Hepatitis Monthly
Volume 24 · Issue 1 · e136838

OPEN PEER REVIEW

Targeted Screening for Viral Hepatitis Among Various Ethnic Groups in Amsterdam, the Netherlands

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SUBMITTED	REVISED	ACCEPTED	DOI
15 Apr 2023	1 Sep 2023	20 Sep 2023	10.5812/hepatmon-136838

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

4 comments · 19 Jun 2023 – 28 Jun 2023

Heidar Sharafi Reviewer

ACCEPT 19 Jun 2023

Dear editor,

Thank you for your invitation. I enjoyed reading the manuscript. I have no comment/correction.

Thank you.

Referee 1 Reviewer

MINOR REVISION 20 Jun 2023

The authors attempted to demonstrate that targeted screening for HBV and HCV in various ethnic groups of immigrants in Amsterdam is more beneficial than generic screening. The manuscript provides informative insights; however, there are some issues that need to be addressed in the second revision:

Minor revisions:

Including information about the composition of the immigrant population in Amsterdam would help readers understand the communities of immigrants in the city.
Please add the exclusion criteria to the Materials and Methods section.
I kindly request the authors to mention the names of the serological kits used in this study, along with their sensitivity and specificity.
Were there any HIV mono-infected or co-infected patients in this cohort?
Does the total number of participants (403 out of 10,585) provide enough statistical power to support the conclusions drawn?
On page 9, line 26, please remove the word "unfortunately."
While the focus of this study has been primarily on HBV, there is a lack of data regarding the prevalence of HCV in different ethnic groups of non-Dutch immigrants in Amsterdam. Please address this gap.
The discussion section would benefit from additional citations to support the discussed ideas and proposed approaches. Consider including information on the prevalence of HBV and HCV in both the general population and immigrants, as marginal populations such as immigrants are an important target for micro-elimination.
Furthermore, there is a lack of data regarding the vaccination rate against HBV in the Netherlands, particularly among immigrants. Please discuss whether high vaccination coverage can eliminate HBV in these sub-populations, instead of relying solely on different screening approaches.
Addressing these points will improve the manuscript and provide a more comprehensive understanding of the study's findings.

Associate Editor

MINOR REVISION 21 Jun 2023

Dear EIC,
The manuscript explores the efficacy of targeted screening for hepatitis B virus (HBV) and hepatitis C virus (HCV) among different ethnic groups in Amsterdam, the Netherlands. The authors investigate whether screening individuals with metabolic risk factors or elevated non-invasive tests (NITs) improves screening

efficiency compared to a generic screening approach. While the study addresses an important topic, there are several areas that need improvement as mentioned by the reviewer.

Editor-in-Chief MINOR REVISION 28 Jun 2023

Dear Author,
Thank you for submitting the article. It needs some revision. Please revise it based on the reviewers' and AE's comments.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Response to reviewers

Reviewer 1:
Authors attempted to demonstrate that targeted screening of HBV and HCV in various ethnic groups of immigrants in Amsterdam is more beneficial than generic screening.

The manuscript provides informative insights; however, there are some issues that need to be addressed in the second revision:

Reply: We thank the reviewer for their time spent reviewing our manuscript and their helpful comments.

Minor revisions:
Including information about the texture of the immigrant population in Amsterdam would help readers understand the communities of immigrants in the city.

Reply: Agreed. We have added more information regarding these migrant populations to the methods section (page 4, lines 7-10): *"More information on the migration history of these groups can be found in earlier papers (Stronks et al. 2013 (Unravelling the impact of ethnicity on….), Snijder et al. 2017). In short, they are the largest migrant populations living in Amsterdam (i.e. Surinamese, Turkish, and Moroccan), and groups with compara ble backgrounds can also be found in other European countries."*

Please add the exclusion criteria to the Materials and Methods section.

Reply: In the material and methods section, we report excluding participants that used >21 units of alcohol per week from study analysis (page 8, line 33 to page 9, line 1). In the revised manuscript, we've added the second exclusion criterion that was used in our study (page 9, line 2): "*Additionally, individuals with an unavailable blood sample were excluded.*"

I kindly request the authors to mention the names of the serological kits used in this study, along with their sensitivity and specificity.

Reply: We have added the requested information to the materials and methods section (page 6, lines 9-12): *"HBV- and HCV serology results were obtained using Liaison XL (DiaSorin, Saluggia, Italy). Sensitivity and specificity for these tests is above 99.7%.(15) For HCV viral load, Alinity (Abbott, Abbott Park, Illinois, United States of America) was used, which has a >98% HCV RNA detection rate for samples with an HCV RNA viral load near the lower limit of detection (i.e., 5.11 IU/mL).(16)"*

Were there any HIV mono-infected or co-infected patients in this cohort?

Reply: Unfortunately, HIV-related data were unavailable in the HELIUS study. This was added to the limitations section (page 11, line 27): "*HIV data was unavailable for the study."*

Does the total number of participants (403 out of 10,585) provide enough statistical power to support the conclusions drawn?

Reply: We agree with the reviewer that the relatively low number of included participants is one of the main limitations of our study, as mentioned in both the second paragraph of the discussion (page 10, lines 8-10) and the limitation section (page 11, lines 16-19). The HBV and HCV serological testing results were a secondary outcome of the NILE study, and therefore not considered when calculating the necessary number of participants to achieve sufficient power. To emphasize this limitation, we have added to the conclusion paragraph (page 11, line 32): *"In conclusion, although the limited sample size precludes any definitive conclusions, ……"*

On page 9, line 26, please remove the word "unfortunately."

Reply: We have deleted the word referred to by the reviewer.

While the focus of this study has been primarily on HBV, there is a lack of data regarding the prevalence of HCV in different ethnic groups of non-Dutch immigrants in Amsterdam. Please address this gap.

Reply: We agree with the reviewer that regarding HCV prevalence, there is a lack of data for the specific population assessed in our study, i.e. individuals from different ethnic groups in Amsterdam with metabolic risk factors. Nonetheless, we respectfully disagree with the observation that this lack of data applies generally to individuals with a migration background. In the first HELIUS study visit, HCV prevalence was assessed in nearly 2500 individuals with an ethnic background other than Dutch in Amsterdam [Zuure et al. JHEP reports 2019, reference 5 in the manuscript], providing appropriate data on HCV prevalence for these groups. Of note, HCV prevalence was low among all of the included ethnic groups in this study.

The discussion section would benefit from additional citations to support the discussed ideas and proposed approaches.

Reply: To the best of our knowledge, the HBV/HCV screening approach assessed in this study is an entirely novel approach, and therefore we were unable to cite any previous papers on this topic. Instead, in the revised version we have decided to add a citation on the effectiveness of a primary care referral pathway for patients with NAFLD [Srivastava et al, Journal of Hepatology 2019], demonstrating the feasibility of a pathway similar to ours. We have added the following (page 10, lines 28-30): *"For NAFLD, it has already been shown that primary care screening programs are effective in both improving advanced fibrosis and cirrhosis detection rates as well as decreasing the number of unnecessary referrals."*

Consider including information on the prevalence of HBV and HCV in both the general population and immigrants, as marginal populations such as immigrants are an important target for micro-elimination.

Reply: Thank you for this suggestion to provide these data, which will be useful to inform the reader about HBV and HCV epidemiology in the Netherlands. We have added the following to the introduction (page 4, lines 6-9): *"Both estimated HBV- and HCV-prevalence in the Netherlands are generally relatively low, 0.34% and 0.16%, respectively, in 2016.(3) However, the majority of people with chronic HBV or HCV in the Netherlands are migrants from HBV- or HCV-endemic*

countries, with estimated HBV- and HCV-prevalence in these groups of 3.1% and 0.9%, respectively.(3)"

Furthermore, there is a lack of data regarding the vaccination rate against HBV in the Netherlands, particularly among immigrants. Please discuss whether a high vaccine coverage can eliminate HBV in these sub-populations, instead of relying solely on different screening approaches. By addressing these points, the manuscript will be improved and provide a more comprehensive understanding of the study's findings.

Reply: We agree with the reviewer that a high coverage of HBV vaccination is crucial to eventually achieving HBV elimination in the Netherlands. However, we consider HBV vaccination to be outside of the scope of our paper, since it concerns a different component of micro-elimination. Where HBV vaccination is crucial to reduce the *incidence* of HBV infection, our topic of interest concerned increasing *diagnosis* and *treatment* rates with case-finding, through which morbidity and mortality could be reduced. This approach focused on a population of mostly first-generation migrants who were chronically infected with HBV since birth or at a young age in the country of origin.

Reviewer 2:

Dear editor, Thank you for your invitation. I enjoyed reading the manuscript. I have no comment/correction.

Reply: We thank the reviewer for their positive comments on our manuscript.

2 Revision 1

1 comment · 5 Sep 2023

Associate Editor

ACCEPT 5 Sep 2023

Dear EIC,
I read the manuscript, and the authors corrected the requested items. The article could be accepted at this stage.
Sincerely;