Reviewer’s report

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

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Reviewer: Natasha Martin

Reviewer's report:

The authors present a mathematical modeling study examining HCV infection among HIV-infected patients in France, and the impact of HCV treatment coverage on the burden of HCV among HIV-infected risk populations. The aim of the project is important and interesting. The authors find that existing levels of DAA therapy could eliminate coinfection in France within 10 year for most risk groups. This is a very interesting and finding- however I have a few concerns about the model formulation and calibration and am unsure how robust the model is tot these concerns. Nevertheless, they should be addressable by the authors, and if addressed would make for a very interesting study. My comments are below:

Methods: The authors acknowledge in the discussion (pg 13) that they "model HCV transmission among HIV-infected patients only, without considering any other route of transmission such as transmission from the moninfected HCV population." They provide sufficient rationale to justify this for the MSM population, but I do not think this is likely appropriate for the PWID population. The prevalence of HCV among PWID in france is high (roughly half PWID infected). Even if incidence of HCV among HIV-infected PWID is low, PWID are more likely to obtain HCV prior to their HIV infection, therefore the incidence of HCV among HIV-infected PWID is not a true measure of the risk of reinfection among HIV-infected PWID, who are likely at high risk of reinfection from other (non HIV-infected PWID). I think the model really needs to address this somehow for reliability.

Methods: It wasn't clear to me how the authors represent current and former injectors (the latter with no ongoing risk of transmission) in the model? What duration of injecting is used?

Methods: I am unclear whether the model is truly dynamic as stated in the methods. In particular, the authors state (pg 7): "Regarding reinfection we considered a constant risk derived from observed reinfection incidence". Does that mean that primary incidence is dynamic but reinfection is fixed? It would be more robust for the model to be able to dynamically reproduce both primary and reinfection incidence, which should be possible with stratification of the high and low risk groups. Without this I am unsure about the validity of the results, in particular in relation to this subgroup.
Methods (pg 6): Overall I found the methods confusing because of what I believe is a mixing of methods between each subsection. The authors start with the epidemiological data and then describe the model, but this becomes confusing because some of the epidemiological text is related to the modeling, for example "We therefore assumed a heterogeneous risk of HVC infection among MSM". At times I was confused whether the statements were epidemiological data analysis or modeling outputs. For example "We thus estimated the property of high and low risk HIV-moninfected MSM according to these assumptions"- is that estimated from the data (and if so how were high/low risk defined), or estimated with the model.

Model parameterization (pg 7): The authors do not model HIV transmission explicitly, but instead model a fixed inflow of new HIV infections based on french national registry data. Are the number roof new diagnoses increasing/decreasing/stable, and what do the authors assume about the inflow in the future?

Methods: The authors do not consider an external force of infection among non-HIV infected MSM, but acute HCV infections are increasingly reported among HIV-negative MSM, and have been reported in HIV pre-exposure prophylaxis trials. Could the authors explore the implications of this in a sensitivity analysis?

Model parameterization (pg 7): Some of the parameters (like treatment rate and SVR) are time varying- it would be helpful if the authors could present the specific values for each time point instead of the range for clarity..

Methods and calibration: It was unclear to me from the main text what calibration data points the model was fit to as this appears to be calibrated to both incidence and prevalence data overall and among specific subgroups - could this be clearly listed in a table or the main text?

Model calibration: It appears that the model is supposed to represent all HIV-infected individuals in France, yet in the supplement, the authors state they calibrate the model using raw numbers from the Dat’ AIDS cohort: "We calibrated our model using yearly observed incidence and prevalence data (raw numbers) in the Dat’AIDS cohort from 1st January 2012 to 1st January 2016. " Given that the authors state the cohort covers 15 centers and only 25% of HIV-infected patients in France, I am unsure why the authors calibrated to these raw numbers as this presumably excludes the other 75% of infected individuals? If these raw numbers were adjusted (as I suspect they may have been) then perhaps the authors could clarify this in the text and state they used the incidence and prevalence rates combined with information on estimates of total numbers.

Results: Can the authors be clearer about what are model projections and how well these model projections fit to observed data- In particular the estimates of number of patients infected with HIV, numbers diagnosed, under care, and coinfected?
Minor points:

The abstract background would benefit from the inclusion of a sentence including the study aim and general method. E.g. something similar to what is in the methods section "We investigated the impact of scaling-up DAA on HCV prevalence among people living with HIV in France using a compartmental deterministic model". The abstract could also clarify that the authors use a transmission model. The results could specify that the numbers presented are model projections, not epidemiological data (unless they are? I was unclear). The sentence "Sub-analyses showed similar results in most risk groups" was a bit unclear- similar in what way, qualitative (declines) or quantitative (similar magnitude in decline of >x%)?

Methods (pg 7): The authors state "We developed a dynamic and deterministic model of HCV transmission, progression and treatment described in Figure 1. Patients enter the model at HIV diagnosis time." This statement and others in the manuscript would be more helpful if it clarified that the model is among HIV-individuals, and in particular among HIV diagnosed individuals.

Figure 2: Can the confidence intervals of the epidemiological data be presented alongside the point numbers?

Supplementary Table 1-5 It would be clearer if these tables specified in the title they were model outputs/projections. Also, it would be nice to have some credibility intervals around these numbers.

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

Unable to assess

**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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