Reviewer’s report

**Title:** Modeling HIV-HCV coinfection epidemiology in the DAA era: the road to elimination

**Version:** 1  **Date:** 12 Jul 2017

**Reviewer:** Natasha Martin

**Reviewer's report:**

The authors have provided responses to many of the reviewer comments, however unfortunately all three reviewers raised the same major concern with the model that the authors fail to correct: namely, the exclusion of HCV transmission from HIV-negative IDU to HIV-positive IDU. Unfortunately, I feel this exclusion is more than just a model limitation - it could impact the validity of the findings, and overestimate the impact of HCV treatment as prevention among this group. The authors state "Regarding IVDUs, most of them are currently former drug users." - what data do the authors have to support this assumption that most are former injectors? Further, the statement that "Moreover in this population a very low and stable first HCV infection rate was observed between 2012 and 2015 in the database (Pradat P. J Infect. 2017, Supplementary Figure 1A)." is only partially relevant because injectors are far more likely to acquire their initial HCV infection prior to their HIV infection, so HCV primary incidence among HIV+ PWID would be expected to be low, and one might expect that HCV reinfection incidence in this group may be higher than primary incidence. The statement "Another study reported that first HCV infection rate decreased from 7.9% person-year to 4.4% person-year among IVDUs in France between 2004 and 2011 (Leon L. Epidemiol Infect. 2017)." implies that HCV incidence may be decreasing among all PWID, but is still relatively high so should be incorporated I think? Overall I still find the new conclusion inadequate: "Third, we did not take into account a potential external source of HCV transmission for IVDUs, i.e. from HIV negative to HIV positive IVDUs, as no data regarding mixing between these two populations currently support this hypothesis." I, and the other reviewers, clearly feel the opposite-- that in the absence of data suggesting no mixing between these groups, one should assume that HIV+ IDUs are mixing with HIV- IDUs, instead of assuming they are not. Again, the implications of this are quite important as they could overestimate the potential treatment as prevention impact. The authors state their assumption is not overly optimistic by stating "Moreover access to DAA treatment in France is universal and the pool of HCV infections is therefore expected to significantly decrease in the HIV negative population, that's why we did not consider crude incidence rate (i.e. independent of HCV prevalence) for these three risk groups as the projections would be overpessimistic." There is another study modeling the impact of current levels of treatment among IVDU in France (Cousien A Hepatology) and although this does show a reduction in incidence, it does not show that incidence among the broader population will be negligible as perhaps implied by the authors. I am sympathetic to the fact that extending the model further would require additional time and effort, but I really think it is important to justify the current findings of this study.
Perhaps it could be done in a simplified way, with a fixed external force of infection representing seeding from the HIV-PWID population, using HCV incidence among all PWID to parameterize. This would likely underestimate the impact of treatment, but would be a more conservative choice than ignoring it entirely?

In addition to the above point, I am still confused as to why the authors do not dynamically model reinfection? The authors state "Regarding the reinfection rate, we considered it in our model as an external constant force of reinfection (i.e. independent of HCV prevalence), as the reinfection rate is very low in non-MSM subgroups (see Table 1) and because among HIV-HCV coinfected MSM, we could not estimate the number of new reinfections among high-risk and low-risk subgroups respectively”. I'm not sure why a low reinfection rate would be a problem- are the authors having problems fitting to the primary and reinfection data- if so more model heterogeneity would help? Similarly, the model does not have to fit to data on HCV reinfection among the specific subgroups of MSM- this could be an output, not an input of the model?

Overall I still believe this analysis could be very important, but do think that for validity the model should be extended to include transmission among HIV-negative PWID in some way (albeit perhaps in a simplified manner applied to the force of infection?). Or perhaps the model findings could be limited to MSM?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

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No

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Not relevant to this manuscript

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