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Global policy and access to new hepatitis C therapies for people who inject drugs

Authors:

Joseph S. Doyle^{1,2,3,4}, Esther J. Aspinall^{5,6}, Sharon J. Hutchinson^{5,6}, Brendan Quinn¹, Charles Gore⁷, Stefan Z. Wiktor⁸, Margaret E. Hellard^{1,3,4*}

Affiliations:

¹Centre for Population Health, Burnet Institute, Melbourne, Australia; ²Department of Medicine, University of Melbourne, Australia; ³School of Population Health and Preventive Medicine, Monash University, Melbourne, Australia; ⁴Department of Infectious Diseases, The Alfred Hospital, Melbourne, Australia; ⁵Health Protection Scotland, Glasgow, UK; ⁶Glasgow Caledonian University, Glasgow, UK; ⁷World Hepatitis Alliance, Geneva, Switzerland; ⁸Department of HIV/AIDS, World Health Organisation, Geneva, Switzerland.

Author contact details:

Dr Joseph S. Doyle MBBS FRACP

Centre for Population Health, Burnet Institute, 85 Commercial Road, Melbourne VIC 3004.

Email: j.doyle@burnet.edu.au; Telephone: +61 3 8506 2324; Fax: +61 3 9282 2100.

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Abbreviations: APRI, aminotransferase/platelet ratio index; ASSIST, Alcohol, Smoking and Substance Involvement Screening Test; DAA, direct-acting antiviral therapy; FIB4; HCV, hepatitis C virus; HIC, high-income countries; HIV, human immunodeficiency virus; LMIC, low- and middle-income countries ; SVR, sustained virological response; NAT, nucleic acid testing; NSP, needle/syringe program; OST, opioid substitution therapy; PEG-IFN, pegylated-interferon; PWID, people who inject drugs; QALY, quality adjusted life years; QOL, quality of life; RNA, ribonucleic acid; RR, relative risk; WHO, World Health Organization

ABSTRACT

People who inject drugs (PWID) are disproportionately affected by hepatitis C virus (HCV). This review outlines policy recommendations made in the 2014 World Health Organisation (WHO) Guidelines on Screening, Care and Treatment of HCV and their relevance to PWID. It also canvasses issues that will affect translation of these global guidelines into practice. The first global HCV guidelines released by WHO have recently advocated targeted HCV testing for PWID, assessment of liver disease and support for alcohol reduction during care. They also strongly advocate treatment using currently licenced direct-acting antiviral agents for all individuals, in particular PWID as a key affected population. New HCV treatment regimens have the potential to cure more than 90% of treated individuals. Scaling-up treatment among PWID has the potential to improve individual and population health by reducing HCV transmission, improving quality of life and supporting behaviour modifications that lead to less risk-taking over time.

PWID face several barriers to accessing HCV care and treatment that need to be overcome. Testing services need re-orientation toward PWID, individuals need to be informed of their results and provided with direct linkage to ongoing care. Health services need to provide care in the community using simpler, cheaper and more accessible modes of delivery. Healthcare costs and pharmaceutical costs need to be minimised so PWID, who are highly marginalised, can access HCV treatment. Sustained scale-up of treatment for PWID could simultaneously improve individual health and achieve the goal of eliminating HCV transmission among this high-risk and vulnerable group.

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Introduction

Chronic hepatitis C virus (HCV) infection is a significant global health problem, affecting approximately 185 million individuals globally, many of whom are unaware of their infection [1, 2]. Among people who inject drugs (PWID), HCV prevalence is estimated at 60-70%, although there is substantial variation in burden of disease regionally and nationally [3] (Figure 1). Most new HCV infections in high-income countries (HIC) occur among PWID, while in low- and middle-income countries (LMIC), injecting behaviour is still a key risk factor for transmission [3]. Whilst HCV treatment uptake remains low, PWID in particular lack access to care and treatment due to practical, systematic and perceived barriers. Arising from its framework for global action on HCV, the World Health Organization (WHO) produced the first global Guidelines for the Screening, Care and Treatment of Persons with Hepatitis C Infection in April 2014 [4]. Along with other professional guidelines and community action programmes, the WHO guidelines aim to improve access to care and treatment, especially among key affected populations like PWID.

This article first outlines key recommendations from the WHO guidelines, how PWID were considered in their development, and the relevance of each recommendation to care and treatment for PWID. Second, it considers the impact of treatment of PWID beyond the individual medical benefits to broader public health and social benefits. It then examines the translation of guidelines into practice exploring the current barriers to care and treatment, including finding cases, health service orientation, cost, and perceptions about behaviour modification and reinfection in the era of simpler treatment. Finally, this article identifies features that will enable treatment scale-up for PWID, including health infrastructure, community engagement and affordable care. It demonstrates that the confluence of new, simpler and highly-effective HCV antiviral agents overcome many of the perceived barriers for treating PWID; coupled with policy recommendations that promote equitable access to medical care for PWID, there is hope that we can now dramatically decrease the burden of HCV infection among injecting populations worldwide.

Global policy and guidelines

The WHO Guidelines of 2014 are the first global HCV treatment guidelines issued by WHO. They are primarily targeted at policy-makers in LMIC formulating country-specific treatment programmes. Unlike clinical management guidelines issued by professional associations [e.g., 5], they use a public-health approach that aims to evaluate scientific evidence and make recommendations mindful of feasibility of implementation in resource-limited settings. These

guidelines are informed by the results of several systematic reviews directed at key questions in HCV testing, care and treatment. They employ a standardised method to grade strength of evidence and make recommendations, taking into account benefits and harms, values and preferences, and resources [6]. These factors are evaluated by a guidelines development group comprising clinicians, researchers, programme managers, and community representatives (including people living with HCV and PWID), among other stakeholders. The key recommendations and levels of evidence developed from this process are summarised in Table 1.

Recommendations on HCV screening and diagnosis

The WHO Guidelines first address how best to identify people with chronic HCV infection; a systematic review examined interventions that promoted HCV testing of asymptomatic individuals [7]. This review investigated the effectiveness of targeted testing interventions on HCV case detection, treatment uptake, and prevention of liver-related morbidity. Studies evaluating targeted interventions – those directed at groups at higher risk of HCV, chiefly including PWID – were compared with no target intervention or routine practice. Targeted testing, compared to no targeted testing, was associated with increased cases detected [number of studies (n)=14; pooled relative risk (RR) 1.7, 95% CI 1.3-2.2] and patients commencing therapy (n=4; RR 3.3, 95% CI 1.1-10.0). Testing interventions delivered by practitioners increased test uptake and cases detected (n=12; RR 3.5, 95% CI 2.5-4.8; and n=10; RR 2.2, 95% CI 1.4-3.5, respectively), whereas more general media/information-based interventions were less effective (n=4; RR 1.5, 95% CI 0.7-3.0; and n=4; RR 1.3, 95% CI 1.0-1.6, respectively). As a result, the WHO guidelines strongly recommend focusing HCV testing efforts on individuals in populations with a high HCV prevalence, which includes PWID in most contexts. Careful consideration of resources, testing modalities and local epidemiology would influence implementation of this recommendation.

Since most laboratory testing or point-of-care diagnosis involved HCV antibody detection initially, a question arises as to when chronic HCV should be confirmed using nucleic acid testing (NAT) to detect HCV ribonucleic acid (RNA). HCV RNA testing immediately after antibody diagnosis provides individuals with their current infection status which might affect health-seeking or risk-taking behaviour [8, 9], as well as lead to linkage to care and treatment. In many contexts, particularly resource-poor settings, NAT testing is largely deferred until an individual is being considered for treatment which may be many years after diagnosis. No direct evidence was available to answer this question. Yet given the potential for PWID and

others to reduce risk-taking behaviour or seek care with awareness of their HCV infection status, the WHO guidelines suggest that NAT testing be performed directly following a positive HCV antibody test, in addition to any HCV RNA testing as part of the assessment for receiving treatment for HCV.

Recommendations on HCV care

Models of HCV care, health resources and infrastructure vary widely. Moreover, HCV treatment is frequently delayed or is unavailable – particularly in LMIC – during which time liver disease may progress or behaviours might influence health status. Given the potential for alcohol to accelerate HCV-associated liver disease [10], screening and counselling for alcohol use and fibrosis assessment were considered two key elements of HCV care requiring comment in the WHO Guidelines. A systematic review was conducted to determine whether alcohol reduction interventions among people with HCV, compared with no intervention, were associated with reduced alcohol intake, changes in fibrosis or liver-related morbidity or mortality [11]. Five small, heterogeneous trials or cohort studies were identified that provided limited evidence that alcohol reduction interventions might be associated with a modest reduction in alcohol consumption among HCV-infected individuals with moderate-to-high alcohol intake [11]. An earlier meta-analysis of brief alcohol reduction interventions among people without HCV infection, compared with no intervention, found a similar, small reduction in total alcohol consumption from 313g/week to 275g/week; a 38g (3 standard drinks) mean reduction [12]. Accordingly, the WHO guidelines recommend that alcohol intake assessments be performed for all persons with HCV infection followed by the offer of a behavioural alcohol reduction intervention for persons with moderate-to-high alcohol intake. The WHO Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) package is one standardised tool designed for use in primary care, validated internationally, and can be helpful in screening PWID for co-morbid substance use and enable early intervention [13].

Fibrosis stage is frequently used to determine urgency of HCV treatment. Assessment of fibrosis for those with chronic HCV is largely dependent upon access to testing resources and trained staff. After reviewing the evidence for non-invasive, low-resource fibrosis assessment, the WHO Guidelines suggest that in resource-limited settings, the aminotransferase/platelet ratio index (APRI) or Fibrosis-4 score (FIB4) be used for the assessment of hepatic fibrosis rather than other non-invasive tests that require more resources such as elastography or Fibrotest. If it was available and resources allow, transient

elastography was also recommended. A series of systematic reviews were conducted to assess the diagnostic yield of more complex and expensive tests (eg elastography) and simple biochemically and haematologically-derived indices (eg APRI and FIB4) [14]. They are summarised in a health technology assessment supporting the use of the APRI score (or FIB4) with high and low cut offs to determine the likelihood of cirrhosis or absence of significant fibrosis, respectively [14]. Easier, primary care assessment of fibrosis stage could help ensure that PWID with advanced liver damage are promptly referred for treatment.

Recommendations on HCV treatment

A series of systematic reviews were conducted of all approved HCV antiviral agents (at April 2014), which included boceprevir, telaprevir, simeprevir and sofosbuvir using pegylated-interferon (PEG-IFN) and ribavirin as the comparator. Given the need for guidance on treatment for LMIC settings, the effectiveness of pegylated-interferon was also appraised against standard interferon, which is still used in some contexts due to its lower cost.

While new HCV agents have not been directly compared among PWID with non-PWID, an earlier meta-analysis that pooled responses in six studies using PEG-IFN and ribavirin among PWID demonstrated a sustained virological response (SVR) of 37% (95% CI 26-48%) among individuals with HCV-genotype-1 infection and 67% (95% CI 56%-78%) in genotypes-2 or -3 infection [15]. These real-world virological responses among PWID are comparable to non-injecting populations, supporting recommendations for HCV treatment among PWID. Given high-quality evidence for the benefits of HCV treatment on virological response, liver morbidity and mortality [4], the WHO strongly recommend that all adults and children with chronic HCV infection, including PWID, should be assessed for antiviral treatment.

Moreover, a strong statement was made recommending PEG-IFN and ribavirin over standard interferon and ribavirin to discourage the use of standard interferon in LMIC.

The additional effectiveness of the HCV protease inhibitors boceprevir, telaprevir and simeprevir added to PEG-IFN and ribavirin has been described elsewhere [16, 17]. In light of simpler, safer direct-acting antiviral therapies (DAAs), WHO conditionally recommended the addition of boceprevir or telaprevir with PEG-IFN and ribavirin. However, it strongly recommended simeprevir, PEG-IFN and ribavirin over PEG-IFN and ribavirin alone. A key consideration when using these regimens among PWID will be drug-drug interactions, which need individualising depending on co-morbidities such as HIV, substance use, and opioid substitution therapy (OST). Evidence for the use of sofosbuvir with PEG-IFN and ribavirin,

and sofosbuvir with ribavirin alone, indicated SVR greater than 90% can be achieved with few significant side effects in clinical trial settings [18-20]. While these registration studies did not make a direct comparison of sofosbuvir regimens with PEG-IFN and ribavirin, the WHO guidelines strongly recommend sofosbuvir with or without PEG-IFN depending on genotype based on the evidence for high efficacy and low toxicity.

Since the WHO Guidelines were published, further drug combinations have been licenced by the US Food and Drug Administration. Fixed-dose sofosbuvir and ledipasvir was licenced in October 2014 and is active against all genotypes (except with less genotype-3a activity, in particular), with >90% SVR when used for 12 weeks [18-20]. This combination tablet has the potential to reduce treatment complexity and improve treatment uptake dramatically [21]. Different oral combinations by other manufacturers have also completed phase-three evaluation and will soon follow or have followed through regulatory approval into clinical practice [22, 23]; their simplicity and low toxicity may be particularly helpful for overcoming barriers to treating PWID.

Benefits of expanding HCV treatment to PWID

The global policy environment promoted by WHO and scientific and community associations is now explicitly orientated toward expanding treatment access for PWID. The medical benefits for individuals with HCV infection and equity arguments are reflected strongly in such guidance. However, additional public health and social benefits also justify expanded treatment access, and might help allay residual reservations in some sectors about treatment of PWID.

Public health benefits of treating PWID

Despite the well-established effectiveness and low cost of current harm reduction strategies for PWID, including OST and needle-syringe programmes (NSP), these methods have been only partially effective at reducing HCV transmission, which is in part due to poor coverage [24]. Expanded treatment access, in addition to widely-implemented harm reduction strategies, could greatly reduce or eliminate ongoing HCV transmission. Mathematical modelling using Australian, British and Canadian data suggest that treating a relatively small proportion of PWID with chronic HCV infection could significantly reduce HCV prevalence over 15 years [25-29]. These models demonstrate that the impact on prevalence varies on the number of individuals treated, the background prevalence of HCV, treatment effectiveness, and the speed of treatment scale-up. HCV prevalence could halve if treatment with >90%

SVR was scaled-up from the current rate of approximately 5 per 1000 PWID treated annually to 15, 40, or 76 per 1,000 PWID treated annually in Edinburgh (Scotland), Melbourne (Australia), and Vancouver (Canada), respectively (Figure 2) [28].

Moreover, treating recent HCV infection may have a greater impact on transmission. The impact of injecting networks on HCV transmission are critical in understanding spread of disease, since individuals with more injecting partners have a greater incidence of infection and reinfection [30]. Based on social network models, treating an individual in conjunction with all their known partners could have the greatest prevention benefit and be practically implemented [31]. Two large clinical trials have been designed to examine this concept of HCV “treatment as prevention” and are currently underway among both community PWID and prison populations (see [clinicaltrials.gov NCT02363517](https://clinicaltrials.gov/ct2/show/study/NCT02363517) and [NCT02064049](https://clinicaltrials.gov/ct2/show/study/NCT02064049)).

Social benefits of treating PWID

Chronic HCV infection adversely influences health-related quality of life (QOL) [32-34]. QOL changes in HCV may be related to cirrhosis or awareness of infection [33-35], since the natural history of HCV infection is to remain largely asymptomatic. Treatment with PEG-IFN can impair QOL [32], while SVR has also been associated with improved QOL, albeit not in all studies [33, 36]. Since PWID are already a marginalised and vulnerable population, global access to interferon-free treatment would clearly be ideal for such individuals, may avoid treatment-related impairment of QOL, and could improve long-term QOL and enhance treatment uptake and utilisation of other health and support services.

Diagnosing and linking PWID to care might also reduce needle-sharing out of concern for injecting partners. Two longitudinal cohort studies have evaluated the impact of HCV diagnosis on behaviour in the short term and over time [8, 9]; both found a reduction in frequency and prevalence of injecting drug use after diagnosis. While these benefits are small, such findings suggest that expanding access to care and treatment for PWID would increase diagnosis and lead to some positive behaviour change. Social functioning, which relates to stable accommodation, employment and inter-personal relationships, is often limited in PWID and is known to influence treatment uptake and side effects during HCV treatment [37-39]. Policies that promote simpler and less toxic therapies are less likely to affect social functioning during treatment.

Translating policy into practice

Despite the medical, public health and social benefits of HCV treatment for PWID, many practical, financial and knowledge barriers need to be overcome to translate global policy into practice.

Testing and linkage to care

Globally, low frequency of HCV testing among PWID is often a result of limited health-seeking behaviours, lower uptake of preventative medical care and under-disclosure of injecting behaviour to clinicians due to real and perceived stigma [40, 41]. Confirmation of current HCV infection using NAT testing, given the additional healthcare episode, expense and follow-up of results also limits accurate diagnosis of chronic HCV. UNITAID have recently evaluated potential costs of diagnosis US\$300-1400, excluding liver biopsy, and costs to patients can be highly variable [42]. Studies describing the HCV care cascade from diagnosis to treatment completion demonstrate attrition of individuals at every step in the care pathway [43]; this attrition is often exaggerated for PWID. Moreover, laboratory and public health surveillance systems largely lack the ability to determine new-onset HCV which reflects a period of high risk of onward HCV infection in PWID [44]. Innovate interventions that deliver testing, results and immediate pathways to care in the community, and surveillance systems that assist in identify recent infection could have substantial public health benefits for PWID.

Health service organisation

HCV care has traditionally been the provenance for specialists and tertiary care given the complexity of care, liver complications when treatment was initiated in advanced fibrosis, and funding models that favour clinician-led care. In order to offer HCV treatment to everyone living with infection, including PWID, an expansion in treatment services will be necessary. Task-shifting to primary care or other healthcare workers accompanied by appropriate workforce training and development will be critical given constraints on human resources and costs. It may also have the important benefit of accommodating patient preference, which might facilitate treatment uptake, adherence and quality of life. Peer workers will also be critical in designing models of care, providing education and support, and integrated into delivering care if treatment scale up is to be achieved and simplified. Several factors make a simplified model for HCV treatment delivery achievable: less individualised and more standardised pharmaceutical regimens; fewer side effects; less monitoring; and community HCV education. While the delivery of oral HCV therapies have

not yet been evaluated outside of tertiary care settings, the safe use of PEG-IFN based treatment in prisons [45], primary care [46] and using nurse-led models of care [47] suggests new antivirals will be easier to deliver. Health services and programme managers have the opportunity – and challenge – to re-design their models of care to accommodate those with HCV and the needs of key populations like PWID.

HCV treatment services frequently prioritise therapy for those with advanced liver disease given the risk of progression to liver failure and cancer, and resource limitations. However, current PWID compared to past PWID are, in general, more likely to have milder liver disease and so clinical guidelines [e.g. 5] that prioritise treatment for individuals with advanced fibrosis pose a potentially significant barrier to treatment for PWID [48]. Different public health outcomes could result from re-orientating HCV services at PWID versus those with advanced fibrosis. United Kingdom modelling indicated that prioritising treatment uptake among PWID will substantially impact on incident transmission; however, this approach foregoes the optimal impact on liver-related mortality. Conversely, targeting those with moderate or advanced fibrosis could have greater impact on liver mortality but may be suboptimal at averting incident infection [48]. The challenge for health systems will be whether they can orientate health services to offer therapy to individuals with both advanced fibrosis and PWID in the context of the current high drug prices.

Affordable treatment

Current policy to offer treatment to everyone will be impossible to implement without substantial falls in the cost of HCV antivirals. At the time of writing, treatment using sofosbuvir could cost as much as US\$1000 per pill or US\$84,000 for a 12 week course of treatment [49]. The current market price of medicines is likely to fall in some jurisdictions with generic manufacturing through voluntary licensing and competition from soon-to-be-approved medications. Tiered pricing arrangements – where a manufacturer varies price by country and income status – are also likely to expand treatment access slightly by lowering prices at the country level. Nevertheless, individual PWID may still face unacceptably high barriers to treatment if out-of-pocket costs for medicines, laboratory tests and health care visits are not minimised or subsidised locally. Short of compulsory licensing to grant generic manufacturers authority to produce patented drugs, in the immediate future, cooperation between the pharmaceutical industry, governments and advocacy from healthcare providers and scientific and affected communities will be necessary to make treatment affordable for PWID.

Ongoing innovation could further assist in price reductions. Potent pan-genotypic antiviral agents will further simplify treatment, avoid the need for expensive genotyping prior to therapy, and probably reduce the frequency of NAT testing during therapy. The licensing of fixed-dose combination therapy of sofosbuvir and ledipasvir for 12 weeks, with high SVR, with activity against most genotypes, and few side-effects makes treatment simplification realistic [18-20]. Newer regimens and research into treatment of acute HCV – which is particularly relevant to PWID given their risk of new infection – might also reduce the length of therapy further, and therefore lower cost substantially.

The cost-effectiveness of chronic HCV treatment among PWID compared to former-PWID and non-injectors has been evaluated in some HIC settings. Modelling based on Australian healthcare costs and utility estimates derived from internationally has explored whether treatment of current PWID and former injectors, compared with those who have never injected, is cost-effective [50]. This research found that despite comorbidities, increased mortality from substance use, and reduced adherence, PEG-IFN and ribavirin treatment of both current and former PWID is cost-effective at under US\$8,000 per quality-adjusted-life-year gained, compared with under US\$4,000 per quality-adjusted-life-year (QALY) gained in non-injectors. The model is highly sensitive to drug costs; the cost of first-generation protease inhibitors made some scenarios of early treatment not cost-effective. United Kingdom derived modelling among PWID prior to interferon-free therapy has come to similar cost-effective conclusions [51]. However, if treatment of PWID were to have a significant prevention benefit and avert new cases of HCV infection, treatment could even be cost-saving by averting future health costs. Despite the benefits and even if the new treatment regimens are “cost-effective”, assuming no immediate changes in drug prices, the financial challenge posed by medication and delivery costs for all people needing treatment would overwhelm current health systems.

In this context, treatment aimed at people at risk of transmitting infection – including PWID – could become especially important since preventing new infections may make both public health *and* economic sense. A recent abstract evaluating scale-up of HCV treatment in the UK assessed the cost effectiveness of IFN-free DAAs delivered immediately compared with deferral until cirrhosis. The model assumed both individual and population prevention benefits of successful treatment. It found the greatest net monetary benefit and lowest cost per QALY among PWID with mild (GB£4650) or moderate (GB£2855) liver disease, while

treatment of non-PWID cost GB£13,100-22,900 for each additional QALY. This analysis indicates that treatment of PWID – especially in low prevalence settings – averts HCV infections hence it becomes cost-effective to treat PWID early rather than delay treatment [52].

Perceptions about risk behaviours and treatment access

HCV reinfection rates after chronic HCV treatment among PWID are generally low, estimated by one meta-analysis of five studies at 2.4 (95% CI, 0.9–6.1) per 100 person-years [15]. Nevertheless, concerns that risk-taking behaviour will increase as fear of disease and treatment declines in the era of highly-effective therapy – so called “risk compensation” – still persist and need addressing. The arguments mounted against treatment of PWID are three-fold: first, that as treatment becomes easier, individuals will be less concerned about reinfection and re-treatment; second, that PWID are unlikely to adhere to prolonged, self-administered, oral therapy given perceived social instability; and third, that PWID accessing DAA treatment may no longer see HCV treatment as a key moment to make broader changes to their lifestyle.

Insights from human immunodeficiency virus (HIV) infection – another chronic viral infection where highly active antiviral therapy has been available for nearly two decades – suggest that any correlation between risk-taking behaviour and treatment commencement is often overstated. In a meta-analysis of 60 studies, injecting risk-taking (measured by sharing needles/syringes) and sexual risk-taking (measured by inconsistent condom use and new sexually transmitted infection diagnoses) were not associated with commencement of HIV antiretroviral therapy [53]. Moreover, among those individuals on therapy, sexual risk-taking was marginally lower, reflecting that individuals commencing long-term therapy are probably self-selecting and lower risk-takers than those not undertaking therapy. Engagement with healthcare, support services and counselling coupled with treatment may have some role in reinforcing positive behaviour. Extrapolating from our knowledge of HIV, it is plausible that HCV therapy will not adversely influence risk-taking behaviour. Future research among PWID cohorts starting novel therapy should explicitly aim to measure changes in behaviour associated with treatment to assess whether simpler treatment has this theoretical impact.

Treatment scale-up for PWID is also an opportunity to reinforce other established harm reduction measures, including increasing coverage of opiate substitution therapy [54, 55], needle and syringe programs [54, 56, 57], and frequent repeat HCV testing and counselling,

particularly where cheap, reliable and rapid testing is available [58]. Expanded access to treatment should not come at a cost to these services; moreover it could facilitate their delivery and better integrate a range of HCV services.

Conclusions

Despite being a highly marginalised population, PWID can be engaged in care and treatment programmes, achieve comparable response to treatment in real-world settings, and have so far demonstrated low rates of reinfection long-term. The reasons for PWID traditionally being excluded from treatment can be largely overcome through treatment advances, advocacy and changes in policy. Moreover, there is an exciting prospect that treatment of PWID may confer both individual benefits and substantial population prevention benefits. To achieve this, national and international policy must facilitate the rapid scale-up of treatment and include PWID specifically in treatment access campaigns. Policies must also adapt rapidly to evolving research and effectively engage PWID in order to plan and deliver treatment services. It is conceivable that long-term goals could be set to eliminate HCV from within PWID in countries where testing and treatment programmes are widely available and accessible. The hope is that with widespread, efficacious treatment targeted at PWID, prevalent HCV will decline and HCV transmission will be effectively prevented.

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FIGURE LEGENDS

Figure 1: Burden of HCV among PWID

Estimated global population with history of HCV infection, chronic HCV infection, and PWID with chronic HCV infection. The estimated number of PWID globally is 16 million (range 11-21 million). PWID living with chronic HCV estimates (10 million, range 6-15 million) compares to 2.8 million (range 1-6 million) PWID living with HIV infection [1, 3].

Figure 2: DAA treatment scale up among PWID

Chronic prevalence over time in (A) Edinburgh, (B) Melbourne, and (C) Vancouver. Simulations show no treatment scale-up from baseline, or scale-up to 10, 20, 40, or 80 per 1,000 PWID treated annually assuming no treatment prior to 2002, a linear scale-up to baseline treatment rates during 2002-2007, and baseline treatment rates during 2007-2012. A linear scale-up from baseline to scaled-up rate during 2015-2017 was modelled. Reproduced from Martin et al, *Hepatology*, 2013 under Creative Commons Attribution License; copyright with authors [28].

TABLES

Table 1: WHO recommendations for the screening, care and treatment of persons with HCV infection (April 2014)[4]

Recommendations on screening for HCV infection	
<i>Screening to identify persons with HCV infection</i>	It is recommended that HCV serology testing be offered to individuals, who are part of a population with high HCV prevalence or who have a history of HCV risk exposure/behaviour. (Strong recommendation, moderate quality of evidence)
<i>When to confirm diagnosis of chronic HCV infection</i>	It is suggested that nucleic acid testing (NAT) for HCV ribonucleic acid (RNA) be performed directly following a positive HCV antibody test to establish the diagnosis of chronic HCV infection, in addition to HCV RNA testing as part of the assessment for receiving treatment for HCV. (Conditional recommendation, very low quality of evidence)
Recommendations on care of people infected with HCV	
<i>Screening for alcohol use and counselling to reduce moderate and high levels of alcohol intake</i>	An alcohol intake assessment is recommended for all persons with HCV infection followed by the offer of a behavioural alcohol reduction intervention for persons with moderate-to-high alcohol intake. (Strong recommendation, moderate quality of evidence)
<i>Assessing degree of liver fibrosis and cirrhosis</i>	In resource-limited settings, it is suggested that the aminotransferase/platelet ratio index (APRI) or FIB4 be used for the assessment of hepatic fibrosis rather than other non-invasive tests that require more resources such as elastography or Fibrotest. (Conditional recommendation, low quality of evidence)
Recommendations on treatment of HCV infection	
<i>Assessing for HCV treatment</i>	All adults and children with chronic HCV infection, including people who inject drugs, should be assessed for antiviral treatment. (Strong recommendation, moderate quality of evidence)
<i>Treatment with pegylated interferon and ribavirin</i>	Pegylated interferon in combination with ribavirin is recommended for the treatment of chronic HCV infection rather than standard non-pegylated interferon with ribavirin. (Strong recommendation, moderate quality of evidence)
<i>Treatment with telaprevir or boceprevir</i>	Treatment with direct-acting antivirals (telaprevir or boceprevir), given in combination with pegylated interferon and ribavirin, is suggested for genotype 1 chronic HCV infection rather than only pegylated interferon and ribavirin. (Conditional recommendation, moderate quality of evidence)
<i>Treatment with sofosbuvir*</i>	Sofosbuvir, given in combination with ribavirin with or without pegylated interferon (depending on the HCV genotype), is recommended in genotypes 1, 2, 3 and 4 HCV infection rather than pegylated interferon and ribavirin alone (or no treatment for persons who cannot tolerate interferon). (Strong recommendation, high quality of evidence)
<i>Treatment with simeprevir*</i>	Simeprevir, given in combination with pegylated interferon and ribavirin, is recommended for persons with genotype 1b HCV infection and for persons with genotype 1a HCV infection without Q80K polymorphism rather than only pegylated interferon and ribavirin. This recommendation applies to persons with HCV mono-infection as well as those with HIV/HCV coinfection. (Strong recommendation, high quality of evidence)

**These recommendations were made without taking resource use into consideration, as pricing information was not available for any country other than the United States at the time this recommendation was formulated.*