BJS Open, 2023, zrad054
https://doi.org/10.1093/bjsopen/zrad054
Systematic Review

Global cost of postoperative ileus following abdominal surgery: meta-analysis

Luke Traeger[1,2,*], Michalis Koullouros[1,2], Sergei Bedrikovetski[1,2], Hidde M. Kroon[1,2], James W. Moore[1,2] and Tarik Sammour[1,2]

[1]Colorectal Unit, Department of Surgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia
[2]Faculty of Health and Medical Sciences, Adelaide Medical School, University of Adelaide, Adelaide, South Australia, Australia

*Correspondence to: Luke Traeger, Colorectal Unit, Department of Surgery, Royal Adelaide Hospital, Port Road, Adelaide, South Australia, 5000, Australia (e-mail: luke.traeger@sa.gov.au)

Poster presented at the Royal Australasian College of Surgeons Annual Scientific Congress, Brisbane, Australia, May 2022

Abstract

Background: Following abdominal surgery, postoperative ileus is a common complication significantly increasing patient morbidity and cost of hospital admission. This is the first systematic review aimed at determining the average global hospital cost per patient associated with postoperative ileus.

Methods: A systematic search of electronic databases was performed from January 2000 to March 2023. Studies included compared patients undergoing abdominal surgery who developed postoperative ileus to those who did not, focusing on costing data. The primary outcome was the total cost of inpatient stay. Risk of bias was assessed using the Newcastle–Ottawa assessment tool. Summary meta-analysis was performed.

Results: Of the 2071 studies identified, 88 papers were assessed for full eligibility. The systematic review included nine studies (2005–2022), investigating 1 860 889 patients undergoing general, colorectal, gynaecological and urological surgery. These studies showed significant variations in the definition of postoperative ileus. Six studies were eligible for meta-analysis showing an increase of €8233 (95 per cent c.i. (5176 to 11 290), $P < 0.0001$, $I^2 = 95.5$ per cent) per patient with postoperative ileus resulting in a 66.3 per cent increase in total hospital costs (95 per cent c.i. (34.8 to 97.9), $P < 0.0001$, $I^2 = 98.4$ per cent). However, there was significant bias between studies. Five colorectal-surgery-specific studies showed an increase of €7242 (95 per cent c.i. (4502 to 9983), $P < 0.0001$, $I^2 = 86.0$ per cent) per patient with postoperative ileus resulting in a 57.3 per cent increase in total hospital costs (95 per cent c.i. (36.3 to 78.3), $P < 0.0001$, $I^2 = 85.7$ per cent).

Conclusion: The global financial burden of postoperative ileus following abdominal surgery is significant. While further multicentre data using a uniform postoperative ileus definition would be useful, reducing the incidence and impact of postoperative ileus are a priority to mitigate healthcare-related costs, and improve patient outcomes.

Introduction

Patients are at risk of impaired gastrointestinal function following intra-abdominal surgery, frequently leading to postoperative ileus (POI). The resulting diet intolerance, abdominal distention, nausea and vomiting are uncomfortable and distressing for patients[1]. POI is also associated with significant morbidity such as pneumonia, delayed wound healing, increased risk of anastomotic failure and organ failure, which prolong the duration of stay, increase 30-day readmission rates and carry a mortality risk[1–4]. Depending on the type of surgery, the incidence of POI ranges from 7 to 27 per cent, with colorectal surgery having the highest incidence, despite implementing enhanced recovery protocols (ERPs)[1–5]. To improve current ERPs with the aim of reducing the incidence of POI, several novel therapies, such as alvimopan, and trials using laxatives have been investigated with varied success[6,7]. Despite these efforts, however, incidences of POI remain high[1,8].

The cost of hospital admission approximately doubles regardless of the severity and type of complication following abdominal surgery[9]. As a result, in the Australian healthcare system in 2003–2004, an extra €180 (AU$460) million (16 per cent of total expenditure on healthcare costs) was spent on complications[10]. In the USA, future expenditure on surgical healthcare is set to exceed €900 million (US$1 trillion) by 2025, accounting for one-fourteenth of the US economy[11]. Unfortunately, surgical complications will contribute significantly to this financial burden.

The increased morbidity and prolonged hospital stay secondary to POI are significant contributors to the financial burden of complications on healthcare systems, as POI remains one of the most common complications after abdominal surgery. Previous studies have demonstrated a 50–100 per cent increase in total hospital costs per patient due to increased staffing costs, imaging, pharmacy and laboratory services[12–19]. In the authors' single-centre experience, an approximate €5000

Received: December 15, 2022. **Revised:** April 02, 2023. **Accepted:** April 09, 2023

(AU$8000) increase in total hospital costs was found, amounting to a 26.4 per cent increase in total hospital costs per patient after the development of POI[20]. International efforts to mitigate this cost are urgently needed.

The aim was to undertake the first systematic review and meta-analysis to identify the costs attributable to POI for patients after intra-abdominal surgery and better understand the financial burden of POI on the healthcare system globally.

Methods

This study was registered prospectively with the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42021275071) and is reported in adherence to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[21].

Search strategy

A systematic search was performed by two independent reviewers (L.T. and M.K.) of PubMed (2000–2023), OVID MEDLINE (2000–2023), EMBASE (2000–2023), Cochrane Library (2005–2023), Clinicaltrials.gov, and Cumulative Index of Nursing and Allied Health Literature (CIANHL) databases (2000–2023). Studies were included until 9 March 2023. Medical subject headings (MeSH) and keyword search terms related to 'cost', 'economics', 'abdominal', 'surgery' and 'ileus' were used. The search strategies are provided in *Table S1*.

Eligibility criteria

Studies were included for full-text review if they were related to POI following intra-abdominal surgery. Inclusion criteria were RCTs or non-RCTs, including human patients over 18 years of age undergoing abdominal surgery diagnosed with POI, investigating the cost of POI. Articles were excluded if they were short communications, reviews, opinion pieces and case reports. Spinal surgery studies were also excluded as from the articles it was unclear if the surgery was performed via an intraperitoneal approach and/or there was a neurogenic cause of intestinal paralysis. Pancreatic studies were also excluded as it was unclear if delayed return of gastrointestinal function was related to delayed gastric emptying or POI. Finally, patient studies with a mechanical cause of bowel obstruction were also excluded.

Study selection

Studies were selected using Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). Both reviewers individually screened titles and abstracts. The reference lists of the articles that were reviewed full text were also checked to identify potential additional articles. Any disagreements were resolved by consensus arbitrated by a third author (S.B.).

Data extraction and synthesis

Two reviewers (L.T. and M.K.) extracted the data independently using a predefined standard data extraction form. Extracted baseline data included author name, country, year, study design, patient population, surgery type, number of patients, definition of POI and incidence of POI.

Risk of bias in individual studies

Risk of bias was recorded using the Newcastle–Ottawa scale and was tabulated, assessed by L.T. and M.K.[22]. A rating of 0 to 9 was allocated to each study, using parameters of patient selection, comparability of the study groups and outcomes reported. Good quality studies had a score of more than or equal to 7.

Outcomes and statistical analysis

The primary outcomes extracted included total hospital cost. The currency of total hospital cost and percentage change between the POI and non-POI groups was recorded. Secondary outcomes included total hospital costs per department. Data were corroborated following extraction and any discrepancies in the extracted data were resolved by the third reviewer (S.B.). Descriptive statistics were used for individual patient data analysis. No assumptions for missing data were made. Costing data were adjusted to euros (€) for 2021. Costs were adjusted for consumer price inflation dependent on the study countries[23–25]. Exchange rates were taken on 31 December 2021[26].

Summary statistics (mean (standard deviation)) were provided or able to be extracted from the included studies[27–29]. For analysis, mean difference and standard error were calculated using MedCalc for Windows®, version 19.4 (MedCalc Software, Ostend, Belgium). Summary meta-analysis of data was performed using StatsDirect software Version 3 (StatsDirect Ltd, Birkenhead, Wirral, UK). Results are presented as total pooled mean difference in total cost (€), with 95 per cent c.i. and forest plots. For overall effect $P < 0.050$ was considered statistically significant. Heterogeneity was estimated using Cochran's Q test and I^2 was considered statistically significant when $P < 0.050$ for the Cochran's Q test and $I^2 > 50$ per cent. Given the heterogeneity of the data, random weights were used for pooled meta-analyses. Risk of bias was analysed using Egger's method, in which $P < 0.050$ indicated significant bias.

Results

The literature search identified 2071 studies of which 953 were duplicates and were removed. Of the 1118 studies screened for title and abstract, 1030 were irrelevant. Eighty-eight studies were screened in full-text review, with nine studies meeting the inclusion criteria (*Fig. 1*)[12–20].

Characteristics of studies

The nine included studies came from four countries and were published between 2005 and 2022. They included a total of 1 860 889 patients, undergoing a range of procedures from general surgical, colorectal, gynaecological and urological surgery[12–20]. No studies were randomized. Seven studies[12–15,17,19,20] were retrospective in design and two studies[16,18] contained prospectively collected data. The complete study characteristics are provided in *Table 1*.

Surgical procedures

The included studies explored the cost of POI in a wide variety of surgeries, summarized in *Table 1*. Five studies reported colorectal surgical procedures alone[12,15,16,18,20], two studies reported gynaecological, general surgical and colorectal cases together[14,19], one study reported colorectal and general surgical cases[13]. One study explored urological cases[17]. Six studies investigated open and laparoscopic approaches to surgery[12,13,15,16,18,20]. One study investigated an open surgical approach[17] and in two studies the surgical approach was unclear[14,19]. Four studies had postoperative care guided by an

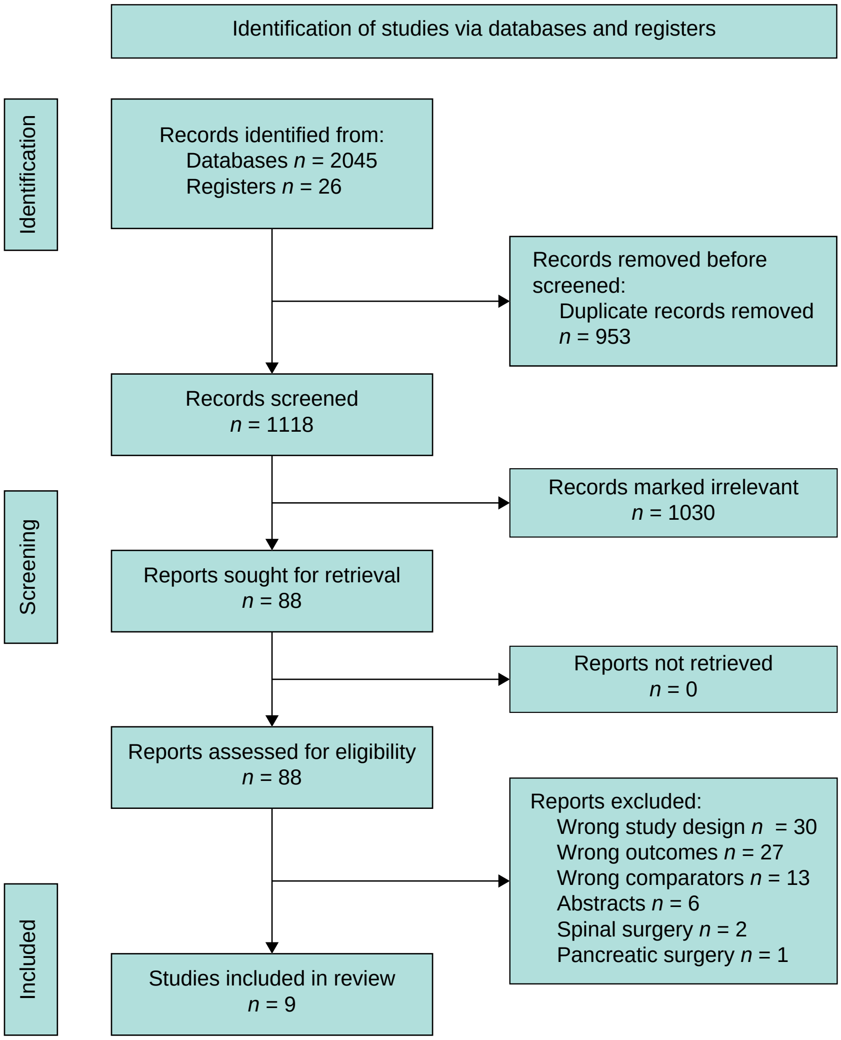

Fig. 1 PRISMA flow chart
Adapted from Page *et al.*[30]

ERP[12,16,18,20], and five studies did not state if an ERP was used after the operations[13–15,17,19].

Definition and incidence of POI

In total, 170 947 (9.2 per cent) patients were diagnosed with POI[12–20]. Five studies diagnosed POI based on clinical factors, provided in *Table 1* and *Table S2*[12,16,18–20]. Four studies diagnosed POI based on ICD-9 codes[13–15,17]. There was heterogeneity in the incidence of POI, 3.2–34.9 per cent, dependent on the type of procedures. In papers reporting colorectal procedures alone, the incidence of POI varied from 17.4 to 34.9 per cent[12,15,16,18,20].

Total cost

Of the available studies, eight studies demonstrated a significant increase in total hospital costs attributable to POI[12–17,19,20]. The one remaining study did report an increase in total cost[18], however, this did not reach significance. This study was the only study that reported estimates of costs billed, while the other studies reported actual billing costs[18]. Percentage increases ranged from 26.3 per cent to 100.5 per cent in total cost (*Table 2*).

Secondary outcomes

Three studies looked at individual departmental costs (*Table 3*)[12,16,20]. Asgeirsson *et al.* found significant increases in hospital costs, pharmacy costs and laboratory tests[12]. Mao *et al.* found statistical increases in medical, laboratory, radiological, medication as well as ward and allied health costs[16]. Traeger *et al.* showed increases in staffing, operating room, pharmacy, supplies and hospital services costs[20]. Two studies found no difference in radiological costs[12,20] and two studies found no difference in operating room costs[12].

Assessment of risk of bias

All studies were of good quality when assessed with the Newcastle–Ottawa scale. Four studies had a score of 7[12,14,16,19], four studies had a score of 8[13,17,18,20] and one study had a score of 9[15]. Risk of bias is summarized in *Table 4*.

Pooled meta-analysis

Of the identified studies, six could be included in the meta-analysis for the primary endpoint of costs of POI[12,13,15,16,18,20]. Three studies provided mean and standard deviation[12,15,20]. For three studies, mean and standard deviations could be derived from available data[13,16,18]. The other

Table 1 Characteristics of included studies

Reference	Country, year	Design	Specialty type	Surgical approach	Perioperative care strategy	No. of patients POI/no POI	Definition of POI	Reported rate of POI
Asgeirrson[12]	USA, 2010	Retrospective single-centred	Colorectal	Open & LAP	ERP	45/141	Clinical	24.2%
Gan[13]	USA, 2015	Retrospective multicentred	Colorectal & general surgery	Open & LAP	Not stated	14 221/123 847	ICD-9 code	Open colectomy: 20.6% LAP colectomy: 14.6% Open cholecystectomy: 11.6% LAP cholecystectomy: 3.2%
Goldstein[14]	USA, 2007	Retrospective multicentred	Gynaecological, colorectal, general surgery	Not stated	Not stated	142 026/1 519 663	ICD-9 code	Abdominal hysterectomy: 4.1% Large bowel colectomy: 14.9% Small bowel resection: 19.2% Appendicectomy: 6.2% Cholecystectomy: 8.5% Nephrectomy: 8.9%
Iyer[15]	USA, 2009	Retrospective multicentred	Colorectal	Open & LAP	Not stated	3115/14 761	ICD-9 code	17.4%
Mao[16]	New Zealand, 2018	Prospective single-centred	Colorectal	Open & LAP	ERP	88/237	Clinical	27.0%
Nutt[17]	USA, 2018	Retrospective multicentred	Urology	Not stated	Not stated	11 155/30 343	ICD-9 code	26.9%
Peters[18]	The Netherlands, 2019	Prospective multicentred	Colorectal	Open & LAP	ERP	66/199	Clinical	24.9%
Salvador[19]	USA, 2005	Retrospective single-centred	Colorectal & gynaecological	Not stated	Not stated	Hysterectomy: 60/331 Colectomy: 35/141	Clinical and ICD-9 code	Hysterectomy: 18.2% Hemicolectomy: 24.5%
Traeger[20]	Australia, 2022	Retrospective single-centred	Colorectal	Open & LAP	ERP	145/270	Clinical	34.9%

ERP, enhanced recovery protocol; LAP, laparoscopic; POI, postoperative ileus.

three studies were contacted for data availability[14,17,19]. Data were not available for one[14], with two studies being unable to be contacted[17,19].

Pooled results showed that total hospital cost for patients with POI was €8233 (95 per cent c.i. (5176–11 290), $P < 0.001$, $I^2 = 95.5$ per cent, Egger's: $P = 0.004$) higher than those without POI (*Table 5* and *Fig. 2*). When comparing percentages, patients with POI had a 66.3 per cent increase of total hospital cost (95 per cent c.i. (34.8 to 97.9), $P < 0.001$, $I^2 = 98.4$ per cent, Egger's: $P = 0.132$). The difference in cost demonstrated significant heterogeneity and bias, however, the percentage difference was not found to be biased.

Pooled results for colorectal-specific studies showed an increase in total hospital costs for patients with POI of €7242 (95 per cent c.i. (4502 to 9983), $P < 0.001$, $I^2 = 86$ per cent, Egger's: $P = 0.080$) (*Table 6* and *Fig. 3*). When comparing the percentages, patients with POI had a 57.3 per cent increase of total hospital cost compared with those without POI (95 per cent c.i. (36.3 to 78.3), $P < 0.001$, $I^2 = 85.7$ per cent Egger's: $P = 0.560$). For colorectal-specific studies, the pooled results demonstrate significant heterogeneity, but were not found to be biased.

Discussion

In this first systematic review of the global financial impact of POI on hospitals, nine studies were identified and eligible for inclusion. The meta-analyses, in which six studies could be included, showed that total hospital costs increased by approximately €8233 or 66.3 per cent per patient with POI. However, there was significant heterogeneity bias between studies[12,13,15,16,18,20].

Defining POI remains contentious. In a systematic review, Vather *et al.* highlighted the range of different definitions commonly used for POI[31]. Consequently, this variety of definitions has implications on the reported POI incidence rates and subsequently on the total hospital costs attributed to POI. To overcome this, the ICD-9 diagnostic codes can be used rather than the clinical signs and symptoms to diagnose POI. However, studies using ICD-9 codes have reported significantly lower incidence rates of POI, leading to an underestimation of the true POI rate and its associated financial burden[12–15]. This was shown clearly in a prospective study in 203 patients, comparing administrative use of ICD-9 codes against a clinical definition of

Table 2 Reported total cost per patient

Reference	Subgroup	Currency, year, statistic	Costing data source (estimate/ actual)	Total cost (per patient)			Total cost (per patient) converted to € (2021)		
				POI	Non-POI	P	Mean (s.d.) POI	Mean (s.d.) non-POI	% change
Asgeirsson[12]	Colectomy	USD, 2010 mean (s.d.)	Hospital accounting system (actual)	$15 914 (13 756) (*n* = 45)	$8316 (4808) (*n* = 141)	<0.05	€17 391 (15 033)	€9088 (5254)	91.4%
Gan[13]	Cholecystectomy and colectomy	USD, 2008–2010 median (i.q.r.)	Premier database (actual)	$21 046 (14 062–35 176) (*n* = 14 212)	$10 945 (7489–16 682) (*n* = 123 847)	<0.001	€25 733 (17 106)	€12 833 (7447)	100.5%
	Open colectomy			$24 078 (*n* = 8303)	$17 044 (*n* = 31 947)	–	–	–	41.3%
	LAP colectomy			$17 505 (*n* = 2577)	$12 521 (*n* = 15 121)	–	–	–	39.8%
	Open cholecystectomy			$20 808 (*n* = 1191)	$13 135 (*n* = 9035)	–	–	–	58.4%
	LAP cholecystectomy			$15 842 (*n* = 2218)	$8529 (*n* = 67 676)	–	–	–	85.7%
Goldstein[14]	Gynaecology, urology, general surgery	USD, 2002 mean	Premier database (actual)	$18 877 (*n* = 142 026)	$9460 (*n* = 1 519 663)	–	–	–	99.6%
Iyer[15]	Colectomy	USD, 2004, mean (s.d.)	Premier database (actual)	$25 089 (35 386) (*n* = 3115)	16 907 (29 320) (*n* = 14 761)	<0.001	€31 650 (44 639)	€21 328 (36 988)	48.4%
Mao[16]	Colorectal surgery	NZD, 2012–2014, median (i.q.r.)	Hospital accounting system (actual)	$27 981 (20 198–42 174) (*n* = 88)	$16 317 (10 620–23 722) (*n* = 237)	<0.005	€20 977 (11 501)	€11 745 (6750)	78.8%
Nutt[17]	Radical cystectomy	USD, 2006–2012, median	USA healthcare Cost and utilization project data (actual)	$32 472 (*n* = 11 155)	$24 600 (*n* = 30 343)	<0.001	—	—	32.0%
Peters[18]	Colorectal	Euro, 2019, mean (95% c.i.)	IMAT MCQ (estimate)	€7549 (4605–10 494) (*n* = 66)	€5052 (3752–6354) (*n* = 199)	0.087	€7760 (12 546)	€5193 (9625)	49.4%
Salvador[19]	Hysterectomy	USD, 2001–2002, Mean (median)	Hospital accounting system (actual)	$12 502 (12 161) (*n* = 60)	$7990 (7375) (*n* = 331)	–	–	–	56.5%
	Colectomy			$28 823 (26 669) (*n* = 35)	$16 407 (11 765) (*n* = 141)	–	–	–	75.7%
Traeger[20]	Colorectal	AUD, 2018–2021, mean (s.d.)	Hospital accounting system (actual)	$37 690 (21 587) (*n* = 145)	$29 822 (20 410) (*n* = 270)	<0.001	€24 093 (13 800)	€19 070 (13 047)	26.3%

AUD, Australian dollars; IMTA MCQ, Institute for Medical Technology Assessment Medical Consumption Questionnaire; LAP, laparoscopic; NZD, New Zealand dollars; POI, postoperative ileus; USD, United States dollars; i.q.r., interquartile range.

POI, demonstrating that 35 per cent of the patients were not coded appropriately[32]. This highlighted that clinicians significantly underestimated the incidence of POI as a complication and represented a missed opportunity for reimbursement of approximately €6700 (US$7400) per patient. Extrapolating these data, Cromwell *et al.* estimated that underreporting of POI represents an annual missed opportunity for reimbursement of €90 (US$100) million[32]. This decreases the reliability of studies defining POI using the ICD-9 method.

The global prevalence of POI is unclear. To estimate the impact of POI in the USA, Solanki *et al.* using ICD codes found 470 110 patients in the USA were hospitalized with POI in 2011[33]. Using our findings, this would represent an increase in total hospital cost by €3.9 billion secondary to POI. This likely represents an underestimation given the inaccuracy of coding data, and the true global value of POI is significantly higher.

Intra-abdominal surgery in particular carries a high risk of POI as a complication. This study highlights the breadth of surgeries affected, with information provided on costs of POI following general, colorectal, gynaecological and urological surgery. Colorectal surgery carries the highest risk of POI due to specific factors such as handling of the bowel, splenic flexure mobilization, stoma formation, open approach and rectal resections[34–36]. In previous studies looking at colorectal procedures, the incidence of POI was reported as 17.4–34.9 per cent[12,15,16,18,20]. When looking at colorectal-specific studies, POI increased total hospital cost by €7242 per patient, and an increase of total hospital costs by 57.3 per cent per patient.

Due to the range of POI definitions used and variation in the collection of costing data, meaningful comparisons between specialties and procedures remain challenging. The present study highlights this heterogeneity between studies. This is

Table 3 Departmental costs–total cost (per patient)

Reference	Department	Currency, year, statistic	POI	Non-POI	P	% Change
Asgeirsson[12]	Hospital	USD, 2010, mean (s.d.)	$7258 ($4110)	$3165 ($2641)	<0.05	129.3% increase
	Pharmacy		$2639 ($3254)	$454 ($1128)	<0.05	481.3% increase
	Radiology		$153 ($110)	$37 ($116)	–	313.5% increase
	Operating room		$4823 ($1261)	$4260 ($11 222)	–	13.2% increase
	Labarotory tests		$579 ($342)	$252 ($282)	<0.05	129.8% increase
Mao[16]	Medical	NZD, 2014 median (i.q.r.)	$4484 ($3498–$6641)	$2583 ($1870–$3943)	<0.005	73.6% increase
	Laboratory		$2688 ($1319–$3666)	$1287 ($401–$2266)	<0.005	108.9% increase
	Radiology		$687 ($109–$1534)	$0 ($0–$247)	<0.005	–
	Medication		$735 ($416–$1745)	$348 ($216–$496)	<0.005	111.2% increase
	Ward and nursing		$8457 ($5742–$13 381)	$3816 ($2598–$6573)	<0.005	121.6% increase
	Allied health		$349 ($184–$438)	$229 ($138–$367)	<0.005	52.4% increase
Traeger[20]	Medical staff	AUD, 2021 mean (s.d.)	$1784 ($2190)	$2544 ($1917)	<0.001	42.6% increase
	Nursing staff		$4365 ($4232)	$6105 ($4014)	<0.001	39.9% increase
	Allied health staff		$217 ($604)	$483 ($1127)	<0.001	122.5% increase
	Indirect salary costs		$2546 ($1991)	$3279 ($2226)	<0.001	28.8% increase
	Critical care		$12 921 ($10 673)	$11 656 ($7831)	0.337	9.8% decrease
	Theatre		$12 759 ($6099)	$13 781 ($5694)	0.046	8.0% increase
	Imaging		$803 ($1117)	$823.21 ($858)	0.452	2.5% increase
	Pathology		$866 ($820)	$977 ($723)	0.096	12.8% increase
	Pharmacy		$326 ($730)	$513.38 ($746)	0.006	57.4% increase
	Supplies		$1900 ($1864)	$2693 ($1736)	<0.001	41.7% increase
	Hospital services		$951 ($835)	$1241 ($819)	<0.001	30.4% increase

USD, United States dollars; NZD, New Zealand dollars; AUD, Australian dollars.

Table 4 Newcastle–Ottawa quality assessment for included studies

Reference	Selection	Comparability	Outcomes	Overall
Asgeirsson[12]	****	*	**	7
Gan[13]	***	**	***	8
Goldstein[14]	****		***	7
Iyer[15]	****	**	***	9
Mao[16]	***	*	***	7
Nutt[17]	****	**	**	8
Peters[18]	***	**	***	8
Salvador[19]	****		***	7
Traeger[20]	****	*	***	8

likely not only the result of variations between surgical specialties and methods of defining POI, but also due to the differences in how healthcare is funded throughout the globe. Of the nine studies included, five were single-centred studies, thus reducing the generalizability. To enhance the analysis and reduce the impact of global differences on the overall total hospital costs, the pooled percentage differences showed a 66.3 per cent increase in total hospital costs. The significance of this increase in total hospital cost highlights the financial burden of POI on the healthcare system globally. Efforts aimed at reducing POI could not only improve patient safety, but also allow the reallocation of these funds to other aspects of healthcare.

The present review identified three studies investigating the breakdown of total hospital costs[12,16,20]. These studies highlighted that total hospital costs were primarily attributable to ward staffing, pharmacy and laboratory costs. The increase in these departmental costs is largely due to the prolonged duration of hospital stay. In Australia, complications during admission have accounted for 15.7 per cent of hospital expenditure[10]. Targeted interventions to reduce the incidence of POI after abdominal surgery, or the impact of this on patients, could significantly reduce this financial burden. Preventing POI, for instance, could remove direct impediments to the recovery of patient autonomy, as well as reduce delayed discharges by 33 per cent, readmissions by 20 per cent and mortality by 20 per cent[8,37].

To reduce the morbidity and associated financial burden of POI, the included papers provide several suggested strategies. Although considered the mainstay of postoperative care, five studies suggested that ERPs target the risk factors for POI by improving postoperative fluid management and nutrition and reducing opioid consumption[12,13,16–18]. Despite this, only four of the nine included studies specified they routinely used an ERP[12,16,18,20]. To reduce the effects of opioid use, peripherally acting μ-opioid receptor antagonists such as alvimopan and methylnaltrexone were also discussed as potential treatments to reduce the incidence of POI[14,16,19]. Three research groups associated with the papers included in this review investigated alvimopan and methylnaltrexone to improve gastrointestinal recovery after operations with varied success[38–40]. However, the current evidence for the use of alvimopan as part of an ERP is low-moderate, and use is supported mainly in open abdominal surgery[41].

Several alternative therapies were also suggested in the reviewed papers. Peters *et al.* highlighted that POI was associated with the systematic inflammatory response and the authors of this paper trialled vagal nerve activation, nutritional interventions and chewing gum in clinical trials to reduce POI[18,42,43]. Gastrografin and prucalopride were also used in clinical trials to treat and prevent POI, following the cost of POI being investigated[44,45]. In our own experience, we are performing an RCT using pyridostigmine, an acetylcholinesterase inhibitor, to modulate the cholinergic anti-inflammatory pathway that is key in the development of POI[46]. The results of this double-blinded RCT are forthcoming.

This meta-analysis has some limitations. In this study we did not include papers that explored the cost due to the patient being readmitted to hospital with delayed POI. Secondly, this study highlights that due to a variety of surgical specialties involved, there was significant heterogeneity in data, which must be considered when interpreting the findings of this analysis. This is likely compounded by differences in healthcare systems between countries. To overcome this limitation, a

Table 5 Summary meta-analysis with values converted to € (2021)

Studies	POI (*n*)	Mean (s.d.) POI	Non-POI (*n*)	Mean (s.d.) non-POI	Mean difference (95% c.i.)	% Weights (random)	Mean percentage difference (95% c.i.)	% Weights (random)
Asgeirsson[12]	45	€17 391 (15 033)	141	€9088 (5254)	€8303 (5377–11 229)	15.7%	91.4% (59.2–123.6)	15.6%
Gan[13]	14 221	€25 733 (17 106)	123 847	€12 833 (7447)	€12 900 (12,745–13 055)	18.3%	100.5% (99.3–101.7)	18.6%
Iyer[15]	3115	€31 650 (44 639)	14 761	€21 328 (36 988)	€10 322 (8837—11 807)	17.5%	48.4% (41.4–55.4)	18.5%
Mao[16]	88	€20 977 (11 501)	237	€11 745 (6750)	€9252 (7213–11 291)	16.9%	78.8% (61.4–96.1)	17.6%
Peters[18]	66	€7760 (12 546)	199	€5193 (9625)	€2567 (−348 to 5482)	15.6%	49.4% (−6.7 to 105.6)	11.7%
Traeger[20]	145	€24 093 (13 800)	270	€19 070 (13 047)	€5023 (2328–7718)	16.0%	26.3% (12.2–40.5)	18.0%
Pooled					€8233 (5176–11,290)	100%	66.3% (34.8–97.9)	100%

Mean difference. Heterogeneity: Cochran Q 112.29 (d.f. 5), $P < 0.001$, $I^2 = 95.5\%$ (95% c.i. 93.3 to 96.8). Z (test) = 5.28, $P < 0.001$. Egger's: bias −4.89 (95% c.i. −7.13 to −2.65), $P = 0.004$. **Percentage difference.** Heterogeneity: Cochran Q 315.50 (d.f. 5), $P < 0.001$, $I^2 = 98.4$ per cent (95% c.i. 98.0 to 98.7). Z (test) = 4.12, $P < 0.001$. Egger's: bias −5.97 (95% c.i. −14.76 to 2.81), $P = 0.132$. POI, postoperative ileus.

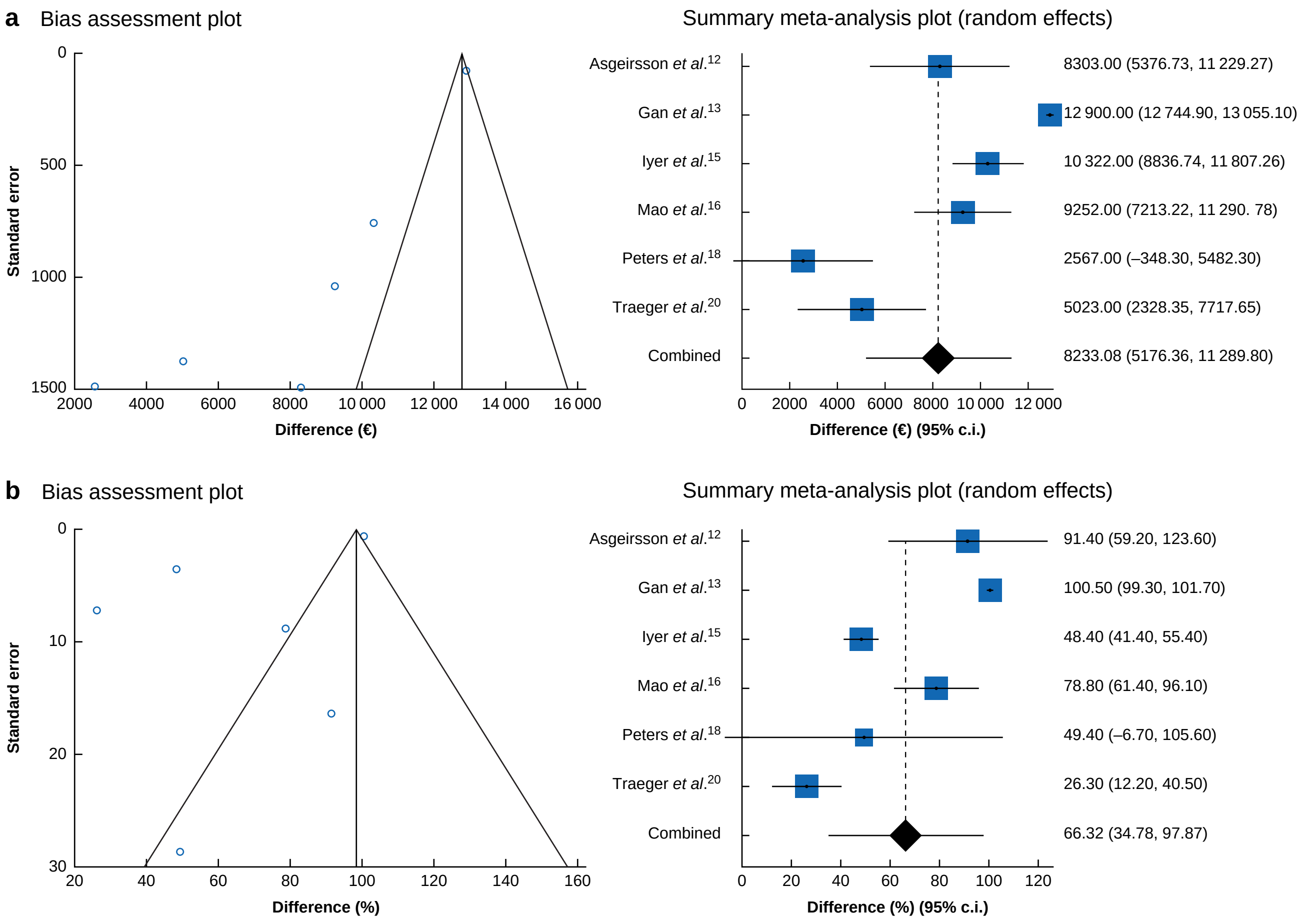

Fig. 2 Meta-analysis plots
a Mean difference and **b** percentage difference.

Table 6 Summary meta-analysis for colorectal studies with values converted to € (2021)

Studies	*n* POI	Mean (s.d.) POI	*n* non-POI	Mean (s.d.) non-POI	Mean difference (95% c.i.)	% Weights (random)	Mean percentage difference (95% c.i.)	% Weights (random)
Asgeirsson[12]	45	€17 391 (15 033)	141	€9088 (5254)	€8303 (5377–11 229)	18.7%	91.4% (59.2–123.6)	16.7%
Iyer[15]	3115	€31 650 (44 639)	14 761	€21 328 (36 988)	€10 322 (8837–11 807)	22.2%	48.4% (41.4–55.4)	26.6%
Mao[16]	88	€20 977 (11 501)	237	€11 745 (6750)	€9252 (7213–11 291)	21.1%	78.8% (61.4–96.1)	23.1%
Peters[18]	66	€7760 (12 546)	199	€5193 (9625)	€2567 (−348 to 5482)	18.7%	49.4% (−6.7–105.6)	9.2%
Traeger[20]	145	€24 093 (13 800)	270	€19 070 (13 047)	€5023 (2328–7718)	19.3%	26.3% (12.2–40.5)	24.4%
Pooled					€7242 (4502–9983)	100%	57.3% (36.3–78.3)	100%

Mean difference. Heterogeneity: Cochran Q 28.49 (d.f. = 4), $P < 0.001$, $I^2 = 86.0\%$ (95% c.i. 64.5 to 92.2). Z (test) = 5.18, $P < 0.0001$. Egger's: bias −7.22 (95% c.i. −16.05 to 1.60), $P = 0.080$. **Percentage difference.** Heterogeneity: Cochran Q 27.88 (d.f. 4), $P < 0.001$, $I^2 = 85.7\%$ (95% c.i. 63.3 to 92.1). Z (test) = 5.35, $P < 0.001$. Egger's: bias 1.48 (95% c.i. −5.73 to 8.69), $P = 0.560$. POI, postoperative ileus.

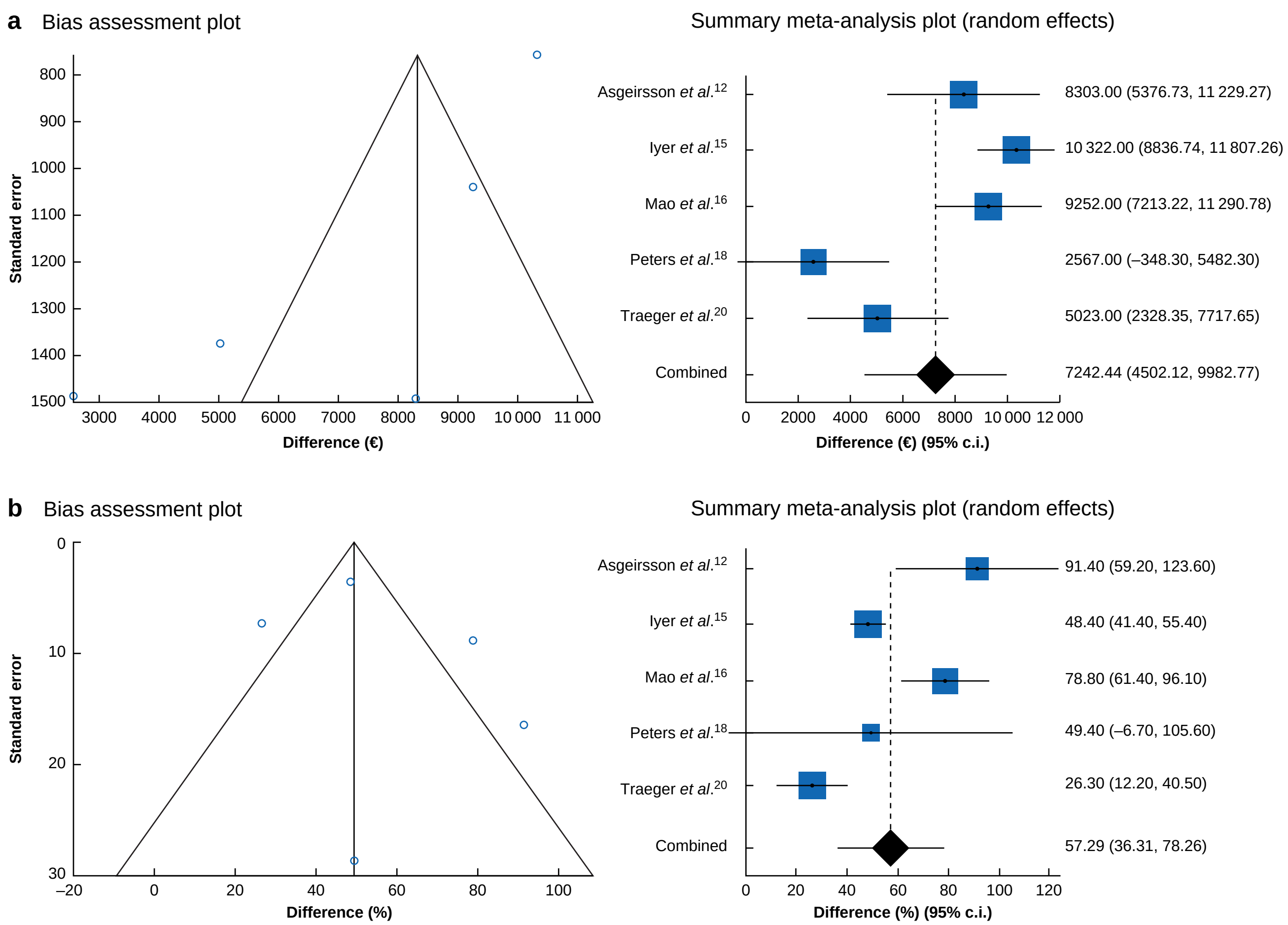

Fig. 3 Meta-analysis plots
a Mean difference and **b** percentage difference for colorectal studies.

colorectal-specific analysis was performed, investigating the percentage increase in total hospital costs in addition to the absolute cost. Moreover, in several of these studies it is unclear if the cost increase is attributable to POI alone and the contribution of other complications to this cost.

The global financial burden of POI following abdominal surgery is significant. While further multicentre data using a uniform POI definition would be useful, it is clear from these data that the costs associated with POI are globally significant. Efforts aimed at reducing the incidence of POI with ERPs and investigating adjunctive therapies such as pyridostigmine are a priority to reduce healthcare-related costs, and improve patient experience and outcome.

Funding

L.T. was supported by the Royal Adelaide Hospital Research Committee Dawes and Colorectal Research Group Scholarship (a1175080) and University of Adelaide Research Training Program Stipend (a1175080). Funding for open access was provided by a Central Adelaide Local Health Network CEO CRIPS grant.

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author contributions

Luke Traeger (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing—original draft), Michalis Koullouros (Data curation, Formal analysis, Investigation, Writing—original draft), Sergei Bedrikovetski (Formal analysis, Investigation, Methodology, Writing—original draft), Hidde Kroon (Methodology, Writing—original draft, Writing—review & editing), James Moore (Supervision, Validation, Writing—review & editing) and Tarik Sammour (Supervision, Validation, Writing—review & editing).

References

1. Vather R, Bissett I. Management of prolonged post-operative ileus: evidence-based recommendations. *ANZ J Surg* 2013;**83**: 319–324
2. Alhashemi M, Fiore JF Jr, Safa N, Al Mahroos M, Mata J, Pecorelli N *et al.* Incidence and predictors of prolonged postoperative ileus after colorectal surgery in the context of an enhanced recovery pathway. *Surg Endosc* 2019;**33**:2313–2322

3. Ceretti AP, Maroni N, Longhi M, Giovenzana M, Santambrogio R, Barabino M *et al.* Risk factors for prolonged postoperative ileus in adult patients undergoing elective colorectal surgery: an observational cohort study. *Rev Recent Clin Trials* 2018;**13**:295–304
4. Wolthuis AM, Bislenghi G, Fieuws S, de Buck van Overstraeten A, Boeckxstaens G, D'Hoore A. Incidence of prolonged postoperative ileus after colorectal surgery: a systematic review and meta-analysis. *Colorectal Dis* 2016;**18**:O1–O9
5. Li Z-L, Zhao B-C, Deng W-T, Zhuang P-P, Liu W-F, Li C *et al.* Incidence and risk factors of postoperative ileus after hysterectomy for benign indications. *Int J Colorectal Dis* 2020;**35**:2105–2112
6. Vaughan-Shaw PG, Fecher IC, Harris S, Knight JS. A meta-analysis of the effectiveness of the opioid receptor antagonist alvimopan in reducing hospital length of stay and time to GI recovery in patients enrolled in a standardized accelerated recovery program after abdominal surgery. *Dis Colon Rectum* 2012;**55**:611–620
7. Dudi-Venkata NN, Kroon HM, Bedrikovetski S, Lewis M, Lawrence MJ, Hunter RA *et al.* Impact of STIMUlant and osmotic LAXatives (STIMULAX trial) on gastrointestinal recovery after colorectal surgery: randomized clinical trial. *Br J Surg* 2021;**108**:797–803
8. Scarborough JE, Schumacher J, Kent KC, Heise CP, Greenberg CC. Associations of specific postoperative complications with outcomes after elective colon resection: a procedure-targeted approach toward surgical quality improvement. *JAMA Surg* 2017;**152**:e164681
9. Vonlanthen R, Slankamenac K, Breitenstein S, Puhan MA, Muller MK, Hahnloser D *et al.* The impact of complications on costs of major surgical procedures: a cost analysis of 1200 patients. *Ann Surg* 2011;**254**:907–913
10. Ehsani JP, Jackson T, Duckett SJ. The incidence and cost of adverse events in Victorian hospitals 2003-04. *Med J Aust* 2006;**184**:551–555
11. Munoz E, Munoz W 3rd, Wise L. National and surgical health care expenditures, 2005–2025. *Ann Surg* 2010;**251**:195–200
12. Asgeirsson T, El-Badawi KI, Mahmood A, Barletta J, Luchtefeld M, Senagore AJ. Postoperative ileus: it costs more than you expect. *J Am Coll Surg* 2010;**210**:228–231
13. Gan TJ, Robinson SB, Oderda GM, Scranton R, Pepin J, Ramamoorthy S. Impact of postsurgical opioid use and ileus on economic outcomes in gastrointestinal surgeries. *Curr Med Res Opin* 2015;**31**:677–686
14. Goldstein JL, Matuszewski KA, Delaney CP, Senagore A, Chiao EF, Shah M *et al.* Inpatient economic burden of postoperative ileus associated with abdominal surgery in the United States. *P&T* 2007;**32**:82–90
15. Iyer S, Saunders WB, Stemkowski S. Economic burden of postoperative ileus associated with colectomy in the United States. *J Manag Care Pharm* 2009;**15**:485–494
16. Mao H, Milne TGE, O'Grady G, Vather R, Edlin R, Bissett I. Prolonged postoperative ileus significantly increases the cost of inpatient stay for patients undergoing elective colorectal surgery: results of a multivariate analysis of prospective data at a single institution. *Dis Colon Rectum* 2019;**62**:631–637
17. Nutt M, Scaief S, Dynda D, Alanee S. Ileus and small bowel obstruction after radical cystectomy for bladder cancer: analysis from the nationwide inpatient sample. *Surg Oncol* 2018;**27**:341–345
18. Peters EG, Pattamatta M, Smeets BJJ, Brinkman DJ, Evers S, de Jonge WJ *et al.* The clinical and economical impact of postoperative ileus in patients undergoing colorectal surgery. *Neurogastroenterol Motil* 2020;**32**:e13862
19. Salvador CG, Sikirica M, Evans A, Pizzi L, Goldfarb N. Clinical and economic outcomes of prolonged postoperative ileus in patients undergoing hysterectomy and hemicolectomy. *P&T* 2005;**30**:590
20. Traeger L, Koullouros M, Bedrikovetski S, Kroon HM, Thomas ML, Moore JW *et al.* Cost of postoperative ileus following colorectal surgery: a cost analysis in the Australian public hospital setting. *Colorectal Dis* 2022;**24**:1416–1426
21. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;**62**:1006–1012
22. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M *et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses*. Ottawa, Canada: The Ottawa Hospital Research Institute, 2022
23. US Bureau of Labour Statistics. CPI Inflation Calculator. https://data.bls.gov/cgi-bin/cpicalc.pl (accessed 4 October 2022)
24. Reserve Bank of New Zealand. Inflation calculator. 2022. https://www.rbnz.govt.nz/monetary-policy/about-monetary-policy/inflation-calculator (accessed 4 October 2022)
25. Reserve Bank of Australia. Inflation calculator. 2021. https://www.rba.gov.au/calculator/annualDecimal.html (accessed 28 September 2021)
26. US Dollar Exchange Rates. 2022. https://www.exchangerates.org.uk (accessed 24 October 2022)
27. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res* 2018;**27**:1785–1805
28. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;**14**:135
29. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. https://www.math.hkbu.edu.hk/~tongt/papers/median2mean.html (accessed 4 October 2022)
30. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;**372**:n71
31. Vather R, Trivedi S, Bissett I. Defining postoperative ileus: results of a systematic review and global survey. *J Gastrointest Surg* 2013;**17**:962–972
32. Cromwell JW, Lund LW. Hospital coding of postoperative ileus: a prospective study. *Cureus* 2022;**14**:e24946
33. Solanki S, Chakinala RC, Haq KF, Singh J, Khan MA, Solanki D *et al.* Paralytic ileus in the United States: a cross-sectional study from the national inpatient sample. *SAGE Open Med* 2020;**8**:2050312120962636
34. Quiroga-Centeno AC, Jerez-Torra KA, Martin-Mojica PA, Castaneda-Alfonso SA, Castillo-Sanchez ME, Calvo-Corredor OF *et al.* Risk factors for prolonged postoperative ileus in colorectal surgery: a systematic review and meta-analysis. *World J Surg* 2020;**44**:1612–1626
35. Millan M, Biondo S, Fraccalvieri D, Frago R, Golda T, Kreisler E. Risk factors for prolonged postoperative ileus after colorectal cancer surgery. *World J Surg* 2012;**36**:179–185
36. Wolthuis AM, Bislenghi G, Lambrecht M, Fieuws S, van Overstraeten A de B, Boeckxstaens G *et al.* Preoperative risk factors for prolonged postoperative ileus after colorectal resection. *Int J Colorectal Dis* 2017;**32**:883–890
37. Viannay P, Hamel JF, Bougard M, Barbieux J, Hamy A, Venara A. Gastrointestinal motility has more of an impact on postoperative recovery than you might expect. *J Visc Surg* 2021;**158**:19–26

38. Earnshaw SR, Kauf TL, McDade C, Potashman MH, Pauyo C, Reese ES *et al.* Economic impact of alvimopan considering varying definitions of postoperative ileus. *J Am Coll Surg* 2015;**221**:941–950
39. Viscusi ER, Goldstein S, Witkowski T, Andonakakis A, Jan R, Gabriel K *et al.* Alvimopan, a peripherally acting mu-opioid receptor antagonist, compared with placebo in postoperative ileus after major abdominal surgery: results of a randomized, double-blind, controlled study. *Surg Endosc* 2006;**20**:64–70
40. Viscusi ER, Rathmell JP, Fichera A, Binderow SR, Israel RJ, Galasso FL *et al.* Randomized placebo-controlled study of intravenous methylnaltrexone in postoperative ileus. *J Drug Assess* 2013;**2**:127–134
41. Alhashemi M, Hamad R, El-Kefraoui C, Blouin MC, Amar-Zifkin A, Landry T *et al.* The association of alvimopan treatment with postoperative outcomes after abdominal surgery: a systematic review across different surgical procedures and contexts of perioperative care. *Surgery* 2021;**169**:934–944
42. van den Heijkant TC, Costes LM, van der Lee DG, Aerts B, Osinga-de Jong M, Rutten HR *et al.* Randomized clinical trial of the effect of gum chewing on postoperative ileus and inflammation in colorectal surgery. *Br J Surg* 2015;**102**:202–211
43. Peters EG, Smeets BJJ, Nors J, Back CM, Funder JA, Sommer T *et al.* Perioperative lipid-enriched enteral nutrition versus standard care in patients undergoing elective colorectal surgery (SANICS II): a multicentre, double-blind, randomised controlled trial. *Lancet Gastroenterol Hepatol* 2018;**3**:242–251
44. Vather R, Josephson R, Jaung R, Kahokehr A, Sammour T, Bissett I. Gastrografin in prolonged postoperative ileus: a double-blinded randomized controlled trial. *Ann Surg* 2015;**262**:23–30
45. Milne T, Liu C, O'Grady G, Woodfield J, Bissett I. Effect of prucalopride to improve time to gut function recovery following elective colorectal surgery: randomized clinical trial. *Br J Surg* 2022;**109**:704–710
46. Dudi-Venkata NN, Kroon HM, Bedrikovetski S, Traeger L, Lewis M, Lawrence MJ *et al.* PyRICo-Pilot: pyridostigmine to reduce the duration of postoperative ileus after colorectal surgery—a phase II study. *Colorectal Dis* 2021;**23**:2154–2160