

Practical steps to improve chronic hepatitis C treatment in people with opioid use disorder

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Objectives: People with a history of injecting drugs have high prevalence of hepatitis C virus (HCV) infection, and many have opioid use disorder (OUD). Modern HCV therapies with improved efficacy and tolerability are available, but access is often limited for this group, who may be underserved for health care and face social inequity. This work develops practical steps to improve HCV care in this population.

Methods: Practical steps to improve HCV care in OUD populations were developed based on clinical experience from Spain, structured assessment of published evidence.

Results: Options for improving care at engagement/screening stages include patient education programs, strong provider–patient relationship, peer support, and adoption of rapid effective screening tools. To facilitate work up/treatment, start options include simplified work up process, integration of HCV and OUD care, and continuous psychosocial support prior, during, and after HCV treatment.

Conclusion: It is important to plan on local basis to set up a joint integrated approach between specific drug treatment services and local points of HCV care. The elements for a specific integrated program should be chosen from options identified, including education services, peer input, organization to make HCV screening and treatment easier by co-location of services, and wider access to prescribing direct-acting antiviral (DAA) therapy.

Keywords: HCV, opioid use disorder, treatment, elimination, practical recommendations

Introduction

Chronic hepatitis C virus (HCV) infection is common in people with a history of injecting drugs and opioid use disorder (OUD).^{1,2} In Europe, it is estimated that 2–3 million individuals have a lifetime history of injecting drug use, including 1.5 million who have a recent history of OUD.² HCV infection is prevalent in 14–84% of such groups.³ Despite high prevalence, individuals in these groups are often marginalized and have limited access to general health care.⁴ Increasing mortality/morbidity due to advanced liver disease defines a major public health problem among people with a history of injecting drugs and OUD⁵ and calls for enhanced access to HCV care for such a marginalized population.⁶

Direct-acting antiviral (DAA) drugs indicated for HCV treatment, with improved efficacy, safety profile, and tolerability, when compared with interferon-based regimens, have transformed outcomes.⁷ DAA regimens are effective in patients receiving opioid agonist therapy (OAT)/opioid substitution therapy (OST) for OUD.^{8–10} Many people with a history of injecting drugs are engaged with OUD treatment services¹¹;

in Europe, the proportion of engagement with OUD care is 40–90%.¹² In Spain, an estimated 60–80,000 people are engaged with OUD treatment services,² of whom 50–80% are infected with HCV.^{2,13} OUD care is often provided by social services, municipal authorities, or the national health service, in different settings within each region or country.^{2,12,13} These centers are separated from potential points of care for HCV.¹² In Spain and other countries, OUD treatment is provided in specialist-led, often standalone offices or clinics; HCV specialist services are not co-located in many cases.^{5,12} Local arrangements for HCV management clinical services are the responsibility of different parts of the health care system, including infectious diseases, internal medicine, and hepatology departments. These organizational factors limit the success of HCV care; social and provider-related barriers to HCV care are also significant.¹⁴

The objective of this work is to identify practical steps to improve HCV treatment in people with a history of injecting drugs and OUD based on clinical experience and relevant evidence in this evolving area.

Methods

Evidence describing interventions that may improve outcomes in the management of HCV treatment in the context of OUD was collected and assessed. A structured approach to organize analysis was followed, applying an existing

framework of a patient journey.^{2,15} This framework describes treatment in steps from potential initial presentation at a drug treatment service through steps of engagement, screening, work up/referral, and treatment (Figure 1).

Evidence collection

A structured search of published literature from PubMed, Web of Science, and Cochrane databases was completed using a set of predefined search terms (Table 1). The search was restricted to publications after 2012, when the first DAA medications became available. A specific additional search of the proceedings of recent, relevant scientific expert meetings was completed to capture the most recent evidence. This focused on the major academic congresses of the leading professional societies, as identified by experts highly familiar with the therapy area. These included American Association for the Study of Liver Diseases (AASLD), European Association for the Study of the Liver (EASL), and British Association for the Study of the Liver (BASL). Two reviewers familiar with structured literature searches and the therapy area assessed evidence independently and analyzed data. A total of 597 articles (PubMed=457, Web of Science=110, and Cochrane=30) and 443 abstracts (AASLD 2017=335, EASL 2017=64, and BASL 2017=44) were screened for relevance (Figure 1). Studies were included if they described effective practice or policy interventions in improving care generally

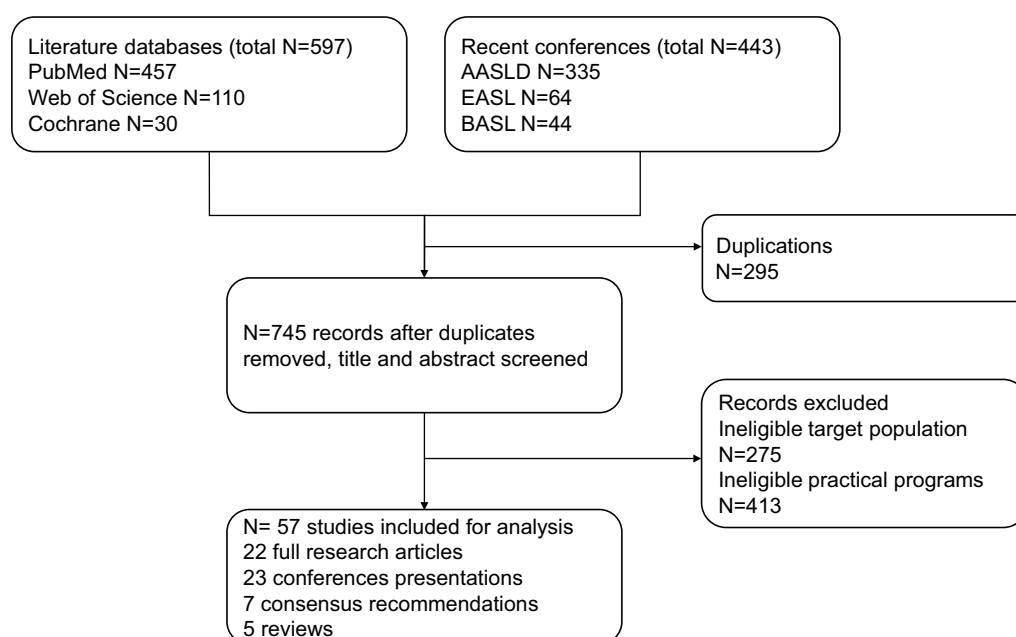


Figure 1 Summary of the process for literature search.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; BASL, British Association for the Study of the Liver; EASL, European Association for the Study of the Liver.

Table 1 Summary of keywords used in literature search

<p>General terms related to HCV care and opioid use disorder ("hepatitis C management" OR "hepatitis C treatment" OR "HCV therapy" OR "Treatment of chronic HCV infection" OR "hepatitis C care" AND "People with a history of injecting drugs" OR "IDU" OR "PWID" OR "Opioid Use Disorder" OR "opioid dependence" OR "opioid addiction" OR "intravenous drugs" OR "intravenous substance" OR "Injecting drug" OR "injecting drug user" OR "heroin").</p> <p>Additional keywords specific to patient journey: "hepatitis C patient presentation" OR "hepatitis C awareness" OR "hepatitis C engagement" OR "Hepatitis C screening" OR "hepatitis C diagnosis" OR "hepatitis C disease staging" OR "hepatitis C fibroscan" OR "hepatitis C workup" OR "assess for hepatitis C treatment" OR "hepatitis C referral" OR "hepatitis C specialist" OR "complete hepatitis C treatment" OR "hepatitis C treatment adherence"</p>
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Abbreviation: HCV, hepatitis C virus; IDU, injecting drug users; PWID, people who inject drugs.

or for HCV specifically in people with a history of injecting drugs and OUD. Evidence from the literature review was then prioritized to identify most important practical steps to improve HCV care for people with OUD. Priorities were chosen by the authors (all with extensive clinical experience in HCV or OUD care) based on the opinion of potential impact. Interventions described in 57 studies, including 22 full research articles, 5 reviews, 23 abstracts/posters from conferences, and 7 consensus recommendations were chosen for analysis.

Results

A series of possible options for improving OUD care at each stage of the patient journey were defined based on an analysis of evidence obtained from the literature search and analysis (Table 2). Studies showing effective practical interventions for improving HCV care in such populations are summarized in Table 2. Results are described according to steps on the patient journey.

Possible tactics to improve patient outcomes

Engagement

Low engagement may be addressed by education programs: for patients, options include brief group sessions at drug treatment services including workshops, Q&A sessions, leaflets, videos on the basics of HCV and risk behaviors for transmission, HCV treatment pathway, right of equal access,^{16,17} and interactive digital health decision aids.¹⁸ Education sessions for health care professionals (HCPs) directed in primary care¹⁹ and drug treatment services,¹⁷ and HCV awareness campaigns directed to the general public may be of benefit. Programs that actively seek patients such as pop-up and short-term services delivered by clinics in neighborhoods with high HCV prevalence are effective in promoting treatment engagement.²⁰

Developing strong provider–patient relationships improves outcomes by creating an “enabling environment”

and avoiding stigma.^{21,22} Peer support improves engagement with medical interventions^{23,24} and can address potential mistrust and fear of discrimination.²⁵

Screening

Adoption of fast and effective screening methods improves efficiency. Dried blood spot testing (DBST) offers antibody testing and RNA confirmation in one step²⁶ and can be effectively implemented in drug treatment services,^{27–29} alcohol clinics, prisons, needle equipment services,²⁸ or via out-reach mobile services.³⁰ A pretesting questionnaire-based screening tool helps identify people who may benefit most from testing in primary care.³¹ Community-based active case finding with rapid antibody oral fluid test, either by peer facilitation³² or by temporary clinics,²⁰ increases screening rate in high-risk populations. Targeted screening at general practices in areas of deprivation and high prevalence of injecting drug use,³³ or at drug treatment services, increases screening outcomes. For people with a history of injecting drugs who tested negative, it is important to offer routine testing every 12 months and following any high-risk injecting episode.^{11,34}

Work up/referral

Simplified work up with access to noninvasive methods such as transient elastography (TE) (also known as Fibroscan) and serum biomarker tests accelerates the workup process and enables triage for immediate care^{35–37} implemented at drug treatment services, primary care, medically supervised injecting centers,³⁸ street-based outreach programs, or in prison.³⁷ Mobile TE further provides convenience in drug treatment services²⁹ or in mobile out-reach programs for hard-to-reach populations of drug users, prisoners, homeless, and psychiatric patients³⁰ or at primary care.³⁹ Noninvasive serum biomarker tests also eliminate many of the concerns associated with liver biopsy.³⁶ The aspartate aminotransferase-to-platelet ratio index (APRI), a calculated score predicting fibrosis,³⁷ is an effective prescreening tool to reduce the number of

Table 2 Summary of effective practical interventions in improving HCV care in patients with a history of injecting drugs and OUD

Step	Country	Intervention	Key findings	Reference
Engagement	Portugal	Patient education program	A multidimensional education program including workshops, educational videos, leaflets, and HCP workshops improved patient knowledge and increased rate of patient referral to a liver specialist	17
	USA		Provision of a formal HCV education class reduced time to the initiation of HCV treatment, increased patient knowledge and interest in treatment, and improved patient-provider communication	19
	USA	Interactive digital health decision aid	A tailored mobile electronic health decision aid developed to support methadone patients acceptable to people in treatment; viewed as useful for supporting engagement with HCPs	18
	USA	HCP education program	Liver health training program for SUD clinic teams improved the implementation of recommended practices for HCV screening and referral	16
	Netherlands	HCV public awareness campaign	A public HCV campaign including radio and newspaper ads and information material distributed at public places increased number of anti-HCV tests 1.36-fold in a 3-month period. Addition of a support program for primary care produced a further 2.2-fold increase in test frequency	76
	Canada	Community "pop-up" clinic	371 previously undiagnosed patients have been identified and 43% linked to multidisciplinary care with promising early results for those receiving treatment	20
	UK	Negotiated flexibility in service provision approach	London health care providers adopted a "negotiated flexibility" approach to appointments, eligibility, substance use, and phlebotomy to facilitate the trust and engagement of PWID	72
	Australia	Peer support service	Peer support service improved engagement, helped to build trusting relationships, and provided instrumental support for clients to access HCV treatment. Peer workers may also contribute to more effective deployment of health resources by preparing clients for clinical engagement with HCV health workers	23
Screening	Australia	Integrated peer support worker model	In an OST clinic with integrated peer support model, peer support workers facilitated broader discussion about HCV treatment, education, and support. This approach allows nurses to focus on assessment and treatment and may address some barriers to care	24
	Scotland	Integrated DBST	DBST was effectively carried out at drug treatment and needle exchange services following appropriate training of staff. A total of 324 "hard to reach" patients tested HCV antibody positive within a 2-year period, 249 of whom attended for further follow-up	27
	UK	Community-based nurse-led DBST	Interim data showed high treatment uptake compared to hospital-based settings and suggested that HCV care can be effectively provided through a community-based model	77
	France	DBST via out-reach mobile services	Hepatitis Mobile Team carried out 944 dry DBST for hard-to-reach patients. A total of 244 new patients identified by DBST screening, 49% achieved HCV cure	30
	Egypt	Questionnaire-based HCV risk screening tool	The first level-screening tool assessed risk factors significantly associated with HCV infection. Integration of such a tool into primary care practice can promote early detection	31
	UK	Community-based active case finding by peer facilitation	379 homeless people were screened over a 1-year period. A total of 68 HCV-positive cases identified and offered referral to NHS Hepatology services	32
	Scotland	Targeted screening at general practices	Test uptake and case yield were approximately 3 and 10 times higher in general practices where HCV testing was offered for IDU compared with control practices	33
Work	USA	Targeted screening at drug treatment services	Implementation of a multifaceted screening program at an SUD clinic increased patient referral rates to specialist care	78
	Australia	APRI score	APRI score may be used as a simple noninvasive biomarker for cirrhosis with reasonable predictive accuracy	37

(Continued)

Table 2 (Continued)

Step	Country	Intervention	Key findings	Reference
	Australia	TE	PWID viewed TE as a highly acceptable diagnostic method; 89% of patients who have undergone TE viewed it as preferable to liver biopsy or blood sample	38
	UK	Community outreach service through addiction clinics	Portable Fibroscan was implemented as a part of an HCV outreach service in a community addiction clinics. Median time from referral to treatment initiation was 32 weeks	39
	Canada	Patient survey	Survey of patient's needs and preferences showed no single preferred approach for different aspects of care; a multipronged and flexible approach at all stages of the patient pathway is most likely to be successful	40
	USA	Peer mentors	Patients receiving usual care with the addition of peer mentors had a significantly higher rate of HCV treatment initiation when compared to usual care alone	41
	Portugal	HCP education program	A multidimensional health education program for patients and HCP at seven drug treatment centers significantly increased rates of patient referral to a liver specialist, from 56.2 to 67.5%	17
Treatment	USA	Integrated treatment in primary care	PCPs were trained to treat HCV through video conferencing, case-based learning, and mentoring. They were generally confident treating patients, and the majority will begin providing care independently after 1 year	43
	Switzerland	Integrated treatment at drug treatment services	Implementation of an onsite multidisciplinary HCV team and noninvasive fibrosis assessment at a drug treatment center increased HCV assessments and treatment uptake when compared with previous model of hospital referral	44
	UK		105 patients were recruited through needle exchange centers over 42 months; 89 patients received treatment in a needle exchange; 74 patients successfully achieved SVR	45
	Spain	Integrated treatment in prisons	The highly successful JailFree-C program involved universal screening of inmates and integrated HCV treatment. A total of 821 inmates tested, 81 identified as viremic, and 64 received treatment. SVR rates were similar to those in community	46
	USA	HCV treatment as a part of integrated OUD treatment plan	HCV care delivered under-one-roof as a part of an OAT program achieved high rates of SVR12 among 136 participants (93%)	47
	USA		HCV care within an office-based OST clinic was successfully set up; 95% of patients achieved early viral response at 4 weeks and SVR was achieved by 100% of patients who completed treatment	48
	UK		Predictive modeling and sensitivity analyses used to project future HCV population suggested that combining HCV antiviral treatment with OAT and needle equipment programs could have chronic HCV prevalence over 10 years	49
	Ukraine		A community-involved model providing integrated HCV treatment and drug treatment services has successfully enrolled over 1,200 patients for HCV treatment, 546 achieved SVR 12 weeks posttreatment	50
	USA		Embedding of addiction specialists in an HCV clinic to provide integration between methadone clinic and hepatitis clinic sites improved patient's adherence with HCV care in comparison to standard referral practices	51
	USA	Education program for PCP	Training program allowed 700 patients to be treated at clinics not previously authorized to provide care for HCV demonstrating the power in this approach to facilitate up-scaling of effective HCV treatment	52
	Australia	DAA prescribing by PCP	Innovative teleconferencing approach allowed HCV care to be effectively provided by PCPs and may facilitate treatment in populations engaged with other treatment services	53
	Australia	DAA prescribing in nurse-led drug treatment services	A nurse-led model of HCV care provision in OST clinics was implemented and has reviewed over 300 patients with viral hepatitis with therapy initiated in 40 patients and notable increase in GP referrals	54

(Continued)

Table 2 (Continued)

Step	Country	Intervention	Key findings	Reference
	Australia	Community hepatitis service	Community-based nurse-led hepatitis service produced reasonable rates of fibrosis staging (72%) and treatment initiation (20%) for PWID. A total of 70% of genotype 1 patients and 54% of genotype 3 patients achieved SVR	55
	USA	DAA prescribing in primary care	Access to HCV treatment at a primary care clinic under the supervision of a hepatologist resulted in high screening rates and cure rates similar to those reported elsewhere	56
	Australia	DAA prescribing in prisons	APRI score was used for patient evaluation and DAA therapy prescribed to relevant patients to provide successful care in a resource-limited prison setting	37
	USA	DAA prescribing at pharmacist-led clinics	HCV treatment including DAA therapy provided through pharmacist-managed clinics recorded similar SVR rates to those achieved in primary care. Pharmacists can be used to help widen access to effective care for HCV	58
	Switzerland	Digital platform for clinical decision making	Smartphone application for access to national treatment guidelines provided faster access to more detailed and specific information to facilitate clinical decision making when compared with traditional web-based publications	59
	USA	Teleconsultation	Patients approved assessment by two-way video conferencing, and there have been high rates of medication adherence in the telemedicine-based HCV care program	60
	Canada	Community HCV program with psychosocial support	A community-based highly supportive model (which included counseling, case management, peer workers, and other services) promoted high levels of treatment and adherence among marginalized groups	61
	Denmark	Tailored treatment duration	4-Week treatment regime with LDV/SOF/RBV \pm PEG2 was highly effective in treating OST patients, with all but one patient in the per protocol population achieving SVR12	62
	Australia	Contingency management	Patients with injecting drug use were significantly more likely to complete an HBV vaccination series if they received a 30 AUD financial incentive per dose compared to those in the no incentive control condition	63
	Canada	Enhanced long-term follow-up post-treatment	A multidisciplinary care program with enhanced long-term follow-up achieved high SVR rates and low rates of recurrent viremia following therapy	65
	Greece		A model developed to simulate HCV transmission among PWID demonstrated the need for scaled-up harm reduction interventions to maintain reductions in HCV prevalence and prevent any resurgence	66

Abbreviations: APRI, aspartate aminotransferase-to-platelet ratio index; AUD, Australian dollars; DBST, dried blood spot testing; GP, general physician; HCPs, health care professionals; HBV, hepatitis B virus; HCV, hepatitis C virus; IDU, injecting drug users; LDV/SOF/RBV, Ledipasvir/ Sofobuvir/ Ribavirin; NHS, National Health System; OAT, opioid agonist therapy; OST, opioid substitution therapy; OUD, opioid use disorder; PCPs, primary care physicians; PWID, people who inject drugs; SVR, sustained virologic response; SUD, substance use disorder; TE, transient elastography.

patients requiring Fibroscan.³⁷ Logistic support such as tailored flexible scheduling facilitates work up completion.⁴⁰

A tailored approach with different options for engagement is most likely to be successful.⁴⁰ Referral processes can be facilitated by education for HCP at drug treatment services¹⁷ and primary care;¹⁹ support from peer mentors facilitates linkage to start HCV treatment.⁴¹

Treatment

A single-location clinic with access to a multidisciplinary team is effective in facilitating the progression from patient identification to HCV treatment.^{20,42} Integrated HCV treatment can

be provided at primary care,^{39,43} drug treatment services,^{39,44} needle equipment services,⁴⁵ or prison.⁴⁶ It can be as a part of a traditional integrated treatment plan for OUD,^{47,48} or as a part of a combined program of integrated drug treatment, HCV, and needle equipment program,^{49,50} or for people who are actively injecting and not receiving integrated treatment for OUD.⁴⁵ Addiction specialists based in HCV clinics⁵¹ or mobile teams for screening, diagnosis, and treatment may address underserved populations.³⁰ Wider prescribing options for DAA including primary care physicians (PCPs) increases treatment access;^{43,52,53} treatment can be delivered in nurse-led drug treatment services,^{39,54} primary care,^{39,55,56} prison,⁵⁷ or pharmacist-led clinics.⁵⁸

Smartphone or desktop digital platforms assist clinical decision making and facilitate treatment initiation.⁵⁹ Teleconsultation is effective in overcoming physical barriers of having to meet with the HCV specialists.⁶⁰

Adherence to treatment can be facilitated with psychosocial support, such as continuous counseling,⁶¹ case management services, actively screening for psychiatric comorbidities with referral to mental health providers including co-located specialists at HCV clinics and referral to peer-support groups with OUD care and buddy systems. Shorter treatment duration tailored to the population of injecting drug users may be effective.⁶²

Peer-led models combined with multidisciplinary care lead to improved knowledge, treatment uptake, and service provision.^{23,25} Contingency management, including monetary incentives, is effective in improving adherence to hepatitis B virus vaccination⁶³ and promotes HCV treatment initiation⁴¹ among people with a history of injecting drugs. Developing or implementing existing national strategies, action plans, and guidelines for HCV treatment in people with a history of injecting drugs helps establish best practices.⁶⁴

Re-infection risk is limited by long-term follow-up with access to multidisciplinary care and harm reduction services after HCV treatment.^{65–67} Regular HCV testing after the treatment and analysis of risk factors for re-infection is helpful for early engagement for potential interventions.^{5,11,68,69}

Discussion

DAA regimens offer the possibility of cure for HCV. People with a history of injecting drugs and OUD represent a major group requiring HCV treatment but find it hard to access care. It is the opinion of the authors that it is essential, now, to address limits to therapy access if HCV treatment uptake is to be available to all and eradication of the infection is to be achieved. Many citizens with great need for HCV therapy cannot navigate pathways to get the HCV care they need. Law, policy, and guidelines in many European countries defines the equality of access to health care for all citizens and increasingly for HCV treatment – it is the reality that despite this and if action is not taken, many with the greatest needs will not be able to access proven treatment for a serious condition.

This structured assessment identifies practical steps from published evidence, which can improve HCV care in people with a history of OUD. Recommendations for practical steps to improve care are shown in Figure 2 and summarized here:

1. Provide peer-led education for patients with OUD including updates on HCV and liver health, DAA therapy, right of equal access to therapy, and how to navigate treatment pathways.^{17,18,70}
2. Develop “enabling” provider–patient relationships^{22,71,72} to support HCV treatment pathway navigation.^{19,73}

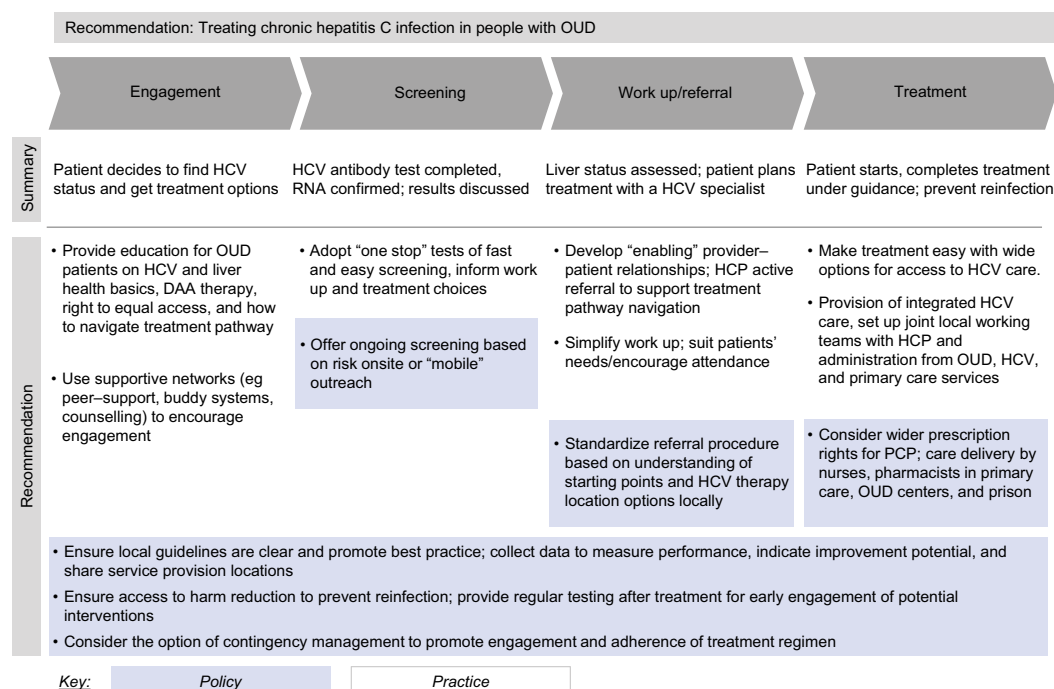


Figure 2 Practical recommendations for best practices of HCV treatment for people with OUD.

Note: A patient journey model, with steps of engagement, screening, workup/referral, and treatment, is used to structure practical recommendations.

Abbreviations: DAA, direct-acting antiviral; HCV, hepatitis C virus; HCP, health care professionals; PCP, primary care physician; OUD, opioid use disorder.

3. Standardize HCV referral procedure based on the understanding of starting points and treatment location options and use supportive networks (eg, peer support, buddy systems, counseling) to encourage engagement.^{23–25}
4. Provide “one stop” fast and easy screening services, providing all necessary diagnostic information.^{5,27–29} Offer ongoing screening based on risk onsite or with “mobile” outreach.^{11,20,30,33,34}
5. Simplify work up to encourage attendance; develop local capability with noninvasive liver assessment within drug treatment clinics.^{29,36,38,70}
6. Make treatment easy with wide options for access to HCV care services. Implement wider prescription rights for PCP^{43,52} and care delivery by nurses and pharmacists in primary care, drug treatment services, and prison.^{39,43,54,57,58}
7. Provide integrated HCV care,^{5,11,39,42,47,51,74} set up joint local working teams of HCP and administration from OUD, HCV, and PCP services focused on HCV treatment.
8. Review service results jointly to set standards of care and inform service development including “all under one roof” models and develop local guidelines to promote best practice.⁶⁴
9. Collect data to measure performance, indicate improvement potential, share results among local service providers and locations.
10. Ensure continuing access to harm reduction to prevent reinfection; provide regular testing after treatment for the early engagement of potential interventions.^{5,11,66–68,75}

This recommendation is based on the clinical experience of clinicians with highly relevant long-term experience and interpretation of a review of current evidence. Evidence is collated from available published sources; this work is limited in this respect – in this evolving field, it is important to reconsider this work in the light of new evidence, in the future. Priorities are set based on clinical experience in Spain and observation of international practices. It is noted that the challenges for HCV and OUD treatment services are common in other countries¹² and that the wide range of models of care and experience in managing HCV in Spain and its regions may be representative of the approach in many other countries. This work identifies practical steps based on clinical factors; there are other social and provider-related factors outside the scope of this article that are important to address in this population.

Conclusion

People with a history of injecting drugs engaged with OUD care services often face considerable barriers for HCV care.

The recommendations advocated here for practical steps to improve care should be considered by all aiming to improve outcomes for marginalized populations who may find it difficult to access treatment for HCV.

Abbreviations

APRI, aspartate aminotransferase-to-platelet ratio index; DAA, direct-acting antiviral; DBST, dried blood spot testing; HCPs, health care professionals; HCV, hepatitis C virus; OAT, opioid agonist therapy; OST, opioid substitution therapy; OUD, opioid use disorder; PCPs, primary care physicians; TE, transient elastography; IDU, injecting drug users; PWID, people who inject drugs.

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Disclosure

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