Evidence Review Title: Treatment for Hepatitis C Virus: a Systematic Review and Meta-Analysis

**Review Checklist**

Thank you again for reviewing this evidence review. The evidence review focuses on *Treatment for Hepatitis C Virus: a Systematic Review and Meta-Analysis* and will be used to develop a guideline.

**INSTRUCTIONS:**

* Please use this form to provide feedback on the evidence review
* Please e-mail this document no later than July 12, 2016 to *Ernesto.Delgado@phac-aspc.gc.ca*
* If you have any questions related to the review process, please contact Alejandra Jaramillo Garcia via e-mail at *Nathalie.Holmes@phac-aspc.gc.ca*
* Please check the appropriate box to answer the questions, and elaborate in the space provided if necessary.

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| **Question** | **Yes** | **No**  |
| 1. Are the objectives and methods of this evidence review clear?
 |[x] [ ]
|  | Yes, the objectives and methods of this evidence review are clear. What is not clear is the reasoning behind the development of this paper. The paper does little more than re-iterate what is already well known about the improved efficacy and reduced harms associated with DAA treatments as compared to older HCV treatment options. We are concerned that the development of this paper is redundant and serves to further delay progress towards the establishment of sensible screening guidelines for an infectious virus for which there is a cure.  |
| 1. Were the results clearly stated?
 |[x] [ ]
|  | The results presented in this paper were clearly stated. However, the paper itself also clearly states that the connection between the questions being studied in this paper and the core question at hand relating to the potential establishment of screening guidelines for HCV in Canada is tenuous at best. |
| 1. Are the conclusions in the review supported by the data that were reviewed?
 |[ ] [ ]
|  | Mostly - See below comment regarding Sheef 2002 paper. |
| 1. Do you have any additional comments?
 | The purpose of this paper is stated as the following: to conduct a systematic review examining the effectiveness and harms of newer hepatitis C treatments regimens compared to older treatment regimens. It is stated in this paper that ‘if this systematic review finds that treatment is effective, and with an acceptable level of harms, the CTFPHC could use this indirect information to recommend for screening in its recommendations.’ With this in mind, and the subsequent presentation of facts in this paper showing that DAA treatments for HCV are both highly effective and minimally harmful (as compared to older treatments), we are pleased that the CTFPHC will be recommending screening for HCV. We do however have several concerns about the content of this review and analysis: This paper makes several misleading references to a study conducted in 2002 by Dr. Sheef. The findings of the Sheef paper are dangerously misrepresented stating that ‘It is also important to note that most people, estimated at 80% or more, who do go on to develop HCV will not progress to end-stage liver disease such as cirrhosis’ (pg. 16). This paper goes on to reference Sheef 2002 to caution against ‘a real possibility of overtreatment’ (pg. 57). We have reviewed the Sheef paper and found that it did not project disease progression beyond 20 years post infection. In fact, Sheef states that the slope of disease progression after 20 years was unknown when the paper was published. We would encourage an examination of more current evidence that projects at least 40-50 years post infection when making statements about the progression of HCV. Related to this point, we are uncomfortable with the implication on page 57 of this paper that treating people living with HCV before they have end-stage liver disease such as cirrhosis would somehow equate to a potential of ‘overtreatment’. The concept of ‘overtreatment’ is a complex one and one that should not be mentioned in passing. We question the concept of ‘overtreatment’ of an infectious virus that is curable with treatments of short duration, low toxicity and high SVR rates. We would encourage more time to be spent reviewing current evidence relating to the health effects of living with HCV pre end-stage liver disease. We would also expect that a statement regarding potential ‘overtreatment’ would have examined evidence pertaining to other related issues including the psychological effects of knowingly living with a treatable, curable disease until it has progressed to have caused significant liver damage. We are curious about the ongoing reluctance in this series of papers examining the potential of screening guidelines to acknowledge middle-aged Canadians as a group that have an elevated risk of living with HCV (pg 16). We would also like to highlight that further context is required on page 17 when the paper states that ‘in Canada, treatment can be limited to patients with later fibrosis stages (F2-F4).’ The use of the word ‘can’ in this phrase might mislead a reader to understand that limiting treatment to later stages of disease progression is an acceptable, or evidence-based practice. In fact, we know that evidence shows that early treatment is more beneficial than later treatment and that the principle issue driving restriction of treatment eligibility is that of the cost and price of medicines, not the health or well-being of people living with HCV. |