

# BMJ Open Gastrointestinal recovery after surgery: protocol for a systematic review

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## ABSTRACT

**Introduction** Gastrointestinal recovery after surgery is of worldwide significance. Postoperative gastrointestinal dysfunction is multifaceted and known to represent a major source of postoperative morbidity, however, its significance to postoperative care across all surgical procedures is unknown. The complexity of postoperative gastrointestinal recovery is poorly defined within gastrointestinal surgery, and even less so outside this field. To inform the clinical care of surgical patients worldwide, this systematic review and meta-analysis will aim to characterise the duration of postoperative gastrointestinal recovery that can be expected across all surgical procedures and determine the associations between factors that may affect this.

**Methods and analysis** MEDLINE, Embase, Cochrane Library and CINAHL will be searched for studies reporting the time to first postoperative passage of stool after any surgical procedure. We will screen records, extract data and assess risk of bias in duplicate. Forest plots will be constructed for time to postoperative gastrointestinal recovery, as assessed by various outcome measures. Because of potential heterogeneity, a random-effects model will be used throughout the meta-analysis. Funnel plots will be used to test for publication bias. Meta-regressions will be undertaken where the outcome is the mean time to first postoperative passage of stool, with potential predictors and confounders being patient characteristics, postoperative outcomes and surgical factors.

**Ethics and dissemination** This study will not involve human or animal subjects and, thus, does not require ethics approval. The outcomes will be disseminated via publication in peer-reviewed scientific journal(s) and presentations at scientific conferences.

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## INTRODUCTION

Collections of large data help characterise broad problems in surgical care and inform the development of systems to improve patient outcomes worldwide.<sup>1 2</sup> Surgery is associated with diverse adverse sequelae, for which any information regarding postoperative recovery, even if unorthodox,<sup>3</sup> has the

## Strengths and limitations of this study

- To our knowledge, this will be the first systematic review to characterise postoperative gastrointestinal recovery across all surgical procedures.
- Findings from this study may inform the optimal postoperative care of all surgical patients, irrespective of procedure, and be applicable on a global scale.
- Future prospective research in the area of gastrointestinal recovery after surgery is likely to benefit from the proposed comprehensive characterisation of the relevant literature.
- This study will adhere to globally accepted full systematic review methods for evidence screening, assessment of risk of bias and data analysis to optimise reliability and translatability to global surgery.
- Given the substantial scope of the proposed research questions, it is anticipated that there will be heterogeneity within the collected data, which will be acknowledged in interpreting the outcomes.

potential to inform beneficial multimodal interventions.<sup>4</sup> Optimisation of the postoperative recovery period relies, in particular, on the utilisation of both surgical and anaesthetic data that can be relied on with certainty.<sup>5</sup> Within this space, the implementation of Enhanced Recovery After Surgery programmes across most surgical specialties is an area of certainty that has led to significant improvements to clinical outcomes and healthcare efficiency at a global level.<sup>6</sup>

Gastrointestinal recovery after surgery is of worldwide significance. Postoperative gastrointestinal dysfunction is multifaceted and a common form of postoperative morbidity, which frequently delays hospital discharge after surgery.<sup>7-9</sup> While it is accepted as prominent consideration in patients undergoing bowel surgery,<sup>10</sup> its significance to postoperative care across all surgical procedures is an area of uncertainty that is poorly defined.



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As with other areas of healthcare, surgical care benefits from the application of standardised metrics that increase certainty.<sup>11</sup> For colorectal surgery, the composite measure of time to tolerance of solid food and first defaecation (GI-2) has been proposed as the best measure to assess postoperative recovery of gastrointestinal transit in that population.<sup>12</sup> However, a 2018 systematic review by Chapman *et al* concluded that postoperative ileus (reduced or uncoordinated intestinal transit resulting in prolonged postoperative gastrointestinal recovery)<sup>10</sup> after major colorectal surgery has no established definition, aetiology or treatment.<sup>13</sup> Furthermore, for gastrointestinal surgery, the outcome reporting for return of bowel function in the evidence base is variable.<sup>14</sup> For surgical operations outside of the field of gastrointestinal surgery, the intricacies of postoperative gastrointestinal recovery are even less defined and have even more associated uncertainty. Therefore, to inform the clinical care of surgical patients worldwide, this systematic review and meta-analysis will aim to characterise the period of postoperative gastrointestinal recovery that can be anticipated across all surgical procedures and determine factors that may affect this.

## METHODS AND ANALYSIS

The methods for this systematic review and meta-analysis, including review question, search strategy, inclusion and exclusion criteria and risk of bias assessment, are established within this protocol prior to the conduct of the review. The study protocol was prospectively registered with PROSPERO, within which the start and end dates are listed as 21 May and 31 December 2021, respectively. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020)<sup>15</sup> and Meta-analyses Of Observational Studies in Epidemiology (MOOSE)<sup>16</sup> reporting guidelines will be adhered to. This protocol has followed the PRISMA protocols (PRISMA-P) 2015 reporting guidelines (online supplemental appendix 1).<sup>17</sup>

### Search strategy and selection criteria

The Population, Intervention, Comparator group, Outcome framework was used to formulate the research question and inclusion criteria. The population will be adult patients undergoing surgery. The intervention will be all surgical procedures, which will be compared against each other. The outcome will be time to first postoperative passage of stool. This will be reported in hours, and in any study reporting this metric in days, data will be converted to hours with the assumption that 1 day is equivalent to 24 hours. Studies will be excluded when the population is comprised of patients under the age of 18 years, if individual surgical procedure or study intervention cohort sample size is less than 200, and/or if the study has an inappropriate design that precludes meaningful observational data.

The literature search will be performed by an information specialist using a peer-reviewed search strategy (online supplemental appendix 2). The search strategy will be reviewed according to Peer Review of Electronic Search Strategies guidelines.<sup>18</sup> Published literature will be identified by searching the following bibliographic databases from inception to May 2021: MEDLINE (1946–) with in-process records and daily updates via Ovid; Embase (1974–) via Ovid; The Cochrane Library via Wiley and CINAHL via EBSCO. The search strategy will consist of both controlled vocabulary, such as the National Library of Medicine's Medical Subject Headings and keywords. The main search concepts will be postoperative ileus or gastrointestinal function, after surgery, and first bowel movement. No filters will be applied to limit the retrieval by study type. Where possible, retrieval will be limited to human studies. Retrieval will not be limited by publication date or language. Searches will be supplemented by pearling of current contents, reviews and original research relating to postoperative gastrointestinal recovery after surgery identified through targeted searches of Google Scholar and PubMed.

### Data extraction

Two reviewers will independently screen titles and abstracts, review full texts and extract data using a standard extraction form. Screening of titles and abstracts will be facilitated through the use of a web application (Rayyan, Qatar Computing Research Institute, Ar-Rayyan, Qatar).<sup>19</sup> Disagreements will be resolved by consensus, with a third reviewer acting as arbitrator, if required. Extracted data will include: research design, study setting, population characteristics, intervention characteristics, comparator characteristics, timeframe for follow-up, quantitative and qualitative outcomes, source(s) of funding and reported conflicts of interest, methodological quality information and other information relevant to the review questions. Data will be synthesised in narrative and tabular formats. The primary outcome will be the time to first postoperative passage of stool. Other outcomes of interest will include, but not necessarily be limited to the following outcome factors: time to the GI-2 composite measure (time taken for patient to tolerate solid food and to pass stool postoperatively),<sup>12</sup> time to first postoperative passage of flatus, time to first postoperative tolerated solid oral intake, time to first postoperative tolerated liquid oral intake, in-hospital mortality, postadmission mortality measures such as 30-day and 90-day mortality, postoperative complications, nausea during the postoperative admission, vomiting during the postoperative admission, postoperative length of stay, need for intensive care unit admission and other relevant surgical and perioperative datapoints. Further outcomes of interest will include, but not necessarily be limited to the following exposure factors: type of surgical procedure, grade of surgery (major therapeutic vs minor therapeutic), surgical urgency (elective vs emergency), surgical approach (open vs laparoscopic vs conversion to open), medication and other factors that may influence

gastrointestinal function, history of diabetes, age, sex and other relevant surgical and perioperative datapoints. The inclusion of the most commonly used surrogate measures for postoperative return of gastrointestinal function will be used to analyse for heterogeneity in gastrointestinal recovery after surgery. Where appropriate, surgical procedures will be coded according to the International Classification of Diseases, Tenth Revision Procedure Codes,<sup>20</sup> which will inform stratification for relevant comparisons within the collected data.

### Quality assessment

Two reviewers will independently perform risk of bias assessments. Included randomised controlled trials will be appraised critically using the Cochrane Risk of Bias tool V.2.0 for assessing risk of bias in randomised trials.<sup>21</sup> Included non-randomised observational studies will be appraised critically using the Downs and Black checklist.<sup>22</sup> Methodological quality of other included study designs will be assessed using appropriate validated tools that are globally accepted.<sup>23</sup> The certainty of evidence will be rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and findings presented in GRADE evidence profiles and summary of findings tables<sup>24</sup> using standardised terms.<sup>25 26</sup>

### Data analysis

A meta-analysis of systematically obtained data was seen as the most appropriate study design as it provides an approach to identify, appraise, synthesise and combine the results of the relevant studies in the global literature<sup>16</sup> to characterise the period of gastrointestinal recovery after any surgical procedure. This will be undertaken using Stata Statistical Software: Release V.15.1 College Station, Texas: StataCorp. Forest plots will be constructed for mean time to first postoperative passage of stool, and subsequently for mean time to postoperative tolerance of solids, liquids, passage of flatus and composite tolerance of solids and passage of stools. Subgroup and sensitivity analyses will be performed where there are sufficient data to do so.

The  $I^2$  statistic will be used to evaluate heterogeneity (with  $I^2 > 50\%$  indicating significant heterogeneity) as will Cochran's  $Q$  p value (with p value  $< 0.05$  indicating significant heterogeneity). In view of potential heterogeneity in this meta-analysis, a random-effects model will be used throughout. Funnel plots will be used to test for publication bias.

Meta-regression will be undertaken where the outcome is mean time to first postoperative passage of stool, with predictors and confounders being patient characteristics, postoperative outcomes and surgical factors. The role of meta-regression in assessing the included observational data is to summarise the existing surgical literature to characterise the period of gastrointestinal recovery after any surgical procedure. Univariate and multivariable meta-regressions may be performed. A p value of  $< 0.05$  will denote statistical significance.

### Limitations

The design of this study has multiple limitations. Limiting inclusion to individual surgical procedure or study intervention cohort sample sizes of at least 200 excludes a large number of studies that would potentially contribute data to this review. However, this sample size limit was set to avoid the inclusion of smaller studies that may be accompanied by biases and outcomes that have limited reliability. Exclusion of paediatric patients under the age of 18 also limits the applicability of this study's findings to this population, however, this exclusion criterion was set to prevent bias stemming from the inclusion of patients whose gastrointestinal tracts were at different stages of development. The primary outcome of time to first postoperative passage of stool has been shown in the literature to not carry the same degree of validity for measuring return of gastrointestinal function as the time to GI-2 composite measure,<sup>12</sup> however, was selected as the primary outcome for this study as it was thought to be more widely reported across the surgical literature, particularly in study cohorts outside of general surgery and colorectal surgery. Where reported in the included studies, time to GI-2<sup>12</sup> will also be analysed. To address many of the limitations of this study, we will include all adult surgical populations and any study designs reporting meaningful observational data. The broad review question of this study was set with the aim of characterising many clinical aspects of the period of postoperative gastrointestinal recovery after all surgical procedures. Accordingly, findings from this study may inform optimal postoperative care of all surgical patients, irrespective of procedure, and be applicable on a global scale.

### Patient and public involvement

No patients will be involved in this study.

### ETHICS AND DISSEMINATION

This study will not involve human or animal subjects and, thus, will not require ethics approval. Results of the study will be disseminated via publication in peer-reviewed scientific journal(s) and presentations at scientific conferences. Any protocol amendments that may arise will be appropriately disseminated within the peer-reviewed literature and academic community.

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