

Dear Professor,

We would like to express our gratitude for your thorough review of our manuscript. Furthermore, we sincerely appreciate the opportunity you've given us to resubmit our revised manuscript. We have diligently addressed the revisions based on your valuable feedback, as outlined below. Red sections are language modifications and yellow highlights are content modifications.

Reviewer #1:

1. HDV can progress to chronic liver disease, please modify it in the Introduction.

R: Thank you for your professional guidance. In the introduction, we have included information stating that HDV can develop into chronic hepatitis.

2. Since the European GWAS dataset did not contain CHB & CHC data, how can you conclude that no significant relationship was found between VH and T2D in Europeans?

R: Although GWAS does not provide CHB and CHC data for Europeans, it does provide VH data for Europeans. We analyzed the overall impact of VH on European T2D. Therefore, we inferred no significant association between VH and T2D in Europeans. This inference describes VH as a whole, not a specific kind of VH. To elaborate further, we provide an additional description in the limitations: "Second, GWAS only provides the overall dataset of VH in Europeans with availability, and it does not include the dataset of different types of VH. Therefore, the results of this study can only infer that VH is not associated with T2D risk in Europeans but cannot explain the effect of different types of VH on T2D risk in Europeans."

3. Please address on what are the most significant differences between the current study and other published clinical articles on the causal relationship between CHC and T2D since many hepatologists were convinced to accept the positive relation in this scenario.

R: (i) We conducted a comprehensive review of literature regarding HCV's action in obesity, metabolic syndrome, and T2D and inferred that the mechanism by which CHC increases the risk of T2D is related to the promotion of hepatic steatosis and the

mediation of fatty liver, hepatic fibrosis, and cirrhosis. (ii) Based on this foundation, we analyzed the reasons that led to MR results that differed from those of clinical studies. Due to the assumption of exclusivity of MR, SNPs associated with known risk factors for T2D, such as fatty liver, liver fibrosis, and cirrhosis, were excluded as confounding factors, which may be the main reason for the negative MR results.

Reviewer #2:

1. Abbreviations in the abstract CHB, CHC are not explained.

R: Thank you for the reminder. We have added the full names of CHB (chronic hepatitis B) and CHC (chronic hepatitis C) to the abstract.

2. “which helps early detect T2D induced by CHC-mediated other factors. “ this is unclear, please rewrite.

R: We have rewritten the sentence: "This helps in early detection of T2D induced by CHC-mediated pathways of hepatic steatosis, liver fibrosis, and cirrhosis."

3. “direct-acting antiviral agent (DAA),” this has to be corrected.

R: Thank you for your professional guidance. We have reviewed the original literature providing this full title and corrected "direct-acting antiviral agent (DAA)" to "direct-acting antiviral agents (DAAs)".

4. “Type 2 diabetes (T2D), Type 2 diabetes (T2D),“ please delete one „diabetes mellitus” may be replaced by T2D.

R: We have deleted the redundant "Type 2 diabetes (T2D)" in "Abbreviations" and replaced "diabetes mellitus" with "T2D" in some of the modifiable text. For other papers that do not distinguish between types of diabetes, we have retained the term "diabetes mellitus."

5. Data on HAV, HDV, and HEV have not to be mentioned because this was not analyzed in this study.

R: Due to the lack of relevant datasets, we could not analyze the impact of HAV, HDV, and HEV on T2D risk. To provide clarity, we outline their possible impact on T2D risk in the Discussion in the context of the published literature. And this unavoidable

problem is acknowledged in the limitations.

6. Authors should discuss the role of obesity / metabolic syndrome in HBV / HCV.

R: Having reviewed relevant literature, we have incorporated a discussion on the role of HBV and HCV in obesity and metabolic syndrome. This additional information strengthens the support for the findings of our study.

We are immensely grateful for your guidance, which has significantly contributed to the refinement of our manuscript.

If you identify any further issues that require attention, please do not hesitate to inform us. Thank you.

Best regards,

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