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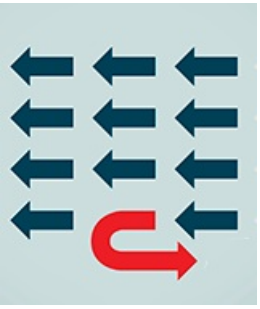

Risks, realities and responses:Hepatitis C re-infection among people who inject drugs and HIV-positive MSM

By Melisa Dickie and Suzanne Fish

There is now strong evidence that direct-acting antivirals (DAAs) can cure the vast majority of people with hepatitis C with successful outcomes across all population groups, including people who inject drugs and people co-infected with HIV. This has led to the hope that hepatitis C can be eliminated as a public health threat.

However, DAAs do not protect against re-infection. If an individual is cured of hepatitis C or spontaneously clears the virus, they can be re-infected with hepatitis C if they are exposed to the virus again. There is an emerging concern that re-infection may compromise the benefits of DAA treatments and pose a challenge to eliminating hepatitis C. Some clinicians and policy makers are reluctant to spend the high cost of treatment on individuals who they believe are likely to become re-infected. In Canada, we are just beginning to expand access to DAAs, we have yet to see how re-infections will be addressed in policy and programming, and there is very limited research on re-infection in the context of DAAs. This article will examine the realities of re-infection rates across two priority populations and explore effective responses.

Hepatitis C treatment and re-infection

Direct-acting antivirals can cure the vast majority of people with chronic hepatitis C.[1,2,3] There was originally some concern that DAAs may be less effective, safe and tolerable for some priority populations, including people who inject drugs and people who are co-infected with HIV. There is now strong evidence to suggest that DAAs bring successful outcomes across all population groups with similar cure rates to the general population.[2,3]

The effectiveness of DAAs has led to optimism about the possibility of eliminating hepatitis C. However, broad-scale treatment efforts across priority populations are now being met with a new concern of re-infection. If an individual clears the virus (either through treatment or spontaneous clearance) they can become re-infected with hepatitis C if they are exposed to the virus again.[2,4,5] There are those who believe that this may post a challenge to eliminating the virus.[3,4,5,6,7,8,9] These concerns make some physicians and policy makers reluctant to treat certain populations who may be at high risk of re-infection.[4]

What do we know about hepatitis C re-infection?

Two of the routes of hepatitis C transmission in Canada are sharing needles/syringes and other drug use equipment, and high-risk sexual practices among HIV-positive men who have sex with men (MSM). As such, people who inject drugs and MSM are the main two priority populations at risk of re-infection for hepatitis C. This section will explore re-infection rates in these two populations.

Hepatitis C re-infection among people who inject drugs

The sharing of injection drug use equipment is the leading cause of hepatitis C transmission in Canada. Hepatitis C is more prevalent among people who inject drugs than in any other group.[10] Based on national hepatitis C estimates from 2011, 66% of people who inject drugs are antibody positive for hepatitis C.[10]

It is important to note that studies of re-infection after successful hepatitis C treatment among people who inject drugs are limited by small sample sizes, retrospective study designs, incomplete longitudinal follow up, and a lack of sensitive methods. Also, almost all of the studies examine re-infection after treatment with interferon-based regimens as opposed to the newer DAA treatments. Although some evidence is beginning to emerge related to re-infection following treatment with DAAs, there is very limited data to date.[11]

Overall, the evidence suggests that the incidence of hepatitis C re-infection among people who inject drugs is low.[3] The life time re-infection incidence in people who inject drugs is 0 to 5 per 100 person years).[2,3,12] In the first published study of hepatitis C re-infection following cure, it was found that people who inject drugs had low re-infection rates despite frequent relapse to drug use following a period of abstinence during treatment.[13] Most of the subsequent studies have reported similarly low rates of re-infection ranging from 0.8 to 4.7 per 100 person years.[14] A review examining studies across Canada, Germany, Norway, the United States, the Netherlands and Australia concluded that re-infection rates are low even among persons who continue to inject drugs during and after treatment.[14]

An ongoing three-year observational study in Australia (of patients who have achieved a cure with new DAAs found a similarly low re-infection rate of 2.3 infections per 100 person years.[9,15] The participants in the study (including those who continue to inject drugs) were enrolled in opioid substitution therapy. This is the only study to date with reported data on re-infection in the DAA era.

Risk of re-infection has been shown to vary depending on the local background epidemic among the group of people who inject drugs.[14] It has been demonstrated that in communities with higher local background levels of hepatitis C, people who inject drugs are likely to have a higher risk of re-infection. This is because they are more likely to be exposed to the virus if they participate in a community with a high prevalence of hepatitis C.

Sub-populations of people who inject drugs

Although on a broad scale re-infection rates across people who inject drugs are low, several studies have pointed to a higher risk of re-infection among particular sub-groups of this population. The broad category of ‘people who inject drugs’ is quite heterogeneous and encompasses people with a diverse range of drug use behaviours, as well as other risk factors. This broad category encompasses people who have only injected once, those who have ceased injecting, those who continue to inject, and people who have injected in a prison context.[3,12,16] There is also a great deal of heterogeneity among people who continue to inject drugs. The frequency of injection can range significantly, and accessibility to clean needles and harm reduction services, including opioid substitution therapy, creates further distinctions between groups.[2,11]

A systematic review and meta-analysis examining hepatitis C re-infection rates among people who inject drugs found varying rates of hepatitis C re-infection.[3] The pooled risk of hepatitis C re-infection was low (2.4 per 100 person years), with higher re-infection rates among people who reported ongoing drug use following their cure (6.4 per 100 person years).[3]

However, screening for high-frequency injection drug use pre-treatment does not seem to be a strong predictor of re-infection[16] because injecting behaviours can change post-treatment.[16] Instead of screening before treatment, it may be more important to support individuals post-treatment to access harm reduction and support services to try to prevent re-infection. Some studies have found that younger age and lower educational attainment may be strong predictors of re-infection.[16] Focusing efforts around this group may help to support lower risk behaviours post-treatment.

Another important sub-population is people with HIV co-infection who inject drugs. The risk of re-infection among this subpopulation is 3.2 per 100 person years.[12] It is unclear if immune suppression plays a role in re-infection for this population.[12]

Hepatitis C re-infection among MSM

In the past decade, an increase in the incidence of acute hepatitis C infection has been reported among HIV-positive MSM in Europe, North America, Australia and Asia.[16] A systematic review found that the incidence of acute hepatitis C from 2000 to 2012 was approximately four times higher in HIV-positive MSM (0.61 per 100 person years) than HIV-negative MSM (0.15 per 100 person years).[17] In Canada, 5% of MSM overall were antibody positive for hepatitis C (2005–2007),[18] and HIV-positive MSM are emerging as a group more likely to acquire hepatitis C.[5,16,17]

There are a number of factors that may facilitate hepatitis C transmission among MSM. Sexual transmission is likely the predominant route of hepatitis C acquisition among MSM, especially among HIV-positive MSM.[16] Hepatitis C viral loads are higher in semen, blood and rectal fluid in MSM with HIV co-infection,[16] which may increase the likelihood that hepatitis C is transmitted sexually.[16]

Some activities can facilitate the sexual transmission of hepatitis C. Examples include condomless anal sex; enema use prior to receptive anal sex; rectal trauma with bleeding; fisting; and group sex.[5,6,16,19]

Recreational drug use, in the context of sexual networks, commonly referred to as “chemsex” or Party and Play (PnP), is also thought to facilitate hepatitis C transmission among some MSM.[5,6] “Chemsex” refers to the use of recreational drugs (injecting and non-injecting drug use before, during and after sex) to enhance sexual experience and to facilitate extended sexual sessions, often with multiple sexual partners. This puts men at high risk of hepatitis C infection and other sexually transmitted infections.[5,6,8,19,20,21,22]

While similar risk behaviours are observed in HIV-positive and HIV-negative MSM, hepatitis C incidence is significantly higher among HIV-positive MSM.[5,16,17] Hepatitis C prevalence among HIV-negative MSM who don’t inject drugs is comparable to the general population.[16]

The reported incidence rates of re-infection among HIV-positive MSM following cure[5,11] are higher than in people who inject drugs.[16] The cumulative risk of re-infection calculated from studies of MSM is 12.8 per 100 person years,[16] compared to 2.4 per 100 person years for people who inject drugs.[3] In the largest cohort of HIV-positive MSM in Western Europe, it was estimated that almost one-quarter (24.6%) of enrolled patients were re-infected within five years of cure. This amounts to an incidence of 7.3 per 100 person years, with the median duration to re-infection being two years.[6] This study confirmed findings from numerous regional European studies. Many of these studies have underscored the importance of sexual networks among MSM, and that hepatitis C re-infection patterns are primarily occurring within existing sexual networks.[5,6,8,16,19]

“Chemsex” is now largely accepted as facilitating hepatitis C transmission within certain sexual networks, driving both primary and secondary re-infections.[5,16,19,21]

In Canada we have generally seen lower rates of hepatitis C infection among MSM (both HIV positive and negative) than in Europe;[7] however, the implications for the Canadian context are important and relevant to consider.

Sub-populations of MSM

HIV-positive MSM are not a homogenous group and re-infection rates may be higher among certain sub-populations. MSM who inject drugs are at significantly higher risk for hepatitis C re-infection than HIV-positive MSM who do not inject drugs.[2,6,16] HIV-positive MSM who engage in “chemsex” may be at even higher risk for re-infection.

Treatment as prevention

Despite the evidence, concerns about re-infection continue to be cited as a reason for withholding treatment to individuals at high risk of re-infection. However, 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 level.[16,19,23]

Treatment as prevention public health approaches have been utilized in the HIV field and lessons can be transferred to hepatitis C. Yet there are some important distinctions between HIV and hepatitis C treatment as prevention. Hepatitis C treatment has the advantage of being short and results in a cure, which may strengthen the cost-saving and public health outcomes.

Treatment as prevention is not only an important public health approach with potentially broad epidemic control benefits. It is also important for the long-term health benefits to individuals. There can be danger in treating individuals because they are 'vectors of infection' as opposed to treating individuals because they are deserving of the individual health and well-being benefits of hepatitis C treatment.

Programming and policy implications: Re-infection in a new era of hepatitis C cure

The starting place, when considering programming and policy responses to re-infection, is to appreciate that the majority of individuals treated for hepatitis C do not become re-infected.[2,11] While re-infection rates are not overwhelming, the re-infection dynamic cannot be ignored and there are important programming and policy implications.

Acknowledgement and acceptance

As the uptake of DAAs become more feasible with the anticipated lifting of restrictions across Canada in the next few years, ongoing risk behaviours in some individuals after successful treatment means that re-infections should be anticipated and acknowledged. Acknowledgement of this reality without discrimination and further stigma associated with high-risk drug use and sexual practices is important. Service providers will undoubtedly see hepatitis C re-infection among some of their clients who continue to engage in high-risk sexual and drug use behaviours after successful treatment.

Re-infection confirms that community health programs are reaching, diagnosing, connecting to care and treating individuals at continued risk. If no cases of re-infection are seen, it is likely that those clients at the highest risk of hepatitis C acquisition are not being reached and treated.[5,15,16,24]

Individual-level strategies and programming implications

Individual-level prevention of re-infection should follow similar approaches to primary prevention approaches. Clients should be offered accessible and culturally appropriate information, education and counselling about the risks of transmission, infection and re-infection associated with drug use and sexual practices.

- Treatment should occur in concert with sexual health and harm reduction counselling from healthcare providers and peers. High coverage needle and syringe programs, opioid substitution therapy, and safer consumption facilities have a role to play in decreasing re-infection rates, as do harm reduction services within rural and remote communities and in prison settings.
- For all clients with ongoing risk behaviours after treatment, it is important to expand testing opportunities to identify those in the early stages of re-infection at the earliest opportunity so they can be re-engaged in care.[2,25]
- Testing and treatment of injecting and sexual partners and networks may also play a role in reducing re-infection rates by reducing the overall prevalence of hepatitis C in the community.
- Individuals who become re-infected should be offered re-treatment, without discrimination or shame. Re-infection will continue to occur until treatment and prevention programs are scaled-up over a significant period of time.

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