastroenterology & Hepatology*. 2019;4(6):435–44.
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32. CATIE. Hepatitis C treatment. 2020. Available from: <https://www.catie.ca/hepatitis-c-an-in-depth-guide/hepatitis-c-treatment> Accessed February 2, 2023.
33. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, Fried MW, Segal JB, Sulkowski MS. Oral direct-acting agent therapy for hepatitis C virus infection: A systematic review. *Annals of Internal Medicine*. 2017;166(9):637–48.
34. Asselah T, Marcellin P, Schinazi RF. Treatment of hepatitis C virus infection with direct-acting antiviral agents: 100% cure? *Liver International*. 2018;38 Suppl 1:7–13.
35. Grebely J, Bruneau J, Bruggmann P, Harris M, Hickman M, Rhodes T, et al. Elimination of hepatitis C virus infection among PWID: The beginning of a new era of interferon-free DAA therapy. *The International Journal on Drug Policy*. 2017;47:26–33.



after treatment completion (10). A gift card to Target stores or CVS pharmacies for USD 15 was provided to patients who attended any visit, for a maximum payout of USD 45 (10). Appointment attendance during the intervention (April–June 2017) was compared to a historical control (April–June 2016) (10). During the intervention period, 198 visits were scheduled for 149 unique patients; during the control period, 129 visits were scheduled for 94 patients (10). Nearly 73% of visits were attended in the intervention group, relative to 61.2% attended appointments in the comparison group ( $p=0.03$ ) (10). In the intervention group, patient appointments were more likely to be attended (adjusted odds ratio 1.94, 95% confidence interval 1.16–3.24,  $p=0.01$ ) (10). Authors suggest that a randomized trial to establish efficacy and broader implementation is warranted (10).

### **Peer involvement and support**

We identified four studies that integrated peers into interventions to increase engagement and retention in HCV care (9, 15–17).

#### **Examples:**

A study conducted in Toronto evaluated the feasibility of using peer mentors to deliver point-of-care HCV testing to marginalized populations, and determined if testing by peer workers had an impact on engagement in HCV care (15). Peer outreach workers ( $n=11$ ) were current or former clients of the Toronto Community Hep C Program, and recruited their personal network members in non-healthcare settings who had a lifetime history of injection drug use and no prior knowledge of HCV antibody status ( $n=380$ ) (15). The primary outcome was the number of participants who visited the HCV treatment program nurse at one of three sites within six months of outreach engagement among those who received point-of-care testing ( $n=195$ ) compared to the testing as usual group ( $n=185$ ) (15). The entire sample had a history of injection drug use, and approximately 66% reported injection drug use within the past 30 days; HIV status was not reported (15). Peer workers were able to successfully administer point-of-care tests and provide antibody status information (15). However, within six months of study enrollment, there was no change in rates of engagement in HCV care among those who received the peer point-of-care test and those who did not (15). Authors concluded that the model was insufficient to promote engagement in HCV care (15).

The ETHOS Engage Study, conducted across 25 drug treatment clinics and needle and syringe programs in Australia, evaluated HCV treatment initiation among people who inject drugs following an intervention campaign (16). The intervention consisted of “campaign days”: days where peer connection, point-of-care HCV RNA screening, and nurse-led linkage to care were integrated into the operations of the drug treatment clinics and needle and syringe programming (16). This allowed for opportunistic engagement of participants who were attending the sites for standard services,

36. Shah H, Bilodeau M, Burak KW, Cooper C, Klein M, Ramji A, et al. The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver. *Canadian Medical Association Journal*. 2018;190(22):E677–E87.
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39. Hajarizadeh B, Cunningham EB, Reid H, Law M, Dore GJ, Grebely J. Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: A systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology*. 2018;3(11):754–67.
40. Sacks-Davis R, Doyle JS, Rauch A, Beguelin C, Pedrana AE, Matthews GV, et al. Linkage and retention in HCV care for HIV-infected populations: Early data from the DAA era. *Journal of the International AIDS Society*. 2018;21 Suppl 2:e25051.

who were approached by peers to participate in the study (16). Peers offered education about HCV treatment and testing, and discussed any HCV-related questions or concerns (16). The primary outcome of the study was initiation of HCV treatment following diagnosis of HCV infection, and the secondary outcome was time to treatment initiation in the 24 months following diagnosis (16). Of the 1,443 participants who were recruited between May 2018 and September 2019, 23% (n=331) had a current HCV infection, though 14 (4%) were deemed ineligible for participation in the study (16). Of the 317 individuals who received a positive HCV RNA result and were eligible for treatment, 70% (n=221) injected drugs within the past month, and 30% (n=96) injected drugs more than a month ago (16). Authors found that this intervention facilitated treatment uptake: 15% (n=47) initiated treatment at 3 months, 27% (n=85) initiated treatment at 6 months, 38% (n=120) initiated treatment at 12 months, and 49% (n=155) initiated treatment at 24 months (16).

### Telemedicine

Two studies occurring in the DAA era examined the impact of telemedicine on engagement and retention in HCV care (13, 14); both are described below and included in Table 1. Of note, one Canadian study from 2017 by Cooper *et al.* (not included in Table 1) found that a telemedicine intervention had favourable engagement and retention outcomes, though participants were not all on a DAA regimen as the study period was from 2012–2016 (70).

Talal *et al.* (2019) delivered an HCV telemedicine intervention among individuals participating in methadone treatment (14). The rationale of the authors was that integrating onsite delivery of HCV care (i.e. telemedicine sessions, paired with coadministration of DAAs and methadone) would foster treatment pursuit (14). Following two virtual education sessions, HCV testing was offered; if the individual was HCV RNA positive, a virtual evaluation with a hepatologist and opioid substitution therapy practitioner was scheduled, and a treatment plan was formulated (14). A specialty pharmacy was used to order the DAAs, which were then delivered to the clinic and dispensed with methadone (14). During the course of treatment, biweekly telemedicine evaluations occurred to monitor adherence and adverse events (14). Sixty-two patients engaged in the initial virtual consultation; of these, 73% (n=45) were prescribed DAAs (14). Approximately 22% (n=10) of individuals who started treatment were living with HIV (14). Authors concluded that virtual HCV care for individuals attending an opioid substitution program is a feasible model for HCV treatment delivery with excellent virologic effectiveness. (14).

An interdisciplinary telehealth model of comprehensive care was developed to address the HCV-opioid epidemic in Southwest Virginia (13). This telehealth model features referrals to/from harm

41. Cunningham EB, Hajarizadeh B, Amin J, Litwin AH, Gane E, Cooper C, et al. Adherence to once-daily and twice-daily direct-acting antiviral therapy for hepatitis C infection among people with recent injection drug use or current opioid agonist therapy. *Clinical Infectious Diseases*. 2020;71(7):e115–e24.
42. Mason K, Dodd Z, Guyton M, Tookey P, Lettner B, Matelski J, et al. Understanding real-world adherence in the directly acting antiviral era: A prospective evaluation of adherence among people with a history of drug use at a community-based program in Toronto, Canada. *International Journal of Drug Policy*. 2017;47:202–8.
43. Jiang X, Song HJ, Wang W, Henry L, Childs-Kean LM, Re VL, 3rd, et al. The use of all-oral direct-acting antivirals in hepatitis C virus-infected patients with substance use disorders. *Journal of Managed Care & Specialty Pharmacy*. 2021;27(7):873–81.
44. Gibbs D, Price O, Grebely J, Larney S, Sutherland R, Read P, et al. Hepatitis C virus cascade of care among people who inject drugs in Australia: Factors associated with testing and treatment in a universal healthcare system. *Drug & Alcohol Dependence*. 2021;228:109050.
45. Lourenco L, Kelly M, Tarasuk J, Stairs K, Bryson M, Popovic N, et al. The hepatitis C epidemic in Canada: An overview of recent trends in surveillance, injection drug use, harm reduction and treatment. *Canada Communicable Disease Report*. 2021;47(12):561–70.

reduction programs and office-based opioid therapy, with HCV training provided to practitioners (13). Program referrals were bidirectional, coming to/from harm reduction sites and office-based opioid therapy programs (13). After referral, three total “visits” are required: an initial nurse visit for diagnostic testing, a telehealth visit with an HCV provider, and a follow-up visit 12 weeks after therapy completion (13). Of the 123 individuals included in the telehealth analysis, 62% (n=76) were referred from harm reduction or office-based opioid therapy sites (13). Of the 123 individuals, 84% (n=103) were linked to care by attending an appointment, 80% (n=98) completed required diagnostic testing, and 76% (n=93) initiated treatment; the time from referral to initial visit was 17.5 days (13). Of those who completed the treatment course (n=93; 76%), 61 (50%) achieved SVR (13). Authors concluded that this model of care was an efficient way to treat HCV among patients referred from harm reduction and opioid therapy programs (13).

### ***Integrated services and case management***

The majority of identified HCV care interventions fell into the category of integrated services and case management, where HCV care was co-located within an already established service (e.g. HIV care clinic, substance use treatment centre). Studies have noted the critical nature of these types of care models; Rich *et al.* (2018) states that:

“The design and scale-up of integrated or co-located, multidisciplinary care models that engage and retain individuals in HIV, HCV, opioid use disorder (OUD), and mental health care are critical to preventing the continued spread of HIV and HCV in the context of the current opioid epidemic.” (71)

The number of studies evaluating integrated services models is considerable, though many of them only describe outcomes at the final stage of the HCV care cascade (i.e. treatment adherence, treatment completion, SVR), and do not necessarily report on outcomes related to linkage and engagement in care (i.e. visits and treatment initiation). For example, a study reporting high levels of treatment adherence and cure was most likely successful at engaging and retaining individuals, but those outcomes have not been explicitly described. Thus, only 15 integrated service and case management models that detail engagement and retention in care outcomes are included in Table 1. However, this may not be an exhaustive list of integrated service models that work to improve engagement in HCV care.

Examples:

One study that detailed outcomes across all the steps in the HCV care cascade occurred in pharmacies in Scotland (19, 72). Participants were individuals who had been receiving opioid substitution therapy at one of 55 community pharmacies for approximately

46. Tarasuk J, Zhang J, Lemyre A, Cholette F, Bryson M, Paquette D. National findings from the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019. *Canada Communicable Disease Report.* 2020;46(5):138.
47. Bajis S, Dore GJ, Hajarizadeh B, Cunningham EB, Maher L, Grebely J. Interventions to enhance testing, linkage to care and treatment uptake for hepatitis C virus infection among people who inject drugs: A systematic review. *International Journal of Drug Policy.* 2017;47:34–46.
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49. Hashim A, Macken L, Jones A, McGeer M, Aithal G, Verma S. Community-based assessment and treatment of hepatitis C virus-related liver disease, injecting drug and alcohol use amongst people who are homeless: A systematic review and meta-analysis. *International Journal of Drug Policy.* 2021;96:103342.
50. Lazarus JV, Picchio CA, Byrne CJ, Crespo J, Colombo M, Cooke GS, et al. A global systematic review of hepatitis C elimination efforts through micro-elimination. *Seminars in Liver Disease.* 2022;42(2):159–72.



three months and who were infected with HCV; testing had been facilitated by the pharmacy (19). Pharmacies were randomized to provide conventional care or pharmacist-led care (19). In the conventional care pathway, pharmacists opportunistically discussed HCV infection with individuals receiving opioid substitution therapy and offered referral to treatment (19). Similarly, in the pharmacist-led pathway, pharmacists opportunistically discussed HCV infection with individuals receiving opioid substitution therapy; however, treatment occurred in the pharmacy with no referral to outside services (i.e. DAAs were dispensed with medication for opioid use disorder) (19). The pharmacist was responsible for evaluation, with a nurse or phlebotomist visiting the pharmacy for assessment blood tests; the pharmacist was also able to contact the specialist hepatitis team for queries regarding contraindications or suitability for treatment (19). The primary outcome of the study was SVR, 12 weeks after treatment completion; secondary outcomes were the proportion of patients receiving dried blood spot testing at the pharmacy, proportion of patients initiating treatment, and the proportion of patients adhering to treatment (19). Authors found that using pharmacists to deliver an HCV care pathway made testing and treatment more accessible for patients, improved engagement, and maintained higher treatment success rates compared to the conventional treatment pathway (19).

A randomized controlled trial in Baltimore among individuals co-infected with HIV/HCV tested the effect a nurse case management intervention had on linkage to HCV care and time to initiating DAA therapy (66). Participants (n=68) were attending a large outpatient infectious disease practice, and were engaged in HIV care; however, each had chronic, untreated HCV (66). The usual care group (n=33) consisted of normal outpatient processes plus provision of an HCV fact sheet; the nurse case management intervention (n=35) included nurse-initiated HCV referral, education, and patient navigation (66). The primary outcome was linkage to care, defined as attendance at an appointment in the viral hepatitis clinic within 60 days of study enrollment; the secondary outcome was time to HCV treatment initiation (66). Compared to patients in the usual care condition, a higher proportion of individuals who received the nurse case management intervention were linked to care within 60 days of enrollment (47% vs 25%; p=0.031) (66). However, there was no significant difference between the two conditions when average time to treatment initiation was compared (66).

51. Ortiz-Paredes D, Amoako A, Ekmekjian T, Engler K, Lebouche B, Klein MB. Interventions to improve uptake of direct-acting antivirals for hepatitis C virus in priority populations: A systematic review. *Frontiers in Public Health*. 2022;10:877585.
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55. Abdelwadoud M, Mattingly TJ, 2nd, Segui HA, Gorman EF, Peretto EM. Patient centeredness in hepatitis C direct-acting antiviral treatment delivery to people who inject drugs: A scoping review. *The Patient: Patient-Centered Outcomes Research*. 2021;14(5):471–84.

## Factors That May Impact Local Applicability

There is a vast amount of literature examining HCV among people who use drugs; thus, the interventions presented in this review are limited to full-text articles published since 2016 in a peer-reviewed journal that were conducted in Canada, the U.S., the UK, or Australia, where at least 50% of the participants had ever used/were currently using drugs. Furthermore, only studies that reported outcomes for engagement in and linkage to HCV care for participants on DAAs were considered. Consequently, all efficacious interventions published in the literature may not have been included. Additionally, while treatment initiation of DAAs is now widespread, some retrospective cohort studies occurred in a timeframe where DAAs were novel, or where DAA uptake was not widespread due to jurisdictional variations in treatment coverage, which may have impacted samples sizes and applicability of examined interventions and their outcomes.

## What We Did

We searched Medline using a combination of (text terms [Injecting drug use\* or Injection drug use\* or who inject or IDU\* or intravenous drug use\* or who use\* drugs or use\* adj2 drug\* or drug use] or MeSH terms exp Substance-Related Disorders/ or exp Substance Abuse, Intravenous/ or terms ((intravenous\* or parenteral\* or inject\* or IV) adj3 (drug\* or substance\*) adj8 (abuse or addict\* or use\* or using or people or person\*)) or PWID\* or PWUD\* or (substance use\* or use\*) adj5 substance\*] in titles or abstracts) AND (terms hepatitis C or HCV in titles or abstracts) AND terms (((treat\* or therap\*) adj5 (uptake\* or start\* or initiat\* or begin\* or access\* or link\* or referr\*)) or ((adhere\* or comply\* or compliance or complied) adj5 (care or healthcare or treat\* or therap\*)) or (engage\* or retention or retain\* or management or treat\* or adherence or uptake) in titles or abstracts or MeSH term exp patient compliance/). Searches were conducted on October 21, 2022 and results limited to English articles published from 2016 to present. Studies from low- and middle-income countries were excluded. Reference lists of identified articles were also searched. Google (grey literature) searches using different combinations of these terms were also conducted. The searches yielded 2,041 references from which 77 were included.

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57. Nouch S, Gallagher L, Erickson M, Elbaharia R, Zhang W, Wang L, et al. Factors associated with lost to follow-up after hepatitis C treatment delivered by primary care teams in an inner-city multi-site program, Vancouver, Canada. *International Journal of Drug Policy*. 2018;59:76–84.
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61. Read P, Lothian R, Chronister K, Gilliver R, Kearley J, Dore GJ, et al. Delivering direct acting antiviral therapy for hepatitis C to highly marginalised and current drug injecting populations in a targeted primary health care setting. *International Journal of Drug Policy*. 2017;47:209–15.
62. Lazarus JV, Wiktor S, Colombo M, Thursz M. Micro-elimination – A path to global elimination of hepatitis C. *Journal of Hepatology*. 2017;67(4):665–6.
63. Leong SL, Teoh SL, Fun WH, Lee SWH. Task shifting in primary care to tackle healthcare worker shortages: An umbrella review. *European Journal of General Practice*. 2021;27(1):198–210.
64. Bartholomew TS, Grosgebauer K, Huynh K, Cos T. Integration of hepatitis C treatment in a primary care federally qualified health center; Philadelphia, Pennsylvania, 2015–2017. *Infectious Diseases*. 2019;12:1178633719841381.
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71. Rich KM, Bia J, Altice FL, Feinberg J. Integrated models of care for individuals with opioid use disorder: How do we prevent HIV and HCV? *Current HIV/AIDS Reports*. 2018;15(3):266–75.
72. Radley A, Tait J, Dillon JF. DOT-C: A cluster randomised feasibility trial evaluating directly observed anti-HCV therapy in a population receiving opioid substitute therapy from community pharmacy. *International Journal of Drug Policy*. 2017;47:126–36.
73. Burton MJ, Voluse AC, Anthony V. Integrating comprehensive hepatitis C virus care within a residential substance use disorder treatment program. *Journal of Substance Abuse Treatment*. 2019;98:9–14.
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75. Morris L, Selvey L, Williams O, Gilks C, Kvassy A, Smirnov A. Hepatitis C cascade of care at an integrated community facility for people who inject drugs. *Journal of Substance Abuse Treatment*. 2020;114:108025.
76. Rowan SE, Kamis KF, Beum R, Bryan K, Gawenus L, Colon Sanchez D, et al. Viral hepatitis and human immunodeficiency virus testing and linkage to care for individuals enrolled in an opioid treatment program. *Journal of Infectious Diseases*. 2020;222(Suppl 5):S384–S391.
77. Wade AJ, Doyle JS, Gane E, Stedman C, Draper B, Iser D, et al. Outcomes of treatment for hepatitis C in primary care, compared to hospital-based care: A randomized, controlled trial in people who inject drugs. *Clinical Infectious Diseases*. 2020;70(9):1900–6.



Table 1. Characteristics of studies examining interventions to improve engagement and retention in HCV care among people who use drugs

Author, year	Country	Objective	Study design	Study population and setting	Proportion of individuals with HIV/HCV co-infection (if reported)	Description	Reported outcomes related to linkage and retention in HCV care (visits/coming into contact with a care provider, treatment initiation of DAAs)
<b>CONTINGENCY MANAGEMENT</b>							
Wohl <i>et al.</i> , 2017 (11)	U.S.	To assess the feasibility of financially incentivizing adherence to HCV care	Experimental (RCT)	Patients of either the University of North Carolina Infectious Diseases Clinic or Liver Center, reporting substance use for at least one year	HIV+: n=19/59 (32%)	<ul style="list-style-type: none"> <li>Participants (n=59) were randomized 1:1 to one of two study arms: either fixed financial incentive (n=28), or lottery-based financial incentive (n=31) to reinforce clinic attendance and medication adherence</li> </ul>	<ul style="list-style-type: none"> <li>More than 90% of scheduled visits were attended; no significant differences between arms</li> </ul>
Alimohammadi <i>et al.</i> , 2017 (11)	Canada	To determine the efficacy of community pop-up clinics offering incentives to engage in HCV care	Observational (prospective cohort)	Vancouver's Downtown Eastside; 68% past or current people who inject drugs	Data not provided	<ul style="list-style-type: none"> <li>A mobile community pop-up clinic offered point-of-care referrals as a prelude to HCV treatment initiation</li> <li>Participants received a gift card to complete a rapid HCV test and receive results; a meal voucher was received when an appointment was scheduled</li> </ul>	<ul style="list-style-type: none"> <li>Of the patients who attended the pop-up clinic who were not engaged in care elsewhere (n=83), 100% redeemed the voucher and successfully engaged in care</li> <li>Of these 83, 61% (n=51) initiated HCV treatment; the remaining 32 (39%) were waiting for treatment funding from the government or through compassionate care programs from pharmaceutical companies</li> </ul>
Ward <i>et al.</i> , 2019 (8) <i>could also be classified under PEER INVOLVEMENT AND SUPPORT</i>	U.S.	To determine if an intervention of cash incentives and peer mentors would increase the rate of HCV treatment initiation and cure	Experimental (RCT)	Individuals with HIV/HCV co-infection who use drugs, receiving HIV care at the Johns Hopkins Moore Clinic for HIV Care, who had not engaged in co-located HCV care within 8 months of entry	n=144/144 (100%)	<ul style="list-style-type: none"> <li>The CHAMPS (Chronic Hepatitis C Management to Improve OutcomeS) study randomized 144 individuals into three treatment groups: usual care (n=36), usual care plus cash incentives (n=54), and usual care plus peer mentors (n=54) to evaluate HCV treatment uptake and cure</li> <li>Cash incentives were contingent on visit attendance</li> </ul>	<ul style="list-style-type: none"> <li>Of the 144 participants, 76% (n=110) initiated treatment</li> <li>Treatment initiation rates were higher in participants randomized to peer mentors or cash incentives compared to usual care, but the differences were not statistically significant</li> </ul>
Norton <i>et al.</i> , 2019 (10)	U.S.	To assess the effectiveness of contingency management on HCV care outcomes compared to enhanced standard of care	Experimental (non-randomized sequential two-arm trial)	Clients of a needle and syringe program in New York City	n=4/16 (25%)	<ul style="list-style-type: none"> <li>The enhanced standard of care arm (n=20) consisted of an expedited appointment at the health centre, a round-trip transit voucher, plus reminder phone calls</li> <li>The contingency management intervention (n=19) consisted of enhanced standard of care plus financial incentives for attendance at HCV visits, return of medication blister packs, and successful early clinical outcome while on HCV treatment</li> </ul>	<ul style="list-style-type: none"> <li>Of the 20 individuals in the enhanced standard of care arm, six were linked to care, four were treatment eligible, and four initiated treatment</li> <li>Of the 19 individuals in the contingency management arm, 14 were linked to care, 12 were treatment eligible, and nine initiated treatment</li> <li>Participants receiving the contingency management intervention were more likely to be linked to HCV care compared to enhanced standard of care (75% vs 30%, p=0.01)</li> </ul>

Table 1 (continued). Characteristics of studies examining interventions to improve engagement and retention in HCV care among people who use drugs

Author, year	Country	Objective	Study design	Study population and setting	Proportion of individuals with HIV/HCV co-infection (if reported)	Description	Reported outcomes related to linkage and retention in HCV care (visits/coming into contact with a care provider, treatment initiation of DAAs)
<b>CONTINGENCY MANAGEMENT (continued)</b>							
Lee <i>et al.</i> , 2020 (9)	U.S.	To evaluate the effectiveness of a financial incentive program to improve appointment attendance at a hospital-based HCV treatment program	Experimental (non-randomized two-arm trial with historical control)	Adult Primary Care HCV Treatment Program at Boston Medical Center, a safety-net hospital serving many patients with substance use disorder	None: HIV+ individuals excluded	<ul style="list-style-type: none"> <li>A gift card incentive was implemented at three different steps of the HCV care continuum: 1) the initial visit; 2) the follow-up visit; and 3) the follow-up visit with an HCV provider 3 months after treatment completion to ascertain SVR</li> </ul>	<ul style="list-style-type: none"> <li>Of patient visits in the intervention group, 72.7% of appointments were attended relative to 61.2% of comparison group visits (p=0.03)</li> <li>Appointments in the intervention group were more likely to be attended (adjusted odds ratio 1.94, 95% confidence interval 1.16-3.24, p=0.01)</li> </ul>
<b>PEER INVOLVEMENT AND SUPPORT</b>							
Ward <i>et al.</i> , 2019 (8) see CONTINGENCY MANAGEMENT for description							
Falade-Nwulia <i>et al.</i> , 2020 (16)	U.S.	To examine the feasibility of a peer-based recruitment strategy to promote HCV testing, linkage to care, and treatment	Observational (prospective cohort)	Conducted at an urban infectious disease clinic in Baltimore, people who inject drugs with HCV antibodies were recruited	n=25/100 (25%)	<ul style="list-style-type: none"> <li>Primary indexes received education on HCV and treatment, and then recruited injection drug use "network members" for HCV testing, linkage to care, and treatment</li> </ul>	<ul style="list-style-type: none"> <li>Prior to enrollment in the study, 69 participants were not linked to care; of these 69: 45% (n=31) went on to schedule an appointment with a provider, 36% (n=25) completed an appointment, 26% (n=18) were prescribed DAA, and 20% initiated therapy (n=14)</li> </ul>
Broad <i>et al.</i> , 2020 (14)	Canada	To determine if using peer outreach workers to deliver HCV point-of-care testing would improve engagement in HCV care	Experimental (RCT)	Peer outreach workers were current or former clients of the Toronto Community Hep C Program; they recruited their personal network members in non-health care settings who had a lifetime history of injection drug use and no prior knowledge of HCV antibody status	Data not provided	<ul style="list-style-type: none"> <li>After receiving education about HCV and harm reduction, participants (n=380) were randomized to receive either a point-of-care test (n=195) or referral to a program treatment nurse for testing (n=185)</li> </ul>	<ul style="list-style-type: none"> <li>Within six months of study enrollment, there was no change in rates of engagement in HCV care among those who received the peer point-of-care test and those who did not</li> </ul>
Conway <i>et al.</i> , 2022 (15)	Australia	To evaluate HCV treatment uptake and factors associated with enrollment following an intervention of "campaign days" promoting HCV care	Observational (retrospective cohort)	Individuals attending drug treatment clinics and/or needle and syringe exchange programs (25 sites across Australia) who had recently injected or were on opioid substitution therapy	Data not provided	<ul style="list-style-type: none"> <li>The ETHOS Engage Study integrated peer connection, point-of-care HCV RNA testing, and nurse-led linkage to care on "campaign days" hosted at drug treatment clinics and/or needle and syringe programs</li> </ul>	<ul style="list-style-type: none"> <li>Of the 317 individuals who received a positive HCV RNA result and were eligible for treatment, 15% (n=47) initiated treatment at 3 months, 27% (n=85) initiated treatment at 6 months, 38% (n=120) initiated treatment at 12 months, and 49% (n=155) initiated treatment at 24 months</li> </ul>

Table 1 (continued). Characteristics of studies examining interventions to improve engagement and retention in HCV care among people who use drugs

Author, year	Country	Objective	Study design	Study population and setting	Proportion of individuals with HIV/HCV co-infection (if reported)	Description	Reported outcomes related to linkage and retention in HCV care (visits/coming into contact with a care provider, treatment initiation of DAAs)
<b>TELEMEDICINE</b>							
Talal <i>et al.</i> , 2019 (13) <i>could also be classified under INTEGRATED SERVICES AND CASE MANAGEMENT</i>	U.S.	To assess the effectiveness of HCV care delivered virtually in a substance use program	Observational (prospective cohort)	Individuals attending a substance use program in New York City for methadone treatment	n=15/62 (24%)	<ul style="list-style-type: none"> <li>Biweekly telemedicine sessions for HCV were delivered to individuals; DAAs were co-administered with methadone</li> </ul>	<ul style="list-style-type: none"> <li>Sixty-two individuals underwent telemedicine-based HCV evaluations of which 73% (n=45) received treatment</li> </ul>
Sherbuk <i>et al.</i> , 2020 (12)	U.S.	To evaluate the effectiveness of an interdisciplinary telehealth model in treating HCV	Observational (prospective cohort)	Individuals living in Southwest Virginia, an area with a high burden of HCV and opioid use disorder	Data not provided	<ul style="list-style-type: none"> <li>A collaborative telehealth model featuring referrals to/from harm reduction programs and office-based opioid therapy, with HCV training provided to practitioners</li> </ul>	<ul style="list-style-type: none"> <li>From the 123 individuals included in the telehealth analysis, 62% (n=76) were referred from harm reduction or office-based opioid therapy sites</li> <li>Of these 123, 84% (n=103) attended a visit, 80% (n=98) completed required diagnostic testing, and 76% (n=93) initiated treatment</li> <li>The time from referral to initial visit was 17.5 days</li> </ul>
<b>INTEGRATED SERVICES AND CASE MANAGEMENT</b>							
Talal <i>et al.</i> , 2019 (13) <i>see TELEMEDICINE for description</i>							
Sherbuk <i>et al.</i> , 2020 (12) <i>see TELEMEDICINE for description</i>							
Rizk <i>et al.</i> , 2019 (21)	U.S.	To improve linkage to care and initiation of treatment by co-locating HCV care in an HIV clinic	Observational (retrospective cohort)	People living with HIV receiving care at a hospital-based clinic in Connecticut; more than half the sample were actively using drugs	n=173/173 (100%)	<ul style="list-style-type: none"> <li>Clinic leadership convened a multidisciplinary team focused on management of individuals co-infected with HIV/HCV to establish an onsite co-infection clinic</li> <li>Patient registry regularly updated with cascade data; customized engagement plans created for patients who were not being linked, referred, or treated</li> </ul>	<ul style="list-style-type: none"> <li>Of the 173 individuals eligible, 93% (n=161) were referred, 85% (n=147) were linked to care, and 71% (n=122) initiated treatment</li> </ul>
Bartholomew <i>et al.</i> , 2019 (71)	U.S.	To describe a comprehensive HCV treatment program developed at a clinic without specialist staff	Observational (retrospective cohort)	A clinic serving low-income, marginalized people in Philadelphia, where two-thirds of the population reported injection drug use	n=65/190 (34%)	<ul style="list-style-type: none"> <li>Using physician assistants and nurse practitioners, HCV care was delivered onsite</li> <li>A community testing initiative referred individuals to the clinic site where they received medical evaluation and a comprehensive, individualized treatment plan</li> </ul>	<ul style="list-style-type: none"> <li>Of the individuals referred to care at the clinic (n=190), 75% (n=143) received approval from insurance</li> <li>Of these, 93% (n=133) initiated treatment</li> </ul>



Table 1 (continued). Characteristics of studies examining interventions to improve engagement and retention in HCV care among people who use drugs

Author, year	Country	Objective	Study design	Study population and setting	Proportion of individuals with HIV/HCV co-infection (if reported)	Description	Reported outcomes related to linkage and retention in HCV care (visits/coming into contact with a care provider, treatment initiation of DAAs)
<b>INTEGRATED SERVICES AND CASE MANAGEMENT (continued)</b>							
Burton <i>et al.</i> , 2019 (72)	U.S.	To promote HCV screening, education, referral, and treatment within a residential treatment program	Observational (retrospective cohort)	Veterans admitted to a substance use disorder program in a Mississippi hospital	n=1/74 (<1%)	<ul style="list-style-type: none"> <li>All veterans admitted to the program are screened for HCV; if positive, education and evaluation are provided and treatment is started</li> <li>Following discharge from the program (typically four or more weeks), follow-up appointments for aftercare and the HCV clinic (located in the same building) are scheduled on the same day</li> <li>Follow-up letters and phone calls remind individuals of their appointments</li> </ul>	<ul style="list-style-type: none"> <li>Of the 597 unique admissions, 13% (n=74) had HCV; of these, all were evaluated for DAA treatment</li> <li>Seventy percent (n=51) initiated treatment</li> </ul>
Beiser <i>et al.</i> , 2019 (73)	U.S.	To evaluate HCV engagement and treatment outcomes in a primary care program	Observational (retrospective cohort)	Individuals referred to the Boston Health Care for the Homeless HCV program, where >80% identified injection drug use as a risk factor	n=95/510 (19%)	<ul style="list-style-type: none"> <li>Individuals were referred to the HCV program through various pathways and received a standardized intake assessment; those who attended their initial nurse appointment were considered "linked", with other supports given to encourage engagement in care</li> </ul>	<ul style="list-style-type: none"> <li>Of the individuals linked to treatment (n=510), 59% (n=300) initiated DAA treatment; of these, 95% (n=285) completed treatment</li> </ul>
Falade-Nwulia <i>et al.</i> , 2019 (22)	U.S.	To examine outcomes of an HCV care program functioning within an HIV care clinic	Observational (retrospective cohort)	Individuals receiving HIV care at the Johns Hopkins HIV clinical practice co-infected with HCV; almost three-quarters had a history of injection drug use	n=593/593 (100%)	<ul style="list-style-type: none"> <li>The co-located viral HCV clinic provides comprehensive care, testing, evaluation, treatment, and pharmacy authorization within the infrastructure of the multidisciplinary HIV care clinic</li> </ul>	<ul style="list-style-type: none"> <li>Of the 593 individuals with chronic HCV, 92% (n=547) were referred for HCV care, 87% (n=517) attended an HCV appointment, 77% (n=457) were prescribed HCV therapy, and 72% (n=426) initiated HCV therapy</li> </ul>
Radley <i>et al.</i> , 2020 (19)	Scotland, UK	To determine if a pharmacist-led pathway increased HCV treatment outcomes	Experimental (RCT)	People receiving opioid substitution therapy across pharmacies in Scotland	None: HIV+ individuals excluded	<ul style="list-style-type: none"> <li>Individuals presenting for opioid substitution therapy at 55 participating pharmacies were offered HCV testing (co-located at the pharmacies)</li> <li>Pharmacies in the conventional care group referred individuals to receive outside HCV care; pharmacies in the pharmacist-led pathway would manage HCV care on-site (HCV treatment co-located with opioid substitution therapy)</li> </ul>	<ul style="list-style-type: none"> <li>Participants in the pharmacist-led pathways were more likely to initiate treatment (8% [n=112] vs 4% [n=61]; p=0.0015)</li> </ul>

Table 1 (continued). Characteristics of studies examining interventions to improve engagement and retention in HCV care among people who use drugs

Author, year	Country	Objective	Study design	Study population and setting	Proportion of individuals with HIV/HCV co-infection (if reported)	Description	Reported outcomes related to linkage and retention in HCV care (visits/coming into contact with a care provider, treatment initiation of DAAs)
<b>INTEGRATED SERVICES AND CASE MANAGEMENT (continued)</b>							
Morris <i>et al.</i> , 2020 (59)	Australia	To determine the impact an integrated, community-based service has on the HCV cascade of care	Observational (prospective cohort)	People who inject drugs attending a treatment management program in Queensland that delivers care within a case management framework	Data not provided	<ul style="list-style-type: none"> <li>Case managers are responsible for a variety of duties, including blood test reminders, medication notifications, referral to appropriate services, and crisis intervention</li> </ul>	<ul style="list-style-type: none"> <li>From a sample of 476 individuals, 72% (n=342) initiated treatment</li> </ul>
Rowan <i>et al.</i> , 2020 (74)	U.S.	To determine if an opioid treatment program is successful in promoting linkage and engagement in care for viral hepatitis	Observational (prospective cohort)	Individuals with substance use disorder attending an opioid treatment program in Colorado	n=4/508 (<1%)	<ul style="list-style-type: none"> <li>A program for all new clients was implemented, which included screening for viral hepatitis, reengaging individuals with a past diagnosis who were untreated, and facilitating patient navigation to promote linkage to care</li> </ul>	<ul style="list-style-type: none"> <li>Of the 532 individuals who were screened for HCV, 20% (n=108) were HCV RNA positive; 60 others who were previously diagnosed but untreated were also identified (total: n=168)</li> <li>57% (n=95) of individuals who received post-test counselling from a patient navigator attended an appointment with an HCV treatment provider</li> <li>Of the individuals who attended an appointment, 76% (n=72) started HCV treatment</li> </ul>
Wade <i>et al.</i> , 2020 (61)	Australia, New Zealand	To compare DAA uptake and treatment outcomes between primary care and usual care (specialist-based hospital care)	Experimental (RCT)	People who inject drugs attending primary care (n=13) sites in Australia and New Zealand	None: HIV+ individuals excluded	<ul style="list-style-type: none"> <li>Primary care sites were equipped with nurses to provide support through the HCV care cascade while general practitioners prescribed opioid substitution therapy; outcomes were compared to usual care</li> </ul>	<ul style="list-style-type: none"> <li>In the primary care arm, 48 individuals were eligible for treatment; 90% (n=43) initiated treatment</li> <li>In the hospital care arm, 29 participants were eligible for study treatment, and 62% (n=18) initiated treatment</li> </ul>
Starbird <i>et al.</i> , 2020 (17)	U.S.	To evaluate the impact of nurse case management on engagement in the HCV care continuum	Experimental (RCT)	Individuals were HIV/HCV co-infected, but not engaged in HCV care, at a large outpatient infectious disease clinic in Baltimore	n=68/68 (100%)	<ul style="list-style-type: none"> <li>Usual care consisted of normal outpatient processes plus provision of an HCV fact sheet; the nurse case management intervention included nurse-initiated HCV referral, education, and patient navigation</li> </ul>	<ul style="list-style-type: none"> <li>Compared to patients in the usual care group, a higher proportion of individuals who received the nurse case management intervention were linked to care within 60 days of enrollment (47% vs 25%; p=0.031)</li> <li>There was no significant difference between the two groups for time to treatment initiation</li> </ul>
Metsch <i>et al.</i> , 2021 (65)	U.S.	To determine if a care facilitation intervention improved steps along the HIV/HCV care cascade	Experimental (RCT)	People co-infected with HIV/HCV attending care in eight U.S. cities	n=113/113 (100%)	<ul style="list-style-type: none"> <li>The care facilitation group received motivation and strengths-based case management to support engagement in HIV/HCV care and medication adherence</li> <li>The control group received referral to HCV care and assistance in appointment scheduling</li> </ul>	<ul style="list-style-type: none"> <li>The average number of care cascade steps completed was significantly higher in the intervention group compared to the control group</li> </ul>

Table 1 (continued). Characteristics of studies examining interventions to improve engagement and retention in HCV care among people who use drugs

Author, year	Country	Objective	Study design	Study population and setting	Proportion of individuals with HIV/HCV co-infection (if reported)	Description	Reported outcomes related to linkage and retention in HCV care (visits/coming into contact with a care provider, treatment initiation of DAAs)
<b>INTEGRATED SERVICES AND CASE MANAGEMENT (continued)</b>							
Losikoff <i>et al.</i> , 2022 (18)	U.S.	To examine the relationships between integrated (opioid use disorder and HCV) treatment interventions on both HCV and opioid use outcomes	Observational (retrospective cohort)	Individuals attending an OUD treatment program for substance use disorders in Massachusetts living with chronic HCV	None: HIV+ individuals excluded	<ul style="list-style-type: none"> <li>The intervention group engaged in integrated HCV treatment with DAA (dispensed with their OUD medication) and were compared to patients with HCV who only received OUD treatment</li> </ul>	<ul style="list-style-type: none"> <li>Of the 646 individuals who met the criteria for HCV treatment, 74 received the integrated (HCV and opioid use disorder) treatment regimen</li> <li>Patients who received integrated treatment were 13.4 times more likely to be retained in care with medication for opioid use disorder than patients who were not in the intervention group</li> </ul>
Bartlett <i>et al.</i> , 2022 (20)	Canada	To determine the association between opioid substitution therapy and HCV treatment initiation	Observational (retrospective cohort)	Individuals in the British Columbia C Hepatitis Testers Cohort who use drugs who had ever taken opioid substitution therapy	n=1,409/13,803 (10%)	<ul style="list-style-type: none"> <li>Of participants followed in the DAA era, 33% (n=4,594) had never received opioid substitution therapy</li> <li>Of participants followed in the DAA era, 68% (n=9,321) were untreated</li> </ul>	<ul style="list-style-type: none"> <li>One year after diagnosis, those currently on opioid substitution therapy had higher probability of starting HCV treatment compared to those not on opioid substitution therapy</li> </ul>