Author's response to reviews

Title: Trends in Liver Transplantation for Primary Biliary Cirrhosis in The Netherlands 1988-2008

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Author's response to reviews:

Concerning Ref.: Ms. No. 1592935376371563
Title: “Trends in Liver Transplantation for Primary Biliary Cirrhosis in The Netherlands 1988-2008”.

Dear Sir,

Thank you very much for the opportunity to submit a revised version of our manuscript.

Several modifications following the useful Reviewer’s comments were made in the new version of the manuscript.

We here address the comments point-to-point:

Referee 1: An article whose findings are important to those with closely related research interests

Question 1: It would valuable for this manuscript if the authors can include the overall incidence of PBC in Netherlands during the two study periods. Is it remained the same and only the incidence of transplantation in PBC is decreased or is the incidence in transplantation decreased due to decreased overall incidence of PBC?

Answer 1: Unfortunately, with respect to the incidence of PBC in the Netherlands, we don’t know whether this remained stable, decreased or increased. This has not been established. Studies performed elsewhere, particularly in the UK, indicate that if the incidence has changed over the last decades it might rather be an increase than a decrease (James et al. Hepatology 1999;30:390-394). Studies in several other countries have suggested the same trend.
This is also mentioned in the discussion: “The incidence of PBC in our country has not been defined and therefore the potential importance of changes in time cannot be addressed properly. A noticeable increased incidence of PBC has been documented in the UK while other data suggest that the incidence worldwide at least seems stable but may be increasing.”

referee 2: An article of importance in its field

Question 1: The manuscript and tables are inconsistent with regard to the time periods studied and analysed. In the abstract as well as in the Manuscript, the two decades are stated as 1988-1998 and 1998 - 2008, while in the table the decades are separated as 1988-1997 and 1998 - 2008. In the "patients and methods" section the time period is stated as "all patients who underwent LTX in the Netherlands from January 1988 until January 2008". Either patients in 1998 have been counted twice, which would be a serious flaw, or this is just a misprint. In any case, two precise decades would be 1.1.1988 - 31.12.1997 and 1.1.1998 - 31.12.2007. Notably, in the figures no case is recorded for 2008.

Answer 1: The reviewer is absolutely right that the correct annotation for the 2 decades is 1.1.1988 - 31.12.1997 and 1.1.1998 - 31.12.2007, and therefore in the figures no case is recorded for 2008. Throughout the new version of the manuscript the time periods are now provided correctly.

Question 2: Five patients died on the waiting list, and these only during the second decade. Waiting time was longer during the second decade. If the 5 patients that died had been transplanted, the statistical analysis given the small numbers would perhaps be different. One might argue that - for whatever reasons – the health care system during the second decade was not as effective as during the first decade in delivering liver transplantation to affected individuals with PBC in a timely manner.

Answer 2: Indeed, 5 patients died on the waiting list, but these patients have been included in the analysis shown in figure 1 and 2.

Moreover, regarding patients characteristics, these patients were comparable to patients at the time of transplantation regarding age, MELD score and time on the waiting list.

Question 3: Page 5: spell out SBP - spontaneous bacterial peritonitis

Answer 3: The abbreviation has been spelled out in the text.

Question 4: you may consider briefly explaining "Schirmer's Test" e.g.(schirmer's test (for assesing tear production to diagnose xerophthalmia))

Answer 4: we added this information.

In addition, we added competing interest and author’s contributions to the manuscript. Competing interests: the authors declare that they have no competing interests (between conclusions and authors’ contribution).

Also the authors' contributions section is added to the manuscript: EK: study concept and design, acquisition of data, analysis and interpretation of data,
drafting of the manuscript, statistical analysis. BEH: analysis and interpretation of data, statistical analysis. HM, RM, BVH and HB: acquisition of data, critical revision of the manuscript for important intellectual content. HB: study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, study supervision.

(inserted before the reference list).

Abbreviations were added.

We very much hope that our manuscript can be accepted for publication, and look forward to your reply.

Yours sincerely,

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