

## PEER-REVIEW REPORT

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**Title:** Viral hepatitis in 2021: The challenges remaining and how we should tackle them

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**Professional title:** Doctor

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**Author's Country/Territory:** United Kingdom

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [ ] Yes [Y] No

## SPECIFIC COMMENTS TO AUTHORS

This is a very timely review with respect to the WHO goals of viral hepatitis elimination. It is great that the authors included all the hepatitis viruses. It is well-written but I feel the authors may have glossed over the problems of diagnosing and managing HBV in low-middle-income countries. They mention POC tests but these are yet to be universally adopted and there is certainly a need to improve the sensitivity, cost and availability of these. Perhaps it is beyond the scope of this review, which is not diagnosis-based. The authors make many valid points but I do have a few individual comments, suggestions and recommendations below. For the sake of easier editing, I have added page and line numbers. Minor comments: • Page 2: In the methods section, authors mention chronic kidney disease as a term used for searching. Should this include and/or liver disease? • Page 4: The authors categorically state that “Use of this vaccine in children has reduced the incidence of HAV infection by 80%”. I think this should be amended to “reportedly reduced” as it was only found in 1 study. • Page 4: Can the authors please elaborate on “who are likely to be exposed to HAV from their employment”. What sort of employment? • Page 5: “people who inject drugs (PWIDs)”, this acronym should be introduced on the previous page where “people who inject drugs” was first mentioned. • Page 5: The MSM acronym was also introduced on the previous page and doesn’t need to be mentioned again. • Page 5: ?re-phrase “offering of vaccination” - line 121 • Page 9: ?Elaborate here on the issues in resource- poor settings • Page 9: Under defining cure – HBsAg, HBeAg, cccDNA etc is used here without an explanation or introduction, ie – surface antigen of HBV... • Page 10: Functional cure is first mentioned here but the definition is incomplete, ie it doesn’t mention HBV DNA suppression off Rx etc. It is introduced again on page 12 but here it is misleading as

functional cure is not “HBsAg loss in more than 30% of patients”. This is inaccurate. • Page 11: POC testing is mentioned again but it should be specified that we need HBV viral load and/or HBeAg –status to inform decisions on maternal prophylaxis. These diagnostic assays are not readily available, costly etc • Page 11: Instead of “seroconversion occurs below the age of 30 years and where a low or undetectable HBV-DNA level was maintained”, suggest replacing “was” with “has been” to avoid the tense change • Page 13: Another categorical statement - “HBsAg loss after the development of advanced fibrosis does not negate the risk of development of HCC”. Suggest “while HBsAg loss minimises the risk, it does not negate....” • Page 14: Line 341 – “hepatitis B core-related antigen” – the acronym has already been introduced so this should be HBcrAg • Page 15: For consistency, suggest putting (HDV) next to subheading. • Page 15: Other studies suggest a higher prevalence of HDV. This should be acknowledged. See Rizzetto et al, The Changing context of hepatitis D. JHepatol. 2021 • Page 16: ?mention that HDV RNA is needed to diagnose current infection. • Disagree with the comment “novel approach”. Testing of newly diagnosed HBsAg-pos patients for anti-HD should be adopted. • Page 17: Again for consistency put (HCV) after subheading • Page 18: SVR needs to be defined – ie sustained virologic response... • Page 21: Line 504 – use “times” instead of “x” • Page 21: Define BBV • End Page 22 to top 23: “treatment” is used 7 times in as nearly as many sentences • Page 23: ? comment on the use of anti-HC testing in re-infections • Page 25: introduce abbreviation for “HCV-positive”, ie (HCV RNA+) • Page 26: For consistency add “virus” to Hepatitis E subheading and include (HEV) • Page 28: Define SOT • Page 29: ?comment on need to understand source of infections to guide public health decisions • Figure 2: ?comment on education/harm reduction • Table 2: Under Hep B - ? after “ Identifying undiagnosed individuals “add linkage to care • Under Hep C - ? add “Harm reduction” under pub health priorities