# PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

# ARTICLE DETAILS

| TITLE (PROVISIONAL) | Evaluation of Published Assessment Tools for Comorbidity in Liver Transplantation: A Systematic Review Protocol |
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| AUTHORS | Qu, Zhi; Gwiasda, Jill; Schrem, Harald; Kaltenborn, Alexander; Harries, Lena; Beneke, Jan; Amelung, Volker; Krauth, Christian |

# VERSION 1 – REVIEW

| REVIEWER | APARNA REGE<br>DUKE UNIVERSITY MEDICAL CENTER, DURHAM, NC, USA |
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| REVIEW RETURNED | 24-Feb-2018 |

| GENERAL COMMENTS | 1.In current study, we are interested in the comorbidities that potentially influence the prognosis and clinical management of liver transplant patients, rather than the disease co-occurred with the indication for liver transplantation or results and complications of transplant....this is a controversial statement as co-existing diseases contribute to pre-op comorbidity. You can elaborate on this in limitations of the study. review of coexisting conditions or diseases may also add some insight to influence of comorbidity indices on outcomes.<br>2.In the search strategies database, please add PubMed..it has been mentioned previously.<br>3. In data extraction: Addition of MELD scores at listing and at transplantation would provide some information. Also if easily derived Karnofsky scores/scales could add information about functional impairment.<br>4. In Discussion: could you please enroll the commonly used comorbidity indices and a brief description of their advantages and disadvantages.<br>5. Please have the study proof read for small grammatical errors. |
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| REVIEWER | Martin Bøgsted<br>Department of Clinical Medicine, Aalborg University |
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| REVIEW RETURNED | 17-Mar-2018 |

| GENERAL COMMENTS | Very intersting review. I have doubt meta analyses can be conducted as the authors also points out. |
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# VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dear Dr. Rege,
Thank you for your comments from a clinical perspective, please find our responses below:

1. In current study, we are interested in the comorbidities that potentially influence the prognosis and clinical management of liver transplant patients, rather than the disease co-occurred with the indication for liver transplantation or results and complications of transplant....this is a controversial statement as co-existing diseases contribute to pre-op comorbidity. You can elaborate on this in limitations of the study. Review of coexisting conditions or diseases may also add some insight to influence of comorbidity indices on outcomes.

Response: We fully agree with the reviewer that co-existing diseases contribute to pre-op comorbidities as well as postoperative complications. We have added the relevant text on this issue in the limitation section of the revised manuscript to elaborate on the complex relationships between comorbidity-related constructs. We have also indicated in the revised manuscript how we will further review this issue in the systematic review.

2. In the search strategies database, please add PubMed. It has been mentioned previously.
Response: We have added the PubMed database in the search strategy in the main text of the revised manuscript.

3. In data extraction: Addition of MELD scores at listing and at transplantation would provide some information. Also if easily derived Karnofsky scores/scales could add information about functional impairment.

Response: MELD score at listing will certainly provide important information on the patients' condition and severity of liver disease. We have therefore added the MELD score in our list of data for extraction accordingly in the revised manuscript. With the respect to the Karnofsky scores, we did not include this scale to our list of data for extraction, because the purpose of the present systematic review is focused on the measurement of comorbidity and not functional physical impairment. This scale will be considered for use in our future studies.

4. In Discussion: could you please enroll the commonly used comorbidity indices and a brief description of their advantages and disadvantages.

Response: This is an excellent suggestion. On the basis of our pilot search and review we found that the Charlson comorbidity index and the Elixhauser index are still the most commonly used in this context. We have added the description of their advantages and disadvantages in the discussion section as has been suggested by the reviewer.

5. Please have the study proof read for small grammatical errors.
Response: The revised manuscript has been carefully proof read by a native speaker to eliminate all grammatical errors.

Reviewer: 2
Response: Dear Prof. Bøgsted, thank you very much for your comment that raises doubts on ability to conduct meta-analyses. We fully agree as we have outlined in our manuscript in detail. Due to the scope of current research, a meta-analysis is unlikely to be performed, because of many different comorbidity measuring tools that are applied until today to describe patient characteristics, risk adjustment and outcome prediction in this field, and there is no gold standard yet. According to your suggestion, we are planning to perform a meta-analytical comparison as recommended by Sharabiani et al. to summarize the results of different assessment tools in comparative studies, if appropriate. The corresponding contents were revised in the abstract and analyses section accordingly.