

WJG 20<sup>th</sup> Anniversary Special Issues (2): Hepatitis C virus**Hepatitis C virus control among persons who inject drugs requires overcoming barriers to care**

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**Abstract**

Despite a high prevalence of hepatitis C virus (HCV) infection, the vast majority of persons who inject drugs (PWID) have not engaged in HCV care due to a large number of obstacles. Education about the infection among both PWID and providers remains an important challenge as does discrimination faced by PWID in conventional health care settings. Many providers also remain hesitant to prescribe antiviral therapy due to concerns about adherence and relapse to drug use resulting in reinfection. Presently, however, as a result of improvements in treatment efficacy combined with professional society and government endorsement of

HCV treatment for PWID, a pressing need exists to develop strategies to engage these individuals into HCV care. In this article, we propose several strategies that can be pursued in an attempt to engage PWID into HCV management. We advocate that multidisciplinary approaches that utilize health care practitioners from a wide range of specialties, as well as co-localization of medical services, are strategies likely to result in increased numbers of PWID entering into HCV management. Pursuit of HCV therapy after stabilization through drug treatment is an additional strategy likely to increase PWID engagement into HCV care. The full impact of direct acting antivirals for HCV will only be realized if innovative approaches are pursued to engage all HCV infected individuals into treatment.

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**Key words:** Treatment of hepatitis C; Viral infection; Human immunodeficiency virus; Hepatitis C virus coinfection; Persons who inject drugs; Obstacles to treatment

**Core tip:** Despite persons who inject drugs (PWIDs) representing the majority of the hepatitis C virus (HCV) disease burden, few receive treatment for HCV. Barriers to treatment uptake exist at multiple levels. Co-localization of HCV management with substance abuse facilities may result in greater treatment uptake for PWID.

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## INTRODUCTION

Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease affecting more than 120 million people worldwide<sup>[1,2]</sup> and at least 3.2 million in the United States<sup>[3-5]</sup>. Among HCV-exposed individuals, up to 80% will develop chronic infection that can ultimately lead to hepatic fibrosis, cirrhosis, hepatocellular carcinoma and death<sup>[6]</sup>. The prevalence of cirrhosis is estimated to increase from 25% in 2010 to 45% by 2030 in untreated patients with chronic HCV infection, and liver-related deaths are projected to increase by 175% over the next decade<sup>[7]</sup>. Currently, HCV is the leading indication for liver transplantation in the United States<sup>[8]</sup>.

As the virus is most effectively transmitted via blood, injection drug use is currently the primary route of HCV transmission in the United States and other developed countries. Among persons who inject drugs (PWID), estimated HCV prevalence ranges from 30% to 70%, depending on frequency and duration of use, while incidence ranges from 16% to 42% per year<sup>[9,10]</sup>. Additionally, up to 20% of human immunodeficiency virus (HIV)-infected PWID in the United States are co-infected with HCV<sup>[11]</sup>. A recent study predicted that for a PWID population with 20% baseline chronic HCV prevalence, treatment rates of 5, 10, 20 or 40 per 1000 annually can lead to a 15%, 30%, 62% and 72% reduction in prevalence after 10 years, respectively<sup>[12]</sup>. The same authors have also estimated that novel treatments, expected to result in viral clearance rates of 90%, can halve HCV prevalence of 25%, 50%, and 65% within 15 years with treatment rates of 15, 40, or 76 per 1000 PWIDs annually<sup>[13]</sup>. Therefore, addressing HCV infection among PWID is a crucial step toward its successful control and prevention.

Despite the fact that PWID represent the majority of the HCV disease burden in developed countries, only 21%-65% have been evaluated for HCV, with less than 20% of evaluated patients receiving treatment<sup>[14-16]</sup>. Moreover, while the majority (> 70%) of PWID initially express willingness to undergo HCV treatment, only a minor percentage (1%-6%) actually receives therapy<sup>[14,16,17]</sup>. A variety of factors limit enrollment of PWID into HCV care and treatment. Identification of these barriers is therefore a key step toward formulating interventions to increase access to HCV care for PWID. Our goal in this article is to highlight the obstacles to providing HCV care to PWID and to propose interventions by which these barriers can be overcome.

## BARRIERS TO HCV TREATMENT IN PWID

Obstacles to providing HCV care to PWID emanate from patients, health care providers and the health care system<sup>[18]</sup> (Table 1). One of the most important patient level obstacles to receiving care is lack of HCV-related knowledge resulting in a low perceived need for treatment. Between 65%-75% of HCV-infected patients are unaware of their status<sup>[19]</sup>. While many patients are aware that treatment for HCV exists, few are cognizant that it

**Table 1 Most common barriers to engagement of persons who inject drugs into care for hepatitis C virus infection**

Domain	Specific barrier
Patient-level	Low perceived treatment need
	Fear of side effects
	Lack of knowledge of serostatus
	Fear of liver biopsy
	Needles may promote relapse
	Coexisting mental health diagnosis
Physician-level	Lack of insurance, poverty, low socioeconomic status
	Concerns about reinfection
	Biases against PWID
	Adherence concerns
Health system-level	Dual diagnoses
	Navigation can be complex
	Mistrust between PWID and medical community
	High cost of HCV treatment
	Stigmatization in health care venues

HCV: Hepatitis C virus; PWID: Persons who inject drug.

is curative. Some PWID are reluctant to undergo liver biopsy, an invasive procedure that has been frequently required prior initiation of HCV treatment. The presence of needles that are required for interferon injection might also be an obstacle to treatment in some persons who previously injected drugs. Additionally, many PWID perceive treatment-related side effects to be worse than the virus itself. Finally, mistrust of the health care system and difficulty keeping medical appointments may also contribute to PWID's unwillingness to initiate HCV therapy<sup>[14]</sup>. PWID are also more likely to be uninsured, have limited access to health care services, be affected by poverty, and have reduced social support<sup>[20]</sup>.

Provider barriers also contribute to low rates of treatment provision to PWID. Patients who report injecting drugs are less likely to be referred for HCV evaluation and less likely to receive HCV treatment<sup>[21,22]</sup>. Many health care providers remain hesitant to treat patients with a history of drug use due to concerns about adherence to the therapeutic regimen. Some providers avoid treatment of PWID due to the misconception that reinfection occurs at a high level following relapse to injection drug use<sup>[23]</sup>. Finally, people with drug addiction have been perceived as challenging patients because they are more likely to be dually diagnosed with psychiatric co-morbidities, such as depression and anxiety, compared to non-addicted individuals<sup>[24]</sup>.

The health care system itself may pose numerous obstacles to HCV treatment of PWID. The United States health care system is complex and the referral and scheduling process, as well as insurance and payment issues, can be difficult to navigate. Long-seated, distrusting relations between PWID and the medical community have contributed to feelings of stigmatization among those seeking HCV treatment. PWID often experience health care providers as judgmental, unresponsive to their medical needs, and disdainful, all of which serve as systemic barriers to care.

Finally, high cost of HCV therapy is another treatment barrier. For example, the estimated total cost of

telaprevir-based therapy, including the cost of side effect management, can be as high as \$147000<sup>[25]</sup>. Although this problem is not specific to PWID, it certainly affects them to a greater extent compared to general population, particularly as PWID are more likely to be uninsured and to have less financial resources.

Excluding PWID from HCV treatment contradicts current recommendations issued by several United States governmental and relevant professional organizations. Governmental bodies, including the Institute of Medicine (IOM)<sup>[26]</sup> and the Department of Health and Human Services (HHS)<sup>[27]</sup>, now advocate for increased awareness and resources to address the issue of disparities in HCV treatment for PWID. Professional organizations such as the American Association for the Study of Liver Disease (AASLD)<sup>[28]</sup>, have stated in their guidelines that PWID should be treated for HCV. Yet despite these recommendations, PWID are frequently excluded from therapy by the health care system.

## OVERCOMING THE OBSTACLES TO HCV TREATMENT FOR PWID

Through advances in HCV management, we are now experiencing partial resolution of the obstacles to HCV treatment among PWID. The rapid acceleration of HCV treatment toward an all oral regimen with improved efficacy and fewer adverse effects will likely result in the elimination of the liver biopsy as a requirement to initiate treatment. Additionally, the avoidance of needle exposure associated with interferon injection would eliminate anxiety among persons who no longer inject drugs. The onus now moves toward strategy development to address other obstacles in the management of HCV in PWID.

As patient-related obstacles can derive from misconceptions and lack of HCV-related knowledge, appropriately designed educational interventions could prove beneficial in promoting HCV care and treatment. Unfortunately, while nationwide surveys in the United States have documented that most opioid agonist treatment (OAT) facilities provide at least some form of HCV education<sup>[29,30]</sup>, patients infrequently avail themselves of these opportunities<sup>[31]</sup>. Increased awareness of potential benefits of such programs and the addition of patient incentives, such as financial compensation or travel stipends, might increase participation. Peer support groups, directed by treatment-experienced patients, could encourage treatment acceptance and provide emotional support through shared treatment experiences. Support from mental health and allied health professionals to assist with procurement of social and mental health services, temporary disability, accessing Medicaid, and obtaining transportation, may potentially increase involvement in HCV treatment. These interventions can be incorporated into an individualized treatment plan to maximize adherence rates and successful outcome achievement.

Other obstacles to provision of HCV care and treatment result from lack of HCV-related knowledge and

misconceptions among health professionals regarding PWID. These barriers may be overcome by provider education about PWID or by close collaboration between health care providers from diverse specialties<sup>[32]</sup>. Involvement of a multidisciplinary team consisting of representatives of hepatology, addiction medicine, generalists, and mental health experts in the treatment of HCV for PWID has been shown to result in increased treatment efficacy<sup>[32]</sup>. Besides direct interaction for the purposes of patient care, mentoring programs conducted between HCV specialists, substance abuse treatment staff, and peers could increase knowledge and build the skills necessary to treat this population. Mentoring programs could be conducted in person or via telemedicine.

A recent meta-analysis demonstrated that HCV treatment outcomes among PWID were improved among those treated for opioid addiction compared to untreated individuals<sup>[32]</sup>. In addition, rates of successful treatment outcomes for PWID were shown to be almost identical to outcomes achieved in registration trials<sup>[32,33]</sup>. However, while occasional drug use does not impact on adherence, treatment completion or treatment efficacy, frequent drug use (daily or every other day) does<sup>[34]</sup>. Consequently, successful outcomes for HCV are more likely to be achieved if PWID who inject frequently are initially stabilized for their addiction and subsequently undergo HCV therapy.

By co-localizing both HCV preventive and treatment services at venues where PWID receive care for drug addiction, uptake of HCV services might increase. For example, due to annual HCV serologic testing in some OAT facilities, HCV-infected patients have been more readily identifiable. At present, however, offsite referral to HCV specialty-care clinics is a common practice among drug treatment providers<sup>[29,35]</sup>. However, its effectiveness is limited as the majority of referred patients often fail to schedule or appear at appointments<sup>[14,36,37]</sup>. Yet, OAT facilities that do offer on-site HCV evaluation and treatment have achieved improved outcomes<sup>[38-41]</sup>. Similar findings have been previously reported for HIV-infected PWID, many of whom voluntarily use primary care services if they are offered onsite in OAT facilities<sup>[42]</sup>. Unfortunately, a recent study of substance abuse treatment programs affiliated with academic medical centers conducted through the National Drug Abuse Treatment Clinical Trials Network found a significant lack of comprehensive HCV counseling, testing, and treatment both on-site or by referral<sup>[43]</sup>. The same programs, however, offered significantly more HIV/AIDS-related health services<sup>[44]</sup>.

OAT facilities that do offer integrated HCV care programs may also provide comprehensive on-site primary care services administered by health care providers with training in diverse disciplines including infectious diseases, hepatology, addiction medicine, and mental health<sup>[45-47]</sup>. Many of these programs also offer active case management and have diverse staff consisting of physicians, physician assistants, nurse practitioners, nurses, counselors, and social workers. To improve adherence, some programs utilize directly observed therapy as well

as offering counseling sessions, motivational interviewing, peer-based support groups, and HCV-related education<sup>[45,47-50]</sup>. Improvement over offsite referral has also been achieved through an integrated model combining addiction medicine physicians with hepatologists in a viral hepatitis clinic<sup>[51]</sup>.

Finally, overcoming the financial obstacles for HCV treatment will not be easy, especially in developing countries. In the United States, health care reform will promote integration of specialty services into primary care, promote prevention, and will likely provide an opportunity for development of innovative models for previously medically-marginalized populations such as PWID. In contrast, in developing countries, pharmacy assistance programs will most likely be necessary in order to enable patients to access novel HCV treatments.

## PARALLELS BETWEEN HIV AND HCV

The issue of increasing awareness and funding for HCV treatment among PWID has many similarities to HIV; indeed, HIV treatment is often touted as one of the great medical successes of our time. As the gravity of the emerging HIV epidemic became apparent in the 1980s, national attention and subsequent funds were directed toward combating the infection. Although similarities exist between both viral infections, so do important differences. For example, HCV is curable in a majority of cases while HIV presently requires costly lifelong treatment. Prevention activities among PWID that have been highly effective in controlling HIV have not been as effective in the control of HCV, largely due to limited funding and advocacy<sup>[52]</sup>. Additionally, the ultimate consequences of HCV infection, such as development of end-stage liver disease, hepatic decompensation, or hepatocellular carcinoma leading to liver transplant and subsequent lifelong immunosuppression, are largely preventable through screening and subsequent treatment. With implementation of improved therapies, the HCV field hopes to achieve the same levels of success accomplished by the HIV field.

## CONCLUSION

As many HCV-infected PWID acquired the virus decades ago, they suffer from cirrhosis and other complications of end-stage liver disease with increasing prevalence. Therefore, strategies to increase HCV care and treatment among PWID are critically needed. Achieving higher treatment rates among this population will require overcoming existing barriers at the patient, provider, and institutional levels. Co-localization of HCV management with substance abuse treatment may be a strategy that could facilitate HCV diagnosis as well as promote treatment acceptance and adherence. This approach would reduce the prevalence of end-stage liver disease, viral transmission, and HCV-associated mortality. Additionally, early identification and treatment of HCV infection

is more cost-effective compared to management of end-stage liver disease<sup>[53]</sup>. Tremendous advances are presently occurring in the HCV field, and we hope that PWID will be included in these changes.

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