**Author’s response to reviews**

**Title:** Risk of De Novo Post-Transplant Type 2 Diabetes in Patients Undergoing Liver Transplant for Non-Alcoholic Steatohepatitis

**Authors:**

Maria Stepanova (maria.stepanova@inova.org)
Linda Henry (linda.henry@inova.org)
Rishi Garg (rishi.garg@inova.org)
Shirley Kalwaney (shirley.kalwaney@inova.org)
Sammy Saab (SSaab@mednet.ucla.edu)
Zobair Younossi (zobair.younossi@inova.org)

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**Author’s response to reviews:** see over
Reviewer 1

Q1. It is unclear if the authors are reporting "new onset diabetes mellitus (NODM)" rates post transplant? If so, suggest use NODM instead of post transplant DM which is line with other papers.

A1. We changed the dx of DM to de novo DM by excluding patients with history of pre-transplant type 2 DM.

Q2. Although a major fraction of cryptogenic cirrhosis is due to NASH, the authors use NASH synonymously with Cryptogenic cirrhosis. Were the authors able to scrutinize the data of explant pathology to discern what fraction of cryptogenic cirrhosis are in fact NASH related?

A2. >90% of cryptogenic cirrhosis in SRTR does not have additional information on its etiology. We, however, believe, and now included 8 references in support, that in the United States (unlike some other countries) cryptogenic cirrhosis is unlikely anything but burned out NASH. This matter is now discussed in Methods.

Q3. I think patients who underwent re-transplantation should be excluded from the analysis as it can skew the data significantly as they might have received higher doses of steroids and immunosuppression during the first graft failure. Table 2 shows 145 patients with re-LT.

A3. We excluded liver re-transplants as recommended.

Q4. A significant fraction of liver transplant (LT) recipients are insulin dependent. It is possible that patients who have type 1 DM prior to LT are more prone to remain diabetic post LT. Could the authors provide data whether pre LT insulin dependency has a role in risk prediction?

A4. The type of DM is specifically recorded in SRTR data collection, so for the purpose of this study we only considered type 2 DM. As a note, only 3.0% of included liver transplant recipients had t1DM.

Q5. It has been shown that HCV is an important risk factor for NODM in both liver and kidney transplant literature. Although it is appropriate for the authors to exclude them in their study, HCV + patients could also serve as controls and thus their exclusion is a limitation.

A5. Indeed, HCV is widely known to have its own diabetogenic effect. So, we believe that inclusion of HCV to controls might mask the effect of the condition which, as we suggest, causes both NASH and DM.

Q6. It is interesting to note that calendar year came out as an important predictor (line 320). Suggest the authors to create a bar histogram showing the trend with each calendar year vs rates of NODM.

A6. We added a bar graph (Figure 2).
Q7. Were any post LT liver biopsies looked at to show whether recurrent NASH is a predictor of NODM?

A7. Unfortunately, SRTR does not collect such information in follow-up.

Q8. Can authors comment in their discussion about higher rates of transient hyperglycemia (at least 1 episode; Table 3) in controls at every time point than the NASH subjects.

A8. We changed the control cohort per recommendation of the other reviewer, so this is no longer the case.

Reviewer 2

Q1. which such large numbers not sure why they decided to lump crypt + NASH and somewhat misleading in the body of the paper they state that the entire cohort of patients is 'NASH' which by their own admission it is not

A1. We believe, and now included 8 references in support, that in the United States (unlike some other countries) cryptogenic cirrhosis is unlikely anything but burned out NASH. This matter is now discussed in Methods.

Q2. what % of the 5890 were NASH and what % were crypt

A2. After exclusion of subjects with pre-transplant DM, the target cohort became smaller. The distribution of diagnoses in both cases and controls is now included in Methods. In particular, 59.6% of patients with supposed NASH were included with the diagnosis of cryptogenic cirrhosis.

Q3. liver transplantation for NASH is a cure for 'NASH' why are we assuming it is a cure for the metabolic syndrome?

A3. We are not. In fact, we explicitly show that this is not the case, since NASH patients continue to have a higher rate of DM even after curing NASH.

Q4. no distinction is made from the ~ 33% of patients going into liver tx with diabetes versus those without i would of seperated out the cohort into patients with diabetes going into tx and those without

A4. We changed the dx of DM to de novo DM by excluding patients with history of pre-transplant type 2 DM.

Q5. why did they decide to use ALD as a control the baseline demographics of these two populations is very different?

A5. We changed the control cohort to include other CLD diagnoses as well, with the exception of HCV which is known to impair glucose metabolism by itself.