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# Letter: association of circulating bile acid concentrations and non-alcoholic fatty liver disease—authors' reply

We agree with Dr Sun and colleagues that a number of conditions, including hyperlipidemia, diabetes, acute and chronic hepatitis, cirrhosis and liver cancer have been reported to be associated with abnormal bile acid metabolism.<sup>1</sup> Dr Sun and colleagues raised several concerns about our report,<sup>2</sup> however, including that "only diabetes but no other concurrent metabolic and hepatobiliary diseases were mentioned between patients with and without NAFLD in the study." In addition, Dr Sun et al. note that as "Guatemala has a high incidence of hepatitis B, liver cirrhosis, and liver cancer, the incidence of these relatively common liver diseases should be investigated in the study". Further, it was noted that cholelithiasis should have been considered in our study and that information on whether the bile acid levels were determined in fasting vs non-fasting samples should have been provided.

In regard to several of the concerns, it may be worth emphasising that our study was a cross-sectional epidemiologic investigation of persons in the general population of Guatemala. The study was conducted to determine the prevalence of various factors. We did not study a clinic population; thus, the participants were not patients. Cholelithiasis is a diagnosis determined by imaging modalities in a clinical setting. In regard to the presence of other medical conditions among the study participants, our report noted that persons with HBV, HCV and/or heavy alcohol consumption were excluded from the statistical analysis. In a subsequent analysis that excluded persons with diabetes, the results of the adjusted bile acid analysis were essentially unchanged.

In regard to hepatitis B, liver cirrhosis and liver cancer being "relatively common" in Guatemala, it should be noted that the reference cited by Dr Sun and colleagues<sup>3</sup> was written by our group. The manuscript reported that the prevalence of hepatitis B virus infection was quite low (<1%) and while the incidence rate of liver cancer in Guatemala is considered to be high (15.6 cases per 100,000 persons) in comparison to liver cancer rates elsewhere, liver cancer is not a common condition in the general population. Lastly, in regard to participants' state at the time of blood draw, all participants in the study were fasting.

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### AUTHOR CONTRIBUTIONS

Alvaro Rivera-Andrade: Writing – original draft (equal). Jessica Petrick: Writing – review and editing (equal). Christian S Alavarez: Writing – original draft (equal). Barry I Graubard: Writing – original draft (equal). Andrea A Florio: Writing – original draft (equal). Fernanda Kroker-Lobos: Writing – review and editing (equal). Dominick Parisi: Writing – review and editing (equal). Neal D Freedman: Writing – review and editing (equal). Mariana Lazo: Writing – review and editing (equal). Mariana Lazo: Writing – review and editing (equal). Eliseo Guallar: Writing – review and editing (equal). John D Groopman: Writing – review and editing (equal). Manuel Ramirez-Zea: Writing – review and editing (equal). Katherine A McGlynn: Writing – original draft (equal).

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# LINKED CONTENT

This article is linked to Rivera-Andrade et al papers. To view these articles, visit https://doi.org/10.1111/apt.16948 and https://doi.org/10.1111/apt.16986

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