

Response to comment on: Perioperative probiotics or synbiotics in adults undergoing elective abdominal surgery: a systematic review and meta-analysis of randomized controlled trials

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Reply

We thank Wu et al, for their interest in our systematic review and meta-analysis¹ and for their comments.

Our primary end point was postoperative infectious complications, and to achieve this aim, we ensured that studies met the criterion of reporting infectious complications. Indeed, if the primary aim of using probiotics or synbiotics is to reduce infectious complications, then any study that failed to report this fundamental outcome was not deemed appropriate for inclusion. Based on the Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (section 3.2.4.1), the measurement of certain outcomes in a study may be an eligibility criterion; especially when the review addresses the potential for an intervention (probiotics or synbiotics) to prevent a particular outcome (infectious complications).² In accordance with this rationale, studies that used the intervention (probiotics or synbiotics) for purposes other than preventing infectious complications and, therefore, did not record infectious complications were ineligible.

Moreover, Berman and Parker³ recommended that meta-analyses should address only one or two primary outcomes to focus the analytic process. It is unlikely that all studies relating to secondary outcomes would be obtained from the initial electronic search as they were not the initial purpose of our analysis.¹ Therefore, a completely different protocol and search strategy would be required to perform a rigorous meta-analysis on secondary outcomes such as length of stay and mortality. This was beyond the scope of our meta-analysis.¹

We restricted our inclusion criteria to patients undergoing abdominal surgery in an effort to maintain sufficient clinical homogeneity in terms of population to provide a meaningful

summary. We argue that patients undergoing surgery for congenital heart disease are sufficiently different from patients undergoing liver transplantation to the point of introducing significant clinical heterogeneity. That, however, does not suggest that probiotics are of no benefit in extra-abdominal surgical procedures.

In the trial sequential analysis (TSA) performed by Wu et al. on our meta-analysis¹ the cumulative Z-curve crossed both the conventional boundary and the trial sequential monitoring boundary for benefit. That is supportive of our conclusion that the use of the probiotics led to significant reduction in infectious complications.

However, it is important to stress that different probiotics and synbiotics differ significantly in their effects on the gut microbiome and that it would be inappropriate to extrapolate the beneficial effect of one strain or combined preparation to another. Therefore, a TSA confirming the efficacy of probiotics or synbiotics taken in isolation could inadvertently be misinterpreted. It was for this reason we were cautious not to include a TSA, as it would have highlighted benefits of “all probiotics” without the caveat that this benefit is limited to only the strains utilised in the studies included in this meta-analysis.¹

There is a fundamental issue in several levels of subgroup analysis in the absence of enough studies as all it does is reduce power and reintroduces selection bias. The Cochrane Handbook acknowledges the usefulness of subgroup analyses in investigating heterogeneity, but stipulates that findings from multiple subgroup analyses may be misleading.⁴ The observational nature of subgroup analyses (as opposed to randomised comparisons) increases the risk of false negatives and false positives.⁵ Due to the potential errors that can be introduced by subgroup analyses, we opted to be careful regarding splitting participant information into separate analyses.

Our meta-analysis strengthens the confidence in the overall benefit of probiotics and synbiotics in patients undergoing abdominal surgery.

References

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