

A systematic review and meta-analysis of baseline risk factors for the development of postoperative ileus in patients undergoing gastrointestinal surgery

MJ Lee^{1,2}, P Vaughan-Shaw⁵, D Vimalachandran⁴, on behalf of ACPGBI GI Recovery Group

¹Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

²The Medical School, University of Sheffield, Sheffield, UK

³Western General Hospital, Edinburgh, UK

⁴Countess of Chester Hospital, Chester, UK

ABSTRACT

INTRODUCTION Postoperative ileus occurs frequently following abdominal surgery. Identification of groups at high risk of developing ileus before surgery may allow targeted interventions. This review aimed to identify baseline risk factors for ileus.

METHODS A systematic review was conducted with reference to PRISMA and MOOSE guidelines. It was registered on PROSPERO (CRD42017068697). Searches of MEDLINE, EMBASE and CENTRAL were undertaken. Studies reporting baseline risk factors for the development of postoperative ileus based on cohort or trial data and published in English were eligible for inclusion. Dual screening of abstracts and full texts was undertaken. Independent dual extraction was performed. Bias assessment was undertaken using the quality in prognostic studies tool. Meta-analysis using a random effects model was undertaken where two or more studies assessed the same variable.

FINDINGS Searches identified 2,430 papers, of which 28 were included in qualitative analysis and 12 in quantitative analysis. Definitions and incidence of ileus varied between studies. No consistent significant effect was found for association between prior abdominal surgery, age, body mass index, medical comorbidities or smoking status. Male sex was associated with ileus on meta-analysis (odds ratio 1.12, 95% confidence interval 1.02–1.23), although this may reflect unmeasured factors. The literature shows inconsistent effects of baseline factors on the development of postoperative ileus. A large cohort study using consistent definitions of ileus and factors should be undertaken.

KEYWORDS

Gastrointestinal surgery – Ileus – Prognosis

Accepted 8 September 2019

CORRESPONDENCE TO

Matthew Lee, E: m.j.lee@sheffield.ac.uk

Introduction

Postoperative ileus remains a challenging and frustrating clinical problem for clinicians and patients alike. Prolonged postoperative ileus occurs in up to one in eight patients undergoing gastrointestinal surgery,¹ and results in patient discomfort, prolonged hospital stay. It is associated with increased postoperative complications.² It is unsurprising, therefore, that a 2017 patient and public consultation study reported prevention of postoperative ileus as an important and unanswered issue.⁵

The causes of postoperative ileus are likely to be multifactorial,⁴ with risk factors for the development of prolonged postoperative ileus conceptually divided into patient and operative factors.⁵ Studies that have attempted to both elucidate the risk factors or strategies to reduce

postoperative ileus have been hampered by lack of consistent definitions of what actually it constitutes and when transient it becomes prolonged.¹

Several clinical intervention studies have sought to reduce the incidence of postoperative ileus. Agents such as steroids,⁶ opioid agonists⁷ and intravenous lidocaine⁸ have all been investigated. However, studies assessing such novel agents are hampered by the absence of clear and robust definitions and a consensus-derived core outcome set.⁹ Development of a validated gastrointestinal recovery score would greatly aid this endeavour. To achieve this, the relevance and effect of preoperative and operative risk factors for development of postoperative ileus, outcome variables, interventions and natural history of ileus requires further investigation.

The UK Medical Research Council-funded PROgnosis REsearch Strategy (PROGRESS) initiative aims to develop multidisciplinary and collaborative research into improving research into quality of care outcomes such as postoperative ileus.¹⁰ Thus, identification of risk factors and development of a gastrointestinal recovery score to better assess strategies to reduce postoperative ileus would fit within two of the remits of this initiative ‘prognostic factor research’ and ‘prognostic model research’.

The aim of this review was to identify preoperative factors associated with the development of postoperative ileus as part of a larger collaborative effort overseen by the Association of Coloproctology of Great Britain and Ireland (ACPGBI) to develop a gastrointestinal recovery score.

Methods

This review was undertaken with reference to the Cochrane Handbook, reported meta-analysis of observational studies in epidemiology (MOOSE) and the preferred reporting items for systematic reviews and meta-analyses guidelines.^{11–15} The review was registered at the outset on PROSPERO, an international prospective register of systematic reviews (CRD42017068697).

Our primary aim was to derive a list of candidate risk factors for postoperative ileus following gastrointestinal surgery through systematic review of published literature. The secondary aim was to perform a meta-analysis of candidate risk factors to examine the significance and magnitude of effect on the risks for postoperative ileus.

We undertook a systematic review of MEDLINE (via OvidSP), EMBASE (via OvidSP) and Cochrane Library databases according to a predefined protocol up to May 2017. The search strategy is presented in Appendix 1.

Inclusion and exclusion criteria

Studies assessing baseline (preoperative) factors and their association with development of postoperative ileus following gastrointestinal surgery in adults were eligible for inclusion. In order to review literature as widely as possible, the definition of postoperative ileus was accepted as defined by authors of individual studies rather than being set by the research team. There was no time limit placed on date of publication, and only studies written in the English language were included. Retrospective and prospective cohort or case-control studies, together with randomised controlled trials, were eligible for inclusion in the review. Owing to the risk of bias, case series, case reports, commentaries and editorials were excluded.

Data extraction

Article titles and abstracts were exported into Covidence, an established online screening and data extraction tool (www.covidence.org) screened for eligibility independently by two authors (PVS and/or ML and/or DV) with disagreements resolved by discussion. Review of the full text was undertaken by two authors for each candidate article. Bibliographies of included studies were hand searched to identify further relevant primary studies. Two

authors independently extracted information from each primary studies using a standardised Microsoft Excel proforma. Data on study design and size, surgical approach (laparoscopic or open), background disease (eg cancer, inflammatory bowel disease) and definition of postoperative ileus were collected. Data on all reported characteristics were collected, including non-modifiable patient characteristics (eg gender, age) modifiable patient characteristics (eg smoking status), physiology characteristics (eg white cell count) and disease characteristics (eg indication for surgery).

Bias assessment

The methodological quality of all studies included in the systematic review was performed using the Quality in Prognostic Studies (QUIPS) tool.¹⁴ Two authors independently applied the QUIPS tool to each study to generate summary quality judgement with the bias assessment considered in the evaluation of the strength of findings. Funnel plots and visual tests of asymmetry were used to assess the risk of publication bias.

Statistical analysis

Studies that reported odds ratios and 95% confidence intervals were considered for meta-analysis. This was selected as many studies reported OR from logistic regression, but no underlying data. A meta-analysis was performed if two or more studies reported a risk factor in this way. Meta-analysis used inverse variance and random effects included in the final synthesis were pooled using meta-analysis to construct relative risk estimates and presented using forest plots.

Results

Initial searches identified 2,430 unique papers. Following screening, 105 papers were retrieved for full-text analysis. Following assessment, 28 papers were included in the qualitative analysis and 12 were included in quantitative analysis. This is summarised in the PRISMA flow chart (Fig 1). These papers reported assessments of 57,767 patients, of whom 6127 developed postoperative ileus. This included 6 prospective cohort studies and 21 retrospective cohort studies. Study characteristics are presented in Table 1.

Bias assessment

The QUIPS tool found concerns around outcome measurements (ie the definition of ileus). It also identified a high risk of bias associated with statistical analysis, as many small studies reported univariate assessments, without adjustment for other factors. A summary of bias assessment is shown in Table 2.

Definition of postoperative ileus

Postoperative ileus was defined in all studies. This was typically a compound definition including aspects of tolerance of diet, absence of distention, passage of stool or

flatus. The definitions of postoperative ileus used are presented in Table 5.

Demographic characteristics associated with postoperative ileus

Twelve studies assessed sex for association with postoperative ileus. Seven studies found no significant relationship between sex and postoperative ileus,^{4,15-20} and a further five found a positive association with male sex.^{5,21-24} It should be noted that those finding a significant association tended to be larger studies which used multivariate regression methods. Nine studies assessed age for association with postoperative ileus. Three studies found that increasing age had no association with increased rates of postoperative ileus.^{15,16,25} Three studies found an association between postoperative ileus and increasing age when a cut-off point at 65 years^{26,27} or 70 years²⁸ was used within univariate analyses. Three studies

using multivariate analysis found increasing age was significantly associated with increased rates of postoperative ileus.^{17,22,25} The association between prior abdominal surgery and postoperative ileus was assessed in eight studies. No relationship with postoperative ileus was seen in five studies,^{4,17,21,29,50} and a positive association was found in three studies.^{25,51,52} Again, positive relationships were typically seen in larger studies which used multivariate regression analysis.

Comorbidity characteristics associated with postoperative ileus

Reported studies tended to support respiratory disease or chronic obstructive pulmonary disease as risk factors for postoperative ileus, with three studies supporting this^{21,22,29} and one disagreeing.¹⁷ The presence of cardiac disease or congestive heart failure were reported as having a significant positive association with postoperative ileus

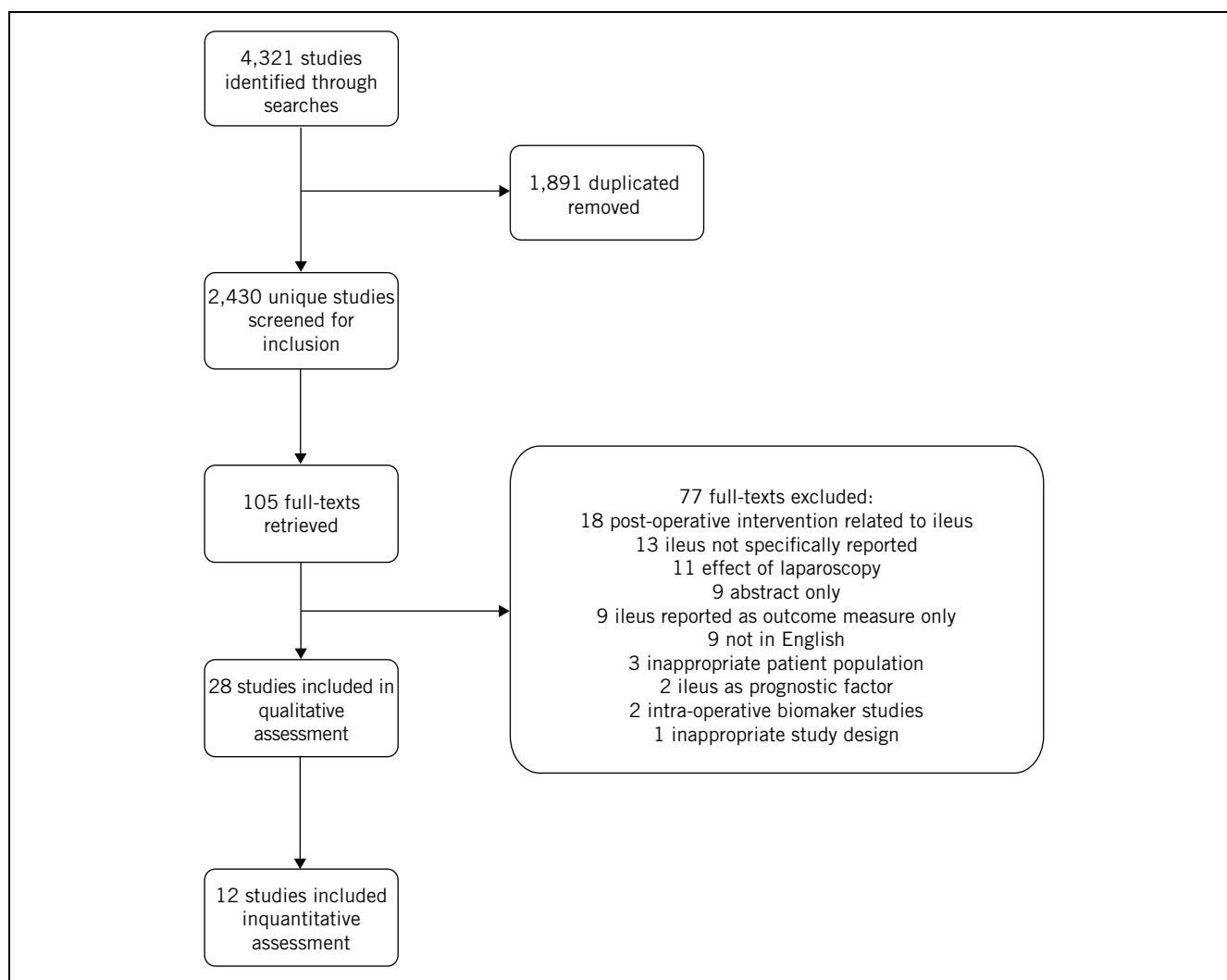


Figure 1 PRISMA flow chart.

rates in two studies^{22,29} and no relationship in a large retrospective cohort.

Renal failure or dialysis were not found to be risk factors,^{22,25,29} while in a single study pre-existing constipation was significantly associated with postoperative ileus (odds ratio, OR, 3.67 95% confidence interval, CI, 1.40–9.67).²² Obesity was assessed in seven studies. Obesity had a positive association in two studies,^{55,54} but this was not replicated across other studies.^{16,27,29,55,55} Weight showed no relationship with postoperative ileus in two studies.^{15,16} Smoking was associated with increased rates of postoperative ileus in a retrospective study.²⁵

Physiological factors

Increasing American Society of Anesthesiologists (ASA) status was associated with postoperative ileus in two large studies. Milan *et al* reported an odds ratio for postoperative ileus of 1.6 for ASA II and 7.0 for ASA IV, albeit with large confidence intervals.²⁹ Moghadamyeghaneh *et al* reported that the risk of developing postoperative ileus was increased for patients judged to be higher than ASA II (OR 1.2, 95% CI 1.07–1.36).²² White cell count raised above $12 \times 10\text{mm}^3$ was a risk factor in one small retrospective study,³⁶ but this was not reflected in a large retrospective study using multivariate analyses.²²

Table 1 Study characteristics.

Study	Study design	Surgical population	Operative approach	Patients (n)	Rate of POI (%)
Akiyoshi <i>et al</i> (2011) ³³	Prospective cohort	Colorectal resection	Laparoscopic	1,194	1.08
Artinyan <i>et al</i> (2008) ⁴	Retrospective cohort	Abdominal surgery	Open	88	100
Bakker <i>et al</i> (2015) ⁴⁵	Prospective cohort	Colorectal resection	Mixed	816	11.64
Barletta <i>et al</i> (2011) ¹⁵	Retrospective cohort	Colorectal resection	Mixed	279	8.60
Bickenbach <i>et al</i> (2013) ³⁵	Retrospective cohort	Gastric cancer resection	Not reported	1,853	8.60
Bisanz <i>et al</i> (2008) ¹⁶	Retrospective cohort	Abdominal surgery	Not reported	101	43.56
Chapuis <i>et al</i> (2013) ⁵	Retrospective cohort	Colorectal resection	Mixed	2,400	14.00
Englesbe <i>et al</i> (2010) ⁴⁶	Prospective cohort	Colorectal resection	Mixed	1,553	5.34
Franko <i>et al</i> (2006) ³¹	Retrospective cohort	Colorectal resection	Laparoscopic	820	4.52
Grosso <i>et al</i> (2012) ²⁶	Retrospective cohort	Colorectal resection	Mixed	446	5.38
Hamel <i>et al</i> (2000) ³⁰	Retrospective cohort	Colorectal resection	Laparoscopic	85	17.64
Huang <i>et al</i> (2015) ²⁷	Prospective cohort	Gastric cancer resection	Mixed	296	32.43
Ichikawa <i>et al</i> (2016) ⁴⁷	Retrospective cohort	Colorectal resection	Laparoscopic	172	2.91
Juarez-Parra <i>et al</i> (2015) ¹⁷	Retrospective cohort	Colorectal resection	Mixed	95	21.11
Kim <i>et al</i> (2013) ²⁸	Retrospective cohort	Gastric cancer resection	Laparoscopic	389	1.80
Kronberg <i>et al</i> (2011) ²⁵	Retrospective cohort	Colorectal resection	Laparoscopic	413	10.17
Le <i>et al</i> (2011) ²¹	Retrospective cohort	Ileal pouch–anal anastomosis	Open	91	21.98
Millan <i>et al</i> (2012) ²⁹	Retrospective cohort	Colorectal resection	Mixed	773	15.91
Moghadamyeghaneh <i>et al</i> (2016) ²²	Retrospective cohort	Colorectal resection	Mixed	27,560	12.69
Murphy <i>et al</i> (2016) ²³	Retrospective cohort	Colorectal resection	Mixed	9,734	14.01
Petros <i>et al</i> (1995) ¹⁸	Retrospective cohort	Colorectal resection	Open	358	16.20
Pikarsky <i>et al</i> (2002) ³⁴	Retrospective cohort	Colorectal resection	Laparoscopic	162	12.34
Tian <i>et al</i> (2017) ¹⁹	Retrospective cohort	Colorectal resection	Mixed	5,533	7.95
Valenti <i>et al</i> (2007) ⁴⁸	Retrospective cohort	Colorectal resection	Open	273	9.15
Vather <i>et al</i> (2013) ²⁰	Prospective cohort	Colorectal resection	Mixed	255	19.61
Vather <i>et al</i> (2015) ²⁴	Prospective cohort	Colorectal resection	Mixed	327	26.91
Yamamoto <i>et al</i> (2013) ³²	Retrospective cohort	Colorectal resection	Laparoscopic	1,701	2.70

POI, postoperative ileus.

Meta-analysis

Meta-analysis was considered where two or more studies reported on association between the same factor and postoperative ileus. For age, the heterogeneity in factor classification and reported outcome measure precluded meta-analysis. Therefore only the demographic characteristics of male sex and prior abdominal surgery were assessed using meta-analysis. Data from five studies was pooled and showed a non-significant effect odds ratio (OR 1.05, 95% CI 0.83–1.28, I2 = 0%; Fig 2a). Data from eight studies showed a significant positive association between male sex and development of postoperative ileus (OR 1.12, 95% CI 1.02–1.23, $p=0.01$) with no heterogeneity (I2 = 0%; Fig 2b).

Meta-analysis of comorbidity factors did not show significant effect of any factors, and demonstrated consistently low heterogeneity. Visual inspection of funnel plots did not demonstrate asymmetry.

Discussion

This is the first systematic review with meta-analysis to examine the relationship between baseline demographic or physiological factors and incidence of postoperative ileus in patients undergoing gastrointestinal surgery. Our review confirms significant heterogeneity in the definition of postoperative ileus used in clinical studies, which limits the synthesis of the published evidence.

Table 2 Bias assessment using quality in prognostic studies tool.

Study	Participation	Attrition	Prognostic factor measurement	Outcome measurement	Confounding	Statistical analysis and reporting
Akiyoshi <i>et al</i> (2011) ³³	L	L	L	H	M	M
Artinyan <i>et al</i> (2008) ⁴	H	M	M	M	H	M
Bakker <i>et al</i> (2015) ⁴⁵	L	L	L	M	M	H
Barletta <i>et al</i> (2011) ¹⁵	L	L	L	L	M	M
Bickenbach <i>et al</i> (2013) ³⁵	H	L	L	H	H	H
Bisanz <i>et al</i> (2008) ¹⁶	L	L	L	M	H	M
Chapuis <i>et al</i> (2013) ⁵	L	L	L	L	L	L
Englesbe <i>et al</i> (2010) ⁴⁶	M	M	M	M	H	H
Franko <i>et al</i> (2006) ³¹	L	L	L	L	M	M
Grosso <i>et al</i> (2012) ²⁶	L	L	L	M	M	H
Hamel <i>et al</i> (2000) ³⁰	L	L	L	M	M	H
Huang <i>et al</i> (2015) ²⁷	L	L	L	L	L	L
Ichikawa <i>et al</i> (2016) ⁴⁷	M	L	M	H	H	H
Juarez-Parra <i>et al</i> (2015) ¹⁷	M	L	L	M	M	H
Kim <i>et al</i> (2013) ²⁸	M	L	L	M	M	H
Kronberg <i>et al</i> (2011) ²⁵	L	L	M	H	H	M
Le <i>et al</i> (2011) ²¹	L	L	L	M	M	H
Millan <i>et al</i> (2012) ²⁹	L	L	L	L	L	L
Moghadamyeghaneh <i>et al</i> (2016) ²²	L	L	M	M	L	L
Murphy <i>et al</i> (2016) ²³	M	L	M	M	L	L
Petros <i>et al</i> (1995) ¹⁸	L	L	L	L	M	M
Pikarsky <i>et al</i> (2002) ³⁴	H	M	L	L	M	H
Tian <i>et al</i> (2017) ¹⁹	L	L	L	M	M	L
Valenti <i>et al</i> (2007) ⁴⁸	L	L	L	M	L	L
Vather <i>et al</i> (2013) ²⁰	M	M	L	H	M	M
Vather <i>et al</i> (2015) ²⁴	L	M	L	L	L	L
Yamamoto <i>et al</i> (2013) ³²	L	L	L	H	H	H

H, high risk of bias; L, low risk of bias; M, medium risk of bias.

Table 3 Definitions of postoperative ileus used in studies.

Study	Definition of postoperative ileus
Akiyoshi <i>et al</i> (2011) ³³	'Persistent ileus' – not otherwise defined.
Artinyan <i>et al</i> (2008) ⁴	Patient's ability to tolerate a solid diet in the absence of nausea, vomiting or abdominal distention.
Bakker <i>et al</i> (2015) ⁴⁵	Prolonged inability to pass flatus and stool resulting in nausea and vomiting and requiring the use of a nasogastric tube and/or total parenteral nutrition.
Barletta <i>et al</i> (2011) ¹⁵	Three episodes of vomiting over 24 hours, cessation of oral diet or the need for a nasogastric tube within 5 days after surgery.
Bickenbach <i>et al</i> (2013) ³⁵	Not defined.
Bisanz <i>et al</i> (2008) ¹⁶	Lack of return of bowel function; no passage of flatus; unable to tolerate oral intake; abdominal distention, nausea and vomiting, and absence of bowel movement by postoperative day 3.
Chapuis <i>et al</i> (2013) ⁵	Presence of abdominal distension with lack of bowel sounds in a patient who has experienced nausea or vomiting and has failed to pass flatus or stool for more than 3 days postoperatively, in the absence of mechanical bowel obstruction.
Englesbe <i>et al</i> (2010) ⁴⁶	An ileus lasting more than 7 days from the index operation.
Franko <i>et al</i> (2006) ³¹	Ileus defined as the inability to tolerate any diet combined with abdominal distension beyond the third postoperative day.
Grosso <i>et al</i> (2012) ²⁶	Not defined.
Hamel <i>et al</i> (2000) ³⁰	Any placement of a nasogastric tube during the initial hospitalisation; the criterion was vomiting 200ml or more, two or more times.
Huang <i>et al</i> (2015) ²⁷	Two or more of the following five criteria met on or after postoperative day 4 without prior resolution of 'postoperative ileus': nausea or vomiting, inability to tolerate oral diet over 24 hours, absence of flatus over 24 hours, abdominal distension and radiological confirmation of ileus.
Ichikawa <i>et al</i> (2016) ⁴⁷	Not defined.
Juarez-Parra <i>et al</i> (2015) ¹⁷	The absence of passage of flatus/stool or inability to tolerate oral diet on or after four postoperative days.
Kim <i>et al</i> (2013) ²⁸	Absence of adequate bowel function on postoperative day 5 or the need for insertion of a nasogastric tube in the absence of a mechanical obstruction.
Kronberg <i>et al</i> (2011) ²⁵	Not defined.
Le <i>et al</i> (2011) ²¹	Any transient cessation of coordinated bowel motility following surgery that prevented the effective transit of intestinal contents or tolerance of oral intake within 7 days of surgery.
Millan <i>et al</i> (2012) ²⁹	No bowel recovery at postoperative day 6.
Moghadamyeghaneh <i>et al</i> (2016) ²²	No return of bowel function within 7 days.
Murphy <i>et al</i> (2016) ²³	Nasogastric tube or nil by mouth on postoperative day 4 or later.
Petros <i>et al</i> (1995) ¹⁸	Passage of flatus or stool, or the ability to tolerate a clear liquid diet, were regarded as evidence of the resolution of postoperative ileus. Postoperative ileus \geq 7 days.
Pikarsky <i>et al</i> (2002) ³⁴	Ileus defined as a condition requiring reinsertion of a nasogastric tube due to two or more episodes of emesis of more than 200ml.
Tian <i>et al</i> (2017) ¹⁹	ICD-10 diagnostic code K56. Abdominal plain x-ray and computed tomography, and the presence of clinical manifestations including nausea, vomiting, abdominal pain, abdominal distension, and/or delay in the passage of flatus and stool for more than 7 days postoperatively, in the absence of mechanical bowel obstruction.
Valenti <i>et al</i> (2007) ⁴⁸	Continued nasogastric tube on the fifth postoperative day or reintroduction of the tube
Vather <i>et al</i> (2013) ²⁰	Prolonged postoperative ileus was recorded as occurring if this was clinically diagnosed and documented by the overseeing surgical team.
Vather <i>et al</i> (2015) ²⁴	Prolonged postoperative ileus was defined as occurring if patients met two of the following five criteria on or after postoperative day 4: nausea or vomiting over the preceding 12 hours, inability to tolerate a solid or semisolid oral diet over the preceding two meal times, abdominal distension, absence of flatus and stool over the preceding 24 hours.
Yamamoto <i>et al</i> (2013) ³²	Not defined.

ICD-10, International Classification of Diseases and Related Health Problems, 10th revision.

A total of 27 studies were included, with some evidence for an association between postoperative ileus and the factors age, male sex, prior abdominal surgery, obesity and pre-existing respiratory disease. However, meta-analysis of the synthesised evidence was limited by heterogeneity in factor and outcome classification, with a significant association seen for male sex only.

Postoperative ileus is a significant clinical problem. It is perhaps the most common complication following gastrointestinal surgery, occurring in up to one in eight patients, and remains poorly understood.¹ There are two traditionally recognised phases of ileus: a short-acting neurogenic phase typified by exaggerated inhibitory reflexes triggered by activation of afferent nerves during the surgical procedure, and a longer inflammatory phase driven by immune mediators.^{57,58} Numerous intervention studies have sought to intervene in the physiology of postoperative ileus, yet the assessment of such studies is limited by both the lack of a standard definition of postoperative ileus and limited understanding of the contribution of baseline demographic and physiological factors.

To better assess strategies to reduce postoperative ileus, we believe that a consensus-derived gastrointestinal recovery score is needed alongside a better understanding of baseline risk factors, with the current study satisfying two remits of the Medical Research Council-funded

PROGRESS initiative: ‘prognostic factor research’ and ‘prognostic model research’.¹⁰ Regardless of the wide application of enhanced recovery programmes, identification of those at high risk of developing postoperative ileus is useful. Proper characterisation of this group could help to identify mechanistic processes underlying the development of postoperative ileus, eventually developing effective targeted treatments.

Some evidence for an association between postoperative ileus and the factors age, male sex, prior abdominal surgery, obesity and pre-existing respiratory disease is reported here and, as such, these variables should be collected and adjusted for in future studies of postoperative ileus. Male sex is associated with postoperative ileus in five studies and the only factor significantly associated with postoperative ileus on meta-analysis. The observed association may result from increased surgical duration and manipulation of the bowel, owing to increased visceral adiposity or a narrow male pelvis necessitating increased manipulation of bowel to complete an operation. Increasing age is associated with increased postoperative ileus in six studies, which could reflect previously reported delayed baseline colonic transit and increased sensitivity to anaesthetic or opiate analgesia.⁵⁹ Obesity was associated with postoperative ileus in two studies assessed and may reflect increased surgical duration, a higher need for open surgery or increased

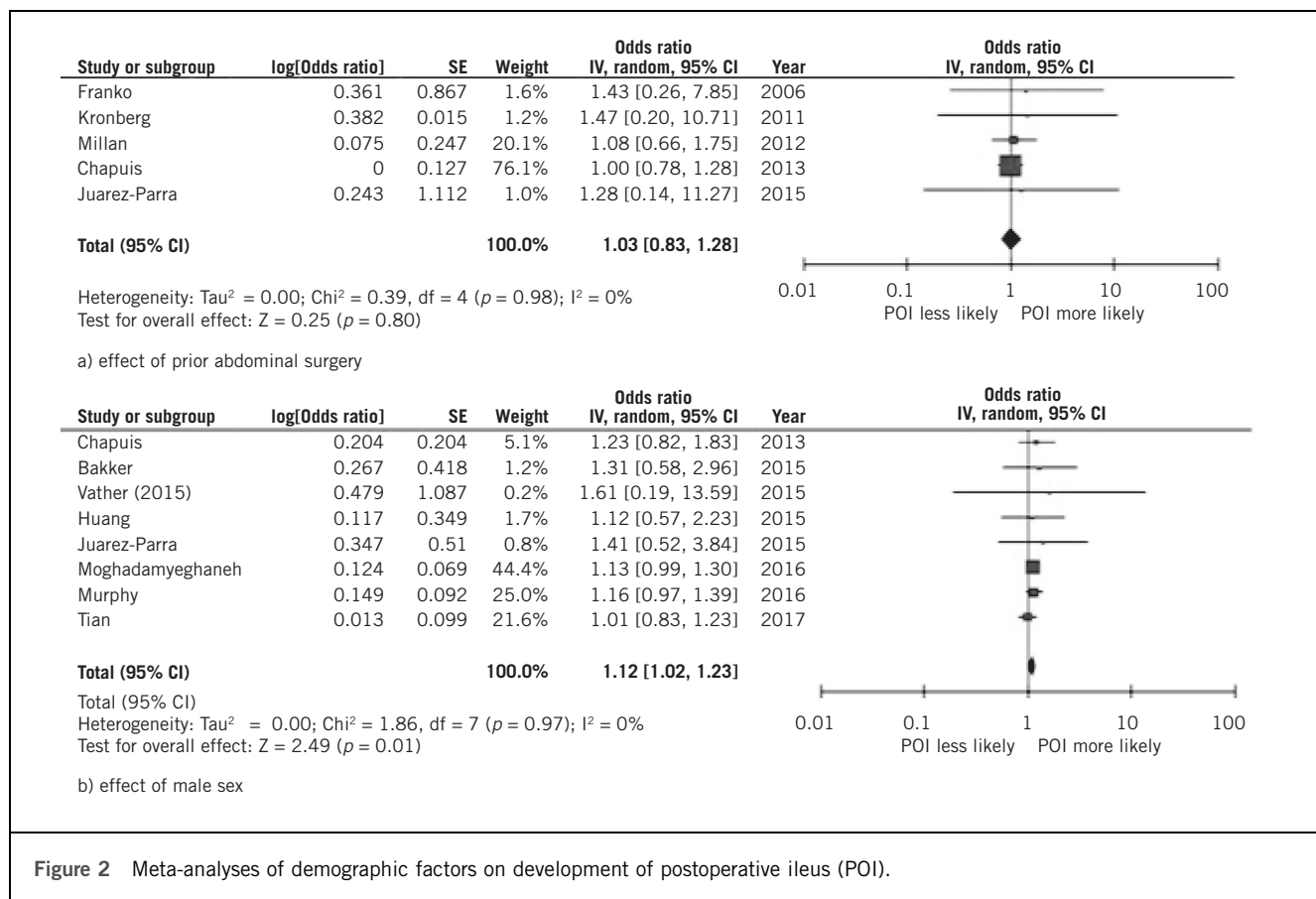
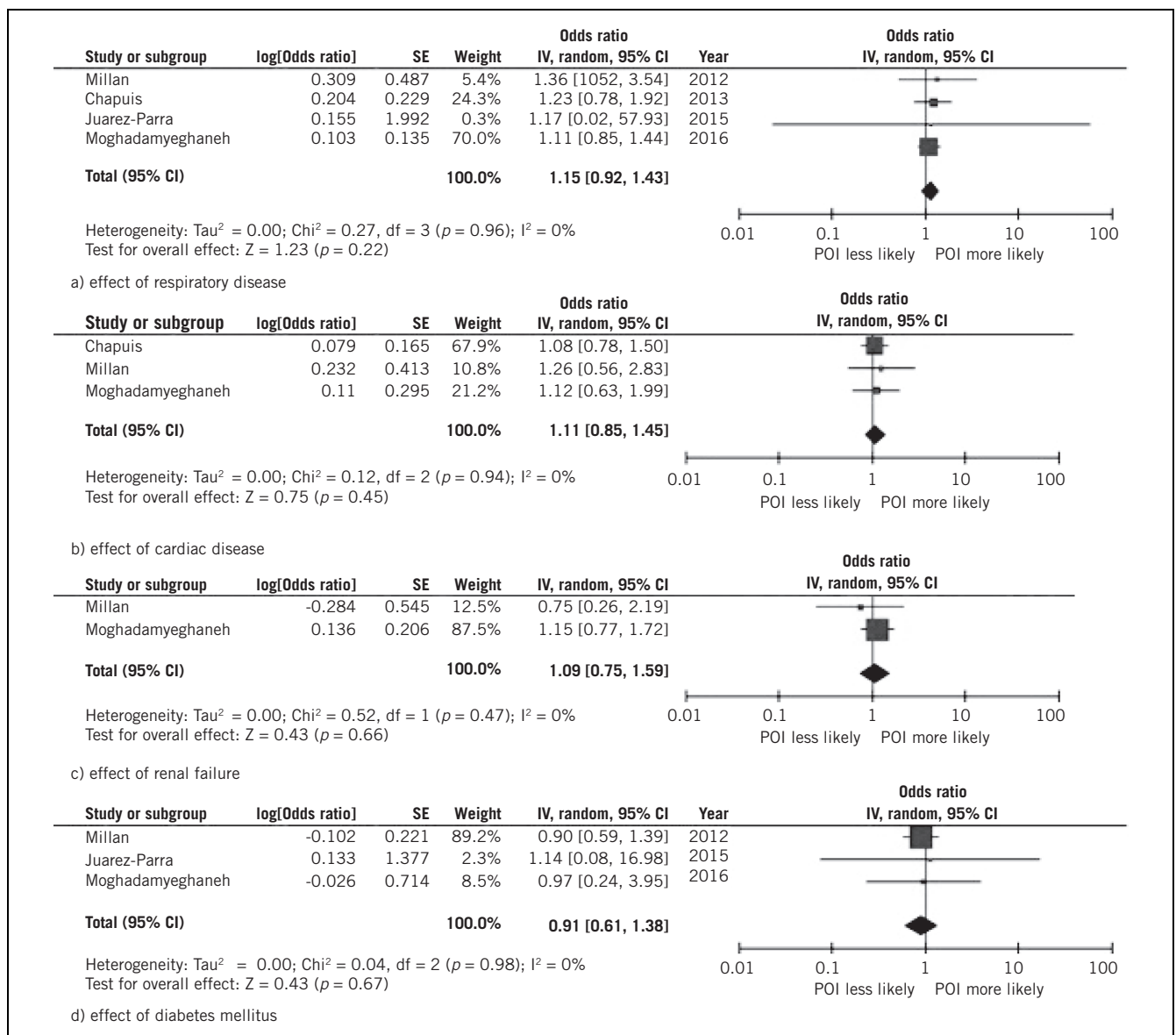


Figure 2 Meta-analyses of demographic factors on development of postoperative ileus (POI).

perioperative anaesthetic or opiate requirement. Finally, three studies reported increased postoperative ileus in patients with baseline respiratory disease, which may reflect a tendency towards greater opiate use in such patients given the fear of postoperative respiratory complications.

Three additional studies that were published recently and therefore outside the years of our search criteria support a number of the above findings.⁴⁰⁻⁴² Hain *et al* assessed risk factors for postoperative ileus in 428 patients undergoing rectal cancer surgery and reported independent significant associations with the baseline factors of male gender (OR 2.5) and age (OR 2.0). Postoperative ileus was also associated with conversion to open surgery and postoperative intra-abdominal

infection, with a rate of 54% in patients with three or more of these risk factors.⁴⁰ Wolthius *et al* reported a series of 523 patients undergoing colorectal resection, with male sex (OR 2.07) and previous abdominal surgery (OR 1.65) associated with postoperative ileus, and a trend towards increased postoperative ileus with increasing age and body mass index.¹ Rybakov *et al* investigated postoperative ileus in 500 patients undergoing colorectal cancer resection, with positive independent associations seen with body mass index (OR 3.20) and previous abdominal surgery (OR 3.02), and a trend towards increased postoperative ileus in male patients.⁴¹ Finally, Sugawara reported a series of 841 patients undergoing major abdominal surgery, of which around 70% were gastrointestinal surgical procedures, with male gender



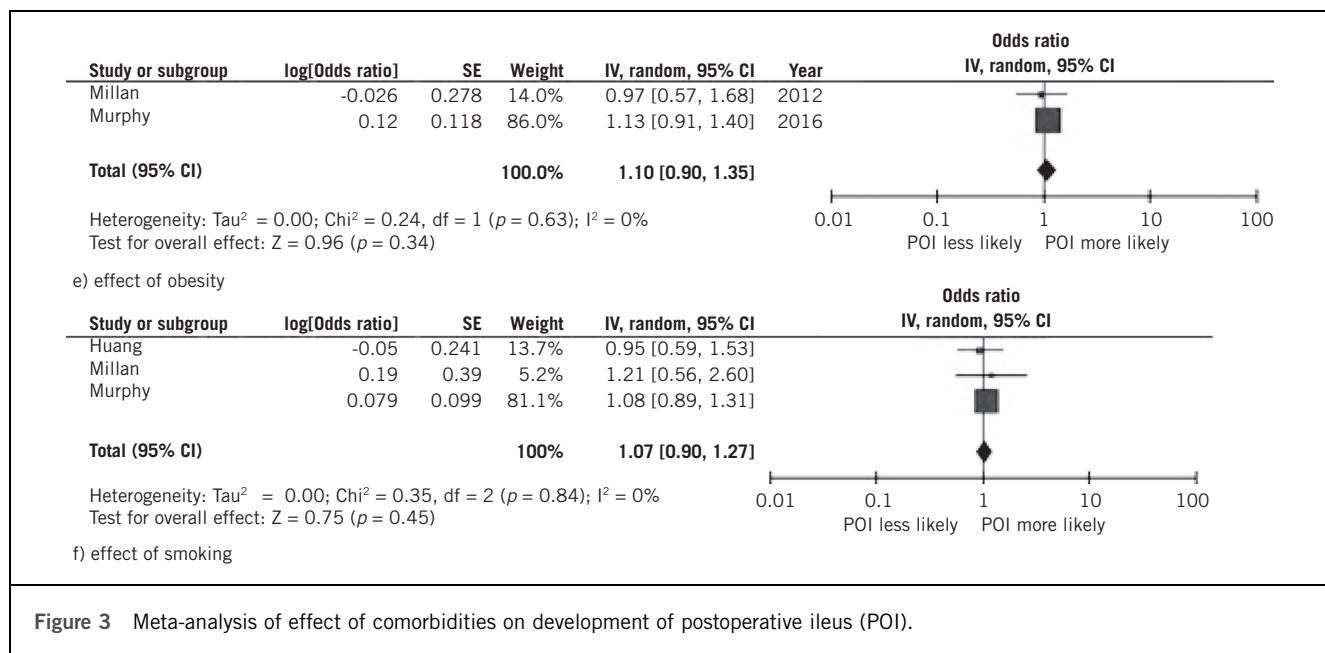


Figure 3 Meta-analysis of effect of comorbidities on development of postoperative ileus (POI).

significantly associated with postoperative ileus, with a non-significant trend towards increased postoperative ileus with age, body mass index and respiratory disease.⁴² It is, however, probable that these studies have similar bias-related issues to those seen in the included studies, so the results should be interpreted with caution.

Limitations

There are some inherent limitations to the present analysis. Crucially, definition of ileus varied across the included studies, confirming findings of a previous systematic review.^{1,45} Some definitions may have been more sensitive than others, leading to wide variation in the incidence of postoperative ileus reported. This may impact upon the ability of statistical methods to ascertain the true effect size. Similarly, many studies conducted univariate analyses only, leaving findings open to critical bias. Similarly, the covariates used to adjust the analysis varied between studies and all studies included in the review were observational studies; hence, unmeasured confounding cannot be ruled out. The number of studies identified examining a single specific factor and postoperative ileus was generally small and this limits the power to detect significant associations. Finally, we recognise that ileus can occur after other surgical procedures, yet have specifically addressed ileus following gastrointestinal surgery to provide some homogeneity in an already heterogeneous field. Even with this relatively narrowed scope, there is significant variation in rates of ileus after different surgical procedures. Controlling for these rates might help to identify some of the underlying factors. The heterogeneity of conditions in this study may have led to a type II error.

Data from the contemporaneous Ileus Management International (IMAGINE) cohort,⁴⁴ and the randomised trial ‘A placebo controlled randomised trial of intravenous

lidocaine in accelerating gastrointestinal recovery after colorectal surgery’ (ALLEGRO) may provide additional information to guide risk stratification of patients. However, it is likely that a large prospective cohort study with robust definitions of postoperative ileus and risk factors will be required to answer this question accurately. Despite advances in other aspects of the art and science, the community seems to have made little progress in the prediction and mitigation of ileus. As a condition seen following most gastrointestinal surgery, this condition should be a focus for researchers and funders.

Acknowledgements

The authors are thankful to all attendees of the Gastrointestinal Recovery Research Day (28 April 2017; Royal College of Surgeons of England, London), supported by the Association of Coloproctology of Great Britain and Ireland Delphi research programme and the Bowel Disease Research Foundation.

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