1) A recently published network meta-analysis of 10 RCTs of SBP primary prophylaxis showed a moderate effect of ciprofloxacin and norfloxacin with low quality evidence for rifaximin use (Facciorusso, et al. Liver International. 2019;39:1448–1458, DOI: 10.1111/liv.14109). Could the authors comment on the findings of that study in relation to theirs?

Thank you for your comments. We have added the following to the Discussion. "A recent network meta-analysis by Facciorusso et al. reported moderate evidence for norfloxacin and ciprofloxacin in primary prophylaxis of SBP, and low quality evidence for the use of rifaximin.{Facciorusso, 2019 #2420} This difference may be accounted for by the inclusion of studies that included both patients with primary prophylaxis and with a history of SBP in our study. Such studies were included in our primary outcome of combined primary and secondary prevention, but not in our subgroup analyses due to lack of subgroup randomization and incomplete information. Analyses of treatment effects in these subgroups are therefore subject to additional biases when compared to complete cohorts.{Assmann, 2000 #2421}"

2) Whether the primary outcome of this study is primary prophylaxis (Line 13, page 5) with secondary prophylaxis as a subgroup analysis (Line 7, page 8) or both primary and secondary prophylaxis (line 25, page 6) should be clarified.

Thank you for your comments. We made it clear that combined primary and secondary prophylaxis (development of SBP) is the primary outcome and the rest are subgroup analyses.

Line 13, page 5 changed to:

"However, evidence for the role and choice of antibiotics in both primary and secondary prophylaxis in the absence of gastrointestinal bleeding remains unclear."

Line 7, page 8 changed to:

"We performed the following subgroup analyses; 1) excluding studies with low quality as assessed with the Jadad scale (≤2), 2) analysis of primary prophylaxis, including only patients without a history of SBP, 3) analysis of secondary prophylaxis including only patients with a history of SBP, and 4) analysis of studies that were reported after 2010 (after rifaximin was approved by US Food and Drug Administration (FDA) to reduce the risk of hepatic encephalopathy)."

3) Risk of death (mortality rate) was the secondary outcome – did individual studies specify whether this was liver related death or all-cause mortality?

The majority of individual studies did not specify cause of death. This was clarified as (like 3, page 8):

"The secondary outcome was the risk of death/transplant as assessed by the proportion of patients who died or were transplanted in each intervention arm due to any cause."

4) If the data were available in the selected studies, an analysis of adverse events or patient tolerability related to specific antibiotics would be useful.

Unfortunately, this data is not available in the majority of individual studies.

5) Figure 2C is difficult to interpret. The bar graph of Rank Probability is labelled “Rank 1 is worst, rank N is best” but it is unclear what each bar in an individual antibiotic treatment group indicates (are these Monte Carlo cycles?). Similarly, the table showing the SUCRA outcomes states (in the figure legend, page 18) that “No. 5 is best” yet Number 5 in the table is placebo.

“Rank N is best” for “Rank Probability” as depicted in the graph contents is correct. The SUCRA rankings in the table were reordered in the conventional ascending sequence. We named the column as SUCRA ranking in the table, so that readers will not be confused with Rank probability.

6) The authors conclude that further RCTs are required. Can this point be elaborated; specifically are trials needed with different designs, greater numbers, and different endpoints? Should all-cause mortality be the primary endpoint?

Thank you for your meaningful comments. This is a pertinent question regarding whether development of SBP could be considered a surrogate outcome in this study, and whether the outcome of importance is all-cause mortality. We believe that both should be evaluated, however it may be appropriate to consider infection prevention as the primary outcome due to the topic focus of prophylaxis and not treatment. Final paragraph, page 16 was edited for clarification as below.

“In conclusion, this systematic review and network meta-analysis of RCTs comparing multiple antibiotics for prophylaxis of SBP suggests that rifaximin is the most effective for the outcomes of preventing SBP and reducing all-cause mortality in high risk cirrhotic patients. Further comparative studies, particularly with appropriate randomization and larger power, are warranted to confirm these findings.”

Minor points TMP-SMX is trimethoprim sulfamethoxazole, not sulbactam (Line 4, page 10)
There are several grammatical errors to be corrected

Thank you for your comments. Additional edits have been made to address these issues.

1) Please add more details how the records were collected, screened and excluded.

The details of search strategy and study selection are explained in the Material&Methods and the Study characteristics of the Results. One and half pages are used, so we have kept it as is due to page limitation.

2) Please explain how the dose affected the result.

Thank you for your meaningful comment. The dose of Rifaximin were 800, 1100, 1200 mg among the three studies whereas the Norfloxacin and TMP-SMX studies all had the same dose. Because there were only three Rifaximin studies, we were unable to separately assess the outcome among each dose.

3) Some of the figures showing the key findings should be placed in the manuscript rather than in the supplementary materials.

We have moved the figures for risk of death/transplant to Figure 3.

4) Make sure all the abbreviations and marks in the figures and tables have explanation in the legends or footnotes.

We have corrected these.