

# Scoping review: The terminology used to describe major abdominal surgical procedures

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## Abstract

**Background:** Major abdominal surgery (MAS) can have a profound impact on the patient but there is currently no consensus as to which surgical procedures constitute MAS. The main objective of this work is to ascertain the terminology used to describe MAS procedures and to apply these findings in order to propose a definition of MAS.

**Methods:** The following databases were searched: Ovid MEDLINE (R) ALL, Embase Classic and Embase (via OvidSP), Global Health (via OvidSP), Health Management Information Consortium (via OvidSP), APA PsycInfo (via OvidSP), PubMed and Web of Science. Original research articles, published between 1980 and April 26, 2022 that contained a description of MAS procedure were included in this study. Article screening and data extraction was undertaken independently by 3 authors. Content analysis was performed to identify key terminology used to describe MAS.

**Results:** Five thousand six hundred and sixty three articles were identified, of which 767 underwent full-text review and 312 were included in the scoping review. Content analysis resulted in 4 main categories: (1) pre-operative factors, (2) intraoperative factors, (3) operation-related factors, (4) post-operative factors. Operation-related factors was the predominant category (1137 references coded). The gastrointestinal resection made the vast majority of the references coded (591).

**Conclusions:** Based on these results, the term “major abdominal surgery” should be defined as an intra-peritoneal operation with no primary involvement of the thorax, involving either luminal resection and/or resection of a solid organ associated with the gastrointestinal tract. However, further work is required to verify this definition using real world data.

## KEYWORDS

definition, major abdominal surgery, scoping review

## 1 | INTRODUCTION

Nearly 10 million open abdominal operations were performed in the US between 2009 and 2013.<sup>1</sup> In the 2021–22 financial year in England, 5.8 million abdominal

operations were recorded in the national hospital statistics database.<sup>2</sup> It has been estimated that the life-time risk of having intra-abdominal surgery is over 40%.<sup>3</sup> Major abdominal surgery (MAS) and its peri-operative complications can have a profound impact on the

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patient's biochemical, physiological, physical and socio-economic function, as well as affect their mental health.<sup>4-6</sup> Multiple sources in the literature refer to this type of surgery, despite the absence of internationally agreed definition of what constitutes MAS. Small and Witt<sup>7</sup> conducted a survey in 1965 in an attempt to distinguish between major and minor surgery. The study identified 12 parameters that equated with major surgery but these could not be considered in isolation. More recently, Martin et al<sup>8</sup> conducted a Delphi in order to arrive at a consensus definition of "major surgery". However, none of the current literature has focused specifically on defining MAS.

Establishing a rational definition for MAS is an important step in the understanding of the recovery trajectory of these patients. Post-operative recovery for these patients is a complex and dynamic process that encompasses multiple domains of health. In order to evaluate the recovery of these patients using patient reported outcome measures, there has to be a defined target population. The main objective of this work is to delineate the terminology used to describe major abdominal surgical procedures and to apply these findings to reach a definition of MAS. A scoping review is ideally suited to achieving this objective as it is designed to address a broader topic with multiple study designs compared to a systematic review that is more appropriate to well-defined concepts.<sup>9</sup> It also facilitates the identification of key concepts and sources of evidence, particularly if there is lack of comprehensive research in that area.<sup>10</sup>

## 2 | MATERIAL AND METHODS

The scoping review was conducted according to the guidance and reporting framework described by Arksey and O'Malley,<sup>9</sup> which was further developed by a number of authors.<sup>11-14</sup> The report was constructed according to PRISMA Extension for Scoping Reviews Checklist.<sup>15</sup>

### 2.1 | Eligibility criteria and sources of evidence

Only original research articles, published between 1980 and April 26, 2022, were included in this study. Articles published prior to 1980 were excluded because laparoscopy was not an established surgical technique prior to this date. Studies were included in the scoping review if they met the following criteria: 1) original research (interventional trials, observational studies, surveys), quality improvement projects, systematic reviews or meta-analysis; 2) adult population  $\geq 18$  years old; 3) specific reference to operation(s) or procedure-related inclusion criteria; 4) published in English

language. Articles were excluded if there was no full text available for review or if they focused on surgery outside of the abdomen (e.g., trauma and orthopedics, plastic surgery, cardiothoracic surgery, neurosurgery, maxillofacial surgery).

### 2.2 | Search

The following databases were searched: Ovid MEDLINE (R) ALL, Embase Classic and Embase (via OvidSP), Global Health (via OvidSP), Health Management Information Consortium (via OvidSP), APA PsycInfo (via OvidSP), PubMed and Web of Science. Searches were carried out between the 12th and April 26, 2022. The search strategy was designed to identify all studies that were focused on major abdominal surgery: (Major OR Complex OR High risk) AND Abdom\* AND (Surger\* OR Procedure\* OR Operat\*). Initially, the strategy was to search across the entire article and keywords. However, it rapidly became apparent that the vast majority of these papers did not contain a specific focus on major abdominal surgery, nor did they provide any reference to the nature of the surgery or procedure inclusion criteria used. Therefore, the search strategy was subsequently modified to only include the articles that contained the relevant keywords within the title. Full electronic search strategy can be found in the supplementary methods.

### 2.3 | Data charting, data items and synthesis of results

Article screening and data extraction was undertaken independently by 3 authors (AC/JC/YD). Any disagreements in assessment were discussed with the senior author (SD). Data were collected into an Excel table that was designed and pre-tested during the preliminary stages of the study. Primary outcome was the description of major abdominal surgical procedures within the introduction or methodology of the article. Secondary outcomes included: study type, study location, region, population, lead specialty conducting the research, operative specialties included the aim of the study. Data were summarized using the following criteria: lead specialty conducting the research, study theme, study type, operative specialties included in the research, region, proportion of geriatric-focused and emergency-focused research.

### 2.4 | Content analysis

All extracted descriptions of major abdominal surgical procedures were imported into NVivo12.<sup>16</sup> Initial word frequency analysis was performed to explore the use of

terminology within the descriptions. Content analysis was performed by becoming familiar with the data and extracting initial codes from the data set.<sup>17</sup> Subsequently, codes were collated into categories and sub-categories, based on their similarities. Categories were reviewed to ensure internal homogeneity within the coded extracts and external heterogeneity with other categories, and used to generate a category “map” of the analysis that was representative of the entire data set. Example quotes for each code and category were collated. The sunburst diagram was generated using Python 3.10.12.<sup>18</sup>

### 3 | RESULTS

A total of 5663 articles were identified within seven databases, of which 767 underwent full text review (Figure 1).<sup>19</sup> Of these 455 studies did not contain a specific description of major abdominal surgical procedure within the introduction or methods and were excluded. 312 studies published between 1983 and 2022 fulfilled the inclusion criteria for the scoping review (Table S1).

Observational research studies were the predominant type of articles that met the inclusion criteria

( $n = 170, 54.5\%$ ), followed by interventional trials ( $n = 118, 37.8\%$ ), systematic reviews ( $n = 13, 4.2\%$ ), meta-analysis ( $n = 6, 1.9\%$ ), quality improvement projects ( $n = 3, 1.0\%$ ) and surveys ( $n = 2, 0.6\%$ ). The majority of these studies were in the field of general surgery ( $n = 247, 79.2\%$ ), with a minority in urology ( $n = 53, 17.0\%$ ), gynecology ( $n = 44, 14.1\%$ ) and vascular surgery ( $n = 33, 10.6\%$ ). A small proportion of studies ( $n = 21, 6.7\%$ ) concentrated specifically on older patients (over 60 years old). Only 7.7% ( $n = 19$ ) of the articles focused on emergency surgery.

Surgical teams led the research in about a third of the included studies ( $n = 86, 31.4\%$ ), with anesthetic teams having the highest interest in the area of major abdominal surgery (47.4%) (Table S2). The most predominant topic was post-operative care and outcomes ( $n = 143, 45.8\%$ ) or perioperative care ( $n = 72, 23.1\%$ ) with only a minority of research investigating pre-operative care ( $n = 20, 6.4\%$ ) or basic sciences ( $n = 39, 12.5\%$ ) (Table S3).

Over half of all studies were conducted in the European countries ( $n = 162, 51.9\%$ ), followed by North America ( $n = 60, 19.2\%$ ), Asia ( $n = 53, 17.0\%$ ), Australia and New Zealand ( $n = 16, 5.1\%$ ), and the rest of the World ( $n = 20, 6.4\%$ ).

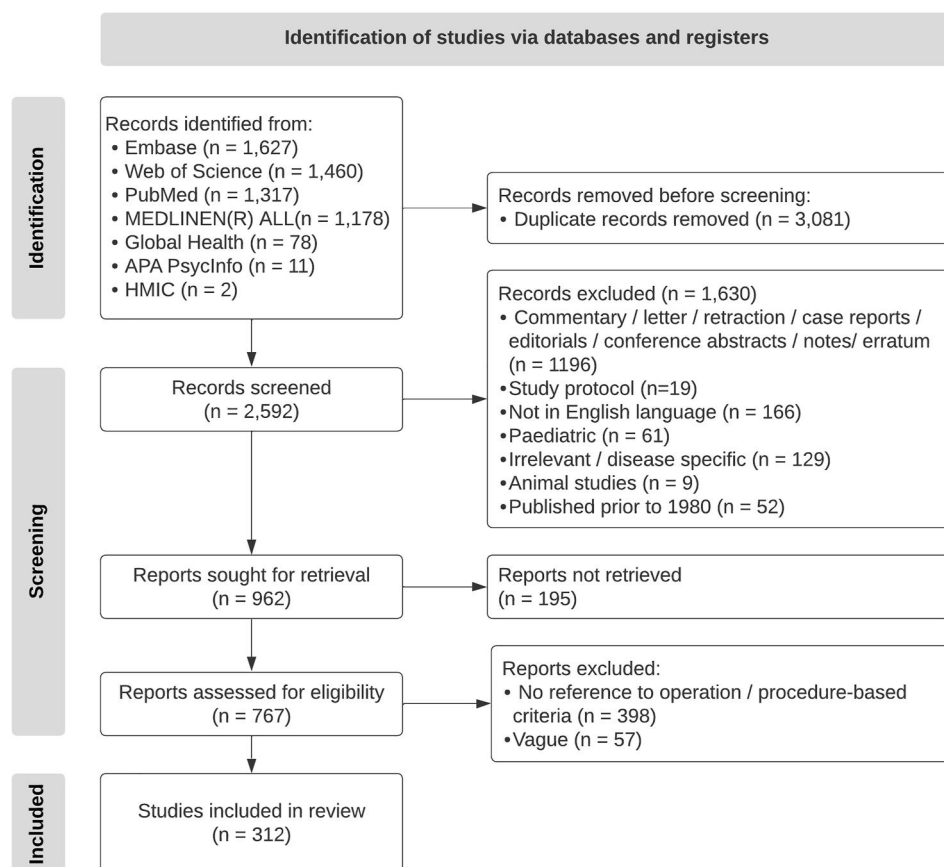


FIGURE 1 PRISMA flow diagram.

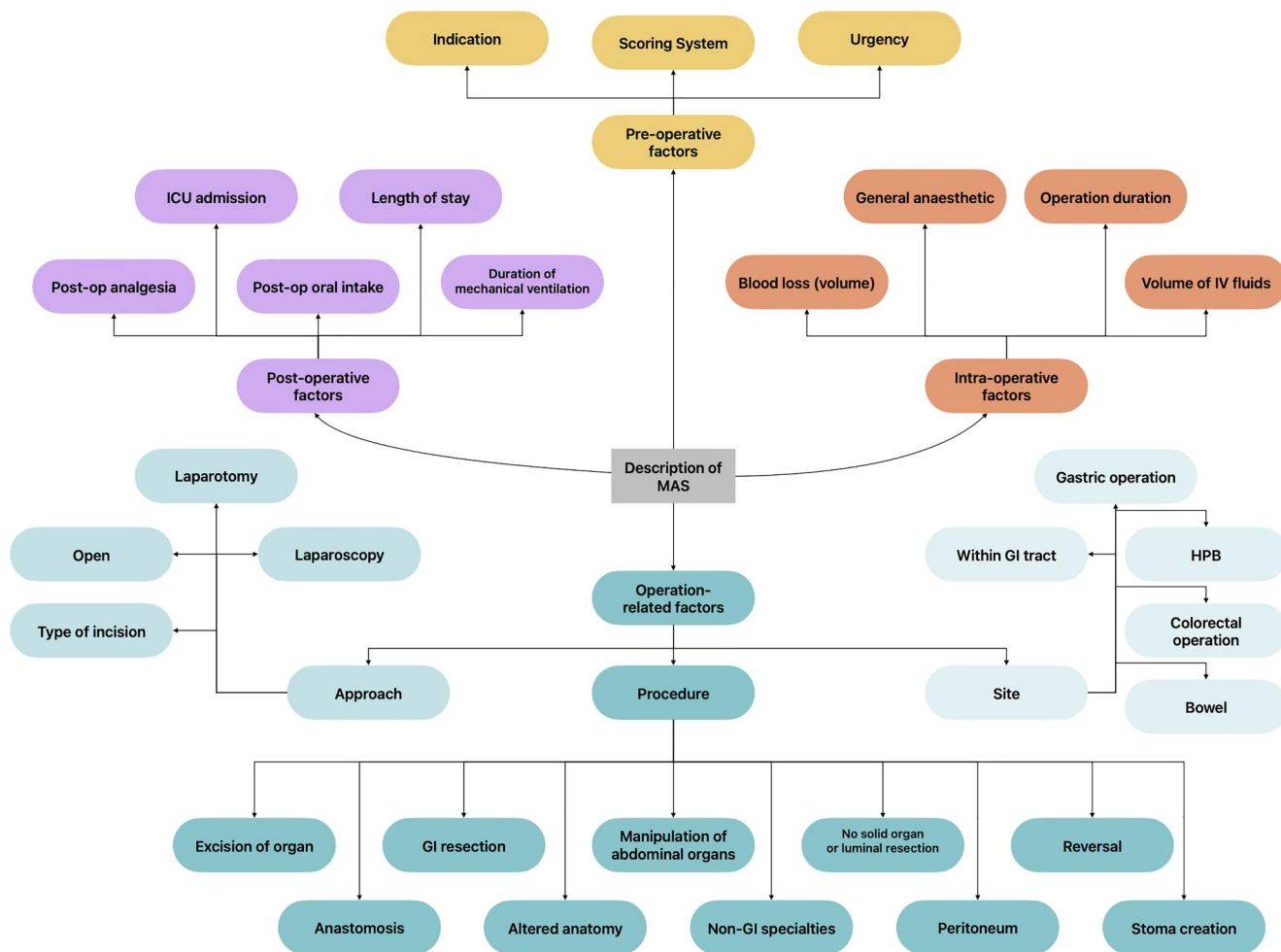
### 3.1 | Content analysis

Initial word frequency analysis revealed that the ten most frequently used words to describe major abdominal surgical procedures were (in order of frequency): resection, open, gastrectomy, elective, bowel, colectomy, pancreatectomy, colorectal, laparoscopic and liver. The following words were excluded from the analysis as these are directly related to the question being studied: surgery, surgical, abdominal, major, procedure(s), defined, included and patients.

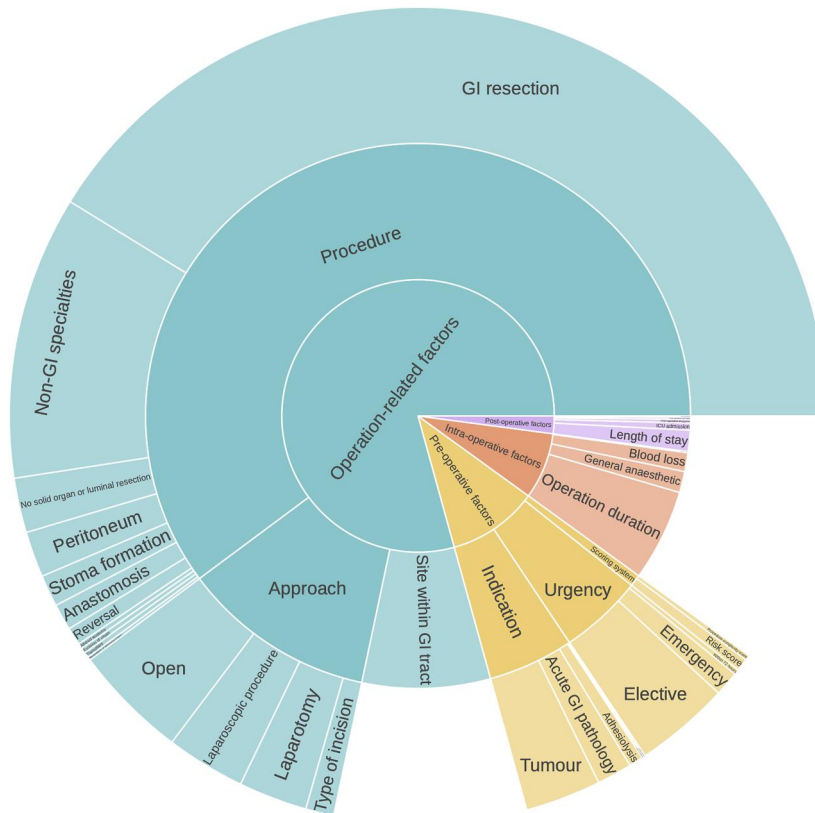
Following refinement and merging of codes based on similarities, 64 codes remained, which amounted to 1434 coded references. These were grouped into 4 main categories that were most internally consistent: 1) pre-operative factors, 2) intraoperative factors, 3) operation-related factors, 4) post-operative factors. The mind-map of categories and sub-categories can be seen in Figure 2. Sunburst diagram illustrates the relative weight of each category and sub-category, based on the number of references coded (Figure 3).

Of the four categories, operation-related factors was the predominant category of the terminology used to

describe major abdominal surgical procedures (1137 references coded), with postoperative factors being rarely used as defining criteria. Preoperative and intraoperative factors were infrequently used to describe MAS, with 154 and 113 references coded respectively. Table 1 provides a summary of all categories and sub-categories with illustrative quotes to aid understanding. Of the subcategories, procedure-related terminology was by far most frequently selected to describe MAS (863 references coded). Gastrointestinal (GI) resection made the vast majority of the references coded (591), predominantly consisting of colectomy, gastric, pancreatic, hepatic and esophageal resections (Table 2). Operations that did not involve solid organ or luminal resection, such as hernia repair, appendectomy and cholecystectomy, were rarely included in the description of MAS, with only 30 references coded to this sub-category. Operations relating to non-GI specialties, such as urology, gynecology, vascular, thoracic and endocrine surgery, were infrequently used as part of a description of MAS. The least frequently used terminology in the description of MAS fell into the following sub-categories and collectively amounted to 5% of the coded



**FIGURE 2** The mind-map of categories and sub-categories of the terminology used to describe major abdominal surgical procedures. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



**FIGURE 3** Sunburst diagram illustrating the relative weight of each category and sub-category, based on the number of coded references. [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

references: scoring system, general anesthetic, blood loss, volume of intravenous (IV) fluids, length of stay, intensive care (ICU) admission, postoperative analgesia, postoperative oral intake and duration of mechanical ventilation.

## 4 | DISCUSSION

We believe that this is the first study to apply a rigorous scientific approach in a scoping literature review using detailed content analysis to identify terminology used to describe MAS. In contrast, previous publications have employed expert opinions to define major surgery.<sup>7,8</sup> The key findings are: (1) a confirmation of a priori hypothesis of the absence of an internationally agreed definition of MAS, (2) a definition for MAS predicated on the content analysis of the terminology used.

Regarding the previous absence of MAS definition, we found that almost 60% of the articles undergoing full text review did not contain any specific reference to the operation or procedure inclusion criteria, undermining the quality of that research and risking introduction of bias. Without a clearly defined patient population, based on a precise description of major abdominal surgical procedures, the interpretation of findings may be difficult. Defining MAS has a much greater

application beyond simply advancing science and theory. A definition that allows careful identification of the MAS patient population permits the development of a number of clinically applicable instruments, such as patient reported outcome measures (PROMs), core outcome measures in effectiveness trials and incorporation into mortality and morbidity predictive tools. These require a clear target population in order to have robust content validity.<sup>20,21</sup> This definition translated into a list of surgical procedure codes has the potential to be used by healthcare providers to identify high-risk and high-cost patients, purely based on the operation code alone.<sup>22</sup>

According to the results of the content analysis, the recommendation of this study would be to include “resection of gastrointestinal organ” as the key terminology in the description of MAS. Not only would this align the definition of MAS with the results of the content analysis, but there is also evidence to support this. Luminal and solid organ resection typically involves use of diathermy, dissection of the peritoneum, tissue manipulation and retraction, mobilization of the bowel and alternation of anatomy, all of which cause significant cellular injury and an autonomic discharge. The ensuing post-operative catabolic stress and inflammatory response, as well as changes in microbiome following intestinal resection, affect patients' recovery.

**TABLE 1** Categories and sub-categories identified in descriptions of major abdominal surgical procedures.

Category/sub-category	Number of coded references	Summary	Illustrative quotes
Pre-operative factors	154		
Indication	73	Indications ranged from acute gastrointestinal pathology, adhesiolysis, control of bleeding, repair of injuries to resection of malignancy	<p>“Perforation, ischemia, abdominal abscess, bleeding, obstruction, evacuation of an intra-peritoneal abscess, intra-peritoneal hematoma, bowel resection with repair due to incarcerated bowel, incisional, umbilical, inguinal and femoral hernias, adhesiolysis, and repair of fascial dehiscence”</p> <p>“Malignant gastrointestinal tumors”</p> <p>“Abdominal tumor resection encompassed a variety of operations for intra-abdominal tumors including benign and malignant diagnoses such as cystic neoplasms and sarcomas”</p>
Scoring system	10	Scoring system consisted of procedure complexity score or a risk score, such as POSSUM score, mortality or morbidity rates, description of complexity	<p>“Operative magnitude score of <math>\geq 4</math> when assessed by the Physiologic and Operative Severity Score for the enumeration of Mortality and morbidity [POSSUM]”</p> <p>“Surgery with an expected postoperative mortality rate <math>&gt; 3\%</math>”</p> <p>“Operative code of major, major plus, or complex major operation”</p>
Urgency	71	Urgency of an operative case ranged from emergency, to within 72 h of admission, to elective.	<p>“Elective”</p> <p>“Immediate emergency”</p> <p>“Performed within 72 h of the admission”</p>
Intra-operative factors	113		
Operation duration	78	Operative duration criteria ranged from at least 30 min to exceeding 4 h	<p>“An expected duration of at least 1.5 h”</p> <p>“Expected operation time of at least 30 min”</p> <p>“Expected duration <math>\geq 2</math> h”</p>
General anesthetic	18	Description of MAS that included general anesthetic as part of the criteria	“Performed under general anesthesia”
Blood loss	16	Blood loss criteria ranged from over 500 mL to $> 20\%$ of blood volume	<p>“An anticipated blood loss of greater than 500 mL”</p> <p>“Estimated blood loss of more than 20% of blood volume”</p> <p>“Blood loss exceeding 1000 mL”</p>
Volume of IV fluids	1	One definition including the volume of fluid administration as part of the criteria for MAS	“Expected intravenous fluid administration of $\geq 2$ L”
Operation-related factors	1137		
Approach	165	Approach ranged from open and laparotomy procedures to laparoscopic procedures, to criteria specifying the type of incision used	<p>“Incision of more than 5 cm”</p> <p>“Surgery through a midline incision”</p> <p>“All surgical procedures under laparoscopic guidance”</p>
Procedure	863	See Table 2	
Site	109	Relates exclusively to GI-related operative sites	<p>“Liver, colorectal, gastric, pancreatic, or esophageal”</p> <p>“Surgery on the gastrointestinal tract (from oropharynx to external anal sphincter)”</p> <p>“All general surgery for the gastrointestinal tract”</p>

(Continues)

TABLE 1 (Continued)

Category/sub-category	Number of coded references	Summary	Illustrative quotes
Post-operative factors	30		
Length of stay	18	Length of stay varied from >1 day to at least 6 post-operative days	<p>“Expected postoperative hospital stay of at least 5 days”</p> <p>“The predictable length of stay for patients in a given diagnosis-related group exceeded 2 days”</p> <p>“Major surgery was defined as a procedure that would normally require a postoperative stay of between one and four nights”</p>
ICU admission	6	Description of MAS included the need for postoperative high dependency unit or intensive care admission as part of the criteria	<p>“Treated postoperatively in the surgical intensive care unit”</p> <p>“Admission to an intensive care unit after the surgery”</p> <p>“Surgery requiring a minimum of 48-h ICU postoperative therapy”</p>
Post-operative analgesia	3	Description of MAS included the need for postoperative analgesia	<p>“Requiring morphine for postoperative analgesia”</p> <p>“Any surgery that would qualify for <math>\geq 2</math> days of scheduled parenterally administered NSAIDs”</p> <p>“Planned postoperative epidural analgesia”</p>
Post-operative oral intake	2	Description of MAS included the need for limitations in oral intake post-operatively	<p>“At least 48 h postoperative fasting”</p> <p>“No significant oral nutrient intake for at least 5 days postoperatively”</p>
Mechanical ventilation	1	Single description of specific duration of mechanical ventilation	“Cumulative duration of postoperative mechanical ventilation >24 h”

Complications, such as postoperative ileus and gastrointestinal tract dysfunction occur in this patient group,<sup>23–25</sup> regardless of the approach used to enter the peritoneal cavity. This can result in an altered recovery trajectory with prolonged hospital stay and increase morbidity.<sup>25</sup>

Contrary to the relatively hard criteria of GI resection, the categories of preoperative, intraoperative and postoperative factors are a lot more fluid and influenced by the variety of hospital, physician and patient factors. Indeed, it can be argued that each of the criteria included in the Martin et al<sup>8</sup> definition of “major surgery” could be subject to such influences. For instance, significant patient comorbidity, such as having a pacemaker (American Society of Anesthesiologists (ASA) class 3), would make an inguinal hernia repair a major surgery. Long operative duration (undefined by Martin et al<sup>8</sup>), blood loss over 1000 mL and degree of organ ischemia can be operator dependent, such that an experienced surgeon can perform a complex procedure faster than inexperienced surgeon,<sup>26,27</sup> result in fewer haemorrhagic complications<sup>28,29</sup> and less visceral ischemia times.<sup>29</sup> Similarly, the presence of post-operative metabolic stress response and the risk of 30-day morbidity and mortality is dependent on

patients' pre-morbid and functional status, their regular medications and the acuteness of presentation. Additionally, the decision to admit to a high dependency or intensive care unit is often resource-dependent and varies between institutions. Basing a definition on patient and operator-dependent criteria risks significant variability in procedure selection, ultimately resulting in an inconsistent MAS cohort.

Specifying MAS as an intra-peritoneal operation would exclude surgery solely involving the abdominal wall, particularly since only 0.6% of references coded included this term within the description of MAS. We deliberated over the inclusion or exclusion of non-gastrointestinal surgical specialties, such as urology, gynecology, endocrine, thoracic and vascular surgery, and transplant surgery from the definition. Certainly, excluding these specialties from the definition of MAS would mitigate against the variability in patient characteristics and recovery trajectory following this surgery. Additionally, the overall low frequency of this terminology being coded (11.4%) in the content analysis supports the exclusion of these surgical specialties.

One limitation of this study is the focus of the search strategy on the article titles, rather than the abstracts or the entire article body. This decision was reached

**TABLE 2** "Procedure" sub-categories identified in descriptions of major abdominal surgical procedures.

<b>Procedure sub-categories</b>	<b>Number of coded references</b>	<b>Illustrative quotes</b>
Altered anatomy	3	"Normal anatomy was significantly altered"
Anastomosis	15	"As operations creating any gastrointestinal anastomosis" "Primary anastomosis" "Digestive anastomosis"
Excision of organ	3	"Organs were removed"
GI resection	591	
Bariatric surgery	1	"Bariatric surgery"
Bypass	1	"Bypass surgery"
Colectomy	109	"Hemicolectomy" "Colectomy (e.g. right hemicolectomy, left hemicolectomy, anterior resection and ultra-low anterior resection)" "Total colectomy"
Cytoreductive surgery	10	"Cytoreductive surgery with HIPEC for PMP" "Cytoreductive surgery with or without hyperthermic intraperitoneal chemotherapy (HIPEC), low anterior resection" "Radical transabdominal tumor debulking"
Exenteration	2	"Pelvic exenteration"
Gastric resection	92	"Total/partial gastrectomy" "Gastrectomy [both total and partial resection] with Roux and Y reconstruction" "Partial and total (radical) gastric resection"
Hepatic resection	83	"Hepatectomy (except for simple wedge resections of segments III, IVb, V or VI)" "Hepatic resections with biliodigestive anastomosis" "Liver resection (in detail, right lobectomy, trisegmentectomy, and bisegmentectomy)"
Esophageal resection	42	"Esophagectomy with gastric conduit reconstruction" "Partial and total (radical) esophageal resection" "Resection of the esophagus"
Pancreatic resection	127	"Pancreatic resections (pancreaticoduodenectomy or distal pancreatectomy with or without splenectomy)" "Pylorus preserving pancreatico-duodenectomy" "Total pancreatectomy/Whipple's procedure"
Rectum resection	47	"Rectum resections" "Abdominoperineal excision of rectum" "Low anterior resection"
Small bowel resection	20	"Small bowel resection" "Small intestinal resections" "Partial resection of intestine"
Manipulation of abdominal organs	2	"Manipulation of an abdominal organ" "Gut manipulation"

(Continues)



TABLE 2 (Continued)

Procedure sub-categories	Number of coded references	Illustrative quotes
No solid organ or luminal resection	31	
Appendectomy	4	"Open appendectomy", "appendectomy"
Cholecystectomy	13	"Open cholecystectomy", "laparoscopic cholecystectomy"
Hernia	9	"Obstructed inguinal hernia" "Incisional hernia repair" "Giant ventral hernia repair (defined as a hernia larger than 10 cm in diameter with loss of domain)"
Lymph node dissection	2	"Retroperitoneal lymph node dissection" "Pelvic lymph node dissection"
Rectopexy	1	"Abdominal rectopexy"
Vagotomy	2	"Highly selective vagotomy"
Non-GI operations	161	
Endocrine surgery	1	"Adrenalectomy"
Gynecological surgery	40	"Radical abdominal hysterectomy with pelvic lymphadenectomy" "Hysterectomy with pelvic and lumbo-aortic lymphadenectomy" "Simple or radical hysterectomy"
Splenectomy	10	"Splenectomy" "Extirpation of the spleen" "Surgery of the spleen"
Thoracic resection	1	"Pneumonectomy"
Urological surgery	75	"Cystectomy and ileal conduit" "Nephrectomy" "Radical prostatectomy with lymph node dissection"
Vascular surgery	34	"Reconstructive abdominal aortic surgery" "Aorto-iliac reconstruction for arteriosclerotic occlusive disease" "Repair of an abdominal aortic aneurysm"
Peritoneum	26	"Deliberate breach of peritoneum or retro-peritoneum" "Surgical procedure in which the peritoneum is entered" "An intra-peritoneal approach"
Reversal	10	
Reversal of Hartmann's	3	"Reversal of hartmann procedure"
Stoma reversal	7	"Reversal of defunctioning ileostomy/colostomy" "Closure ileostomy" "Reversal of ileostomy"
Stoma creation	18	"Construction of temporary loop ileostomy" "Creation of definitive stoma" "Stoma formation"
Transplant surgery	3	"Liver transplantation"

following the outcome of a preliminary search where many of the returned articles had no specific focus on major abdominal surgery. Although it is possible that some articles were omitted, the impact of this is unlikely to have a major bearing on the conclusions and the ensuing definition of MAS. We concede that our derived definition is theoretical and is based on previously published literature, which is invariably subject to a publication bias. However, the large number of articles included in the analysis would, in part at least, mitigate against this. Additionally, it should be emphasized that the purpose of this study was to derive an unambiguous definition of MAS, which in itself cannot predict short-term or long-term patient outcomes, determine resource allocation or assist with patient consent. Rather it serves as a robust scientific platform for future development of clinically-relevant applications, such as PROMs.

In conclusion, we propose that “major abdominal surgery” should be defined as an intra-peritoneal operation with no primary involvement of the thorax, involving either luminal resection and/or resection of a solid organ associated with the gastrointestinal tract. Undoubtedly, further research is required to verify this definition using real world patient data.

## AUTHOR CONTRIBUTIONS

**Alona Courtney:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; visualization; writing – original draft; writing – review & editing. **Jonathon Clymo:** Data curation; formal analysis. **Yasmin Dorudi:** Data curation; formal analysis. **Suneetha Ramani Moonesinghe:** Conceptualization; methodology; supervision; writing – review & editing. **Sina Dorudi:** Conceptualization; methodology; supervision; writing – original draft; writing – review & editing.

## CONFLICT OF INTEREST STATEMENT

Nothing to declare.

## ETHICS STATEMENT

Ethical approval was not required for this scoping review.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.