Reviewer's report

Title: The case for a universal hepatitis C vaccine to achieve hepatitis C elimination

Version: 0 Date: 03 May 2019

Reviewer: Reza Yaesoubi

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The authors have used mathematical models of hepatitis C transmission to study the impact of different test and treat elimination strategies on the incidence of hepatitis C in 167 counties. My comments are as follows:

Definition of Optimality. My primarily concern about this study is how the authors define optimality, which is not consistent (and maybe even in conflict) with the principals of health care resource allocation. The authors indicate:

"For each country, we determined which approach could achieve the WHO elimination target of an 80% reduction in hepatitis C incidence by 2030 at the lowest cost, and where this target was not achievable, we determined the strategy that resulted in the maximum possible incidence reduction."

This approach may result in a selection of strategies that are suboptimal. The standard approach in resource allocation is to select a strategy that is expected to have the lowest ratio of cost per unit of health produced. For example, compared to the status quo, a strategy that cost $10 per case averted is preferred to the strategy that cost $20 per case averted. I suggest authors to follow the standards of cost-effectiveness analysis in presenting their results [1,2].

The WHO elimination target of an 80% reduction in hepatitis C incidences by 2030 may be seemed arbitrary by policy makers in different counties. Therefore, instead of putting so much emphasis on this target, I recommend authors to focus more on the comparative performance of strategies in terms of health and financial outcomes. Using cost-effectiveness analyses, the authors could then identify the strategies that are on the cost-effectiveness (efficiency) frontier for each county and highlight the strategy that is also expected to meet the WHO elimination target. That way, for each county, you can conclude whether the WHO elimination target can be achieved in a cost-effectiveness fashion, and if not, you can suggest an alternative strategy that is cost-effective and is expected to approach the WHO elimination target.

Validation. Not enough efforts have been made to establish the validify of the proposed mathematical models in terms of their ability to accurately describe the key characteristics of hepatitis C epidemics in the counties studied here. I recommend showing the time-series of prevalence and incidence rates (maybe stratified by population sectors, general community vs. PWI, and whether reached by healthcare system vs. not engaged) produced by the model (refer to Appendix Figure 1 in [3] for an example). For countries where observations on these time-
Parameter uncertainty. There is considerable uncertainty in many parameters of the proposed models. The authors have attempted to account for uncertainties through extensive one-way sensitivity analysis, but I think that has not been done in a strategic way and has made the presentation hard to follow and to some extend convoluted. One-way sensitivity analysis would be ideal for scenarios where the goal is to investigate whether the main conclusions of the study would change by changing the value of an input parameter. I recommend the authors to select a small number of parameters to include in one-way sensitivity analysis (for example, vaccine price would be a good candidate) and use probabilistic sensitivity analysis (PSA) to propagate the uncertainty in other parameters onto model projections.

Minor Comments:

1. The current model structure assumes that all 'infected but not diagnosed' cases will eventually get diagnosed. Is this a reasonable assumption? Is it possible that someone be infectious and remain asymptomatic?

2. Please provide in the Abstract and the main text for how many years the simulation is run.

References


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?
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Not applicable

Are the conclusions drawn adequately supported by the data shown?
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No

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