

Answer to the reviewers and editor

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The study by De Weggheleire et al is an excellent work. Even if the proposed score is not applicable in western countries, as also stated by the writers themselves, it may be proven extremely useful in countries with low and middle income. Additionally we should keep in mind that these specific countries, do carry the greatest burden of HIV-HCV co-infection.

Answer: Thank you for this encouraging review. We have added still a phrase at the end of the 2nd paragraph of the discussion to highlight the point of largest burden in low and middle income countries, and also added this notion in the last phrase of the conclusion.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: overall very good manuscript.....No major changes required except that the conclusion portion could be more specific and add a note on limitations...

Answer: We added some further specifications in the conclusion and hope this responds to the comment of the reviewer. The limitations of our study are specified in the 5th paragraph of the discussion: *There are also several limitations. It is a model development study, with internal validation to correct for over-optimism by bootstrapping, but no external validation was done yet. Further validation in different settings will thus be crucial before decisions on generalizability can be taken [33]. Inherent to the score building method used (Spiegelhalter Knill-Jones), continuous variables had to be categorized. This may have led to information loss [34,35]. The SKJ method adjusts for dependency between predictors (confounding), but in a more restricted manner than the conventional logistic regression. Each result (present or absent) of a particular predictor/test is being shrunk to the same degree [30].*

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: It is an interesting manuscript about "Development of a risk score

for hepatitis C coinfection among HIV patients in Cambodia with potential to guide prioritization of hepatitis C testing in resource-constrained settings". My concern is determined in the following points. HIV-infected patients should be screened regularly for HCV co-infection, particularly if they are in high-risk groups. Sexual transmission of HCV needs to be included in patient counseling both for HIV-infected men and women. Increased progression rates to AIDS and liver disease in co-infected individuals may require earlier and more aggressive treatment of both infections. However, following treatment initiation, patients should be monitored for AEs, with prompt intervention to support continued treatment. For most co-infected patients, HAART should be initiated before anti-HCV therapy to slow liver progression and increase CD4 counts. Above mentioned should be referred to.

Answer: We agree with the reviewer that HIV patients should be screened regularly for HCV co-infections if they are in high-risk groups. In the cohort we studied, high-risk groups were very rare as specified in the first paragraph of the methods section, and also in the first paragraph of the discussion (primarily heterosexually-infected HIV patients). In the conclusion, we also emphasized more that the score is aimed for targeted screening in HIV cohorts with few key populations.

However, to acknowledge this point and also the other valid points raised by the reviewer we modified paragraph 3 of the discussion. The additions we made are underlined here: *With this paper, we do not intend to advocate in a general manner for targeted HCV testing in all HIV populations. We agree with the WHO guidelines that HIV populations are a convenient population sub-group to be targeted as a whole, as they often have a higher HCV prevalence than the general population, and are easy to reach [4,26]. 'Testing all repeatedly for HCV, accompanied by appropriate preventive counselling' should be aimed for whenever feasible as part of a comprehensive package of care for people living with HIV (including timely initiation of ART and treatment of comorbidities as HCV), especially as nearly 100% curative HCV treatment options are now available. However, lack of resources, and low in-country HCV coinfection prevalence in large HIV cohorts with little ongoing transmission risk, are valid contextual arguments that countries may use to opt differently [8-10,27]. As also the argument that HIV coinfection leads to faster HCV disease progression (and therefore priority) has become debatable in the early ART era [8-10,27,28], some countries may indeed opt for a more restricted HCV testing approach combined with early initiation of ART. Anticipating this, it seemed to us timely to develop this score for targeted HCV testing.*

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The manuscript describes a clinical and translational research of the development of a risk score for hepatitis C coinfection among HIV patients in Cambodia with potential to guide prioritization of hepatitis C testing in resource-constrained settings. The topic is within the scope of the WJH.

(1) Classification: Grade C, Grade B and Grade A;

(2) Summary of the Peer-Review Report: The authors found an excellent and interesting work. However, the conclusion portion could be more specific and add a note on limitations. The questions raised by the reviewers should be answered; and

(3) Format: There are 5 tables and 3 figures.

(4) References: A total of 36 references are cited, including 1 reference published in the last 3 years;

(5) Self-cited references: There is 1 self-cited reference. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and

Answer: We consider the self-cited reference as essential to provide the background information of the HIV cohort and prevalence study done in Cambodia, so would prefer that it can be kept in the list.

(6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2 Language evaluation: Classification: Grade A, Grade B and Grade A.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Clinical Trial Registration Statement, and the Institutional Review Board Approval Form. Written informed consent was waived. No academic misconduct was found in the Bing search.

4 Supplementary comments: This is an unsolicited manuscript. The study was supported by 2 grants.

Answer: We have removed the information on the institutional programs of the Institute of Tropical Medicine of Antwerp through which the implementation of the HCV program in Cambodia was supported. These programs (framework agreement, SOFI program) were no specific external grants so probably better not to mention them.

The topic has not previously been published in the WJH.

5 Issues raised:

(1) The title is too long, and it should be no more than 18 words;

Answer: The title has been shortened in the revised version, and is now 16 words.

(2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Answer: see answer above

(3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and

Answer: The figures have been uploaded now in a ppt. All parts can be processed now by the editor.

(4) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Answer: These items have been added in the revised version.

6 Recommendation: Conditional acceptance.

(2) *Company editor-in-chief:* I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Answer: The title has been shortened and is now 16 words.