

# Moving the Agenda Forward: The Prevention and Management of Hepatitis C Virus Infection Among People Who Inject Drugs

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The majority of hepatitis C virus (HCV) occurs among people who inject drugs (PWID) [1], and the burden of HCV-related liver disease is still increasing [2]. HCV treatment is safe and effective among PWID [3], and international guidelines encourage HCV treatment in this group [4, 5], but HCV treatment uptake remains low among PWID [6, 7], mainly due to patient-, practitioner- and systems-related barriers to care. However, strategies have emerged to improve the prevention and management of HCV infection among PWID.

To foster the dissemination of knowledge in the field of viral hepatitis among PWID, the International Network on Hepatitis in Substance Users (INHSU) was established. INHSU established the International Symposium on Hepatitis in Substance Users (held every 2 years), focused on the management of viral hepatitis among PWID, specifically HCV infection. The first symposium was held in Zurich, Switzerland, in 2009 and the second was held in Brussels, Belgium, in 2011. The symposium is attended by researchers, practitioners, and community members and includes sessions on the epidemiology and natural history of viral hepatitis, clinical applications of basic science research, management of medical comorbidities and social science- and community-based perspectives. At the meeting in 2011, a panel of international experts was assembled in collaboration with the European Liver Patients Association to develop the first international recommendations

for the management of HCV among PWID. This supplement presents original research from the most recent meeting, highlights recent advances in the field, and presents recommendations for the clinical management of HCV infection among PWID.

## HCV PREVENTION AMONG PWID

It is estimated that 10 million PWID were HCV antibody positive in 2010, with a global HCV prevalence of 67% among PWID [8]. HCV incidence also remains high among PWID [9].

In the first article of this supplement, Page et al review and highlight the challenges of behavioral interventions for HCV prevention [9]. The authors demonstrate that harm-reduction programs successful in preventing human immunodeficiency virus (HIV) infection among PWID have been less effective for preventing HCV infection and that combined strategies are likely required [9]. Martin et al use mathematical modeling to project the impact of combining opiate substitution treatment (OST), high-coverage needle and syringe programs (NSPs), and HCV treatment on HCV prevalence and incidence among PWID [10]. Data from their study suggest that large reductions (>45%) in HCV chronic prevalence over 10 years requires HCV antiviral treatment, with the scale-up of combined interventions, including OST and NSPs, substantially reducing the treatment rate required to achieve specific HCV prevalence reductions. An alternative way of preventing HCV infection would be through the availability of an HCV vaccine. Cox and Thomas highlight the need for an HCV vaccine for PWID, demonstrate that protective immunity against persistent HCV infection is possible, and summarize

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recent advancements in HCV vaccine research, including recent phase 1/2 trials of an HCV candidate vaccine among PWID [11].

## ENHANCING HCV ASSESSMENT AMONG PWID

Although HCV treatment is successful among PWID [3], assessment and uptake remain low [6,7]. Understanding the barriers and facilitators of HCV care is critical in the design of strategies and programs for effectively increasing the proportion of PWID assessed and treated for HCV.

In this supplement, Treloar et al discuss barriers to HCV care and stigmatization, considering components required for the design programs to effectively engage PWID in HCV care [12]. Bruggmann et al review the spectrum of HCV care models among PWID, highlighting that “one size does not fit all” and that when barriers are systematically addressed within a supportive environment, HCV assessment and treatment among PWID can be very successful [13]. This is consistent with data from Alavi et al from the Enhancing Treatment for Hepatitis C in Opioid Substitution Settings (ETHOS) Study, demonstrating that when HCV nursing and specialist support are integrated into existing OST or community health clinics, a high proportion of PWID with chronic HCV assessed by a nurse can be engaged in HCV care [14]. Another setting with opportunity for expanding HCV assessment and treatment is prisons. Post et al review the considerable burden of HCV in prisons, highlight potential challenges, and illustrate programs that have successfully integrated HCV screening, assessment, and treatment for prisoners with HCV [15]. One important consideration as we move forward with the development of new models of care is the involvement of the affected community. In this supplement, Crawford et al review different peer support models [16] and highlight the importance of involving community-based groups early into the design and implementation of these programs to achieve the greatest opportunity for engagement by PWID.

## ENHANCING HCV TREATMENT AMONG PWID

It has been clearly demonstrated that PWID can be successfully treated [3]. However, the populations studied are often heterogeneous (combination of current and former PWID) and there are few data on HCV treatment outcomes among active PWID. Further, few prospective trials have evaluated strategies to enhance adherence and response to treatment among PWID.

In a systematic review and meta-analysis of treatment for HCV infection among active PWID, Aspinall et al demonstrate an overall sustained virologic response (SVR) of 56% [17]. This is the first systematic review of HCV treatment among those with ongoing drug use at the time of treatment and illustrates that active PWID can respond favorably to therapy. In the first

randomized controlled trial performed to date among active drug users, Hilsden et al randomized participants to immediate vs delayed HCV treatment [18]. They demonstrate that directly observed pegylated interferon and self-administered ribavirin can lead to a high proportion of patients with SVR among active drug users, but suggest that delaying treatment may compromise subsequent engagement in HCV treatment [18]. Last, in the largest trial reported to date among people with chronic HCV infection receiving OST, Reimer et al demonstrate that an intervention based on psychoeducation may enhance adherence to HCV treatment and reduce dropouts, particularly among people with longer treatment durations (those with genotypes 1/4) or those with mental health comorbidities [19].

## MANAGING HCV TREATMENT AMONG PWID

Until recently, HCV treatment guidelines (and many practitioners) excluded PWID from consideration, citing concerns about adherence, increased susceptibility to side effects and reinfection. Issues of HIV infection and management of multiple drug interactions (both prescribed and nonprescribed drug use) complicate HCV management in this population. However, until recently there have been no recommendations for the management of HCV among PWID.

Grady et al demonstrate that the rate of reinfection reported to date has been low (1%–5% per year), which does not support decisions to withhold HCV treatment in this group based on concerns of reinfection [20]. Schaefer et al focus on another common barrier to HCV treatment assessment, namely, mental health issues [21]. They review the available evidence in this area, providing practical information for practitioners interested in managing HCV among PWID. Taylor et al summarize the data to date on management of HCV/HIV coinfection, including recent data investigating new direct-acting antivirals and studies of PWID with HCV/HIV coinfection [22]. Mauss et al focus on the problem of drug–drug interactions, which are an issue among PWID, given the potential for HCV direct-acting antivirals to interact with drugs used to treat HIV coinfection, OST (eg, methadone and buprenorphine), and nonprescription drugs [23].

The supplement is concluded with recommendations for the management of HCV infection among PWID [24]. This is meant to supplement existing international guidelines for HCV treatment, focusing on specific issues encountered among PWID. These guidelines should serve as an evidence-based tool for practitioners managing HCV among PWID.

## FUTURE PERSPECTIVES

High rates of HCV infection still occur among PWID. Research is needed to evaluate the efficacy of combined HCV prevention approaches (such as HCV treatment as prevention, OST, NSPs,

and vaccines). In addition to primary prevention, efforts must be expanded to prevent advanced liver disease due to chronic HCV. HCV treatment can reduce morbidity and mortality, but HCV assessment and treatment remains low among PWID. The availability of simple, well-tolerated, and highly effective interferon-free direct-acting antivirals will facilitate engagement among PWID, but research on strategies to enhance HCV screening and assessment is still needed. The evaluation of strategies to enhance adherence and therapy outcomes (eg, directly observed therapy, medication reminders, adherence education, peer support) should also be a research priority.

Research in this area needs to move beyond small, single-center, retrospective studies demonstrating that HCV treatment among PWID is feasible. Larger, prospective clinical trials run through international clinical networks are required to more rapidly evaluate potential treatment strategies. One such trial, ACTIVATE (A Collaborative Trial in Injectors of Individualized Treatment for Genotype 2/3), is a phase 4, open-label, multicenter, international trial of response-guided treatment with directly observed pegylated interferon alfa 2b and self-administered ribavirin for patients with chronic HCV genotype 2 or 3 infection and ongoing injection drug use. It is the first attempt to establish a clinical network and may be a step in the right direction. Further evidence-based research focused on strategies for enhanced HCV prevention, screening, assessment, and treatment among PWID will be required to reduce the HCV-related burden that still exists globally.

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