

Elimination of hepatitis C virus infection among people who use drugs: Ensuring equitable access to prevention, treatment, and care for all

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ARTICLE INFO

Keywords:

HCV
Drug users
Injecting
Treatment
Care
Access
PWID

ABSTRACT

There have been major strides towards the World Health Organization goal to eliminate hepatitis C virus (HCV) infection as a global public health threat. The availability of simple, well-tolerated direct-acting antiviral therapies for HCV infection that can achieve a cure in > 95% of people has provided an important tool to help achieve the global elimination targets. Encouragingly, therapy is highly effective among people receiving opioid agonist therapy and people who have recently injected drugs. Moving forward, major challenges include ensuring that new infections are prevented from occurring and that people who are living with HCV are tested, linked to care, treated, receive appropriate follow-up, and have equitable access to care. This editorial highlights key themes and articles in a special issue focusing on the elimination of HCV among people who inject drugs. An overarching consideration flowing from this work is how to ensure equitable access to HCV treatment and care for all. This special issue maps the field in relation to: HCV prevention; the cascade of HCV care; strategies to enhance testing, linkage to care, and treatment uptake; and HCV treatment and reinfection. In addition, papers draw attention to the 'risk environments' and socio-ecological determinants of HCV acquisition, barriers to HCV care, the importance of messaging around the side-effects of new direct-acting antiviral therapies, the positive transformative potential of treatment and cure, and the key role of community-based drug user organizations in the HCV response. While this special issue highlights some successful efforts towards HCV elimination among people who inject drugs, it also highlights the relative lack of attention to settings in which resources enabling elimination are scarce, and where elimination hopes and potentials are less clear, such as in many low and middle income countries. Strengthening capacity in areas of the world where resources are more limited will be a critical step towards ensuring equity for all so that global HCV elimination among PWID can be achieved.

Introduction

There have been major strides towards the World Health Organization goal to eliminate hepatitis C virus (HCV) infection as a global public health threat. Therapeutic development for HCV infection has reached its pinnacle, with a number of simple, well-tolerated direct-acting antiviral therapies that can achieve a cure in > 95% of patients (Falade-Nwulia et al., 2017), even in "real-world" studies (Afdhal & Serfaty, 2016). Encouragingly, therapy is highly effective among people receiving opioid agonist therapy (OAT) (Hajarizadeh et al., 2018) and people who have recently injected drugs (Hajarizadeh et al., 2018). The major challenge moving forward is to ensure that new infections are

prevented from occurring and that people who are living with HCV are tested, linked to care, treated, receive appropriate follow-up, and have equitable access to care (Lazarus et al., 2018).

This is the third special issue published in the *International Journal of Drug Policy* focused on HCV among people who inject drugs (Grebely et al., 2015; Grebely, Bruneau et al., 2017) that has been published in collaboration with the International Network on Hepatitis in Substance Users (INHSU). INHSU is an international organization dedicated to scientific knowledge exchange, education, and advocacy focused on improving HCV prevention and care among people who use drugs. This special issue includes 21 original research articles (including two systematic reviews), and three commentaries focused on the "Elimination

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<https://doi.org/10.1016/j.drugpo.2019.07.016>

of hepatitis C virus infection among people who use drugs: Ensuring equitable access to prevention, treatment, and care for all". This special issue maps the field in relation to: HCV prevention; the cascade of HCV care; strategies to enhance testing, linkage to care, and treatment uptake; and HCV treatment and reinfection. In addition, papers draw attention to the 'risk environments' and socio-ecological determinants of HCV acquisition, barriers to HCV care, the importance of messaging around the side-effects of new direct-acting antiviral therapies, the positive transformative potential of treatment and cure, and the key role of community-based drug user organizations in the HCV response. While this special issue highlights some successful efforts towards HCV elimination among people who inject drugs, it also highlights the relative lack of attention to settings in which resources enabling elimination are scarce, and where elimination hopes and potentials are less clear, such as in many low and middle income countries.

Epidemiology and prevention of HCV infection among people who inject drugs

Among the 71 million people living with HCV infection globally (The Polaris Observatory HCV Collaborators, 2017), at least 6.1 million (8.5% of all infections globally) are people who have recently injected drugs (Degenhardt et al., 2017; Grebely et al., 2019). There also exists a considerable, unquantified number of people living with HCV who may have contracted HCV by injecting, but who no longer inject drugs (Grebely, Applegate, Cunningham, & Feld, 2017; Grebely, Bruneau et al., 2017; Grebely, Hajarizadeh, & Dore, 2017; Grebely, Lamoury et al., 2017; Larney et al., 2015; Trickey et al., 2019).

HCV transmission continues to occur among people who inject drugs (Des Jarlais et al., 2018; Hahn et al., 2019; Kaberg, Naver, Hammarberg, & Weiland, 2018; Morris et al., 2017; Puzhko et al., 2017; Valencia La Rosa et al., 2018). Transmission among people who inject drugs is estimated to account for 23% of new infections globally (WHO, 2017). Mathematical modelling suggests that globally, if the increased risk for HCV transmission among people who inject drugs was removed, an estimated 43% of new HCV infections could be prevented from 2018 to 2030 (Trickey et al., 2019).

Like other epidemics, patterns of HCV transmission can be subject to changes in the environment, particularly around drug consumption and markets. For example, in the United States, the number of new cases of HCV infection have been increasing, in part due to a rise in prescription opioid use and inadequate access to adequate harm reduction services [e.g. needle and syringe programs (NSP) and OAT] (Campbell et al., 2017; Van Handel et al., 2016; Zibbell et al., 2018). In North America, prescription opioid injecting has been associated with increased incidence (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012) and prevalence of HCV infection (Hadland et al., 2014; Havens et al., 2013; Havens, Walker, & Leukefeld, 2007; Zibbell, Hart-Malloy, Barry, Fan, & Flanagan, 2014). In the United States, rural settings have experienced particular vulnerability to increasing numbers of HCV infections (Van Handel et al., 2016).

In this issue, Cloud et al identify features of rural risk environments that may contribute to the HCV burden in Kentucky, United States (Cloud, Ibragimov, Prood, Young, & Cooper, 2019), with implications for understanding barriers in accessing prevention and care in other rural settings. In-depth, semi-structured interviews were conducted with people who used prescription opioids to "get high" in five rural regions in Kentucky to understand HCV-related risk behaviours and environmental features that shaped vulnerability to engaging in these behaviours. Participants described an economic decline in the region that was associated with intergenerational poverty, reduced employment prospects, and diminished social enrichment opportunities that collectively contributed to substance use and risky injecting practices. Decisions to inject in "trap houses" (similar to shooting galleries) or secluded spaces where they were rushed to inject or they were at increased risk of sharing injecting equipment were shaped by geographic

isolation, poor knowledge about HCV transmission risks, inadequate access to harm reduction services, familial poverty, and fear of law enforcement. Stigma was identified as a key structural barrier to the use of harm reduction services. This paper highlights the importance of education about risks for HCV, expanding harm reduction coverage, strategies to support those who are unemployed or living in poverty and addressing stigma tailored to rural contexts in the United States in efforts to strive to better HCV prevention among people who inject drugs.

The cascade of HCV care among people who inject drugs

Cascades of care provide a framework for monitoring population-level clinical and public health outcomes, identifying gaps in the continuum of care, and provide insight into potential opportunities for intervention (Gardner, McLees, Steiner, Del Rio, & Burman, 2011; WHO, 2017). The cascade of care for HCV infection includes those living with HCV, diagnosed with HCV, linked to care, treated, and cured (Hajarizadeh, Grebely, Martinello et al., 2016; Hajarizadeh, Grebely, Matthews, Martinello, & Dore, 2016; Yehia, Schranz, Umscheid, & Lo Re, 2014). The cascade of HCV care among people who inject drugs in the interferon-era has been described in a variety of settings (Butler et al., 2017; Iakunchykova et al., 2018; Iversen et al., 2017; Stephens, Young, & Havens, 2017; van Santen, van der Helm, Lindenburg, Schim van der Loeff, & Prins, 2017), with suboptimal engagement reported along all stages of the cascade, including testing, linkage to care and treatment. The development of novel mechanisms for surveillance of the HCV cascade of care is critical to monitor progress and identify sub-populations requiring further support to ensure that care is equitable.

In this issue, there were several papers highlighting the potential use of linked administrative datasets for monitoring progression along the HCV cascade and at the population-level (Ireland et al., 2019; Rojas Rojas et al., 2019). Ireland et al used administrative datasets to identify 29,773 people who had been tested for HCV infection and had attended a drug treatment service in England between 2008 and 2016 (Ireland et al., 2019). Half of all people testing positive for HCV antibodies had ≥ 1 positive anti-HCV test, demonstrating wasteful HCV testing and the need for further education and training on HCV testing for general practitioners and other physicians. Among people who were HCV antibody positive ($n = 3,123$), only 75% had received an HCV RNA test and among those who were HCV RNA detectable, only 14% had received treatment for HCV in the interferon-era. While this study is limited by not having data on treatment uptake in the interferon-free era, it highlights how administrative data can be used to monitor progress on HCV service level targets at a population-level.

Understanding barriers to uptake of HCV treatment is also critical for efforts to ensure care is equitable. Rojas Rojas et al used administrative data from France to identify 29,127 people (including 21% who were females) with chronic HCV infection who had received OAT therapy at least once between 2012 and 2016 to evaluate HCV treatment uptake (Rojas Rojas et al., 2019). Overall, 29% had received treatment (12% interferon-based and 17% DAA) up to the end of the follow-up period. After adjusting for potential confounders, women were 41% and 28% less likely to have received interferon-based and DAA-based therapy, respectively. This work clearly highlights the need to address gender-specific barriers to care. Also, this population of people who have received OAT represents a group already engaged in care and further work is needed to engage those not already interfacing with the health system or who are accessing other health services which do not provide HCV care.

Although data linkage studies using administrative data can provide important insights into the HCV care cascade at the population-level, they often lack more detailed individual-level data to better understand factors associated with barriers to care and treatment. In this issue, Makarenko and colleagues evaluated temporal trends in HCV treatment initiation and associated factors during the transition from interferon-based to interferon-free DAA-based therapies between 2011 and 2017

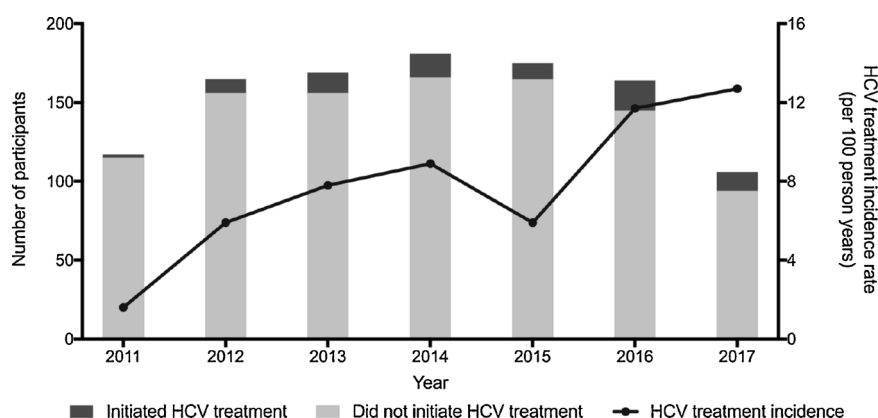


Fig. 1. HCV treatment uptake among people who inject drugs in Montreal, Canada (Makarenko et al., 2019).

in a long-term prospective observational cohort of people who inject drugs in Montreal, Canada (Makarenko et al., 2019). Among 308 participants with either current or previous HCV infection, 26% ($n = 80$) initiated treatment, with treatment increasing from 1.6% (1.6 per 100 person-years) in 2011 to 12.7% (12.7 per 100 person-years) in 2017 (Fig. 1). In adjusted analysis, visiting a primary care physician was associated with increased odds of receiving treatment, while more frequent injecting drug use was associated with a decreased odds of receiving treatment. In the DAA-era, people aged > 40 years, those currently receiving OAT, and people who had previously received treatment were more likely to initiate HCV DAA therapy. These data highlight that although treatment uptake has improved in this setting, barriers have to be addressed to increase treatment among those less engaged in drug treatment and other health services.

Patient, provider, health system, structural, and social barriers and facilitators to HCV treatment uptake among people who inject drugs have been well documented (Doab, Treloar, & Dore, 2005; Grebely et al., 2008; Grebely, Matthews, Lloyd, & Dore, 2013; Grebely, Oser, Taylor, & Dore, 2013; Harris et al., 2018; Harris & Rhodes, 2013; Treloar, Rance, Dore, Grebely, & Group, 2014; Wolfe et al., 2015). Patients report not seeking HCV treatment due to a lack of knowledge of HCV and its treatment, the absence of noticeable symptoms, perceptions around HCV being a benign disease and fears of liver biopsy and treatment side-effects of interferon-based therapies [reviewed in (Grebely, Oser, Taylor, & Dore, 2013)]. Patient perceptions are influenced by the ‘horror stories’ of negative experiences of liver biopsies and the side-effects of interferon-based HCV treatment propagated within peer networks (Swan et al., 2010).

In this issue, Bryant et al evaluated knowledge and perceptions of DAA treatment through surveys and in-depth interviews with people who inject drugs not previously having received HCV treatment in New South Wales, Australia (Bryant, Rance, Hull, Mao, & Treloar, 2019). Interestingly, in the DAA era, one-third of people who had not initiated treatment worried “a lot” about side-effects. Concerns of side-effects were underpinned by a distrust and suspicion of medical institutions and their technologies and widespread negative associations of treatment linked to interferon-based therapies. Bryant et al draw on the concept of ‘counterpublic health’ and its recognition that the everyday health needs, knowledges and aspirations of subordinated citizens frequently contradict the normative frameworks governing public health interventions (Bell & Aggleton, 2012). They highlight that failing to engage with concerns about side-effects could hinder HCV elimination efforts. This article highlights the importance of building educational messages about potential side-effects of HCV therapy that are seen as relevant and trustworthy by people who inject drugs, but also addressing the widespread negative perceptions of interferon-based therapies.

The involvement of people who inject drugs in the design and delivery of HCV services plays a key role in the response to HCV infection

(Bonnington & Harris, 2017; Crawford & Bath, 2013; Henderson, Madden, & Kelsall, 2017). In this issue, Brown et al sought to better understand the role of community-based drug user organizations in the HCV response (Brown et al., 2019). The authors used data from a project using system thinking methods to draw together the insights of 90 peer staff from 10 Australian community and peer organizations to identify how these organisations can be influential in their community and policy system. A strength of peer-based drug user organisations to support scale up of HCV testing and treated was their capacity to mediate between, and navigate within, the complex community and policy/health service systems. Policy and service organisations need recognise their own system role to value and enable peer-based drug user organisations to achieve their potential. If the HCV prevention and treatment system is to reach people who inject drugs living with HCV and achieve HCV elimination goals, then policy and health services need to invest in strengthening peer-based drug user organisations as well as recognise, value and act on quality policy advice from peer leadership among people who inject drugs.

While we consider the broad range of factors that can impact decisions about and access to HCV treatment among people who inject drugs, Hoj and colleagues sought to synthesise and clarify the conceptual underpinnings of access to health care for people who inject drugs, with a view to informing research and practice (Hoj, Jacka, Minoyan, Artenie, & Bruneau, 2019). Hoj et al present a comprehensive theoretical framework to understand, investigate and intervene upon barriers and facilitators to HCV care for people who inject drugs (Fig. 2). Drawing from the concept of candidacy (Dixon-Woods et al., 2006), the framework posits access to care as a negotiated product of the alignment between individuals, health professionals and health systems. The authors highlight that individuals need to first identify themselves as candidates for services and work to stake this claim as health professionals often serve as gatekeepers adjudicating asserted candidacies. Repeated interactions build experiential knowledge and develops relationships between patients and practitioners over time. Importantly, these processes occur within complex social circumstances of interdependent individual, service, system, and policy factors. This paper provides concrete examples of how this framework could be used to specify research questions, identify intervention targets, describe and test plausible effect mechanisms, and identify any threats to research translation. Collectively, this paper provides an important framework to understand and systematically address barriers to HCV care.

Enhancing testing, linkage to care, and treatment for PWID

Targeted strategies to address all stages of the HCV care cascade (diagnosis, linkage to care, treatment, and cure) will be required to reduce the burden of HCV among people who inject drugs and achieve HCV elimination (Scott et al., 2017). In the previous special series

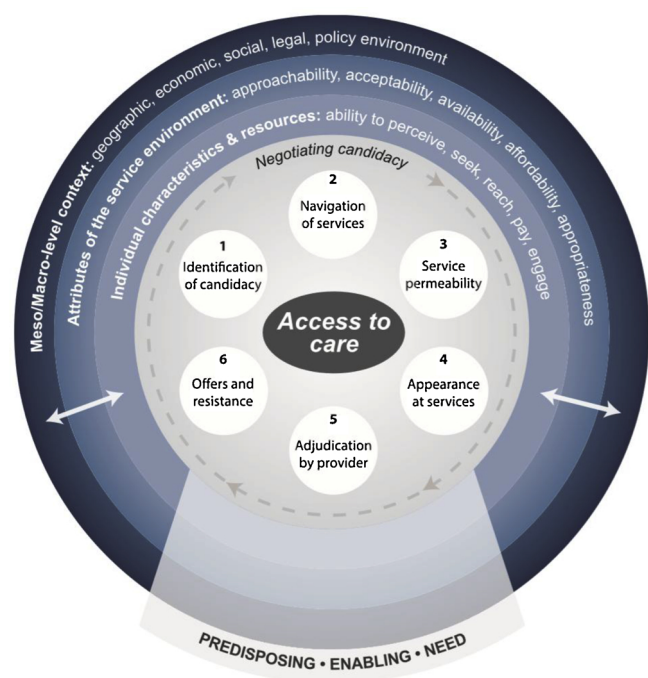


Fig. 2. Integrated framework of access to HCV care for people who inject drugs (Hoj et al., 2019).

(Grebely, Bruneau et al., 2017), Bajis et al performed a systematic review to evaluate the effectiveness of interventions to enhance HCV testing, linkage to care, and treatment uptake among people who inject drugs (Bajis et al., 2017). Interventions with evidence of effectiveness for enhancing HCV testing (on-site testing; and dried blood spot testing), linkage to care (facilitated referral for HCV assessment) and treatment (integrated HCV care) were identified. Further work is still needed to explore strategies to enhance testing, linkage to care and treatment among people who inject drugs.

Strategies to enhance testing and diagnosis will be critical to diagnose those who are unaware of their infection. In a commentary in this issue, Katzman and colleagues propose revisiting the current approaches to screening and consider the potential use of contact tracing programs to enhance HCV screening and diagnosis (Katzman, Mateu-Gelabert, Kapadia, & Eckhardt, 2019). Contract tracing has been a key element of the public health response for tuberculosis, HIV, and other sexually transmitted infections. Katzman et al highlight that contract tracing programs for HCV could supplement existing screening strategies to ensure that people living with HCV and their injecting and sexual partners receive curative DAA therapy, prevent onward transmission by decreasing the time to treatment initiation (thereby reducing the period of infectiousness), and reach people who are not engaged in services.

Point-of-care HCV testing increases testing and linkage to care (Bajis et al., 2017; Bottero et al., 2015; Grebely, Applegate et al., 2017; Grebely, Bruneau et al., 2017; Grebely, Hajarizadeh et al., 2017; Grebely, Lamoury et al., 2017). In this issue, there were several studies evaluating point-of-care HCV testing in different settings beyond traditional access points, including hospital emergency departments (Hutton et al., 2019), needle and syringe programs (Williams, Howell et al., 2019), drug treatment services (Alavi et al., 2019), community-based drop-in centers providing harm reduction services (Alavi et al., 2019), and homeless reception centres (Alavi et al., 2019).

In a paper by Hutton et al, the investigators evaluated risk-based screening, offer of point-of-care HCV antibody testing, and linkage to treatment for HCV at an inner-city hospital in Melbourne, Australia (Hutton et al., 2019). Among 1,122 participants eligible for screening,

34% (n = 378) reported at least one risk factor and 97% (368 of 378) received point-of-care HCV antibody testing (24% of whom were homeless). Among those tested, 14% (n = 50) were HCV antibody positive (88% had ever injected drugs) and 9% (n = 30) were HCV RNA positive (three of these participants died). Of the remaining participants with active HCV infection, 37% (10 of 27) initiated treatment. These data clearly demonstrate the challenges of linkage to HCV testing and treatment in the emergency room setting and highlight the need to improve care in marginalized populations (e.g. people with ongoing injecting and those who are homeless).

NSPs offer a unique opportunity to engage with people who inject drugs who may not be otherwise engaged in health services. Williams et al investigated the feasibility and acceptability of HCV point-of-care testing at NSPs co-located in three community health clinics in Melbourne, Australia between June and November 2017 (Williams, Howell et al., 2019). NSP attendees were offered an oral fluid-based point-of-care HCV antibody test by NSP staff. People who tested HCV antibody positive were then offered point-of-care Xpert HCV RNA testing via venepuncture (time to final result – two hours) and standard of care laboratory testing required for HCV treatment (also via venepuncture). Results were provided on-site, via phone, or via text message. Among 174 participants receiving point-of-care HCV antibody testing, 86% (n = 150) were HCV antibody positive and 93% (n = 140) of these received point-of-care HCV RNA testing. Overall, 54% (76 of 140) were HCV RNA positive. Although only 5% of these people waited on-site for results, 63% were eventually assessed for treatment. The majority of participants reported a preference for point-of-care testing (66%) and supported the involvement of NSP staff in providing testing (90%). The availability of a next generation finger-stick point-of-care Xpert HCV Viral Load assay (Grebely, Lamoury et al., 2017; Lamoury et al., 2018), enabling same-day diagnosis of active infection (HCV RNA) in one hour (sensitivity and specificity, 100%) (Lamoury et al., 2018) provides the opportunity to further evaluate whether finger-stick point-of-care HCV RNA testing could be integrated into routine practice to enhance HCV testing and treatment among PWID.

There are few studies investigating linkage to HCV testing and treatment in low- and middle-income country settings (Bajis et al., 2017). Alavi et al evaluated the impact of an intervention to enhance HCV treatment uptake among people with history of drug use attending drug treatment clinics, community-based harm reduction drop-in centers, and a homeless reception service between April 2018 and December 2018 in Tehran, Iran (Alavi et al., 2019). The intervention incorporated on-site point-of-care HCV antibody testing, venepuncture for HCV RNA testing (among those HCV antibody positive), liver fibrosis assessment, and linkage to care. Among the 632 participants enrolled, 28% had a history of injecting drug use, the HCV antibody prevalence was 27% (n = 170) and 99% (n = 168) received HCV RNA testing. Among people who were HCV RNA positive (n = 134), treatment uptake was 84% overall, including 100% (45/45) of those in drug treatment clinics, 96% (46/48) in drop-in harm reduction centers, and 54% (22/41) in the homeless reception setting (Fig. 3). These data on HCV treatment uptake among people receiving on-site point-of-care HCV testing and linkage to care are encouraging and such models could be explored in other low- and middle-income country settings. It is clear that the setting is important in the delivery of new interventions and populations who are more marginalized might require additional support.

Although there have been advances in the development of strategies to enhance HCV testing, linkage to care and treatment, studies to date have limitations (Bajis et al., 2017). Studies are often limited by small sample sizes, performed in single-centres, and there are few randomized controlled trials or comparative studies in the interferon-free era (Bajis et al., 2017). Although a variety of strategies have been assessed, they lack comparator groups, so measuring the effect of these interventions is difficult. As we move forward, well-designed studies evaluating interventions to enhance HCV testing/treatment among PWID are

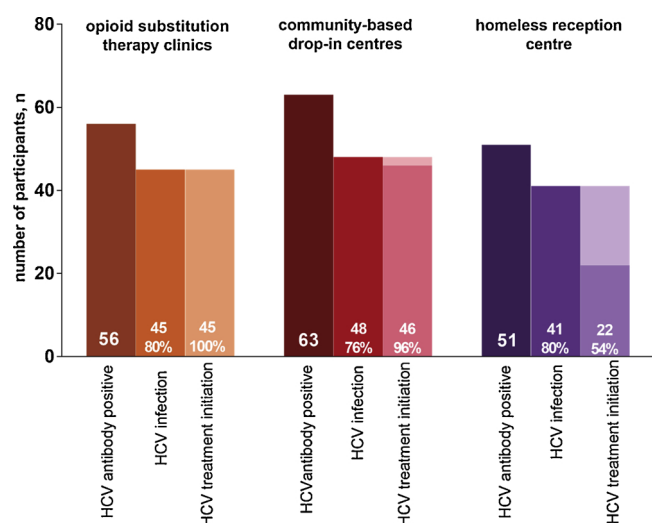


Fig. 3. Hepatitis C virus screening, diagnosis, and treatment uptake among participants with a history of drug use in the ENHANCE study ($n = 632$) (Alavi et al., 2019).

needed, particularly to inform efforts to deliver treatment at scale.

HCV treatment for PWID

Interferon-free DAA therapy is safe and effective among both people receiving OAT and people with ongoing injecting drug use (Hajarizadeh et al., 2018). In meta-regression analyses, studies performed in the real-world were associated with lower SVR compared to clinical trials, mainly due to higher loss to follow-up, not virological failure (Hajarizadeh et al., 2018). Given this evidence, the next challenge is to achieve greater scale-up HCV testing and treatment services while enhancing follow-up interventions to prevent reinfection for people who inject drugs. Enhancing uptake of HCV testing and treatment among people who inject drugs will require moving beyond hospital-based tertiary clinics and integrating HCV services into existing community-based settings where people who inject drug already access other services, including drug treatment clinics, community health centres and primary care, prisons, NSPs, supervised consumption rooms, homelessness settings, and mental health settings.

In this issue, Selfridge et al. evaluated efficacy of DAA therapy, HCV reinfection following successful therapy and mortality among people attending an inner-city community health centre in Victoria, Canada (Selfridge et al., 2019). Among 270 participants who initiated DAA therapy, 98% completed treatment and 92% achieved an SVR. These results are impressive, given the high proportion with cirrhosis (32%), HCV genotype 3 (26%) and HIV co-infection (20%). Recent injecting drug use prior to treatment initiation did not have an impact on SVR. The rate of HCV reinfection was 3.2 cases per 100 person-years. Twenty people died during follow-up (6.3 per 100 person-years), including two people during therapy (drug overdose, $n = 2$) and 18 following therapy completion (drug overdose, $n = 7$). Although the treatment outcomes from this study are encouraging it highlights the importance of integrating HCV care within a framework that addresses drug-related harms.

This point is further emphasized from a study by Krajden et al. evaluating mortality among people with and without HCV infection from a large population-based dataset in British Columbia, Canada (Krajden et al., 2019). Among people with HCV infection, although liver-related mortality increased from 1992 to 2014, it has declined sharply since 2018, coinciding with the introduction and uptake of DAA therapy. However, mortality attributed to HIV infection and illicit drug use increased from 1992 to 2000, declined slowly until 2013, then has rapidly increased, coinciding with the recent surge in opioid overdose

deaths. This clearly highlights the need to look beyond HCV and consider strategies to address drug-related harms and improve the health of people who use drugs.

Prisons represent an important setting for HCV elimination efforts among people who inject drugs (Grebely, Matthews et al., 2013; Hajarizadeh, Grebely, Martinello et al., 2016; Hajarizadeh, Grebely, Matthews et al., 2016; Post, Arain, & Lloyd, 2013). People who inject drugs have high rates of imprisonment, which is in part due to criminalization associated with the possession or use of drugs. Among people with a history of injecting drug use in prison, the prevalence of chronic HCV infection is 48% (95% CI: 44%, 53%) (Larney et al., 2013) and incidence is 6.3–16.4 per 100 person-years (Champion et al., 2004; Cunningham et al., 2017).

In this issue, Overton and colleagues report on the outcomes from a nurse-led model of HCV care across a network of 36 prisons in New South Wales, Australia (Overton et al., 2019). Initial clinical assessments, confirmatory testing for HCV, and liver disease staging (by transient elastography) were performed by the nursing team. The nurse then discussed the case with an infectious diseases physician (via phone or in person) and DAA therapy was prescribed. During the first year of DAA therapy in New South Wales, Australia, 698 participants were initiated on HCV therapy and the intent-to-treat SVR was 57% (396 of 698). Among those with available HCV testing at 12-weeks post-treatment, the SVR was 92% (396 of 430). The main reasons for not having an HCV RNA test was either release from prison during treatment (7%, $n = 52$) or release from prison prior to SVR assessment (30%, $n = 211$). No demographic or clinical characteristics were identified to be associated with lost to follow-up.

These data complement the results observed in other smaller studies of DAA-based therapy in prisons (Aspinall et al., 2016; Hochstatter et al., 2017; Morey et al., 2019; Papaluca et al., 2019; Pontali et al., 2018) and recent studies demonstrating the potential for large reductions in HCV RNA prevalence to achieve HCV “micro-elimination” in prisons (Bartlett et al., 2018; Blogg, Wood, McGrath, & Lobo, 2018; Cuadrado et al., 2018). Further research is needed to identify strategies to engage people who have received HCV treatment in prison in post-treatment follow-up and care.

HCV infection is also highly prevalent in homeless populations, with global estimates ranging from 4 to 36% (Beijer, Wolf, & Fazel, 2012). Homeless people who inject drugs may have a particularly high burden of HCV infection, with HCV antibody prevalence ranging from 55 to 81% (Strehlow et al., 2012). Unstable housing/homelessness has also been demonstrated to be associated with lower uptake of HCV testing and/or treatment (Butler et al., 2017). Two studies in the issue report on models of care to enhance the treatment of HCV in people who are homeless.

In the first study, Harney et al. evaluated the outcomes of a nurse-led outreach service providing HCV treatment to people attending homeless services (Harney et al., 2019). Among the 52 participants who received HCV testing, 75% were HCV RNA positive (46% were sleeping on the street, 74% reported injecting drug use), and 46% (24 of 52) initiated HCV treatment. Sleeping on the street was associated with lower uptake of HCV treatment. Although the overall SVR was 54% (13 of 24), all those with an available SVR ($n = 15$) responded to therapy.

The second study by Beiser et al. examined treatment engagement and outcomes in a cohort of homeless-experienced adults treated through an innovative community-based primary care program in Boston, the United States (Beiser, Smith, Ingemi, Mulligan, & Baggett, 2019). Among 510 people referred for HCV treatment, 59% ($n = 300$) were initiated on DAA therapy for HCV infection. The main reasons for not having initiated therapy among the remaining 41% ($n = 210$), included being lost to follow-up ($n = 93$) or having superseding social issues ($n = 49$). Among the those initiating treatment ($n = 300$, 20% homeless, 59% with opioid dependence), 95% completed treatment and 85% ($n = 255$) achieved SVR. Factors associated with lower SVR included bipolar disorder, opioid dependence, or on-treatment insurance

coverage changes. The rate of HCV reinfection was 13.1 per 100-person years.

Collectively, these data complement studies in the literature (Bajis et al., 2019) demonstrating that HCV therapy can be successful among people who are homeless. Given that lower HCV treatment uptake has been reported among people who inject drugs who are homeless (Butler et al., 2017), further strategies are needed to address engagement in testing and care in this population.

Understanding the motivations and attitudes towards HCV treatment among people who inject drugs is critical for the design of strategies to facilitate broader scale-up. In this issue, Williams et al. explored how the transformative potential may affect treatment success among people who inject drugs within two healthcare for the homeless clinic settings (Williams, Nelons et al., 2019). In-depth interviews were performed with 27 people who inject drugs participating in a pilot clinical trial testing the effective delivery of DAA treatment, including one group receiving OAT and another group frequently attending an NSP. In both groups, participants described significant life projects that motivated them to complete HCV treatment. These projects included social redemption and healthier self-concept, strengthening of relationships, pursuit of abstinence from substance use, and harm reduction. Although the themes were consistent between treatment groups, more participants in the group from the NSP relied on harm reduction than on pursuing abstinence as a strategy to prevent reinfection after successful treatment. Understanding the incentives that help motivate people through treatment is a critical aspect towards identifying and addressing barriers to successful engagement in treatment and optimizing treatment outcomes.

A key theme emerging across the material in this special issue is the need for integrated models of HCV care for people who inject drugs. Socias et al conducted a systematic review of the impact of integrated care (co-location of services) for HCV and drug treatment services (the authors refer to this as substance use services) on engagement in HCV care among people who inject drugs (Socias et al., 2019). The authors conducted a narrative synthesis, categorizing models based on the patient entry point (a: HCV facility; b: drug treatment facility; and c: other facilities) and levels of integrated services offered (a: HCV/substance use testing only; b: HCV/substance use treatment, and c: testing/treatment and other services). Among the 44 original studies identified, a wide range of different models were identified ($n = 26$) for the integration of services within drug treatment services. The authors also identified other models of integrated services in primary care facilities, harm reduction centres, HIV services, and sexual health services. While the narrative analysis indicated, that, overall integrated care improved engagement in HCV care (e.g., testing, treatment uptake and cure), the quality of evidence was predominantly low to moderate. Further, the heterogeneity between the different models of care and the lack of randomized or comparative studies precluded the ability to conduct a meta-analysis. Lastly, 95% of studies were from high-income countries and only 14% were in the interferon-free DAA era. Further well-designed studies to evaluate the effect of integrated HCV care on HCV testing and treatment in drug treatment settings would be a useful addition to inform strategies to optimize HCV care in the future.

Altogether, these studies underscore the critical need for additional research to evaluate the clinical effectiveness of strategies for the integration of care for HCV and drug user health and the cost-effectiveness of such models. In this issue, Barocas et al evaluated the clinical impact, costs, and cost-effectiveness of integrating buprenorphine-naloxone therapy for opioid dependence into onsite HIV/HCV treatment compared with the status quo of offsite referral for medications for opioid dependence (Barocas et al., 2019). Using mathematical modelling, the authors demonstrated that an integrated care strategy (buprenorphine-naloxone with HIV/HCV treatment) could improve HCV-related outcomes by reducing the lifetime prevalence of cirrhosis, the lifetime risk of liver-related death, and the lifetime risk of HCV reinfection after cure. Further, the authors demonstrated that integrated

care was associated with reductions in one- and five-year non-liver related deaths, thereby contributing to improved life expectancy and health-related quality of life. Compared to the status quo, integrated care was cost-effective (assuming a US\$100,000 per adjusted life year willingness to pay threshold) with an incremental cost-effectiveness ratio (ICER) of \$57,100 per quality adjusted life year. This study highlights how the integration of services for HCV and opioid dependence can improve outcomes for both HCV and drug user health more broadly. However, further work is needed to address the high costs related to treatment for HCV and opioid dependence to allow these strategies to be more cost-effective and facilitate broader scale-up and implementation.

Risk behaviours and reinfection following HCV treatment among people who inject drugs

Previous studies have demonstrated that reductions in injecting risk behaviours may occur in the setting of interferon-based treatment (Alavi et al., 2015; Artenie et al., 2017; Artenie et al., 2019; Midgard et al., 2017). In this issue, Caven and colleagues conducted a systematic review of the impact of HCV treatment on drug use risk behaviours among people who inject drugs (Caven, Malaguti, Robinson, Fletcher, & Dillon, 2019). The authors identified five studies evaluating the impact of HCV treatment on behaviour change (including recent injecting drug use and injecting equipment sharing). Comparisons between studies was challenging and a meta-analysis was not possible, given the heterogeneity between studies. However, data from this review suggests that engaging in HCV treatment may be associated with reduced or maintained injecting risk behaviours, with no evidence to suggest that there are increased risk behaviours during or following treatment. It is likely that these findings are attributed to ongoing therapeutic relationships and harm reduction education provided by physicians, nurses, counsellors and other allied health providers. Analysis of injecting risk behaviour must be informed by the availability of the sterile equipment. Given the global under-achievement in distribution of sterile injecting equipment, it cannot be assumed that needle and syringes were available in ways that allowed participants in these studies to increase their use of this equipment. HCV treatment is an opportune time to address unsafe injecting practices to minimize the risk of HCV reinfection following successful therapy and address other health-related outcomes such as other blood borne virus risks (e.g. HIV infection) and other injecting-related infections.

As DAA treatment scale-up expands among populations with ongoing risk behaviours for reacquisition, it is essential to acknowledge that HCV reinfection can and will occur. The rate of HCV reinfection among PWID ranges from 0% to 5% per annum, with higher incidence among people with ongoing injecting drug use (5–22% per annum) (Aspinall, Simmonds) (Cunningham, Applegate, Lloyd, Dore, & Grebely, 2015; Martinello, Hajarizadeh, Grebely, Dore, & Matthews, 2017). The rate of reinfection will depend on the study population (and risk behaviours for HCV acquisition), the HCV RNA prevalence in the population, the population-level incidence of HCV infection, and the coverage of harm reduction programs (e.g. OST and NSP). Although there are fewer data on factors associated with reinfection among PWID, needle and syringe sharing, more frequent injecting and cocaine/methamphetamine injecting have been associated with an increased risk of HCV reinfection (Young et al., 2017).

In this issue, Holeksa et al provide further data on HCV reinfection from a “real-world” study of HCV therapy among people who use drugs at a multidisciplinary HCV treatment program in Vancouver, Canada (Holeksa et al., 2019). Among 243 people with recent drug use (previous 6 months) who received HCV treatment, 80% reported ongoing drug use following treatment. Overall, the rate of HCV reinfection was 1.1 per 100 person-years (95% confidence interval 0.8–5.2). Unfortunately, there was no comparison group and detailed data on injecting risk was not available. Further, Valencia and colleagues

evaluated HCV reinfection among people with recent drug recruited from two mobile harm reduction services in Madrid, Spain (Valencia et al., 2019). Among 121 people with recent injecting drug use (previous 6 months) who received HCV treatment, the rate of HCV reinfection was 9.8 per 100 person-years [95% confidence interval 4.7–18.2]. In adjusted analyses, injecting drug use in the month prior to initiation of HCV therapy was associated with reinfection (adjusted hazards ratio 8.7, 95% CI 1.0, 73.6). Collectively, these data underscore the importance of counselling about the risks of HCV re-infection follow HCV therapy and long-term maintenance in care to ensure regular follow-up for HCV reinfection.

There are few studies that have evaluated HCV reinfection in prisons (Bate, Colman, Frost, Shaw, & Harley, 2010; Simmons, Saleem, Hill, Riley, & Cooke, 2016). In this issue, Marco et al evaluated HCV reinfection and associated factors in a large retrospective cohort of people who had received HCV treatment in prison between January 2002 and December 2016 in Catalonia, Spain and were re-tested yearly or when re-entering prison (Marco et al., 2019). Among 602 participants (74% history of injecting drug use, 29% HIV infected), the overall rate of reinfection was 2.9 cases per 100 person-years (2,155 person-years of follow-up). In adjusted analyses, HIV infection was the only factor associated with HCV reinfection. Unfortunately, data was not available to estimate the rate of reinfection among people with ongoing injecting drug use, and to differentiate reinfection that occurred in prison from those during release. Irrespective of this limitation, it highlights the importance of reinfection among people who are in prison and the need to optimize prevention strategies in prisons, including broader access to HCV treatment, NSP, and OAT, interventions that are already accepted in Spain, but insufficient in terms of coverage.

Evidencing viral elimination

Rhodes and Lancaster (Rhodes & Lancaster, 2019) also reflect on the evidencing of viral elimination. But they offer up an approach to thinking about implementation science which is different to that of the mainstream. In a thought-provoking commentary on the controversies resulting from a Cochrane Collaboration systematic review on the clinical benefits and curative potential of DAA treatments (Jakobsen et al., 2017; Jakobsen, Nielsen, Koretz, & Gluud, 2018), they argue for the need to move beyond questions of method and epistemology to questions of ontology. This invites us to not only reflect on the veracity of evidence and the 'best methods' for evidencing hepatitis C intervention effects, but also to ask how science interacts with other forms of knowledge to 'perform' its evidence. Rhodes and Lancaster are inviting us to step back from our research and intervention efforts to consider how these practices perform things like 'elimination', 'cure', and 'biomedical promise' in particular ways. They describe this 'different' way of thinking as a way of 'knowing' hepatitis C cure and elimination 'more carefully' for it hits home how all knowledge-making practices, including science, are deeply embedded in social and political 'matters-of-concern'. They remind us that there is unavoidably a politics in relation to knowledge-making, and that reflecting on this is an important element of how science 'cares'. This then, is a pointer to how implementation science in relation to hepatitis C elimination might better incorporate ideas from social science going forwards.

Conclusions

As highlighted in this special issue, there have been great advancements in the understanding of strategies to improve HCV prevention, testing, linkage to care, and treatment outcomes for people who inject drugs. Major barriers still persist to achieve the WHO elimination targets, including in access to and delivery of harm reduction strategies, HCV testing, linkage to care, and treatment. As we move forward, a greater understanding of barriers to HCV testing and treatment will be critical, with a greater involvement of the community

of people who inject drugs in the research and conduct of programs to guide the appropriate responses. More emphasis on the development and conduct of larger, well-designed studies (such as comparative studies and randomized controlled trials) evaluating strategies to enhance HCV prevention, testing, linkage to care, and treatment are critical to move this field forward. At the same time, it must be acknowledged that no one service or setting is exactly the same, so we must tailor interventions to meet the needs of the people that they are meant to support.

The important and debilitating role of stigma in the lives of people living with HCV has long been documented (Crofts, Louie, & Loff, 1997). The availability of curative HCV treatments makes this picture more complicated as people achieving a cure can leave behind this unwanted and damaging label. Indeed, stigma can be a motivator to take up and complete treatment (Williams, Nelons et al., 2019) and something that people value as an outcome of treatment (Madden, Hopwood, Neale, & Treloar, 2018). However, stigma remains a barrier to seeking treatment (Madden, Hopwood, Neale, & Treloar, 2018) and something that can endure as a "residual underbelly of shame" (Harris, 2017). What we also need to understand is the relationship of stigma with reinfection with some people with HCV describing this as a "new monster" (Richmond et al., 2018). Work to reduce stigma associated with HCV and with injecting drug use must continue as a priority.

The simplification of HCV testing and treatment provides a unique opportunity for scale-up. But we must also design and implement simple interventions to facilitate greater potential for scalability to achieve a greater impact on HCV-related disease burden and drug user health at a population-level. It will be critical to evaluate the costs of these potential interventions to generate evidence that can be used by policy makers to advocate for broader integration into the health system. The paucity of research from low- and middle-income country settings does not mean that there is not important work being carried out there, but we need to enhance our efforts to encourage knowledge translation to and from these settings. Many of the articles in this special issue of the *International Journal of Drug Policy* highlight the important intersection between HCV and drug-related harms. As such, engagement in HCV care must be used as an opportunity to address the broader health needs of people who use drugs. Lastly, as we move forward, it will be critical that programs and services are developed in a range of different settings and addressing all the needs of people in those settings. At the very least, attention is needed in the areas of HCV prevention especially the provision of NSP and OAT which is documented to be well below target in most areas of the world (Larney et al., 2017). So, while this special issue highlights some successful efforts towards HCV elimination among people who inject drugs, it also highlights the relative lack of attention to settings in which resources enabling elimination are scarce, and where elimination hopes and potentials are less clear, such as in many low and middle income countries. Strengthening capacity in areas of the world where resources are more limited will ensure that there is equitable care for all populations of people who use drugs and no one is left behind in the pursuit of the WHO goal to eliminate HCV infection as a major public health threat.

Disclosures

JG is a consultant/advisor and has received research grants from AbbVie, Cepheid, Gilead Sciences and Merck/MSD. JB is a consultant/advisor and has received research grants from AbbVie, Gilead Sciences and Merck/MSD. JVL is a consultant/advisor and has received research grants from AbbVie, Cepheid, Gilead Sciences and Merck/MSD.

Financial support

The Kirby Institute and the Centre for Social Research in Health are funded by the Australian Government Department of Health and Ageing. The views expressed in this publication do not necessarily represent the position of the Australian Government. JG is supported by a

National Health and Medical Research Council Career Development Fellowship (1112352). JVL is supported by a Spanish Ministry of Science, Innovation and Universities Miguel Servet grant.

Acknowledgements

The authors would like to thank Professor Tim Rhodes for providing thoughtful comments and revisions for this commentary.

References

- Afdhal, N. H., & Serfaty, L. (2016). Effect of registries and cohort studies on HCV treatment. *Gastroenterology*, 151, 387–390.
- Alavi, M., Spelman, T., Matthews, G. V., Haber, P. S., Day, C., van Beek, I., et al. (2015). Injecting risk behaviours following treatment for hepatitis C virus infection among people who inject drugs: The Australian Trial in Acute Hepatitis C. *International Journal of Drug Policy*, 26, 976–983.
- Alavi, M., Poustchi, H., Merat, S., Kaveh-Ei, S., Rahimi-Movaghar, A., Shadloo, B., Hajarizadeh, B., Grebely, J., Dore, G. J., & Malekzadeh, R. (2019). An intervention to improve HCV testing, linkage to care, and treatment among people who use drugs in Tehran, Iran: The ENHANCE study. *J Drug Policy*, 72, 99–105.
- Artenie, A. A., Zang, G., Daniel, M., Fortier, E., Jutras-Aswad, D., Puzhko, S., et al. (2017). Short-term injection drug use changes following hepatitis C virus (HCV) assessment and treatment among persons who inject drugs with acute HCV infection. *International Journal of Drug Policy*, 47, 239–243.
- Artenie, A. A., Cunningham, E. B., Dore, G. J., Conway, B., Dalgard, O., Powis, J., et al. (2019). Patterns of drug, alcohol use and injection equipment sharing among people with recent injecting drug use or receiving opioid agonist treatment during and following hepatitis C virus treatment with direct-acting antiviral therapies: An international study. *Clin Infect Dis*. <https://doi.org/10.1093/cid/ciz633> pii: ciz633. [Epub ahead of print].
- Aspinall, E. J., Mitchell, W., Schofield, J., Cairns, A., Lamond, S., Bramley, P., et al. (2016). A matched comparison study of hepatitis C treatment outcomes in the prison and community setting, and an analysis of the impact of prison release or transfer during therapy. *Journal of Viral Hepatitis*, 23, 1009–1016.
- Bajis, S., Dore, G. J., Hajarizadeh, B., Cunningham, E. B., Maher, L., & Grebely, J. (2017). 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*, 47, 34–46.
- Bajis, S., Grebely, J., Cooper, L., Smith, J., Owen, G., Chudleigh, A., et al. (2019). Hepatitis C virus testing, liver disease assessment and direct-acting antiviral treatment uptake and outcomes in a service for people who are homeless in Sydney, Australia: The LiveLife homelessness study. *Journal of Viral Hepatitis*. <https://doi.org/10.1111/jvh.13112> PMID: 30980785 [Epub ahead of print].
- Barocas, J. A., Morgan, J. R., Fiellin, D. A., Schackman, B. R., Eftekhari Yazdi, G., Stein, M. D., et al. (2019). Cost-effectiveness of integrating buprenorphine-naloxone treatment for opioid use disorder into clinical care for persons with HIV/hepatitis C co-infection who inject opioids. *International Journal of Drug Policy*.
- Bartlett, S. R., Fox, P., Cabatangan, H., Jaros, A., Gorton, C., Lewis, R., et al. (2018). Demonstration of near-elimination of hepatitis C virus among a prison population: The Lotus glen correctional centre hepatitis C treatment project. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 67, 460–463.
- Bate, J. P., Colman, A. J., Frost, P. J., Shaw, D. R., & Harley, H. A. (2010). High prevalence of late relapse and reinfection in prisoners treated for chronic hepatitis C. *Journal of Gastroenterology and Hepatology*, 25, 1276–1280.
- Beijer, U., Wolf, A., & Fazel, S. (2012). Prevalence of tuberculosis, hepatitis C virus, and HIV in homeless people: A systematic review and meta-analysis. *The Lancet Infectious Diseases*, 12, 859–870.
- Beiser, M. E., Smith, K., Ingemi, M., Mulligan, E., & Baggett, T. P. (2019). Hepatitis C treatment outcomes among homeless-experienced individuals at a community health centre in Boston. *International Journal of Drug Policy*.
- Bell, S. A., & Aggleton, P. (2012). Time to invest in a 'counterpublic health' approach: Promoting sexual health amongst sexually active young people in rural Uganda. *Children's Geographies*, 10, 385–397.
- Blogg, J., Wood, J., McGrath, C., & Lobo, C. (2018). Eradicating hepatitis C from the New South Wales prison system. *The Medical Journal of Australia*, 208, 276.
- Bonnington, O., & Harris, M. (2017). Tensions in relation: How peer support is experienced and received in a hepatitis C treatment intervention. *International Journal of Drug Policy*, 47, 221–229.
- Bottero, J., Boyd, A., Gozlan, J., Carrat, F., Nau, J., Pauti, M. D., et al. (2015). Simultaneous human immunodeficiency virus-hepatitis B-Hepatitis C point-of-care tests improve outcomes in Linkage-to-Care: Results of a randomized control trial in persons without healthcare coverage. *Open Forum Infectious Diseases*, 2, ofv162.
- Brown, G., Perry, G. E., Byrne, J., Crawford, S., Henderson, C., Madden, A., et al. (2019). Characterising the policy influence of peer-based drug user organisations in the context of hepatitis C elimination. *International Journal of Drug Policy*.
- Bruneau, J., Roy, E., Arruda, N., Zang, G., & Jutras-Aswad, D. (2012). The rising prevalence of prescription opioid injection and its association with hepatitis C incidence among street-drug users. *Addiction*, 107, 1318–1327.
- Bryant, J., Rance, J., Hull, P., Mao, L., & Treloar, C. (2019). Making sense of 'side effects': Counterpublic health in the era of direct-acting antivirals. *International Journal of Drug Policy*.
- Butler, K., Day, C., Sutherland, R., van Buskirk, J., Breen, C., Burns, L., et al. (2017). Hepatitis C testing in general practice settings: A cross-sectional study of people who inject drugs in Australia. *International Journal of Drug Policy*, 47, 102–106.
- Campbell, C. A., Canary, L., Smith, N., Teshale, E., Blythe Ryerson, A., & Ward, J. W. (2017). State HCV incidence and policies related to HCV preventive and treatment services for persons who inject drugs - United States, 2015–2016. *American Journal of Transplantation: Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, 17, 1945–1948.
- Caven, M., Malaguti, A., Robinson, E., Fletcher, E., & Dillon, J. F. (2019). Impact of Hepatitis C treatment on behavioural change in relation to drug use in people who inject drugs: A systematic review. *International Journal of Drug Policy*.
- Champion, J. K., Taylor, A., Hutchinson, S., Cameron, S., McMenamin, J., Mitchell, A., et al. (2004). Incidence of hepatitis C virus infection and associated risk factors among Scottish prison inmates: A cohort study. *American Journal of Epidemiology*, 159, 514–519.
- Cloud, D. H., Ibragimov, U., Prood, N., Young, A. M., & Cooper, H. L. F. (2019). Rural risk environments for hepatitis C among young adults in Appalachian Kentucky. *International Journal of Drug Policy*.
- Crawford, S., & Bath, N. (2013). Peer support models for people with a history of injecting drug use undertaking assessment and treatment for hepatitis C virus infection. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 57(Suppl. 2), S75–79.
- Crofts, N., Louie, R., & Loff, B. (1997). The next plague: Stigmatization and discrimination related to hepatitis C virus infection in Australia. *Health and Human Rights*, 2, 86–97.
- Cuadrado, A., Llerena, S., Cobo, C., Pallas, J. R., Mateo, M., Cabezas, J., et al. (2018). Microenvironment eradication of hepatitis C: A novel treatment paradigm. *The American Journal of Gastroenterology*, 113, 1639–1648.
- Cunningham, E. B., Applegate, T. L., Lloyd, A. R., Dore, G. J., & Grebely, J. (2015). Mixed HCV infection and reinfection in people who inject drugs—impact on therapy. *Nature Reviews Gastroenterology & Hepatology*, 12, 218–230.
- Cunningham, E. B., Hajarizadeh, B., Bretana, N. A., Amin, J., Betz-Stablein, B., Dore, G. J., et al. (2017). Ongoing incident hepatitis C virus infection among people with a history of injecting drug use in an Australian prison setting, 2005–2014: The HITS-p study. *Journal of Viral Hepatitis*, 24, 733–741.
- Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., et al. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: A multistage systematic review. *The Lancet Global Health*, 5, e1192–e1207.
- Des Jarlais, D. C., Arasteh, K., Feelemyer, J., McKnight, C., Barnes, D. M., Perlman, D. C., et al. (2018). Hepatitis C virus prevalence and estimated incidence among new injectors during the opioid epidemic in New York City, 2000–2017: Protective effects of non-injecting drug use. *Drug and Alcohol Dependence*, 192, 74–79.
- Dixon-Woods, M., Cavers, D., Agarwal, S., Annandale, E., Arthur, A., Harvey, J., et al. (2006). Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. *BMC Medical Research Methodology*, 6, 35.
- Doab, A., Treloar, C., & Dore, G. J. (2005). Knowledge and attitudes about treatment for hepatitis C virus infection and barriers to treatment among current injection drug users in Australia. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 40(Suppl. 5), S313–320.
- Falade-Nwulia, O., Suarez-Cuervo, C., Nelson, D. R., Fried, M. W., Segal, J. B., & Sulkowski, M. S. (2017). Oral direct-acting agent therapy for hepatitis C virus infection: A systematic review. *Annals of Internal Medicine*, 166, 637–648.
- Gardner, E. M., McLees, M. P., Steiner, J. F., Del Rio, C., & Burman, W. J. (2011). The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 52, 793–800.
- Grebely, J., Applegate, T. L., Cunningham, P., & Feld, J. J. (2017). Hepatitis C point-of-care diagnostics: In search of a single visit diagnosis. *Expert Review of Molecular Diagnostics*, 17, 1109–1115.
- Grebely, J., Bruggmann, P., Treloar, C., Byrne, J., Rhodes, T., Dore, G. J., et al. (2015). Expanding access to prevention, care and treatment for hepatitis C virus infection among people who inject drugs. *International Journal of Drug Policy*, 26, 893–898.
- Grebely, J., Bruneau, J., Bruggmann, P., Harris, M., Hickman, M., Rhodes, T., et al. (2017). Elimination of hepatitis C virus infection among PWID: The beginning of a new era of interferon-free DAA therapy. *International Journal of Drug Policy*, 47, 26–33.
- Grebely, J., Genoway, K. A., Raffa, J. D., Dhadwal, G., Rajan, T., Showler, G., et al. (2008). Barriers associated with the treatment of hepatitis C virus infection among illicit drug users. *Drug and Alcohol Dependence*, 93, 141–147.
- Grebely, J., Hajarizadeh, B., & Dore, G. J. (2017). Direct-acting antiviral agents for HCV infection affecting people who inject drugs. *Nature Reviews Gastroenterology & Hepatology*, 14, 641–651.
- Grebely, J., Lamoury, F. M. J., Hajarizadeh, B., Mowat, Y., Marshall, A. D., Bajis, S., et al. (2017). Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: A cohort study. *The Lancet Gastroenterology & Hepatology*, 2, 514–520.
- Grebely, J., Larney, S., Peacock, A., Colledge, S., Leung, J., Hickman, M., et al. (2019). Global, regional, and country-level estimates of hepatitis C infection among people who have recently injected drugs. *Addiction*, 114, 150–166.
- Grebely, J., Matthews, G. V., Lloyd, A. R., & Dore, G. J. (2013). Elimination of hepatitis C virus infection among people who inject drugs through treatment as prevention: Feasibility and future requirements. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 57, 1014–1020.
- Grebely, J., Oser, M., Taylor, L. E., & Dore, G. J. (2013). Breaking down the barriers to hepatitis C virus (HCV) treatment among individuals with HCV/HIV coinfection: Action required at the system, provider, and patient levels. *The Journal of Infectious*

- Diseases*, 207(Suppl. 1), S19–25.
- Hadland, S. E., DeBeck, K., Kerr, T., Feng, C., Montaner, J. S., & Wood, E. (2014). Prescription opioid injection and risk of hepatitis C in relation to traditional drugs of misuse in a prospective cohort of street youth. *BMJ Open*, 4, e005419.
- Hahn, J. A., Tully, D. C., Evans, J. L., Morris, M. D., Briceno, A., Bean, D. J., et al. (2019). Role of HCV viremia in corroborated HCV transmission events within young adult injecting partnerships. *Open Forum Infectious Diseases*, 6, ofz125.
- Hajarizadeh, B., Cunningham, E. B., Reid, H., Law, M., Dore, G. J., & Grebely, J. (2018). Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: A systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology*, 3, 754–767.
- Hajarizadeh, B., Grebely, J., Martinello, M., Matthews, G. V., Lloyd, A. R., & Dore, G. J. (2016). Hepatitis C treatment as prevention: Evidence, feasibility, and challenges. *The Lancet Gastroenterology & Hepatology*, 1, 317–327.
- Hajarizadeh, B., Grebely, J., Matthews, G., Martinello, M., & Dore, G. (2016). *Treatment uptake for chronic hepatitis C in Australia following universal access to interferon-free treatments*. *Hepatology*, Vol. 63, HOBOKEN 07030-5774, NJ USA: WILEY-BLACKWELL 111 RIVER ST948A.
- Harney, B. L., Whitton, B., Lim, C., Paige, E., McDonald, B., Nolan, S., et al. (2019). Quantitative evaluation of an integrated nurse model of care providing hepatitis C treatment to people attending homeless services in Melbourne, Australia. *International Journal of Drug Policy*.
- Harris, M. (2017). Managing expense and expectation in a treatment revolution: Problematising prioritisation through an exploration of hepatitis C treatment 'benefit'. *International Journal of Drug Policy*, 47, 161–168.
- Harris, M., Bonnington, O., Harrison, G., Hickman, M., Irving, W., & Hep, C. T. (2018). Understanding hepatitis C intervention success—Qualitative findings from the HepCATT study. *Journal of Viral Hepatitis*, 25, 762–770.
- Harris, M., & Rhodes, T. (2013). Hepatitis C treatment access and uptake for people who inject drugs: A review mapping the role of social factors. *Harm Reduction Journal*, 10, 7.
- Havens, J. R., Lofwall, M. R., Frost, S. D., Oser, C. B., Leukefeld, C. G., & Crosby, R. A. (2013). Individual and network factors associated with prevalent hepatitis C infection among rural Appalachian injection drug users. *American Journal of Public Health*, 103, e44–52.
- Havens, J. R., Walker, R., & Leukefeld, C. G. (2007). Prevalence of opioid analgesic injection among rural nonmedical opioid analgesic users. *Drug and Alcohol Dependence*, 87, 98–102.
- Henderson, C., Madden, A., & Kelsall, J. (2017). 'Beyond the willing & the waiting' - the role of peer-based approaches in hepatitis C diagnosis & treatment. *International Journal of Drug Policy*, 50, 111–115.
- Hochstatter, K. R., Stockman, L. J., Holzmacher, R., Greer, J., Seal, D. W., Taylor, Q. A., et al. (2017). The continuum of hepatitis C care for criminal justice involved adults in the DAA era: A retrospective cohort study demonstrating limited treatment uptake and inconsistent linkage to community-based care. *Health & Justice*, 5, 10.
- Hoj, S. B., Jacka, B., Minoyan, N., Artenie, A. A., & Bruneau, J. (2019). Conceptualising access in the direct-acting antiviral era: An integrated framework to inform research and practice in HCV care for people who inject drugs. *International Journal of Drug Policy*.
- Holeksa, J., Magel, T., Alimohammadi, A., Thiam, A., Yung, R., Chu, L., et al. (2019). Low rate of reinfection among a cohort of people who use drugs successfully treated for hepatitis C virus infection in Vancouver, Canada. *International Journal of Drug Policy*.
- Hutton, J., Doyle, J., Zordan, R., Weiland, T., Cocco, A., Howell, J., et al. (2019). Point-of-care Hepatitis C virus testing and linkage to treatment in an Australian inner-city emergency department. *International Journal of Drug Policy*, 72, 84–90. <https://doi.org/10.1016/j.drugpo.2019.06.021>.
- Iakunchykova, O., Meteliuk, A., Zelenov, A., Mazhnaya, A., Tracy, M., & Altice, F. L. (2018). Hepatitis C virus status awareness and test results confirmation among people who inject drugs in Ukraine. *International Journal of Drug Policy*, 57, 11–17.
- Ireland, G., Simmons, R., Hickman, M., Eastwood, B., Ramsay, M., & Mandal, S. (2019). Mapping the hepatitis C cascade of care in people attending drug treatment services in England: A data linkage study. *International Journal of Drug Policy*.
- Iversen, J., Grebely, J., Catlett, B., Cunningham, P., Dore, G. J., & Maher, L. (2017). Estimating the cascade of hepatitis C testing, care and treatment among people who inject drugs in Australia. *International Journal of Drug Policy*, 47, 77–85.
- Jakobsen, J. C., Nielsen, E. E., Feinberg, J., Katakam, K. K., Fobian, K., Hauser, G., et al. (2017). Direct-acting antivirals for chronic hepatitis C. *The Cochrane Database of Systematic Reviews*, 9, CD012143.
- Jakobsen, J. C., Nielsen, E. E., Koretz, R. L., & Gluud, C. (2018). Do direct acting antivirals cure chronic hepatitis C? *BMJ*, 361, k1382.
- Kaberg, M., Naver, G., Hammarberg, A., & Weiland, O. (2018). Incidence and spontaneous clearance of hepatitis C virus (HCV) in people who inject drugs at the Stockholm Needle Exchange-Importance for HCV elimination. *Journal of Viral Hepatitis*, 25, 1452–1461.
- Katzman, C., Mateu-Gelabert, P., Kapadia, S. N., & Eckhardt, B. J. (2019). Contact tracing for hepatitis C: The case for novel screening strategies as we strive for viral elimination. *International Journal of Drug Policy*.
- Krajden, M., Cook, D. A., Wong, S., Yu, A., Butt, Z. A., Rossi, C., et al. (2019). What is killing people with hepatitis C virus infection? Analysis of a population-based cohort in Canada. *International Journal of Drug Policy*.
- Lamoury, F. M. J., Bajis, S., Hajarizadeh, B., Marshall, A. D., Martinello, M., Ivanova, E., et al. (2018). Evaluation of the xpert HCV viral load finger-stick point-of-care assay. *The Journal of Infectious Diseases*, 217, 1889–1896.
- Larney, S., Grebely, J., Hickman, M., De Angelis, D., Dore, G. J., & Degenhardt, L. (2015). Defining populations and injecting parameters among people who inject drugs: Implications for the assessment of hepatitis C treatment programs. *International Journal of Drug Policy*, 26, 950–957.
- Larney, S., Kopinski, H., Beckwith, C. G., Zaller, N. D., Jarlais, D. D., Hagan, H., et al. (2013). Incidence and prevalence of hepatitis C in prisons and other closed settings: Results of a systematic review and meta-analysis. *Hepatology*, 58, 1215–1224.
- Larney, S., Peacock, A., Leung, J., Colledge, S., Hickman, M., Vickerman, P., et al. (2017). Global, regional, and country-level coverage of interventions to prevent and manage HIV and hepatitis C among people who inject drugs: A systematic review. *The Lancet Global Health*, 5, e1208–e1220.
- Lazarus, J. V., Pericas, J. M., Colombo, M., Ninburg, M., Wiktor, S., & Thursz, M. (2018). Viral hepatitis: 'E' is for equitable elimination. *Journal of Hepatology*, 69, 762–764.
- Madden, A., Hopwood, M., Neale, J., & Treloar, C. (2018a). Beyond cure: Patient reported outcomes of hepatitis C treatment among people who inject drugs in Australia. *Harm Reduction Journal*, 15, 42.
- Madden, A., Hopwood, M., Neale, J., & Treloar, C. (2018b). Beyond interferon side effects: What residual barriers exist to DAA hepatitis C treatment for people who inject drugs? *PloS One*, 13, e0207226.
- Makarenko, I., Artenie, A., Hoj, S., Minoyan, N., Jacka, B., Zang, G., et al. (2019). Transitioning from interferon-based to direct antiviral treatment options: A potential shift in barriers and facilitators of treatment initiation among people who use drugs? *International Journal of Drug Policy*.
- Marco, A., Guerrero, R. A., Vergara, M., Gallego, C., Sole, C., Planella, R., et al. (2019). Reinfection in a large cohort of prison inmates with sustained virological response after treatment of chronic hepatitis C in Catalonia (Spain), 2002–2016. *International Journal of Drug Policy*.
- Martinello, M., Hajarizadeh, B., Grebely, J., Dore, G. J., & Matthews, G. V. (2017). HCV cure and reinfection among people with HIV/HCV coinfection and people who inject drugs. *Current HIV/AIDS Reports*, 14, 110–121.
- Midgard, H., Hajarizadeh, B., Cunningham, E. B., Conway, B., Backmund, M., Bruggmann, P., et al. (2017). Changes in risk behaviours during and following treatment for hepatitis C virus infection among people who inject drugs: The ACTIVATE study. *International Journal of Drug Policy*, 47, 230–238.
- Morey, S., Hamoodi, A., Jones, D., Young, T., Thompson, C., Dhuny, J., et al. (2019). Increased diagnosis and treatment of hepatitis C in prison by universal offer of testing and use of telemedicine. *Journal of Viral Hepatitis*, 26, 101–108.
- Morris, M. D., Shiboski, S., Bruneau, J., Hahn, J. A., Hellard, M., Prins, M., et al. (2017). Geographic differences in temporal incidence trends of hepatitis C virus infection among people who inject drugs: The InC3 collaboration. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 64, 860–869.
- Overton, K., Clegg, J., Pekin, F., Wood, J., McGrath, C., Lloyd, A., et al. (2019). Outcomes of a nurse-led model of care for hepatitis C assessment and treatment with direct-acting antivirals in the custodial setting. *International Journal of Drug Policy*.
- Papaluca, T., McDonald, L., Craigie, A., Gibson, A., Desmond, P., Wong, D., et al. (2019). Outcomes of treatment for hepatitis C in prisoners using a nurse-led, statewide model of care. *Journal of Hepatology*, 70, 839–846.
- Pontali, E., Fiore, V., Ialungo, A. M., Ranieri, R., Mollaret, O., Barbarini, G., et al. (2018). Treatment with direct-acting antivirals in a multicenter cohort of HCV-infected inmates in Italy. *International Journal of Drug Policy*, 59, 50–53.
- Post, J. J., Arain, A., & Lloyd, A. R. (2013). Enhancing assessment and treatment of hepatitis C in the custodial setting. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 57(Suppl. 2), S70–74.
- Puzhko, S., Roy, E., Jutras-Aswad, D., Artenie, A. A., Fortier, E., Zang, G., et al. (2017). High hepatitis C incidence in relation to prescription opioid injection and poly-drug use: Assessing barriers to hepatitis C prevention. *International Journal of Drug Policy*, 47, 61–68.
- Rhodes, T., & Lancaster, K. (2019). Evidence-making hepatitis C cure: towards a science that knows more carefully. *International Journal of Drug Policy*, 72, 40–46. <https://doi.org/10.1016/j.drugpo.2019.06.023>.
- Richmond, J. A., Ellard, J., Wallace, J., Thorpe, R., Higgs, P., Hellard, M., et al. (2018). Achieving a hepatitis C cure: A qualitative exploration of the experiences and meanings of achieving a hepatitis C cure using the direct acting antivirals in Australia. *Hepatology, Medicine and Policy*, 3, 8.
- Rojas Rojas, T., Di Beo, V., Delorme, J., Barre, T., Mathurin, P., Protopopescu, C., et al. (2019). Lower HCV treatment uptake in women who have received opioid agonist therapy before and during the DAA era: The ANRS FANTASIO project. *International Journal of Drug Policy*.
- Scott, N., Doyle, J. S., Wilson, D. P., Wade, A., Howell, J., Pedrana, A., et al. (2017). Reaching hepatitis C virus elimination targets requires health system interventions to enhance the care cascade. *International Journal of Drug Policy*, 47, 107–116.
- Selfridge, M., Cunningham, E. B., Milne, R., Drost, A., Barnett, T., Lundgren, K., et al. (2019). Direct-acting antiviral treatment for hepatitis C, reinfection and mortality among people attending an inner-city community health centre in Victoria, Canada. *International Journal of Drug Policy*.
- Simmons, B., Saleem, J., Hill, A., Riley, R. D., & Cooke, G. S. (2016). Risk of late relapse or reinfection with hepatitis C virus after achieving a sustained virological response: A systematic review and meta-analysis. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 62, 683–694.
- Socias, M. E., Karamouzian, M., Parent, S., Barletta, J., Bird, K., & Ti, L. (2019). Integrated models of care for people who inject drugs and live with hepatitis C virus: A systematic review. *International Journal of Drug Policy*.
- Stephens, D. B., Young, A. M., & Havens, J. R. (2017). Healthcare contact and treatment uptake following hepatitis C virus screening and counseling among rural Appalachian people who use drugs. *International Journal of Drug Policy*, 47, 86–94.
- Strehlow, A. J., Robertson, M. J., Zerger, S., Ronney, C., Arangua, L., Farrell, E., et al. (2012). Hepatitis C among clients of health care for the homeless primary care clinics. *Journal of Health Care for the Poor and Underserved*, 23, 811–833.
- Swan, D., Long, J., Carr, O., Flanagan, J., Irish, H., Keating, S., et al. (2010). Barriers to

- and facilitators of hepatitis C testing, management, and treatment among current and former injecting drug users: A qualitative exploration. *AIDS Patient Care and STDs*, 24, 753–762.
- The Polaris Observatory HCV Collaborators (2017). Global prevalence and genotype distribution of hepatitis C virus infection in 2015: A modelling study. *Lancet Gastro Hepatol*, 2, 161–176.
- Treloar, C., Rance, J., Dore, G. J., Grebely, J., & Group, E. S. (2014). Barriers and facilitators for assessment and treatment of hepatitis C virus infection in the opioid substitution treatment setting: Insights from the ETHOS study. *Journal of Viral Hepatitis*, 21, 560–567.
- Trickey, A., Fraser, H., Lim, A. G., Peacock, A., Colledge, S., Walker, J. G., et al. (2019). The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: A modelling study. *The Lancet Gastroenterology & Hepatology*, 4, 435–444.
- Valencia, J., Alvaro-Meca, A., Troya, J., Cuevas, G., Gutierrez, J., Morro, A., et al. (2019). High rates of early HCV reinfection after DAA treatment in people with recent drug use attended at mobile harm reduction units. *International Journal of Drug Policy*.
- Valencia La Rosa, J., Ryan, P., Alvaro-Meca, A., Troya, J., Cuevas, G., Gutierrez, J., et al. (2018). HCV seroconversion in a cohort of people who use drugs followed in a mobile harm reduction unit in Madrid: Breaking barriers for HCV elimination. *PloS One*, 13, e0204795.
- Van Handel, M. M., Rose, C. E., Hallisey, E. J., Kolling, J. L., Zibbell, J. E., Lewis, B., et al. (2016). County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among persons who inject drugs, United States. *Journal of Acquired Immune Deficiency Syndromes*, 73, 323–331.
- van Santen, D. K., van der Helm, J. J., Lindenburg, K., Schim van der Loeff, M., & Prins, M. (2017). HIV and hepatitis C treatment uptake among people who use drugs participating in the Amsterdam Cohort Studies, 1985–2015. *International Journal of Drug Policy*, 47, 95–101.
- WHO (2017). In W. H. Organization (Ed.). *Global hepatitis report 2017*. Geneva: World Health Organization.
- Williams, B., Howell, J., Doyle, J., Thompson, A. J., Draper, B., Layton, C., et al. (2019). Point-of-care hepatitis C testing from needle and syringe programs: An Australian feasibility study. *International Journal of Drug Policy*.
- Williams, B., Nelons, D., Seaman, A., Witkowska, M., Ronan, W., Wheelock, H., et al. (2019). Life projects: The transformative potential of direct-acting antiviral treatment for hepatitis C among people who inject drugs. *International Journal of Drug Policy*.
- Wolfe, D., Luhmann, N., Harris, M., Momenghalibaf, A., Albers, E., Byrne, J., et al. (2015). Human rights and access to hepatitis C treatment for people who inject drugs. *International Journal of Drug Policy*, 26, 1072–1080.
- Yehia, B. R., Schranz, A. J., Umscheid, C. A., & Lo Re, V., 3rd (2014). The treatment cascade for chronic hepatitis C virus infection in the United States: A systematic review and meta-analysis. *PloS One*, 9, e101554.
- Young, J., Rossi, C., Gill, J., Walmsley, S., Cooper, C., Cox, J., et al. (2017). Risk factors for hepatitis C virus reinfection after sustained virologic response in patients coinfected with HIV. *Clinical Infectious Diseases: Publication of the Infectious Diseases Society of America*, 64, 1154–1162.
- Zibbell, J. E., Asher, A. K., Patel, R. C., Kupronis, B., Iqbal, K., Ward, J. W., et al. (2018). Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004 to 2014. *American Journal of Public Health*, 108, 175–181.
- Zibbell, J. E., Hart-Malloy, R., Barry, J., Fan, L., & Flanagan, C. (2014). Risk factors for HCV infection among young adults in rural New York who inject prescription opioid analgesics. *American Journal of Public Health*, 104, 2226–2232.