Response to: "Comment on Prehabilitation in major abdominal surgery" by Kehlet.

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

Dear Editor,

We duly note the comments by Kehlet on our recently published study on the impact of prehabilitation on patient outcomes in hepatobiliary, colorectal and upper gastro-intestinal surgery <sup>1</sup>.

Prehabilitation studies to date have provided conflicting reports on clinical outcomes. Emphasizing this fact, we note that the Carli et al. group quoted by Kehlet, have themselves found both no effect on length of stay<sup>2</sup> and a reduced length of stay<sup>3</sup> with prehabilitation in separate studies. Further, several prehabilitation studies have reported reduced length of stay after cardiac<sup>4</sup>, colorectal<sup>3</sup> and hepatopancreatiobiliary<sup>5</sup> surgery. We hasten to add that determining the factors that affect hospital length stay (LOS) especially in a surgical context can be complex, and as quoted in our manuscript discussion '....this phenomenon is often multifactorial...'. We acknowledge the contribution of enhanced recovery programmes (ERP) in reducing LOS<sup>6</sup>. Indeed, this strategy is now commonplace and well established in most modern surgical departments over the last decade. Therefore it would not be unreasonable to assume that this was the minimum perioperative strategy in both the standard and prehabilitated groups; thereby rendering the contribution of prehabilitation clearer.

Concerning the observation of only three studies included in our LOS analysis, we can confirm that all authors of studies included in the data synthesis were contacted on two occasions to provide data on LOS. This data was forthcoming from the three studies included in the meta-analysis on LOS. This may reflect a wider issue of inadequacy in support and collaboration amongst authors within the scientific community. In our judgement we believe that data provided by authors, if inadequate, should be presented with caveats so as to avoid reporting bias.

Kehlet makes a valid point on details of Enhanced Recovery Programme (ERP) reporting. It would be worth noting that some modern ERPs have now evolved to include some aspect of pre-optimisation<sup>7</sup>. This may include several of the strategies employed in 'prehabilitation'. Future reporting of studies involving prehabilitation should seek to clarify the terminology as it relates to what 'standard care' and 'prehabilitation' entails. While the LOS debate within prehabilitation is worthwhile, it may be worth paying some attention to cancer related outcomes such as survival. This issue is important to both patients and clinicians, and there is emerging evidence of prehabilitation improving disease-free survival<sup>8</sup>.

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- 3. Gillis C, Buhler K, Bresee L, et al. Effects of Nutritional Prehabilitation, With and Without Exercise, on Outcomes of Patients Who Undergo Colorectal Surgery: A Systematic Review and Meta-analysis. *Gastroenterology*. 2018;155:391-410.e4.
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- 5. Dewulf M, Verrips M, Coolsen MME, et al. The effect of prehabilitation on postoperative complications and postoperative hospital stay in hepatopancreatobiliary surgery a systematic review. *HPB*. Epub ahead of print April 2021. DOI: 10.1016/j.hpb.2021.04.021.
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- 7. Jones NL, Edmonds L, Ghosh S, et al. A review of enhanced recovery for thoracic anaesthesia and surgery. *Anaesthesia*.;68 . Epub ahead of print February 2013. DOI: 10.1111/anae.12067.
- 8. Trépanier M, Minnella EM, Paradis T, et al. Improved Disease-free Survival After Prehabilitation for Colorectal Cancer Surgery. *Ann Surg.*;270 . Epub ahead of print September 2019. DOI: 10.1097/SLA.00000000003465.