

## Commentary on Barré *et al.* (2019): Identifying remaining barriers to hepatitis C treatment in the DAA era

*Untreated alcohol use disorder delays time to starting hepatitis C virus (HCV) treatment among people who inject drugs, even in the direct-acting anti-virals era. We need to identify and minimize remaining barriers to engaging in HCV care, including alcohol and other social factors.*

Significant increases in hepatitis C virus (HCV) treatment uptake have been observed since the introduction of broad access to direct-acting anti-viral (DAA) therapies in many countries [1]. However, treatment uptake is now beginning to decline in some countries, and those not treated within the first years of DAA access may be more challenging to reach [2,3]. In the interferon era, HCV treatment uptake was extremely low; for example, estimates from France, Australia and Canada reported that 4, 2 and 1%, respectively, of those with hepatitis C viraemia were treated annually before 2014 [4]. Treatment uptake was particularly low among people who inject drugs (PWID), a key group at risk of HCV infection [5,6].

Substantial increases in treatment uptake among PWID since DAA availability have been reported in some contexts. For example, in Australia, treatment uptake among those participating in repeat cross-sectional studies at needle and syringe programmes increased from 10% in 2015 to 41% in 2017 [7], and the incidence of HCV treatment initiation in a cohort of PWID in Montreal, Canada, increased from 1.6/100 person-years in 2011 to 12.7 in 2017 [8].

In this issue of *Addiction*, Barre and colleagues [9] found that treatment uptake in France among PWID who have a history of opioid substitution therapy (OST) remained similarly low in the interferon era (2012–13) and early DAA era (2014–15): treatment initiation among HCV-diagnosed PWID was approximately 6 per 100 person-years in both time-periods. Irrespective of treatment regimen, PWID with untreated alcohol use disorders were less likely to start HCV treatment than PWID living with chronic HCV without alcohol use disorders or on treatment for alcohol use disorder. That said, the magnitude of the reduced likelihood of treatment uptake among those with untreated alcohol use disorders appeared to be larger in the interferon era. These results are in the context of restricted access to DAA therapy in France until May 2016 [10], when advanced liver disease was removed as a treatment criterion.

Barre and colleagues approach involved analyzing untreated alcohol use disorder as a potential barrier to HCV treatment before and after DAA introduction, allowing comparison between these two time-periods. The resulting analysis provided insight into the probable reduction in the

effect size of alcohol use disorder as a barrier to HCV treatment. At the same time it highlighted that, although the effect may have been attenuated, those with untreated alcohol use continue to be less likely to be treated for HCV in France than other PWID. The effect of untreated alcohol use disorder prior to and after the introduction of DAA could be compared even more directly, and this comparison could be quantified by considering DAA introduction as a potential effect modifier.

The authors suggest that treatment of alcohol use disorders will improve access to therapy in this group. Whether or not that is the case, their analysis highlights the group with untreated alcohol use as a potential target for interventions aimed at improving linkage to care, and for qualitative research in order to identify potentially effective interventions.

Barre and colleagues' data, coupled with emerging evidence from the United States, Canada and Australia, reveal that barriers to treatment uptake persist in the DAA era. Treatment uptake has been associated with important social factors, other than alcohol use, including not being on OST, illicit drug use, unstable housing and geographic location of residence [7,8,11–14]. These findings are sobering in an era of optimism that it will be possible to change HCV epidemiology by treating sufficient numbers of people with ongoing risk behaviours [15]. In the DAA era, where treatment courses are short, all-oral, with minimal side-effects and adherence is far less important as a predictor of treatment outcomes [16], the provider-side rationale for reluctance to treat people who use alcohol and illicit drugs no longer applies but some barriers to treatment may persist nonetheless.

Applying Barre and colleagues' comparative approach to other potential remaining barriers to HCV treatment pre- and post- DAA introduction would provide insight into progress made since the introduction of DAAs, the remaining challenges and the potential targets for interventions to connect those remaining HCV infected with DAA treatment. A key point is that we all need to work better to educate prescribers to adopt a patient-centred approach to HCV treatment. Instead of waiting for PWID 'to be ready' for treatment, perhaps we should ask ourselves: 'why are we not discussing treatment today'? This message continues to be relevant in the DAA era.

### Declaration of interests

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### References

1. Marshall A. D., Pawlotsky J. M., Lazarus J. V., Aghemo A., Dore G. J., Grebely J. The removal of DAA restrictions in Europe— one step closer to eliminating HCV as a major public health threat. *J Hepatol* 2018; **69**: 1188–96.
2. Doyle J. S., Scott N., Sacks-Davis R., Pedrana A. E., Thompson A. J., Hellard M. E., *et al.* Treatment access is only the first step to hepatitis C elimination: experience of universal anti-viral treatment access in Australia. *Aliment Pharmacol Ther* 2019; **49**: 1223–9.
3. Saeed S., Strumpf E., Moodie E. E. M., Wong L., Cox J., Walmsley S., *et al.* Eliminating structural barriers: the impact of unrestricted access on hepatitis C treatment uptake among people living with HIV. *Clin Infect Dis* 2019; <https://doi.org/10.1093/cid/ciz833>.
4. Bruggmann P, Berg T, Ovrehus AL, Moreno C, Brandao Mello CE, Roudot-Thoraval F *et al.* Historical epidemiology of hepatitis C virus (HCV) in selected countries. *J Viral Hepat* 2014; **21**(): 5–33. Epub 2014/04/10. <https://doi.org/10.1111/jvh.12247>. PubMed PMID: 24713004.
5. Lazarus J. V., Sperle I., Maticic M., Wiessing L. A systematic review of hepatitis C virus treatment uptake among people who inject drugs in the European region. *BMC Infect Dis* 2014; **14**: S16.
6. Luhmann N., Champagnat J., Golovin S., Maistat L., Agustian E., Inaridze I., *et al.* Access to hepatitis C treatment for people who inject drugs in low and middle income settings: evidence from 5 countries in Eastern Europe and Asia. *Int J Drug Policy* 2015; **26**: 1081–7.
7. Iversen J., Dore G. J., Catlett B., Cunningham P., Grebely J., Maher L. Association between rapid utilisation of direct hepatitis C antivirals and decline in the prevalence of viremia among people who inject drugs in Australia. *J Hepatol* 2019; **70**: 33–9.
8. Makarenko I., Artenie A., Hoj S., Minoyan N., Jacka B., Zang G., *et al.* Transitioning from interferon-based to direct antiviral treatment options: a potential shift in barriers and facilitators of treatment initiation among people who use drugs? *Int J Drug Policy* 2019; **72**: 69–76.
9. Barre T., Marcellin E., Di Beo V., Delorme J., Rojas Rojas T., Mathurin P., *et al.* Untreated alcohol use disorder in people who inject drugs (PWID) in France: a major barrier to HCV treatment uptake (the ANRS-EANTASIO study). *Addiction* 2019; <https://doi.org/10.1111/add.14820>.
10. Delile J.-M., de Ledinghen V., Jauffret-Roustide M., Roux P., Reiller B., Foucher J., *et al.* Hepatitis C virus prevention and care for drug injectors: the French approach. *Hepatol Med Policy* 2018; **3**; <https://doi.org/10.1186/s41124-018-0033-8>.
11. Socias M. E., Ti L., Wood E., Nosova E., Hull M., Hayashi K., *et al.* Disparities in uptake of direct-acting antiviral therapy for hepatitis C among people who inject drugs in a Canadian setting. *Liver Int* 2019; <https://doi.org/10.1111/liv.14043>.
12. Butler K., Larney S., Day C. A., Burns L. Uptake of direct acting antiviral therapies for the treatment of hepatitis C virus among people who inject drugs in a universal health-care system. *Drug Alcohol Rev* 2019; **38**: 264–9.
13. Falade-Nwulia O., Irvin R., Merkow A., Sulkowski M., Niculescu A., Olsen Y., *et al.* Barriers and facilitators of hepatitis C treatment uptake among people who inject drugs enrolled in opioid treatment programs in Baltimore. *J Subst Abuse Treat* 2019; **100**: 45–51.
14. Scott N., Hainsworth S. W., Sacks-Davis R., Pedrana A., Doyle J., Wade A., *et al.* Heterogeneity in hepatitis C treatment prescribing and uptake in Australia: a geospatial analysis of a year of unrestricted treatment access. *J Virus Erad* 2018; **4**: 108–14.
15. Scott N., Iser D. M., Thompson A. J., Doyle J. S., Hellard M. E. Cost-effectiveness of treating chronic hepatitis C virus with direct-acting antivirals in people who inject drugs in Australia. *J Gastroenterol Hepatol* 2016; **31**: 872–82.
16. Grebely J., Dalgard O., Conway B., Cunningham E. B., Bruggmann P., Hajarizadeh B., *et al.* Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): an open-label, single-arm, phase 4, multicentre trial. *Lancet Gastroenterol Hepatol* 2018; **3**: 153–61.