

Article details: 2017-0048	
Title	Model-based projection of health and economic effects of screening for hepatitis C Canada: informing national screening recommendations
Authors	William W. L. Wong PhD, Aysegul Erman PhD(c), Jordan J. Feld MD, Murray Krahn MD MSc
Reviewer 1	Dr. Dena Schanzer
Institution	Public Health Agency of Canada, Centre for Infectious Disease Prevention and Control, Ottawa, Ont.
General comments and author response	<p>1. While technically the Public Health Agency of Canada funds the CTFPHC, if CTFPHC commissioned the work (through a contract signed by the CTFPHC), should the CTFPHC not also be considered the funder? (CHEERS Checklist item 23 and CMAJ Open's policy of full disclosure). As CTFPHC provided the scenarios and some assumptions, this involvement should be disclosed. While PHAC may not have directly influenced the work, the statement "The views expressed in this article are those of the authors and do not represent those of the Public Health Agency of Canada" should be revised to state that the views (ie, some assumptions and scenarios evaluated) are those of the authors and CTFPHC.</p> <p>Response: The funding source is directly from PHAC, not from CTFPHC. We have added an additional statement in the financial disclosure: "Funding for this study was provided by the Public Health Agency of Canada (PHAC). The Canadian Task Force on Preventive Health Care (CTFPHC) Working Group suggested some assumptions and scenarios to be evaluated in this manuscript. However, the views expressed in this article are those of the authors alone, and and do not represent the positions of either the CTFPHC or PHAC" to make it transparent.</p> <p>2. As a general comment on manuscript style, the model assumptions are difficult to find, as some are in the main body and others are in the appendices. It is very difficult to get a full picture of the assumptions used in the model. My recommendation is to provide a full list of all assumptions in one table. The short version in the main text is simply a repetition of parts of the longer version in the appendices, and this style does not work well. (CHEER item 13b should be addressed in the main text).</p> <p>Response: A table regarding all assumptions has been added to the appendix (Appendix Table 2 – Summary of Assumptions).</p> <p>3. Abstract: As per CHEER item 2, the main outcome (ICER) should be reported for each scenario along with the range from the uncertainty analyses. In noting that the CTFPHC report has assessed the quality of evidence used to inform this model as low quality, providing a plausible range of uncertainty may not be possible. Some statement on the methods used to obtain the range of plausible values used is required (expert opinion, a fixed percentage variation). The number of deaths avoided is not really comparable across scenarios (as this figure depends on the size of the cohort and HCV prevalence) and could be dropped from the abstract. Perhaps the proportion of LD deaths avoided by screening and treatment for each scenario would be more informative (about 50%).</p> <p>Response: We have revised the abstract, and included the proportion of liver death as well as the uncertainty information. In economic evaluation, uncertainty are characterized by probability sensitivity analysis. ".....Probabilistic sensitivity analyses indicated that the chance that screening would be cost-effective at \$50,000 willingness-to-pay threshold were 39.5%, 63.2%, 58.4% and 58.1% for scenario 1-4."</p> <p>4. The scenarios are not well described (CHEERS item 4). It appears that the target population for the intervention varies by age range included and average hepatitis C prevalence of the cohort. The age range is provided, however, I could not find the hepatitis C prevalence assumed for each cohort. This should be stated. Are there any other difference? I image so, otherwise I can't explain the differences in Alternative Figure 2. Also the target populations for a one time screening test seem rather unusual. An explanation for these choices is required (CHEERS item 4). I would not think that a one time screening test was under consideration for persons under the age of 30 years. (Personally, I'd choose a baby-boomer age group, 45-64 years of age; older baby-boomers 65-75 perhaps; 35-45 as likely to be most cost effective, and for comparison a cohort such as immigrants from a high prevalence country).</p> <p>Response: The prevalence information regarding to the scenarios were listed in Table 2. An additional sentence has been added to the main text to provide pointer to the reader when we are defining the cohort: ".... Important parameters used in each cohort are provided in Table 2....."</p> <p>5. Outputs: I'd recommend moving the main outputs from the appendices to the main text (Appendix Figure 2). A sensitivity analysis (Tornado diagrams) is a required output and should be in the main document. The range of values for each input parameter should be identifiable in the Tornado diagram. (CHEER item 17, 20b). How these ranges were obtained should also be described, again as part of the main body. I am wondering if these ranges include the new negotiated prices for treatment. (Hard to publish a model when the target is moving so fast!)</p> <p>Response: The Tornado diagrams were moved from the appendix back to the main text. The method to generated the range was indicated in the appendix analyst strategy section: "...We then ran deterministic one-way sensitivity analysis on all model parameters over the plausible ranges using the reported 95% confidence interval (CI) ranges if available or using ± 25% of the reference value as indicated in tables...." Further, an assumption statement was added "Model did not consider negotiated drug prices" to the assumption table.</p> <p>6. Under the section on limitations I would like to see a reference to the CTFPHC statement that the evidence (data) available to inform this model is considered low quality, and a list of the most important data requirements (fibrosis stage in undiagnosed population (screened in) by age; prevalence by age/year of birth by region ...)</p> <p>Response: Statement regarding the CTFPHC statement has been added in the discussion: ".....Our model results was evaluated by CTFPHC using the GRADE approach (8) and were considered as "weak evidence". However, the GRADE approach was not developed to evaluate decision and economic models, and has very limited utility for that purpose (28)....."</p>