

Jin-Lei Wang, Company Editor-in-Chief
Editorial Office
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Dear Dr Wang,

13th June 2022

RE Manuscript NO: 76796

Thank you for your reply and the opportunity to revise our manuscript *Alcohol intake is associated with a decreased risk of developing primary biliary cholangitis*. Thank you for providing us with valuable reviewer suggestions to improve our paper. We have included the reviewer and science editor's comments immediately after this letter and responded to each individually, outlining how we addressed each comment and corresponding changes to the manuscript.

Kind regards,
Dr Janine French & Dr Kate Collins
Department of Gastroenterology
Austin Health

Reviewer #1:

Comment 1.1: They should include a definition of a standard drink in the text to better understand the extent of alcohol consumption in the studied patients.

Answer 1.1: We have amended the manuscript to include the definition of a standard drink (10g of alcohol). This is documented in the methods section under measurement of alcohol intake.

Reviewer #2:

Comment 2.1: Can the authors explain the sentence: "Cases who had been diagnosed during the defined age periods, as well as their linked controls, were not included in the analysis of that specific age period.". According to the description of the model of the study, subjects and controls were divided into age groups according to age at the time of the analysis.

Answer 2.1: We have changed the writing to now read: "Cases who had been diagnosed during the defined age periods, as well as their linked controls, were not included in the analysis of that specific age period or age periods that followed".

Comment 2.2: Could authors clarify how they investigated the role of the length and cumulative amount of alcohol consumption before and after diagnosis of PBC? What is the follow-up period of the patient from diagnosis to evaluation in this study?

Reply to the comments on manuscript 76796 *Alcohol intake is associated with a decreased risk of developing primary biliary cholangitis* French, J et al.

Answer 2.2: In our cohort, the mean time from PBC diagnosis to time of study was 12.6 years (this has now been added to the manuscript under the results section in the second paragraph). However, there was no follow up period as PBC cases were recruited post PBC diagnosis and the data regarding exposures was collected retrospectively using the validated questionnaires.

Comment 2.3 How has the stage of liver disease and the association with alcohol consumption been investigated? Could authors provide information on the baseline PBC stage status?

Answer 2.3 The cumulative alcohol exposure until PBC diagnosis was less than controls for each age band prior to diagnosis. For patients with PBC and cirrhosis at the time of the analysis, the pre-PBC alcohol intake in each 10-year band for both total drinks per week and drinks per session did not impact Child-Pugh score at the time of analysis. This additionally would be an interest for future research if it can be replicated in other environmental cohort studies for PBC.

Comment 2.4: In Supplementary Table 2. replace word “pathology” with “platelets”.

Answer 2.4: Thank you for bringing this to our attention, change has now been made to read as ‘platelets’

Comment 2.5: Language requires polishing to achieve precision, clarity and grammatical correctness.

Answer 2.5: Language within the paper has been reviewed and refined.

Science Editor 3:

Comment 3.1 The response for ursodeoxycholic acid should also be evaluated.

Answer 3.1 Our study was designed to examine environmental and lifestyle-related exposures prior to PBC diagnosis. Thus, we have not analysed the effects of environmental or drug factors after diagnosis of PBC. UDCA response is such an important prognostic factor for PBC patients, a direction for future research could be to analyse UDCA response post-diagnosis in those who consume versus abstain from alcohol.
