

# on hepatitis C treatment efficacy among people who use drugs

### **KEY MESSAGES**

Treatment is highly effective at curing hepatitis C for all people, including people who use drugs. People who use drugs, including those who are on opioid agonist treatment, are just as likely to cure their hepatitis C with treatment as other populations who received treatment. People who use drugs should be offered hepatitis C treatment, regardless of whether they plan to continue, reduce or stop their use of substances.

Hepatitis C reinfections can happen. Treatment protocols are the same whether a person is receiving treatment for their first hepatitis C infection or for a reinfection. People who use drugs should have access to treatment for hepatitis C reinfection.

Hepatitis C treatment should be offered to people who use drugs in conjunction with services to support their overall health, including harm reduction services, which will also help to reduce the likelihood of hepatitis C reinfection.

Hepatitis C treatment can be a positive and stabilizing factor in a person's life, especially when combined with additional care and supports that address underlying health and social issues and align with the person's goals. In addition to improving the health of people with hepatitis C by enabling them to be cured, access to treatment offers the important benefit of helping to prevent onward hepatitis C transmission.

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#### INTRODUCTION

There has been a treatment revolution in hepatitis C: safe and highly effective direct-acting antiviral (DAA) treatment can now cure hepatitis C in as little as eight to 12 weeks. The availability of effective treatments has made the elimination of hepatitis C as a public health threat a possibility. There is strong evidence to suggest that offering treatment to the most high-risk individuals is the most effective and cost-efficient approach to achieving elimination of hepatitis C at both the individual and population levels.

Canadian hepatitis C treatment guidelines now recommend that all people with chronic hepatitis C be considered for treatment, including people who use drugs, a population that is disproportionately affected by hepatitis C in Canada. People who use drugs experience significant stigma and discrimination and are more likely to face socioeconomic disadvantages, experience medical morbidities and experience barriers to accessing health care. These factors are significant barriers to accessing hepatitis C treatment and as such, people who use drugs are traditionally an underserved population when it comes to hepatitis C treatment.

This CATIE statement summarizes the best available evidence on hepatitis C treatment efficacy among people who use drugs. This statement was developed to help service providers in Canada adapt their programs and incorporate this evidence into their messaging and support for clients. This statement begins with simple key messages, followed by recommendations for service providers and a list of available tools and resources. It also provides a review of the evidence that service providers can use for more specific discussions with clients and colleagues.

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For more information, please see the evidence review at the end of this statement.

#### **ABOUT HEPATITIS C TREATMENT**

Hepatitis C treatment has dramatically improved with the advent of DAAs, which cure over 95% of the people with hepatitis C who take them.

DAA treatment for hepatitis C is safe and effective. It usually involves taking one to three pills once a day for eight or 12 weeks. Side effects are usually mild and diminish or go away completely after a few weeks.

Hepatitis C treatment is now widely available, and publicly funded, across the country. For most clients, the cost of treatment is covered through public health insurance plans (provincial, territorial or federal). For many, private insurance may cover the cost of treatment. Most clients will not have to pay out of pocket for hepatitis C treatment, and programs (such as manufacturer patient assistance programs) are available to help cover the cost of deductibles if they exist.

#### **RECOMMENDATIONS FOR SERVICE PROVIDERS**

Canadian treatment guidelines recommend that all patients with chronic hepatitis C infection should be considered candidates for treatment, including people who use drugs. A chronic hepatitis C infection is an infection that persists for more than six months. Despite this recommendation, barriers to accessing hepatitis C treatment exist for people who use drugs. The following recommendations have been made in an effort to address these barriers.

Below are recommendations on how service providers might better support the linkage to and uptake of hepatitis C treatment among people who use drugs. Underpinning each of these recommendations is the need to address the underlying health and social issues clients may be experiencing. The current context of criminalization of drug use; subsequent incarceration; experiences of stigma, discrimination and marginalization; and the overdose crisis are examples of challenges that intersect with all efforts to support people who use drugs. Clients may have additional health or other social issues, and at times addressing these issues may be prioritized above hepatitis C treatment. Part of the service provider role in supporting clients with hepatitis C care is to build a trusting relationship and positive rapport so that service providers and clients can work together to prioritize and achieve their health and other goals.

## **1. Facilitate and support uptake of hepatitis C treatment among people who use drugs.**

Hepatitis C treatment is beneficial and recommended for everyone with a chronic hepatitis C infection, regardless of the amount of liver injury. People who use drugs and who have a hepatitis C infection or reinfection should have access to treatment. Current drug or alcohol use should not be a barrier to receiving treatment, and going on opioid agonist treatment (OAT) or reducing drug or alcohol use is not required for hepatitis C treatment.

Some clients and providers may have questions about how DAA treatment interacts with substances, such as OAT and illicit drugs. No DAAs are contraindicated with OAT or opioids, stimulants, cannabinoids and ethanol (alcohol). The use of these substances should not be a barrier to accessing hepatitis C treatment, although there are some factors for healthcare providers to consider. There is a weak but potentially clinically significant interaction between fentanyl or oxycodone and certain DAAs: the effects of opiates could theoretically be enhanced when a person is taking certain DAAs, increasing the risk of respiratory depression and overdose.

Recommendations to manage this interaction includes monitoring for side effects such as decreased level of consciousness and respiratory depression. Further, in the context of a highly variable, unregulated and poisoned drug supply, harm reduction practices (such as not using alone, using lower amounts of illicit drugs and ensuring access to naloxone) are important at all times, including when clients are taking hepatitis C treatment.

## If a client has hepatitis C, talk to them about the health benefits of treatment and what to expect.

Discuss potential side effects of DAA treatment and how to manage them. Reinforce that hepatitis C treatment is safe and

highly effective at curing hepatitis C. DAA treatment is much simpler to take than the older treatments (e.g., interferon), which were poorly tolerated, more difficult to administer and often inaccessible to people who use drugs.

## Support clients while they are considering and going through hepatitis C treatment to remain engaged in care.

To provide the best care for clients undergoing hepatitis C treatment, it is recommended that service providers take the following steps:

- Work with clients to identify and achieve the goals they have for themselves before they start treatment, and support them when they are ready to start treatment.
- Consider the types of supports that clients may benefit from during treatment, including services that address the underlying health and social issues they may be experiencing. Examples include income support programs, housing programs, food security programs, drug and alcohol programs (including OAT), harm reduction services including supervised consumption/overdose prevention sites, mental health programs, programs that address intimate partner violence, and health care services.
- Continue to emphasize and link clients to harm reduction education and services. Harm reduction supports decrease both the immediate risk of infection and the risk of future re-exposure and reinfection. Discuss and provide supports for overdose prevention.
- Talk about how to address possible missed or lost doses of medication. Offer, or link clients to, supports for medication adherence and continued engagement in care. Supports may include providing regular check-ins, offering flexible dispensing of medications, pairing DAAs with other treatments the person is currently receiving such as methadone or safer supply medications, providing group support, and ensuring treatment continuation and dose delivery across organizations such as prisons, psychiatric units and hospitals. Treatment support workers, case workers or peer support workers may be able to help to provide these services.

Connect clients with hepatitis C to healthcare providers who have good reputations for supporting people who use drugs. Given the stigma and discrimination that people who use drugs can experience while accessing services, the service provider role includes being aware of — and developing partnerships with — local healthcare providers, clinics and health centres that offer low-barrier, welcoming and respectful care for people who use drugs.

#### For clients who experience reinfection, maintain a nonjudgmental environment, link clients to respectful care and offer support through treatment for reinfection.

Some people will develop hepatitis C reinfection when they are re-exposed to the virus. Reinfection is to be expected and can be considered an important indicator of treatment coverage success by demonstrating that services are reaching the highest risk individuals in a community. Reinfection risk is highest in the time period immediately following treatment and among people who are exposed to many incidences of hepatitis C infection. Clients should be given ongoing access to harm reduction support following hepatitis C treatment. Clients should not be denied hepatitis C treatment because of concerns that they might become reinfected. The same treatment protocols are used to treat all hepatitis C infections, whether it is a first-time infection or a reinfection. However, treatment for reinfection can pose additional challenges that will need to be navigated. It is important to refer clients to providers who can provide retreatment, knowledgeable harm reduction conversations and psycho-social supports. In addition, it is important to emphasize client successes in testing and reconnecting to care.

## Consider ways to integrate hepatitis C treatment into services that are already being accessed by people who use drugs.

Integrated services can meet people where they are at and serve people in locations that are easier for them to access, more comfortable to use and more responsive to their health needs, such as harm reduction settings, supervised injection services, OAT programs, community health centres, sexual health services and shelters.

#### Advocate for clients to access treatment.

According to Canadian treatment guidelines, drug use should not affect an individual's eligibility for hepatitis C treatment. The service provider role may include advocating for treatment, reinforcing the point that people who use drugs are eligible for treatment and addressing barriers to treatment access.

# 2. Encourage routine testing for hepatitis C infection and reinfection for clients who use drugs and their networks.

Testing is the only way to identify if a person has hepatitis C. In Canada, regular hepatitis C testing is recommended for people at ongoing risk of hepatitis C, including people who use drugs.

## Encourage clients who use drugs to get tested regularly for hepatitis C.

• Support appropriate education around screening (antibody testing) and confirmatory testing.

- Find out how hepatitis C tests are conducted locally and prepare clients for what to expect.
- It is recommended that people at ongoing risk of hepatitis C infection be tested every six to 12 months. For individuals who have never had hepatitis C, this would mean being tested for hepatitis C antibodies with a screening test.
- Be familiar with, and develop partnerships with, local healthcare providers, clinics and other health centres that offer hepatitis C testing services and have a good reputation for supporting people who use drugs. By establishing these connections service providers can help to ensure that clients who use drugs are able to access testing services without barriers.

#### Encourage clients who have been cured of hepatitis C and are at risk of reinfection to be tested every six to 12 months for hepatitis C with a confirmatory test, typically an RNA test.

- People who have had hepatitis C before will remain antibody positive and thus should be tested for reinfection using a confirmatory test only. Routine testing will help identify a person in the early stages of reinfection and will enable them to be engaged in care and treatment as soon as possible. The frequency of testing will be dependent on risk of re-exposure.
- Provide education to clients regarding hepatitis C transmission before, during and after treatment. Discuss the groups of people a client uses with (networks), support low-barrier peer-led referral pathways and offer hepatitis C testing and treatment for people in the client's networks.

Consider ways to integrate hepatitis C testing into programs that support people who use drugs, such as OAT and harm reduction services, community health centres and shelters. Integrated services can meet people where they are at and serve them in locations that are easier for them to access, more comfortable to use and more responsive to their health needs. Ensure appropriate post-test counselling services are available in conjunction with testing offerings.

# 3. Facilitate access to harm reduction services to reduce the likelihood of hepatitis C infection and reinfection.

The most common route of hepatitis C transmission in Canada is sharing equipment used to inject, smoke and/or snort drugs. Hepatitis C can be passed on when people share drug use equipment that has come in contact with blood that contains hepatitis C. New equipment should be used each time a person injects drugs (including needles and syringes, filters, water, and cookers used for preparing or injecting drugs), and an individual should use their own equipment to smoke drugs (including pipes and mouthpieces) and snort drugs (including straws or rolled paper).

## Inform clients that a person can be reinfected with hepatitis C if they are exposed to the virus again.

There is no vaccine to prevent hepatitis C infection. Hepatitis C reinfection after re-exposure can occur in people who have spontaneously cleared the virus, as well as in people who have been treated and cured. Previous treatment for hepatitis C does not protect against reinfection.

#### Speak with clients about how they are using drugs and support them to use more safely to prevent reinfection by providing:

- counselling about safer drug use, including overdose prevention and naloxone
- resources for safer drug use, such as new drug use equipment
- information on the nearest supervised consumption site or overdose prevention site (if these services are available)

## Offer welcoming and safe services where clients are treated with dignity and respect.

This includes the provision of culturally safe and competent care. Recognize that the criminalization of drug use and resulting stigma may be a barrier to people feeling safe accessing harm reduction services. These conditions may result in people using alone, which puts them at increased risk of death from overdose. If an organization does not provide services that a person needs, discuss their fears and offer warm referrals.

#### **TOOLS AND RESOURCES**

#### **CATIE resources**

- Hepatitis C treatment in harm reduction programs *Prevention in Focus*
- Common hepatitis C drugs available in Canada for adults CATIE poster
- Hepatitis C: Treatment and liver health CATIE resource
- Epclusa (velpatasvir + sofosbuvir) Fact sheet
- Maviret (glecaprevir + pibrentasvir) Fact sheet
- Harvoni (ledipasvir + sofosbuvir) Fact sheet
- Zepatier (elbasvir + grazoprevir) Fact sheet
- Vosevi (sofosbuvir + velpatasvir + voxilaprevir) Fact sheet

- Ibavyr (ribavirin) Fact sheet
- Curing hepatitis C: What you need to know if you use drugs
  CATIE booklet
- Responding to an opioid and stimulant overdose CATIE booklet

## Guidelines, position papers and consensus statements

- The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver - Canadian Medical Association Journal
- Global declaration to eliminate hepatitis C in people who use drugs International Network on Health and Hepatitis in Substance Users
- Blueprint to inform hepatitis C elimination efforts in Canada – Canadian Network on Hepatitis C
- Global health sector strategy on viral hepatitis 2016–2021 World Health Organization

#### **EVIDENCE**

Hepatitis C treatment efficacy and individual and community benefits of treatment

Hepatitis C treatment has dramatically improved with the advent of DAAs. DAAs are all-oral medications, typically taken over eight to 12 weeks, which have minimal side effects and cure over 95% of the people with hepatitis C who take them.<sup>1,2</sup> The previously available interferon-based hepatitis C treatment was poorly tolerated, was taken by injection over 24–48 weeks, had potential psychiatric side effects and was associated with a lower likelihood of cure.<sup>3</sup>

DAA treatment and hepatitis C cure provide significant health benefits, including reducing the risk of liver failure, liver cancer (hepatocellular carcinoma) and cirrhosis and reducing the risk of the development of extrahepatic manifestations, such as cryoglobulinemia, non-Hodgkin lymphoma, cardiovascular disease and diabetes mellitus.<sup>4</sup> Benefits of being cured also include improved health-related quality of life.<sup>5</sup>

While the primary benefit of scaling up testing, treatment and linkage to care is diagnosing hepatitis C infections and curing people, these efforts can also be considered a prevention strategy. Wide-scale treatment and cure means there are fewer people with hepatitis C and therefore there are fewer opportunities for onward transmission of the virus, resulting in a decrease in the number of new infections. This concept is called treatment as prevention. Hepatitis C treatment as prevention initiatives have resulted in reduced incidence of hepatitis C in Iceland,<sup>6</sup> in prison settings in Australia<sup>7</sup> and among HIV-positive men who have sex with men in the Netherlands.8 There is strong evidence to suggest that offering treatment to the most high-risk individuals is the most effective and cost-efficient approach to eliminating hepatitis C at both the individual and population levels.<sup>9-12</sup> In addition to modelling that suggests that treatment as prevention is an effective strategy for addressing hepatitis C among people who use drugs,<sup>12</sup> rapid scale-up of hepatitis C treatment among people who use drugs in Australia demonstrated a decline in the transmission of hepatitis C virus and in the prevalence of hepatitis C virus viremia (the presence of virus in the blood) among a population of people who inject drugs.<sup>13</sup> Adopting an effective treatment as prevention approach targeting people who use drugs also requires concurrent high coverage of harm reduction services.14

#### Hepatitis C treatment access among people who use drugs: gaps in access and barriers to receiving treatment

#### Gaps in access to hepatitis C treatment

People who use drugs are over-represented in the global hepatitis C epidemic.<sup>2</sup> This is also true in Canada, where injection drug use is the most frequently reported risk exposure among people with hepatitis C.<sup>15</sup> A 2017–2019 national survey of people who inject drugs in Canada (formerly called I-Track) found that 64% of participants had a current or past hepatitis C infection and 37% of participants had a current hepatitis C infection.<sup>16</sup>

Despite treatment advances, people who use drugs continue to be an underserved population when it comes to accessing hepatitis C testing, care and treatment. In the same 2017– 2019 national survey of people who inject drugs in Canada, only 50% of people who used drugs with a current hepatitis C infection were aware of their infection. Of those who were aware of their status, only 11% had ever received hepatitis C treatment, and of those who received treatment, 4% were currently on treatment.<sup>16</sup>

In the past, with interferon-based hepatitis C treatments, injection drug use was a contraindication to treatment.<sup>17</sup> However, DAA treatment is safe and effective for people who use drugs.<sup>18,19</sup> and Canadian treatment guidelines recommend that all patients with chronic hepatitis C infection should be considered candidates for treatment.<sup>5</sup>

#### Barriers to receiving hepatitis C treatment

People who inject drugs experience significant stigma and discrimination and are more likely to have socioeconomic disadvantages, experience medical morbidities and experience barriers to accessing health care.<sup>20</sup> Unintended harms of injection drug use, rooted in its criminalization, include bloodborne viral infections, overdose and overdose death, and injecting-related bacterial infections.<sup>20</sup> In Canada, the ongoing overdose crisis presents an urgent challenge to keep people alive;<sup>21</sup> there have been steep drug-related mortality increases among both people living with hepatitis C and those who are hepatitis C negative.<sup>22</sup>

Barriers to accessing hepatitis C treatment among people who use drugs can be categorized as provider-level and systemic barriers and individual-level barriers. Provider-level and systemic barriers include:

- reluctance to treat people who are actively using drugs,<sup>23,24</sup> along with misconceptions regarding treatment effectiveness,<sup>25-28</sup> reinfection<sup>24,29</sup> and adherence<sup>29</sup>
- lack of knowledge of hepatitis C testing and treatment among healthcare professionals, which can lead to the inability to adequately identify and treat people<sup>24,27,30</sup>
- lack of appropriate treatment settings for people who use drugs (e.g., lack of infrastructure for hepatitis C services, complicated or compartmentalized and poorly linked service delivery)<sup>24,28,30,31</sup>
- criminalization of drug use, stigma and discrimination of people who use drugs<sup>19,31</sup> and linked contextual factors related to resulting marginalization such as poverty, homelessness and the overdose crisis<sup>31</sup>
- lack of knowledge of the needs (e.g., health and social support needs) of people who use drugs<sup>27,30</sup>

Individual-level barriers to accessing hepatitis C treatment among people who use drugs are specific to each person and are linked to systemic barriers. They can include:

- experiencing stigmatization,<sup>23,24</sup> being concerned about experiencing stigmatization and mistrusting the health system<sup>24,26,27,29,30,32</sup>
- having multiple competing priorities and not being able to fully engage in care<sup>24,27,30</sup> or prioritizing hepatitis C treatment below other health concerns (e.g., housing, overdose, HIV)<sup>31</sup>
- being unaware of one's hepatitis C status, being asymptomatic<sup>23,27</sup> or perceiving one's need for treatment to be low<sup>23,24,29</sup>

• having limited knowledge of DAA treatments, where to access treatment, or eligibility criteria<sup>23,24</sup>

Some of the barriers at the provider level can be addressed through approaches such as integration, or co-location, of services within harm reduction programs (e.g., safer consumption sites, overdose prevention sites) or other programs or settings (e.g., HIV programs, OAT programs, primary care services, sexual health services).<sup>23,24,31</sup> Other barriers at the provider level can be addressed by improving the competencies and awareness of healthcare providers and addressing any misconceptions they may have about hepatitis C testing and treatment for people who use drugs.<sup>23,24</sup> This can include engaging people with lived and living experience to plan and lead service delivery.<sup>23,31</sup>

Barriers at the individual level can be addressed by linking clients to social and medical supports including income supports, housing and mental health care;<sup>24,31</sup> providing education about hepatitis C and DAA treatment;<sup>24</sup> and building partnerships with healthcare providers and services locally that provide safe and nonjudgmental care for people who use drugs and supporting clients with linkage and navigation to these services.

#### Treatment efficacy among people who use drugs

Current Canadian hepatitis C treatment guidelines recommend that all people with chronic hepatitis C be considered for treatment, including people who use drugs.<sup>5</sup> This is aligned with other national and international guidelines and recommendations.<sup>33-36</sup>

## Sustained virological response (SVR) among people who use drugs

A strong body of evidence demonstrates that DAA treatment is highly effective at curing hepatitis C among people who use drugs and that hepatitis C treatment outcomes among people who use drugs and people on OAT are similar to those among people without a history of drug use. A recent systematic review and meta-analysis found that hepatitis C treatment was highly effective among people with recent drug use and people receiving OAT,<sup>37</sup> and the results of this review were comparable with those of another study.<sup>38</sup> In both studies, SVR was achieved in about 88% of people with recent injection drug use and about 91% of people receiving OAT.<sup>37,38</sup>

Further, in a recent systemic review and meta-analysis of DAA treatment efficacy among people who use drugs, there was no significant difference in the proportion of SVR (or cure) among people receiving OAT and a control group, or among people who inject drugs and a control group.<sup>18</sup> The analysis included

1,702 participants on OAT, 538 participants who injected drugs and 19,723 participants who served as controls. SVR achievement ranged from 90% (OAT group) to 88% (injection drug use group).<sup>18</sup>

All three of these articles included studies on hepatitis C treatment among people with current and recent injection drug use. This affirms that treatment in this population is highly effective and that abstinence from drug use should not be a prerequisite for treatment.

#### Safety of DAA treatment with OAT or drug use

No DAAs are contraindicated with OAT or with illicit drugs; however, there are some factors for healthcare providers to consider. In the practice guidelines for hepatitis C treatment produced by the European Association for the Study of the Liver, fentanyl and oxycodone are identified as having potential interactions with certain DAA treatments.<sup>33</sup>

Recommended management includes monitoring for decreased level of consciousness and respiratory depression.<sup>39</sup> There are no expected interactions with stimulants, cannabinoids and ethanol.<sup>40</sup> It is important to note that these potential drug interactions should not dissuade providers from prescribing DAAs to clients who are taking OAT or using drugs, as real-world studies have shown that hepatitis C treatment is safe and effective in people who use drugs and people on OAT.<sup>18,19</sup>

#### Treatment adherence among people who use drugs

Treatment adherence has been identified as a potential concern among clinicians reluctant to offer hepatitis C treatment to people who use drugs.<sup>37</sup> However, evidence suggests there is no significant difference in treatment adherence among people who use drugs and people who don't use drugs.<sup>18</sup> SVR achievement remains high among people who do not adhere to their DAA treatment, suggesting there is forgiveness to non-adherence with DAA treatment.<sup>41.43</sup> Non-adherence is typically defined as taking less than 90% of doses.

Two large international studies called SIMPLIFY and D3FEAT reported on SVR and adherence among people who use injection drugs and people receiving OAT. Participants received once-daily and twice-daily DAA treatments. Six centres in Canada were included in the study.<sup>41</sup> Median adherence was high at 92%. In total, 40% of participants were categorized as nonadherent (i.e., took less than 90% of their doses); however, SVR remained high in both nonadherent and adherent participants (89% and 95%, respectively). There was no difference in SVR between participants who missed seven

consecutive doses and those who did not. Nonadherence was associated with recent stimulant injection, unstable housing and twice-daily dosing. Adherence also decreased over the course of treatment.<sup>41</sup>

Some clients may benefit from and prefer to access enhanced adherence supports.<sup>44</sup> Such supports may include:

- regular contact by phone or in person<sup>44</sup>
- directly observed dispensing of medications (daily or weekly)<sup>44,45</sup>
- liaison with other organizations or delivery of treatment to prisons, psychiatric units and hospitals<sup>44</sup>
- group treatment<sup>45</sup>

#### Hepatitis C reinfection among people who use drugs

People who engage in ongoing risk behaviours related to drug use, such as sharing injection drug use equipment, may be exposed to the hepatitis C virus and become reinfected with hepatitis C. Canadian hepatitis C treatment guidelines recommend that people who have ongoing risk exposures receive annual RNA testing to assess for reinfection.<sup>5</sup> Hepatitis C reinfection should be managed the same way as a primary infection.<sup>5</sup> This is aligned with other international guidelines.<sup>33</sup>

Hepatitis C reinfection is often cited as a concern among clinicians reluctant to offer treatment to people who use drugs.<sup>18,19</sup> However, being cured of hepatitis C has significant benefits for individuals' health, as well as community benefits such as preventing onward transmission of hepatitis C. From a treatment as prevention perspective, hepatitis C reinfections in a setting with high harm reduction service coverage can be interpreted as a marker of success: it can be considered an indication that treatment is reaching individuals with high-risk drug use who are often not seen accessing services.<sup>14</sup>

A meta-analysis of hepatitis C reinfection among people who inject drugs included international data from 6,311 person-years of follow-up and 36 studies including nine studies from Canada.<sup>46</sup> The pooled rates were 5.9 reinfections per 100 person-years among people with recent drug use, 6.2 reinfections per 100 person-years among people with recent injection drug use and 3.8 reinfections per 100 personyears among people receiving OAT. There are similar rates of reinfection following interferon-based treatments, suggesting that concerns that individuals may change their risk behaviours after receiving DAA treatment (because DAA treatment is less onerous and more successful than the earlier hepatitis C treatments) are unfounded.<sup>46</sup> Receipt of OAT and longer follow-up time were associated with lower reinfection rate. Reinfection rates were lower than primary infection rates in a pooled analysis of seven studies of people who use drugs.<sup>46</sup>

Strategies to address hepatitis C reinfection among people who use drugs include the following:<sup>14,19</sup>

- acknowledge that when treating people with higher risk injection drug use, reinfections are to be expected
- discuss reinfection risk with clients before, during and after treatment
- optimize harm reduction strategies, including offering education and resources for safer injection drug use practices and overdose prevention
- discuss clients' injecting partners and offer screening for their regular partners
- screen for reinfection with annual RNA assessment
- offer treatment for reinfection without stigma or discrimination

#### REFERENCES

- Falade-Nwulia O, Suarez-Cuervo C, Nelson DR et al. Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review. *Annals of Internal Medicine*. 2017;166(9):637-48.
- World Health Organization. Global health sector strategy on viral hepatitis, 2016–2021. Geneva: World Health Organization; 2016 Jun. Available from: https://www.who.int/hepatitis/strategy2016-2021/ghsshep/en/
- Grebely J, Bruneau J, Bruggmann P et al. Elimination of hepatitis C virus infection among PWID: the beginning of a new era of interferon-free DAA therapy. *International Journal of Drug Policy*. 2017;47:26-33.
- 4. Gonzalez HC, Gordon SC. Hepatitis C. Gastroenterology *Clinics of North America*. 2020;49(2):301-14.
- Shah H, Bilodeau M, Burak KW et al. The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver. *CMAJ*. 2018;190(22):E677-E687.
- Olafsson S, Fridriksdottir RH, Tyrfingsson T et al. THU-412-Iceland may already have reached the WHO 2030 targets for diagnosis and treatment of hepatitis C virus infection: results from the Treatment as Prevention for

Hepatitis C (Trap HepC) Program. *Journal of Hepatology*. 2019;70(1);e337–e338.

- Hajarizadeh B, Grebely J, Byrne M et al. Evaluation of hepatitis C treatment-as-prevention within Australian prisons (STOP-C): a prospective cohort study. *Lancet Gastroenterology & Hepatology*. 2021;6(7):533-46.
- Boerekamps A, van den Berk GE, Lauw FN et al. Declining hepatitis C virus (HCV) incidence in Dutch human immunodeficiency virus-positive men who have sex with men after unrestricted access to HCV therapy. *Clinical Infectious Diseases*. 2018 May;66:1360-65.
- Martin NK, Vikerman P, Foster GR et al. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modeling analysis of its prevention utility. *Journal of Hepatology*. 2011 Jun;54(6):1137-44.
- 10. Midgard H, Weir A, Palmateer N et al. HCV epidemiology in high-risk groups and the risk of reinfection. *Journal of Hepatology*. 2016;65:S33-S45.
- Marcellin F, Demoulin B, Suzan-Monti M et.al. Risk factors for HCV reinfection or transmission in HIV-HCV coinfected MSM (ANRS-VESPA2 French National Survey). *Journal of Acquired Immune Deficiency Syndromes*. 2015 Dec 15; 70(5):e179-e182.
- Hickman M, De Angelis D, Vickerman P et al. Hepatitis C virus treatment as prevention in people who inject drugs – testing the evidence. *Current Opinion in Infectious Diseases*. 2015 Dec;28(6):576-582.
- Iversen J, Dore GJ, Catlett B et al. Association between rapid utilisation of direct hepatitis C antivirals and decline in the prevalence of viremia among people who inject drugs in Australia. *Journal of Hepatology*. 2019;70(1):33-9.
- Dore G. HCV reinfection as a positive indication of highrisk population treatment access. *Journal of Viral Hepatitis*. 2019;26:516-8.
- 15. Public Health Agency of Canada. *Report on hepatitis B and C in Canada: 2017*. Ottawa: Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2019. Available from: https://www.canada.ca/content/dam/themes/health/publications/diseases-conditions/report-hepatitis-b-c-canada-2017/report-hepatitis-b-c-canada-2017.pdf

- Government of Canada. Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019: national findings. *Canada Communicable Disease Report.* 2020 May 7;46(11):138-48. Available from: https://www.canada.ca/en/public-health/services/reportspublications/can...
- 17. Myers RP, Shah H, Burak KW et al. An update on the management of chronic hepatitis C: 2015 consensus guidelines from the Canadian Association for the Study of the Liver. *Canadian Journal of Gatroenterology and Hepatology*. 2015;29(1):19-34.
- Graf C, Mücke MM, Dultz G et al. Efficacy of direct-acting antivirals for chronic hepatitis C virus infection in people who inject drugs or receive opioid substitution therapy: a systematic review and meta-analysis. *Clinical Infectious Diseases*. 2020;70(11):2355-65.
- Martinello M, Dore GJ, Matthews GV et al. Strategies to reduce hepatitis C virus reinfection in people who inject drugs. *Infectious Disease Clinics of North America*. 2018; 32(2):371-93.
- 20. Grebely J, Dore GJ, Morin S et al. Elimination of HCV as a public health concern among people who inject drugs by 2030 – What will it take to get there? *Journal of the International AIDS Society*. 2017;20:221-46.
- 21. Selfridge M, Cunningham EB, Milne R et al. 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.* 2019;72:106-13.
- 22. Samji H, Yu A, Wong S et al. Drug-related deaths in a population-level cohort of people living with and without hepatitis C virus in British Columbia, Canada. *International Journal of Drug Policy*. 2020;86:102989.
- 23. Goodyear T, Brown H, Browne AJ et al. "I want to get better, but...": identifying the perceptions and experiences of people who inject drugs with respect to evolving hepatitis C virus treatments. *International Journal for Equity in Health*. 2021;20(1):81.
- 24. Amoako A, Ortiz-Paredes D, Engler K et al. Patient and provider perceived barriers and facilitators to direct acting antiviral hepatitis C treatment among priority populations in high income countries: a knowledge synthesis. *International Journal of Drug Policy*. 2021;103247.
- 25. Norton BL, Akiyama MJ, Zamor PJ et al. Treatment of chronic hepatitis C in patients receiving opioid agonist

therapy: a review of best practice. *Infectious Disease Clinics of North America*. 2018;32(2):347-70.

- Fragomeli V, Weltman M. Addressing viral hepatitis in the opiate substitution setting: an integrated nursing model of care. *Journal of Gastroenterology and Hepatology*. 2015; 30(2):6-11.
- 27. Hashim A, O'Sullivan M, Williams H et al. Developing a community HCV service: Project ITTREAT (integrated community-based test – stage – TREAT) service for people who inject drugs. *Primary Health Care Research & Development*. 2018;19:110-20.
- 28. Lazarus JV, Percias JM, Picchio C et al. We know DAAs work, so now what? Simplifying models of care to enhance the hepatitis C cascade. *Journal of Internal Medicine*. 2019;286:502-25.
- 29. Zeremski M, Zibbell JE, Martinez AD et al. Hepatitis C virus control among persons who inject drugs requires overcoming barriers to care. *World Journal of Gastroenterology*. 2013;19(44):7846-51.
- Bruggman P, Litwin AH. Models of care for the management of hepatitis C virus among people who inject drugs: one size does not fit all. *Clinical Infectious Diseases*. 2013;57(S2):S56-61.
- 31. Goodyear T, Ti L, Carrieri P et al. "Everybody living with a chronic disease is entitled to be cured": challenges and opportunities in scaling up access to direct-acting antiviral hepatitis C virus treatment among people who inject drugs. *International Journal of Drug Policy*. 2020; 81:102766.
- 32. Grebely J, Oser J, Taylor LE et al. 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. *Journal of Infectious Diseases*. 2013 Mar;207 Suppl1(Suppl1):S19-25.
- European Association for the Study of the Liver (EASL). EASL recommendations on treatment of hepatitis C: final update of the series [practice guidelines]. *Journal of Hepatology*. 2020;73:1170-1218.
- American Association for the Study of Liver Diseases (AASLD). HCV guidance: recommendations for testing, managing, and treating hepatitis C [website]. AASLD; 2020. Available from: www.hcvguidelines.org
- 35. Chung, RT, Ghany MG, Kim AY et al. Hepatitis C guidance 2018 update: AASLD-IDSA recommendations for testing,

managing, and treating hepatitis C virus infection. *Clinical Infectious Diseases*. 2018;67(10):1477-92.

- 36. World Health Organization. *Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection*. Geneva: World Health Organization; 2018. https://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/
- Hajarizadeh B, Cunningham EB, Reid H et al. Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: a systematic review and meta-analysis. *Lancet Gastroenterology & Hepatology*. 2018;3(11): 754-67.
- Latham NH, Doyle JS, Palmer AY et al. Staying hepatitis C negative: a systematic review and meta-analysis of cure and reinfection in people who inject drugs. *Liver International*. 2019;39(12):2244-60.
- 39. Hong J, Wright RC, Partovi N et al. Review of clinically relevant drug interactions with next generation hepatitis C direct-acting antiviral agents. *Journal of Clinical and Translational Hepatology*. 2020;8(3):322-35.
- Ing Lorenzini K, Girardin F. Direct-acting antiviral interactions with opioids, alcohol or illicit drugs of abuse in HCV-infected patients. *Liver International*. 2020;40(1): 32-44.
- 41. Cunningham EB, Hajarizadeh B, Amin J et al. Adherence to once-daily and twice-daily direct-acting antiviral therapy for hepatitis C infection among people with recent injection drug use or current opioid agonist therapy. *Clinical Infectious Diseases*. 2020;71(7):e115-e124.
- 42. Brooks KM, Castillo-Mancilla JR, Morrow M et al. Adherence to direct-acting antiviral therapy in people actively using drugs and alcohol: the INCLUD Study. *Open Forum Infectious Disease*. 2021;8(1):ofaa564.
- 43. Heo M, Pericot-Valverde I, Rennert L et al. Hepatitis C virus DAA treatment adherence patterns and SVR among people who inject drugs treated in opioid agonist therapy programs. *Clinical Infectious Diseases*. 2021 April 20; ciab334.
- 44. Read P, Gilliver R, Kearley J et al. Treatment adherence and support for people who inject drugs taking direct-acting antiviral therapy for hepatitis C infection. *Journal of Viral Hepatitis*. 2019;26(11):1301-10.
- 45. Norton BL, Akiyama MJ, Arnsten JH et al. High HCV cure rates among people who inject drugs and have

suboptimal adherence: a patient-centered approach to HCV models of care. *International Journal of Drug Policy*. 2021;93:103135.

 Hajarizadeh B, Cunningham EB, Valerio H et al. Hepatitis C reinfection after successful antiviral treatment among people who inject drugs: a meta-analysis. *Journal of Hepatology*. 2020;72(4):643-57.



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