

Response to: (Comment on “The impact of prehabilitation on patient outcomes in hepatobiliary, colorectal and Upper Gastro-intestinal cancer surgery: A PRISMA-Accordant Meta-Analysis”)

Joel Lambert, Lawrence Hayes, Thomas Keegan, Daren Subar, Christopher Gaffney

Dear Editor,

We read with interest the comments of Fiore et al. on our recent work on the impact of prehabilitation on patient outcomes in hepatobiliary, colorectal and upper gastro-intestinal surgery¹. Indeed, we are familiar with their research and commend them for their publications in this field.

On their first point on PRISMA compliance, we can confirm full and transparent compliance with PRISMA guidelines² (the PRISMA checklist is in our supplemental data)¹. We accept that our meta-analysis was not pre-registered and this as a limitation. We believe that the questions to be answered by the meta-analysis were made expressly clear and enshrined in the aims of the meta-analysis. The inclusion and exclusion criteria were clearly set out in the text in the Methods and taken together with the PRISMA flow diagram, comprehensively deal with how all data were handled.

With reference to how the quality of selected studies was assessed, Fiore et al. have attempted to judge the method we have used to assess study quality by applying a different assessment tool; Assessing the Methodological Quality of Systematic Reviews (AMSTAR-2) to the one we have used in our analysis; Physiotherapy Evidence Database (PEDro). While we accept that the AMSTAR-2 is a validated tool for this purpose, all assessment tools require application with some degree of subjective interpretation and inference in the data extraction phase. The AMSTAR-2 designers themselves concede that as an assessment tool this may further evolve with input and feedback from users³ in the same way that AMSTAR-2 developed from AMSTAR as this first iteration inadequately addressed methodological quality⁴.

With reference to scoring tools for studies included in systematic reviews and meta-analyses, our critics should not be surprised to note that the comparison of two different tools, PEDro versus Cochrane Risk of Bias (CROB) criteria produced different sets of trials of adequate quality⁵. The authors of that meta-epidemiological review suggested the need for a consistent approach in assessing risk of bias (RoB)⁵. Moseley et al. have suggested further that either tool can be used in assessing RoB but cannot be used interchangeably⁶. This probably highlights the need for a universally agreed assessment tool for clinical trials. It may be that certain assessment tools may be more appropriate based on the methodology and type of intervention being assessed. Rather than providing critique on an assessment tool we have not used, Fiore et al. apparent concerns on study quality assessment may have been better served by giving constructive commentary on the assessment tool that we have used (PEDro) within the context of our review. PEDro as an assessment tool has also been well validated to be used for this purpose⁷. As correctly mentioned by Fiore et al., cumulative PEDro scores may give more weighting to poorer quality unrandomized studies which may overestimate effect sizes, however, their concerns were not borne out in our analysis. Indeed, we observed

that included unrandomized/uncontrolled studies tended to receive significantly lower PEDro scores for methodological quality compared with higher quality randomised/controlled trials. Lower PEDro score studies had no undue influence on weighting in the pooled analysis. Additionally, in the interest of transparency we provided all the elementary data on how individual quality scores were accrued for every PEDro criterion (Table S1)¹.

Concerning the reduction in length of hospital stay (LoS) quoted in our paper, this has been caveated in the discussion in our manuscript. Whilst the included number of studies is small, it is nonetheless based on observations from 828 patients. LoS can be nuanced and complex and may be related to other factors such as social and community provisions, discharge endpoints, patient-related social issues. Additionally, it is often impossible to tease out the contribution of other factors such as enhanced recovery.

Concerning the lack of meta-analysed LoS data from the authors listed by Fiore et al., we can confirm that omissions were neither deliberate nor inadvertent. We went through extraordinary lengths to acquire these data from authors of the studies listed by Fiore et al. Only the three authors (studies) who responded with data required, were included in the final meta-analysis. In our opinion, the lack of sufficient data when specifically requested from authors should not preclude reporting of the data. This in itself would contribute to reporting bias. Improving scientific rigour in data gathering, analysis and dissemination requires cooperation and collaboration within the scientific community. We may be able to increase quality of reporting and analysis by simply being more fastidious in data sharing. This may have a greater impact on the quality of research output than modifying, scrutinising or repurposing pre-existing methodological quality assessment tools.

While we concur with Fiore et al. that any intervention that may improve outcomes in surgery has to be cost effective and that data on cost-effectiveness in prehabilitation is currently lacking⁸, we diverge on the suggestion that prehabilitation interventions are costly or cost ineffective. Indeed, prehabilitation programmes have already been successfully rolled out across several NHS Trusts in the United Kingdom. Further, several studies have pointed to prehabilitation approaches with low-cost profiles and high scalability, thereby producing appreciable benefits for large cohorts of patients for smaller inputs. This has been suggested to reduce both direct and indirect healthcare costs related to cancer treatments⁹. According to Cancer Research UK, these interventions in their simplest form may involve lifestyle changes such as smoking cessation or alcohol reduction, increased exercise and stress reduction strategies all of which are patient-driven with low financial outlay.

As a team of surgeons, academics and statisticians, we are fully cognisant of the complexities involved in data gathering and synthesis and value our professional and academic responsibilities in augmenting knowledge in this field. We believe that further clarity and advances in prehabilitation research may come through more high-quality clinical trials to understand some of the mechanisms that underpin observed clinical outcomes. We have endeavoured to further study this aspect of prehabilitation through the SPECS Trial (NCT04880772).

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