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Review

A systematic review of the impact of post-operative oral fluid intake on ileus following elective colorectal surgery

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ABSTRACT

Introduction: Ileus (delayed return of bowel function after surgery) is one of the highest priority research questions in modern day colorectal practice. Current Enhanced Recovery After Surgery (ERAS) guidance either does not include a specific recommendation for volume of postoperative oral fluids/foodstuffs or suggests ad-lib fluids. It is unclear if the volume of intake affects ileus rates. This systematic review aimed to determine the optimal fluid volume for patients to consume day one after elective colorectal surgery.

Methods: The literature was searched across seven databases, September 23, 2020. Randomised controlled trials of adults undergoing elective colorectal surgery, comparing oral intake postoperatively were eligible for inclusion. Two blinded reviewers assessed papers with disagreements resolved by a third independent reviewer. Main outcomes were 'resolution of postoperative ileus' and 'length of hospital stay'. Secondary outcomes included vomiting, mortality and complications.

Results: Of 2175 screened papers, eight were eligible for inclusion. All studies gave a clear liquid diet postoperatively. The comparison groups followed a traditional nil-by-mouth approach. All studies showed a minor reduction in postoperative ileus and hospital stay in the intervention group, but we are unable to determine the optimal postoperative oral fluid volume. The low number and poor quality of studies was a significant limitation. None of the trials were conducted within an ERAS protocol: only 883 patients were included in total.

Conclusions: From the current literature it is unclear how postoperative oral fluid volume intake affects gastrointestinal function and ileus in elective colorectal surgical patients. This remains an important area for further research.

1. Introduction

In the United Kingdom (UK) approximately 20,000 colorectal resections are carried out annually [1]. These procedures are associated with several complications [2], one which is common to all is ileus, defined as 'delayed return of bowel-function following surgery' [3]. The widespread introduction of Enhanced Recovery After Surgery (ERAS) programmes [4,5] include a series of evidence-based multimodal interventions designed to expedite early recovery after surgery. This has led to improvements in the peri-operative management of surgical patients. Despite this, the rate of prolonged ileus remains between 5.3 and 25% [2–6]. Ileus therefore continues to be a significant clinical problem in colorectal surgical practice.

Ileus is associated with nausea, vomiting, abdominal distension and often the requirement for gastric decompression with the placement of a nasogastric (NG) tube. It significantly impacts patient recovery and well-being and increases hospital stay for patients [3–7]. However, its aetiology remains unclear. Attempts to investigate this process are required to further understand the pathology and reduce ileus rates. Indeed, The Association of Coloproctology of Great Britain and Ireland (ACPGBI) Delphi process in 2014 listed reduction of ileus as one of the highest priority non-cancer related questions in modern day colorectal practice [8].

Studies reporting postoperative ileus are limited, primarily due to

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the lack of a consistent definition, leading to conflicting results [3]. The development of ileus is likely multifactorial, with no single action found to prevent it occurring. Thus, a multimodal approach is recommended by current ERAS guidelines for prevention and treatment [9]. One factor that has been demonstrated to increase the risk of increase length of hospital stay and ileus is fluid overload with intravenous (IV) fluids during the peri-operative period [10–12]. The proposed mechanism for this is bowel oedema delaying the return of peristalsis. Oral intake has been less frequently studied as a causal factor for ileus. ERAS guidelines for colorectal surgery do not include a specific recommendation for initial volumes/timing of oral intake following major colorectal resection [9,13]. However, the ERAS guidance specifically for rectal surgery state that 'an oral ad-lib diet is recommended 4 h after rectal surgery' [14].

Previous work has demonstrated that early feeding is safe following anastomosis in both laparoscopic and open procedures [9,15]. Despite this, whether large volumes of oral intake on the first day post-operatively impact the incidence of ileus remains unclear.

This systematic review aimed to assess the current evidence to determine if volume of oral fluid intake in the first 24 h post-elective colorectal surgery affects gastrointestinal recovery and ileus rates, with the intention of making a specific recommendation to update the ERAS guidelines. In short, is there literature to determine the optimal fluid volume to allow patients to consume day one post-elective colorectal surgery?

2. Methods

2.1. Study design

A systematic review assessing the impact of postoperative oral fluid intake on ileus rates following elective colorectal surgery.

2.2. Search strategy

Thirty-five terms (Table 1) were searched in seven databases (Ovid Medline, Ovid Evidence-Based Medicine (EBM) including Cochrane Library, Ovid Commonwealth Agricultural Bureaux (CAB), Ovid Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed and Elsevier Science) September 23, 2020. 2175 papers were found in total. Papers were reviewed using Rayyan Qatar Computing Research Institute (QCRI), Qatar software [16].

2.3. Study selection

After 746 duplicate papers were removed, the population, intervention, comparison, outcome and study (PICOS) inclusion and exclusion criteria (Table 2) were used by two independent, blinded reviewers (EM and FC) to determine papers suitable for inclusion. Studies where there was disagreement were assessed by a third reviewer (GR). 1429 titles, 126 abstracts, and 20 papers were assessed. 8 papers were suitable for inclusion (Fig. 1). The 12 papers read in full that did not meet the inclusion/exclusion criteria are referenced with reason for rejection in Fig. 1 [17–28]. Definitions of postoperative ileus, criteria for NG tube reinsertion and resolution of ileus are summarised in Table 3.

Table 1
Search terms.

Search	Keywords
#1	"surgery" OR "abdominal surgery" OR "colorectal surgery" OR "gastrointestinal surgery" OR "colon"
#2	"fluid therapy" OR "fluid balance" OR "oral fluid" OR "oral intake" OR "oral nutrition" OR "oral rehydration" OR "energy intake" OR "food volume"
#3	"postoperative" OR "post-operative" OR "postoperative care" OR "postop" OR "post-op" OR "postoperative procedure" OR "post surgery" OR "after surgery"
#4	"ileus" OR "complication$" OR "hospital stay" OR "gastrointestinal dysfunction" OR "naso-gastric tube" OR "NG tube" OR "vomiting" OR "delayed discharge"
#5	"randomized controlled trial" OR "randomised controlled trial" OR "randomized" OR "randomised" OR "controlled clinical trial" OR "RCT"
#6	#1 AND #2 AND #3 AND #4 AND #5: Limits English Language, Human, Adult.

Table 2
Inclusion/exclusion criteria.

	Inclusion	Exclusion
Patient	Adult population	Paediatrics/children
	Post surgery	Preoperative
	Postoperative	All non-colorectal surgery
	Colorectal	Emergency operations
	Elective operations	
	Open and laparoscopic	
Intervention	Oral fluids postoperative	Intravenous fluids
	ral nutrition postoperative	Percutaneous endoscopic gastrostomy (PEG) feeding/other forms of enteral feeding
		Total parenteral nutrition
	Volume of oral fluids postoperative	Oral fluids preoperative
		Preoperative carbohydrates
		Intraoperative fluids
Control	No restriction to oral fluids or another suitable control group	No control group
Outcome	Ileus	Infection
	Gastrointestinal Dysfunction	Other complications e.g. wound dehiscence
	Vomiting	
	Hospital Stay	
	Delayed Discharge	
	Nasogastric Tube	
Study	Randomised controlled trial	All other study types
	English language	Non-English language studies
	Human	Animal studies

2.4. Outcomes

Primary outcomes were resolution of postoperative ileus and length of hospital stay (Table 4). Secondary outcomes included vomiting, mortality and complications (Fig. 5, Table 5).

2.5. Data collection, analysis and reporting

Two independent reviewers (EM and FC) used the Cochrane Data Collection Form for Randomised Controlled Trials (RCTs) [30] to collect data. The Scottish Intercollegiate Guidelines Network (SIGN) checklist for RCTs [31] was used for critical appraisal. Bias was assessed following the Cochrane Handbook guidelines [32]. Results were collated and areas of disagreement assessed by a third independent, blinded reviewer (GR). Results have been conducted and reported in line with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) Statement Criteria 2020 [33]. The quality of the review is assessed as a high-quality review using the 'Assessing the Methodological Quality of Systematic Reviews' (AMSTAR) 2 critical appraisal tool [29].

2.6. Statistical analysis

'Hospital stay (days)' and 'days until ileus resolution' between the intervention vs control groups have been analysed by paired multiple t-tests (parametric) to investigate statistical significance (p-value <0.05), t, df, correlation coefficient were also calculated for effective pairing as shown in Fig. 2. Standard deviations for each individual pair were as provided from the source publications. Data were analysed and visualised with GraphPad Prism V 8.4.3. Meta-analysis concerning

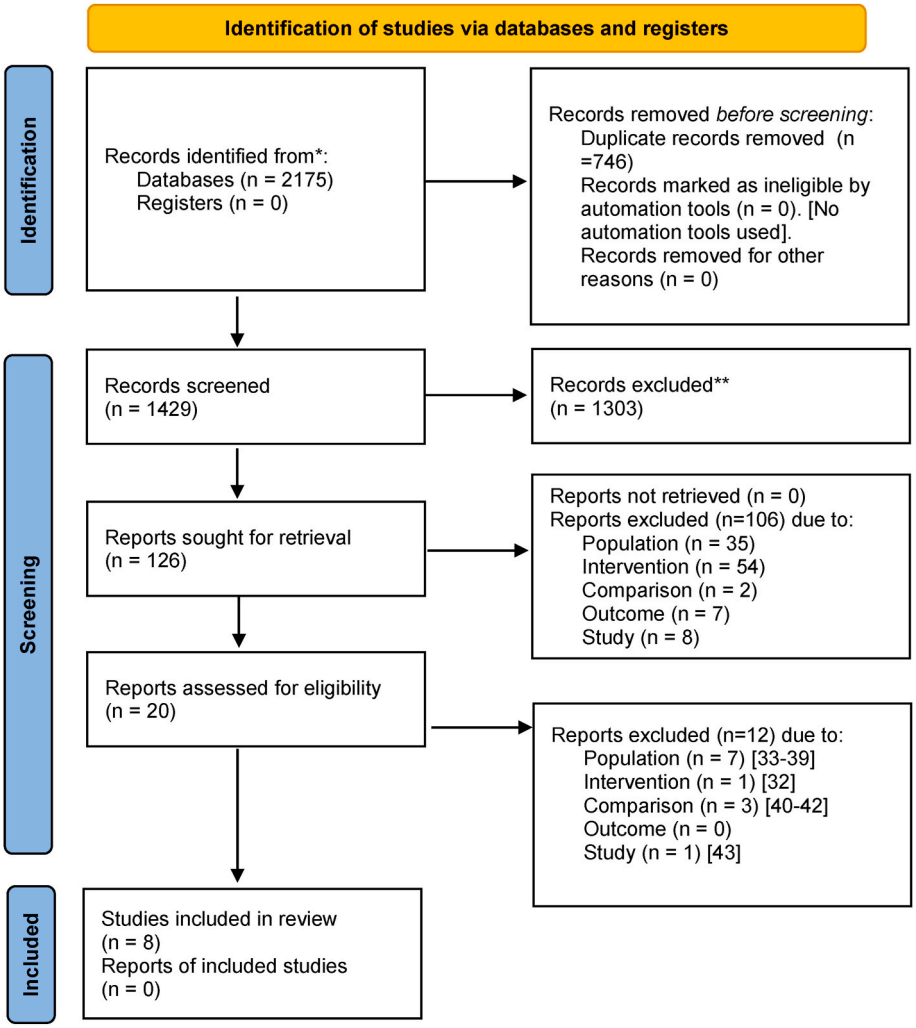

Fig. 1. PRISMA 2020 [29] flow diagram depicts search strategy and reasons for paper exclusions, with papers that were read in full and rejected referenced.

dichotomous secondary outcomes, namely NG tube reinsertion (events), vomiting (events), complications (events), anastomotic leak (events), mortality (events), was conducted by computing the OR from the original data (Table 5) using the Cochrane-Mantel-Haenszel method with Review Manager (RevMan) v5.4 software using a random-effect model. Statistical heterogeneity was quantified using I^2 statistics and Cochrane Q tests (Fig. 5).

2.7. Study registration

Registered with the 'International Prospective Register of Systematic Reviews' (PROSPERO) database: number CRD42020189311. This study is also registered with 'ResearchRegistry', unique identifying number: reviewregistry1332 [34].

3. Results

3.1. Study characteristics

Eight studies were included. All were single centre RCTs aiming to determine the safety/effect of early oral feeding on ileus and length of hospital stay on patients following elective colorectal surgery. Trials were conducted between 1995 and 2014.

Patient demographics are presented in Table 6. 883 patients were enrolled across the trials. The number of patients in each trial varied from 29 to 199. All studies included open operations. Three also included laparoscopic or laparoscopic-assisted operations [35–37].

No study was blinded, with patients/assessors aware of treatment protocols. Stewart *et al.* [38] used a visual analogue scale to assess nausea, and dietary intake was independently assessed by a dietician. None of the studies were conducted within an ERAS protocol. Table 7 summarises patient/population, intervention, comparison and outcome (PICO) data.

3.2. Intervention and comparison

Intervention and comparison treatment arms varied between studies. Reissman *et al.* [39] gave their intervention group a clear liquid diet the first postoperative day then a regular diet within the next 24–48 h as tolerated. The comparison group were nil-per-os (NPO) until resolution of ileus and then the same protocol followed.

Lobato Dias Consoli *et al.* [36] and Da Fonseca *et al.* [37] and both gave their intervention group 500 mL oral liquid diet day one post-operatively then moved onto a regular diet thereafter. Their comparison groups were NPO until the passing of first flatus or first evacuation, and then an oral liquid diet followed by a regular diet within 24 h. Pragatheeswarane *et al.* [40] started patients on a clear liquid diet of 30 cm^3/h at the 24th hour: this was increased to 60 cm^3/h in the next 12 h: then a full fluid diet within 48 h and solid diet over the next 24 h. The comparison group were NPO until the resolution of ileus, then a clear liquid diet, then solid food diet. Stewart *et al.* [38] gave their intervention group free fluids 4 h postoperatively and Dag *et al.* [41] from 12 h, both

Table 3
Definitions and criteria in each trial.

Author (year)	Criteria for Postoperative Insertion of Nasogastric Tube	Definition of Resolution of Ileus	Discharge Criteria
Reissman *et al.* (1995)	Vomited more than 100 mL 2x in 24 h in the absence of bowel movements.	Having a bowel movement in the absence of abdominal distention and vomiting.	Both groups discharged home after they had had a bowel movement and tolerating regular diet for at least 24 h.
Stewart *et al.* (1998)	Vomiting of >100 mL on two occasions within 24 h.	Passage of flatus or bowel motion.	Not recorded and comment in discussion 'without uniform medical criteria for discharge'.
El Nakeeb *et al.* (2009)	Two episodes of vomiting in the absence of any bowel movements.	Bowel movements in the absence of vomiting and abdominal distension.	Eligible for discharge when self-caring, tolerating oral fluid and diet, had bowel function and were independently mobile.
Da Fonseca *et al.* (2010)	Stated no nasogastric tubes used postoperatively and no criteria defined.	Elimination of first flatus.	The hospital discharge criteria were the same for both groups. (1) adequate pain control with oral medication, (2) absence of nausea (3) passage of first flatus, (4) ability to tolerate solid food, and (5) ability to walk safely and without assistance of another person.
Lobato Dias Consoli *et al.* (2010)	Two consecutive episodes of vomiting greater than 400 mL	First flatus or evacuation.	When patients were fully mobile, pain was controlled with only oral analgesics and tolerance of oral food was adequate.
Dag *et al.* (2011)	Two or more episodes of vomiting >100 mL, in the absence of bowel movement.	Passed first flatus or stool.	Both groups discharged once fulfilled all discharge criteria: passage of flatus or stools, toleration of oral liquid and solid food, comfortable on oral analgesia, no complications that required hospital treatment.
Fujii *et al.* (2014)	Not routinely used.	Time of first passage of flatus and defecation. All cases of ileus diagnosed and confirmed by X-ray.	Not recorded.
Pragatheeswarane *et al.* (2014)	Vomited more than 100 mL 2x in 24 h in the absence of bowel movements.	Having a bowel movement in the absence of abdominal distention and vomiting.	Both groups discharged when they had passed flatus and stools and tolerated solid diet for at least 24 h in the absence of other factors affecting discharge such as fever, wound infection, anastomotic leakage etc.

Table 4
Primary outcome data.

Author (year)	Length of Postoperative Hospital Stay (days) [Mean ± standard deviation if available unless otherwise stated].		Resolution of Postoperative Ileus (days) [i.e. time to first flatus] [Mean ± standard deviation if available unless otherwise stated].	
	Intervention Group	Control Group	Intervention Group	Control Group
Reissman *et al.* (1995)	6.2 ± 0.2 (range 2–12)	6.8 ± 0.2 (range 3–12) (p > 0.05)	3.8 ± 0.1 (range 1–8)	4.1 ± 0.1 (range 1–9) (p > 0.05)
Stewart *et al.* (1998)	9 (median) (range 5–28)	11 (median) (range = 6–18) (p = 0.10)	3 (median) (range 1–5)	4 (median) (range 2–6) (p = 0.01)
El Nakeeb *et al.* (2009)	6.2 ± 0.2 (range 3–11)	6.9 ± 0.5 (range 3–12) (p = 0.05)	3.3 ± 0.9 (range 2–8)	4.2 ± 1.2 (range 2–9) (p = 0.04)
Da Fonseca *et al.* (2010)	4.0 ± 3.7	7.6 ± 8.1 (p < 0.001) (reported as p = 0.000)	1.5 ± 0.5	2.0 ± 0.7 (p = 0.019)
Lobato Dias Consoli *et al.* (2010)	3.0 (median)	5.0 (median) (p < 0.05)	Day 1 (specific figures not recorded, and statistical analysis unclear)	Day 2 (specific figures not recorded and statistical analysis unclear) (p < 0.05)
Dag *et al.* (2011)	5.55 (range 4–22)	9.0 (range 4–49) (p = 0.0001)	1.76 (range 1–6)	3.27 (range 1–10) (p = 0.0001)
Fujii *et al.* (2014)	9.6 ± 6.3	9.6 ± 4.6 (p = 0.491)	2.3 ± 0.7	3.1 ± 1.0 (p < 0.001)
Pragatheeswarane *et al.* (2014)	11.1 ± 5.5	14.4 ± 8.5 (p = 0.011)	2.6 ± 0.9	4.5 ± 1.5 (p < 0.0001)

allowed progression to solid diet at patients' discretion. El Nakeeb *et al.* [42] allowed free fluids on the first postoperative day then a solid diet over the next 24–48 h. The comparison groups for these studies were the same as the others (NPO until first flatus/resolution of ileus). Fujii *et al.* [35] gave their intervention group a liquid diet on the first postoperative

Table 5
Secondary outcome data.

Author (year)	Nasogastric Tube Reinsertion Rate		Vomiting		Patients with Complications		Anastomotic Leak Rate		Mortality Rate	
	Intervention Group	Control Group	Intervention Group	Control Group	Intervention Group	Control Group	Intervention Group	Control Group	Intervention Group	Control Group
Reissman *et al.* (1995)	11% (9/80)	10% (8/80) (p > 0.05)	21% (17/80)	14% (11/81) (p > 0.05)	7.5% (6/80)	6.1% (5/81) (p > 0.05)	0% (0/80)	1.2% (1/81) no p value	No mortality In either group.	
Stewart *et al.* (1998)	10% (4/40)	7.5% (3/40) (p = non-significant)	35% (14/40)	35% (14/40) (p = non-significant)	25% (10/40)	27.5% (11/40) no p value	2.5% (1/40)	0 (0/40) no p value	0 (0/40)	2.5% (1/40) no p value
El Nakeeb *et al.* (2009)	6.7% (4/60)	8.3% (5/60) (p = 0.25)	25.0% (15/60)	16.7% (10/60) (p = 0.05)	23.3% (14/60)	36.7% (22/60) no p value	1.7% (1/60)	3.3% (2/60) (p = 0.35)	0	1.66% (1/60) no p value
Da Fonseca *et al.* (2010)	Not used.		16.7% (4/24)	19.2% (5/26)	16.7% (4/24)	34.6% (9/26) (p = 0.480)	0% (0/24)	15.4% (4/26) (p = 0.111)	4.2% (1/24)	0% (0/26) (p = 0.480)
Lobato Dias Consoli *et al.* (2010)	Not reported – unclear.		Values not reported. (p = non-significant between groups)		26.7% (4/15)	35.7% (5/14) (p = non-significant)	Values not reported. (p = non-significant between groups)		One (3.4%) patient died duing follow-up: did not report from which group.	
Dag *et al.* (2011)	8.1% (8/99)	6.0% (6/100) (p = 0.363)	Not recorded.		12.1% (12/99)	14.0% (14/100) (p = 0.541)	2.0% (2/99)	6.0% (6/100) (p = 0.279)	Not reported.	
Fujii *et al.* (2014)	Nasogastric tubes not routinely used, no values for reinsertion rates given.		Not recorded.		12.9% (8/62)	17.2% (10/58) (p = non-significant)	1.6% (1/62)	0% (0/58) (p = 0.517)	No mortality in either group.	
Pragatheeswarane *et al.* (2014)	Values not reported. (p = non-significant between groups)		8.3% (5/60)	11.7% (7/60) (p = 0.543)	Values not reported. (p = non-significant between groups)		1.7% (1/60)	5.0% (3/60) (p = 0.319)	1.7% (1/60)	1.7% (1/60) (p = 1)

Table Analyzed	ILEUS RESOLUTION
Column B	Control
vs.	vs.
Column A	Early enteral feed
Paired t test	
P value	0.0007
P value summary	***
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=5.322, df=8
Number of pairs	9
How big is the difference?	
Mean of differences (B - A)	0.9233
SD of differences	0.5205
SEM of differences	0.1735
95% confidence interval	0.5233 to 1.323
R squared (partial eta squared)	0.7798
How effective was the pairing?	
Correlation coefficient (r)	0.8530
P value (one tailed)	0.0017
P value summary	**
Was the pairing significantly effective?	Yes

Table Analyzed	Hospital stay days
Column B	Control
vs.	vs.
Column A	Early enteral feed
Paired t test	
P value	0.0031
P value summary	**
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
t, df	t=4.168, df=8
Number of pairs	9
How big is the difference?	
Mean of differences (B - A)	1.861
SD of differences	1.340
SEM of differences	0.4466
95% confidence interval	0.8313 to 2.891
R squared (partial eta squared)	0.6846
How effective was the pairing?	
Correlation coefficient (r)	0.8721
P value (one tailed)	0.0011
P value summary	**
Was the pairing significantly effective?	Yes

Fig. 2. Statistical analysis summary tables – paired-t test - analysing ileus resolution and postoperative hospital stay in days.

day then a solid diet within 24 h: they used a different control group to the other studies, allowing oral fluids from day two regardless of resolution of ileus, then a solid diet as tolerated.

Out of the eight studies only three recorded specific volumes of oral fluid they allowed patients to consume [36,37,40].

Table 8 compares study protocols. All studies stated that intra-operative NG tubes were removed immediately in the recovery room or that 'no NG tubes were used postoperatively'. Each used different anti-emetic and analgesic protocols. Within each study the comparison groups appear to have been treated equally.

3.3. Primary outcomes

Resolution of postoperative ileus (days) and length of postoperative hospital stay (days) were primary outcomes in each trial (Table 4). Fig. 3 illustrates that seven studies found a statistically significant reduction in

Table 6
Comparison of population characteristics between groups. I = intervention group and C = control group.

Author (year)	Mean Age (years) (± Standard Deviation if Available)	Percentage Males Per Group	Body Mass Index (kg/m^2)	Co-morbidities/Other	Surgical Procedure	Procedures Included
Reissman *et al.* (1995)	I = 51 (range 16–82) C = 56 (range 20–90) (no p value)	I = 42.5% C = 53.1% (no p value)	Not recorded.	Not recorded.	Matched – no significant difference between groups.	-Segmental colonic, rectal or small bowel resection -Restorative proctocolectomy with ileoanal pouch -Stoma closure -Total proctocolectomy -Stoma creation.
Stewart *et al.* (1998)	I = 58 (range 25–89) C = 59 (range 17–88) (no p value)	I = 47.5% C = 45.0% (no p value)	Not recorded.	Comorbidities not recorded – groups noted to be well matched for age, sex, duration of operation, blood loss, presence/absence of drain.	No significant difference between groups.	- Ileocolic resection - Right hemicolectomy - Subtotal colectomy - Left hemicolectomy - Anterior resection.
El Nakeeb *et al.* (2009)	I = 52.3 ± 12.5 (range 21–70) C = 56.3 ± 11.6 (range 25–69) (no p value)	I = 65% C = 70% (no p value)	Not recorded.	Pathology between groups similar: Rectal cancer (11 vs 12 cases) and colonic cancer (49 vs 48 cases). Diabetes or heart disease (p = 0.41) between groups.	Groups were matched for surgical procedure, numbers similar for each.	- Right colectomy - Left colectomy - Low anterior resection - Closure of colostomy.
Da Fonseca *et al.* (2010)	I = 57.4 (±16.3) C = 51.7 (±13.3) (p = 0.697)	I = 33.3% C = 38.5% (p = 0.706)	Not recorded.	American Society of Anaesthesiologists (ASA) grades not significantly difference between groups (p = 0.443).	No significant difference between groups.	- Right hemicolectomy -Transverse colectomy -Left hemicolectomy -Total colectomy.
Lobato Dias Consoli *et al.* (2010)	I = 54.5 ± 10.1 (35–75) C = 47.4 ± 16.7 (range 21–79) (p value non-significant)	I = 26.7% C = 35.7% (p value non-significant)	On admission all patients were nutritionally assessed by subjective global assessment and body mass index (BMI). Numbers not reported.	Not recorded.	No significant difference between groups.	-Sigmoid resection -Left hemicolectomy -Resection of transverse colon -Right hemicolectomy -Total colectomy.
Dag *et al.* (2011)	I = 62 (range 35–85) C = 61 (range 17–89) (p = 0.479)	I = 52.5% C = 61.0% (p = 0.199)	Not recorded.	No significant difference between groups (p = 0.984). Recorded cardiac, pulmonary, cardiac and pulmonary, urinary and diabetes mellitus, similar numbers for each group.	No significant difference between groups (p = 0.143). However, difference in number of subtotal colectomy operations: I = 10 vs C = 2.	- Very low anterior resection - Low anterior resection - Anterior resection - Sigmoidectomy - Left hemicolectomy - Transverse colectomy - Right hemicolectomy - Subtotal colectomy.
Fujii *et al.* (2014)	I = 67.4 ± 11.7 C = 66.9 ± 10.7 (p = 0.784)	I = 58.0% C = 51.7% (p = 0.607)	I = 22.9 ± 2.8 C = 22.5 ± 3.1 (p = 0.877)	Clinical characteristics of two groups similar - cancer stage (p = 0.106), diabetes (p = 0.225), blood loss (p = 0.486).	Similar number of laparoscopic assisted surgery In both groups (p = 0.299).	- Colorectal resections: specific operation types not recorded.
Pragatheeswarane *et al.* (2014)	I = 46.5 ± 17.2 C = 46.9 ± 16.5 (p value non-significant)	I = 55.0% C = 53.3% (p value non-significant)	Not recorded.	Hypertension, diabetes mellitus, ischemic heart disease – no significant difference found between groups.	No significant difference between groups.	-Abdominoperineal resection - Ileostomy closure - Colostomy closure - Other resection anastomosis procedures - Other diversion procedures.

time for resolution of postoperative ileus in the intervention arm [35–38,40–42]. The remaining study showed a reduction in time between the intervention and control groups but failed to reach the limit of statistical significance [39].

Note that for their length of post-operative hospital stay control group Da Fonseca *et al.* [37] report the standard deviation value as greater than the mean: this shows that the data was not normally distributed and median and range should have been used for analysis. In-addition this paper quotes the associated p value as p = 0.000 – this has been amended to p < 0.001 in Table 4.

Timings for resolution of ileus varied from day 1 [36] to 4.5 days [40]. The largest difference between intervention and control was found by Pragatheeswarane *et al.* [40] at 1.9 days. Only one other study reported a difference of greater than one day [41].

A significant reduction in length of postoperative hospital stay was reported by six studies [36–38,40–42] (Fig. 4). Seven trials showed an overall reduction in length of hospital stay in the intervention arm when compared to the control group. Only Fujii *et al.* [35] showed no difference in length of hospital stay - 9.6 days for both groups, despite finding a statistically significant earlier resolution of ileus in their intervention group (p < 0.001).

The shortest length of postoperative stay was found in the intervention group of Lobato Dias Consoli *et al.* [36] at 3.0 days. Pragatheeswarane *et al.* [40] reported the longest mean length of stay in their

Table 7
Population/intervention/control and outcomes (PICO) summary of trials. I = intervention group and C = control group.

Author (year)	Population		Intervention		Control		Outcomes	Sample Size: total number of patients
	Mean Age (years) [± standard deviation and range if available].	Inclusion and Exclusion Criteria	Diet	Time started postoperatively	Diet	Time started postoperatively	Outcomes Recorded: Primary/ Secondary (if defined in the paper)	
Reissman *et al.* (1995)	I = 51 (range 16–82) C = 56 (range 20–90) (no p value)	Elective laparotomy with bowel resection, November 1992–April 1994. Laparoscopic and emergency procedures excluded.	Clear liquid diet on the first postoperative day - regular diet within the next 24–48 h, as tolerated (absence of vomiting or abdominal distention).	Day one postoperatively.	Nil-per-os until the resolution of the ileus- then clear liquid diet, followed by a regular diet as described for intervention group.	Nil-per-os until resolution of ileus.	1. Tolerated early feeding 2. Vomiting 3. Nasogastric tube reinsertion 4. Resolution of ileus 5. First meal ingestion 6. Length of hospital stay.	161
Stewart *et al.* (1998)	I = 58 (range 25–89) C = 59 (range 17–88) (no p value)	Included - elective colorectal resection with anastomosis and without stoma formation. Excluded – patients having extensive division of adhesions greater than 2h and patients having rectal anastomosis with covering stomas.	Free fluids from 4 h after the operation and progressed to solid diet from the first postoperative day at own discretion.	Four hours postoperatively.	Fasted until passage of flatus or bowel motion, then commenced on clear fluids and progressed to solid diet over 24–48 h at the surgeon's discretion.	Nil-per-os until passage of flatus or bowel motion.	1.Vomiting >100 ml 2. Nasogastric reinsertion 3.Prolonged distension 4.Nausea score 5. Anti-emetic 6. Passage flatus 7. First bowel action 8. Commencement solid diet 9.Full diet 10. Discharge time.	80
El Nakeeb *et al.* (2009)	I = 52.3 ± 12.5 (range 21–70) C = 56.3 ± 11.6 (range 25–69) (no p value)	Included - elective open colonic anastomosis. Excluded – chronic liver disease, emergency laparotomy, stoma formation, those with metastasis, patients unfit for surgery.	Began fluids on the first postoperative day and advanced to a regular diet within the next 24–48h as tolerated (indicated by an absence of vomiting or abdominal distension).	Day one postoperatively.	Nil-per-os until the resolution of ileus then a fluid diet, followed by a regular diet.	Nil-per-os until resolution of ileus.	1. Tolerated early feeding 2. Vomiting 3. Nasogastric tube reinsertion 4. Time to passage of first flatus 5. Time to passage of first stool 6. Hospital stay 7. Patient satisfaction 8. Readmission.	120
Da Fonseca *et al.* (2010)	I = 57.4 ± 16.3 C = 51.7 ± 13.3 (p = 0.697)	Elective colonic surgery patients included. Excluded – emergency operations, low anterior resection, or abdominoperineal resection of the rectum; patients receiving a stoma; patients remaining in the intensive care unit (ICU) for more than 24 h; patients with cognitive deficits that impaired protocol comprehension; American Society of Anaethesiologists (ASA) score > III; patients who chose not to particiate. and patients who chose not to participate.	First post-operative day received an oral liquid diet (approx 500 cm^3) then regular diet within the next 24 h, as tolerated (absence of vomiting or abdominal distention) and at their discretion.	Day one postoperatively.	Nil-per-os until the elimination of the first flatus, then oral liquid diet, followed by regular diet within the next 24 h as per intervention group.	Nil-per-os until first flatus.	Primary* 1.Length of hospital stay 2.Feeding tolerance 3. Time to first flatus and defecation 4.Morbidity Rate particularly anastomotic leak rate 5. Mortality Rate Secondary 1.Readmission rate 2.Surgical reintervention after discharge 3.Use of intravenous fluids intraoperatively.	54 29

(*continued on next page*)

Table 7 (*continued*)

Author (year)	Population		Intervention		Control		Outcomes	Sample Size: total number of patients
	Mean Age (years) [± standard deviation and range if available].	Inclusion and Exclusion Criteria	Diet	Time started postoperatively	Diet	Time started postoperatively	Outcomes Recorded: Primary/ Secondary (if defined in the paper)	
Lobato Dias Consoli *et al.* (2010)	I = 54.5 ± 10.1 (35–75) C = 47.4 ± 16.7 (range 21–79) (p value non-significant)	Included >18 years, either open or laparoscopic elective colonic resection with a primary anastomosis. Excluded - emergency procedures, Hartmann's colonic resection or with protective colostomy and those who did not agree to participate.	First postoperative day 500 mL of restricted fluid and if no nausea and vomits were observed they were able to eat a free diet, immediately thereafter.	Day one postoperatively.	Nil-per-os until flatus or evacuation happened. No record of what this group were then allowed orally.	Nil-per-os until flatus or evacuation.	1. Length of hospital stay 2. Time to first flatus 3.Occurrence of nausea and vomiting 4. Diarrhoea 5.Anastomotic leak rate.	
Dag *et al.* (2011)	I = 62 (range 35–85) C = 61 (range 17–89) (p = 0.479)	Included - Elective open colorectal cancer surgery: all consecutive patients included regardless of American Society of Anaesthesiologists (ASA) score, comorbidity, localisation and stage of tumour, comorbidity, preoperative chemoradiotherapy, diabetes. Excluded – scheduled or unscheduled ileostomy or colostomy. Advanced metastastic disease where colonic resection not performed. Patients who declined to participate.	Early postoperative oral feeding commencing approximately 12 h after the operation with a fluid diet, this was gradually increased to a solid diet as tolerated by the patient.	Twelve hours postoperatively.	Fasting until passage of first flatus or stools, no comment as to diet thereafter.	Nil-per-os until passage of first flatus or stool.	1.Time to intestinal movements 2. Time to defecation 3. Time to toleration of a regular diet 4. Nasogastric reinsertion rate 5. Hospital stay 6. Complications 7. Anastomotic leakage.	199
Fujii *et al.* (2014)	I = 67.4 ± 11.7 C = 66.9 ± 10.7 (p = 0.784)	Included - consecutive patients with colorectal cancer who underwent elective colorectal resection, 2010–2011. Excluded – simple colostomy, colostomy closure, emergency operations, surgery with stoma creation.	Liquid diet on the first postoperative day and advanced to a regular diet in the next 24 h as tolerated.	Day one postoperatively.	Liquid diet on the second postoperative day and advanced to a regular diet in the next 24 h as tolerated.	Day two postoperatively.	1.Liquid diet (day) 2. Solid diet (day) 3. Time to first flatus 4. Time to defaecation 5. Hospital stay after surgery 6. C-Reactive protein (CRP) 7. Albumin 8. Complications including ileus.	120
Pragatheeswarane *et al.* (2014)	I = 46.5 ± 17.2 C = 46.9 ± 16.5 (p value non-significant)	Included - elective open bowel surgeries. Emergency bowel surgeries, laparoscopic bowel surgeries and those not fit for starting oral feeding, e.g. patients on ventilator, unconscious patients and those who underwent feeding procedures like feeding jejunostomy, were excluded.	Clear liquid diet of 30 cm^3/h at the 24th hour: this was increased to 60 cm^3/h in the next 12 h: patients then had a full fluid diet within 48 h and then a solid diet over the next 24 h.	Nil-per-os until 24 h postoperatively.	Nil-per-os until the resolution of the ileus,-then a clear liquid diet, progressing to a solid diet as tolerated. Nasogastric tube removed within 24 h.	Nil-per-os until resolution of ileus.	Primary 1.Total length of hospitalisation 2. Postoperative length of hospitalisation. Secondary 1. Time of the first passage of flatus and stools 2. Time of starting first solid diet 3.Nasogastric tube reinsertion rate 4. Complications.	120

Table 8
Summary of study protocols. I = Intervention Group and C=Control Group.

Author (year)	Laparoscopic vs Open Surgery	Preoperative Protocol	Postoperative Analgesia	Anti-emetics	Intraoperative Nasogastric Tube Removed
Reissman *et al.* (1995)	100% Open.	Not recorded.	- Similar in both groups: patient-controlled analgesia intravenous pump with meperidine hydrochloride 1 mg/mL solution 300 mg–400 mg/24 h for 48–72 h. - Then intramuscular meperidine 50 mg–100 mg or propopoxyphene napsylate (100 mg by mouth) combined with acetaminophen (650 mg) 4 to 6 times daily.	Not recorded.	Immediately after surgery.
Stewart *et al.* (1998)	100% Open.	Patients counselled Preoperatively by a dietician and advised to expect some nausea and one or two episodes of vomiting. No other preoperative protocols recorded.	- Epidural catheter between the 7th and 9th thoracic vertebrae attempted for all patients, if not successful then patient-controlled analgesia containing pethidine used. - Epidural infusions of marcaine (10 mg/ml) + fentanyl (5 μg/ml) for 3–4 days postoperatively. Then once catheters removed intramuscular morphine or pethidine + oral dextropropoxyphene 32.5 mg and paracetamol 325 mg). Narcotic requirements similar between groups.	Drug(s) not recorded. Mean use similar between groups: p value is recorded as NS (non-significant).	Removed in recovery.
El Nakeeb *et al.* (2009)	100% Open.	History and clinical exam, bloods for complete blood count, liver + renal function, electrolytes, tumour marker tests. Barium enema, abdominal ultrasound, pelvic and abdominal computerized tomography, bone survey, chest X-ray, colonoscopy and biopsy. Chemical and mechanical bowel preperation.	Not recorded.	Not recorded.	Immediately after surgery.
Da Fonseca *et al.* (2010)	Laparoscopic I = 54.2% vs C = 46.2% Converted laparoscopic to open I = 4.2% vs C = 0.0% (p = 0.443)	Not recorded.	Dipyrone (2 g intravenous four times daily). Ketoprofen (100 mg intravenous twice daily). Nalbuphine (5 mg intravenous four times daily if required for breakthrough pain). Epidural thoracic analgesia not used.	- Prophylactic use of ondansetron (4 mg) and dexamethasone to prevent postoperative nausea and vomiting. - Metoclopramide (20 mg intravenous three times daily if required).	Postoperatively: no nasogastric tubes or drains used: do not record exactly when removed.
Lobato Dias Consoli *et al.* (2010)	Laparoscopic I = 46.7% vs C = 42.9% (p = non-significant)	Both groups nil-per-os for 12 h preoperatively.	Not recorded.	Not recorded.	Postoperatively: no nasogastric tubes or drains: do not record exactly when removed.
Dag *et al.* (2011)	100% Open.	Standard bowel preperation and prophylactic intravenous antibiotics before surgery.	Similar in all patients: Patient-controlled analgesia with meperidine hydrochloride 1 mg/mL solution 300 mg–400 mg/24 h for 48–72 h then intramuscular dipyrone or acetaminophen (650 mg) 4–6 times daily.	Not recorded.	Immediately after surgery.
Fujii *et al.* (2014)	Lapraroscopic-assisted I = 32.3% and C = 43.1%, (p = 0.299). Does not record if the other procedures were laparoscopic or open.	Not recorded.	Not recorded.	Not recorded.	With exception of cases with intestinal stenosis, nasogastric tubes not routinely used.
Pragatheeswarane *et al.* (2014)	100% Open.	Not recorded.	Non-opioids in both groups. Intramuscular injections of non-steroidal anti-inflammatory agents. Some patients also had postoperative epidural analgesia in either group (no significant difference between groups).	Not recorded.	Within 24 h of recovery from anaesthesia.

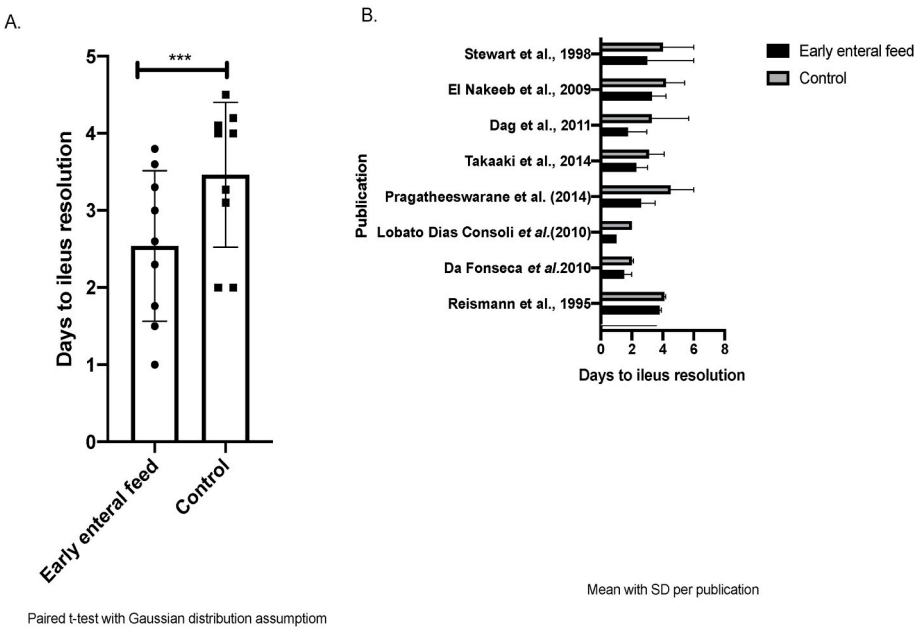

Fig. 3. Primary Outcome Comparison – Days to Resolution of Ileus. Raw data as depicted in Table 4.

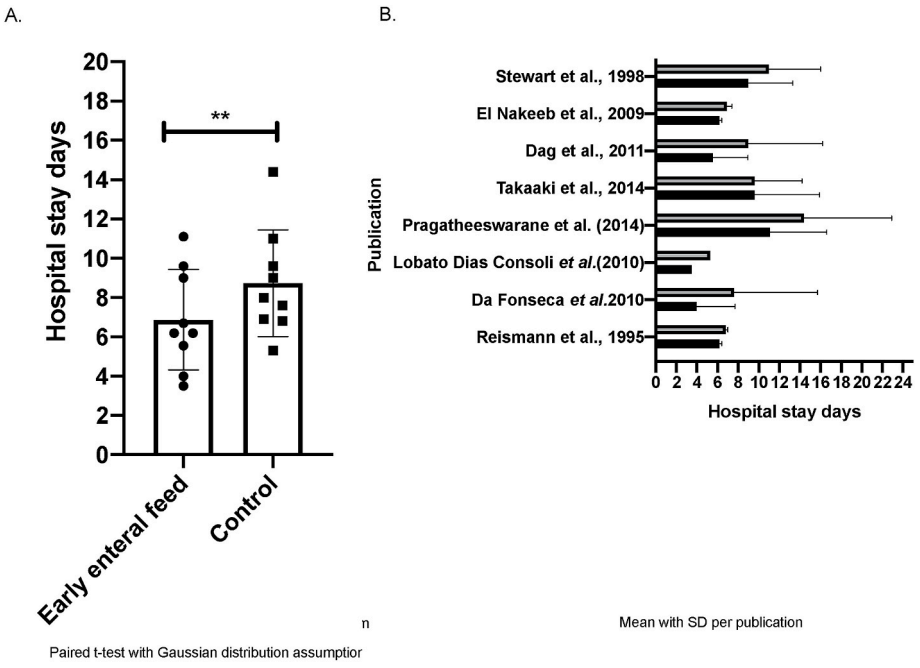

Fig. 4. Primary Outcome Comparison – Postoperative Hospital Stay (days). Raw data as depicted in Table 4.

control group −14.4 days. The largest difference between intervention and control was 3.6 days (4.0 vs 7.6 days, $p < 0.001$) [37].

3.4. Secondary outcomes

Six of the eight trials include data on vomiting. Only one paper [42] found this difference to be statistically significant between study arms with less patients vomiting in their control group (16.7%) vs intervention group (25.0%) ($p = 0.05$). Reissman *et al.* [39] also reported a higher vomiting rate in the intervention arm. The remaining studies reported either greater vomiting rates in the control group [37], no difference between groups [36,38,40] or did not record rates of vomiting [35,41]. Mortality figures were recorded by seven papers [35–40, 42]. No study found a significant difference between groups.

Percentage NG tube reinsertion rate was recorded by five papers [38–42]. Da Fonseca *et al.* [37] did not use NG tubes postoperatively: Fujii *et al.* [35] and Lobato Dias Consoli *et al.* [36] did not record reinsertion rates. No study found a significant difference between groups, but three found a higher rate of insertion in their intervention group [38, 39,41].

The total number of patients with complications was recorded by all studies. Five studies showed a higher rate of complications for the control groups [35–38,41,42], with three reporting particularly high values (34.6% [37], 35.7% [36] and 36.7% [42]). Reissman *et al.* [39] reported much lower complication rates, with the intervention group displaying a slightly higher rate vs control group (7.5% vs 6.1%). No

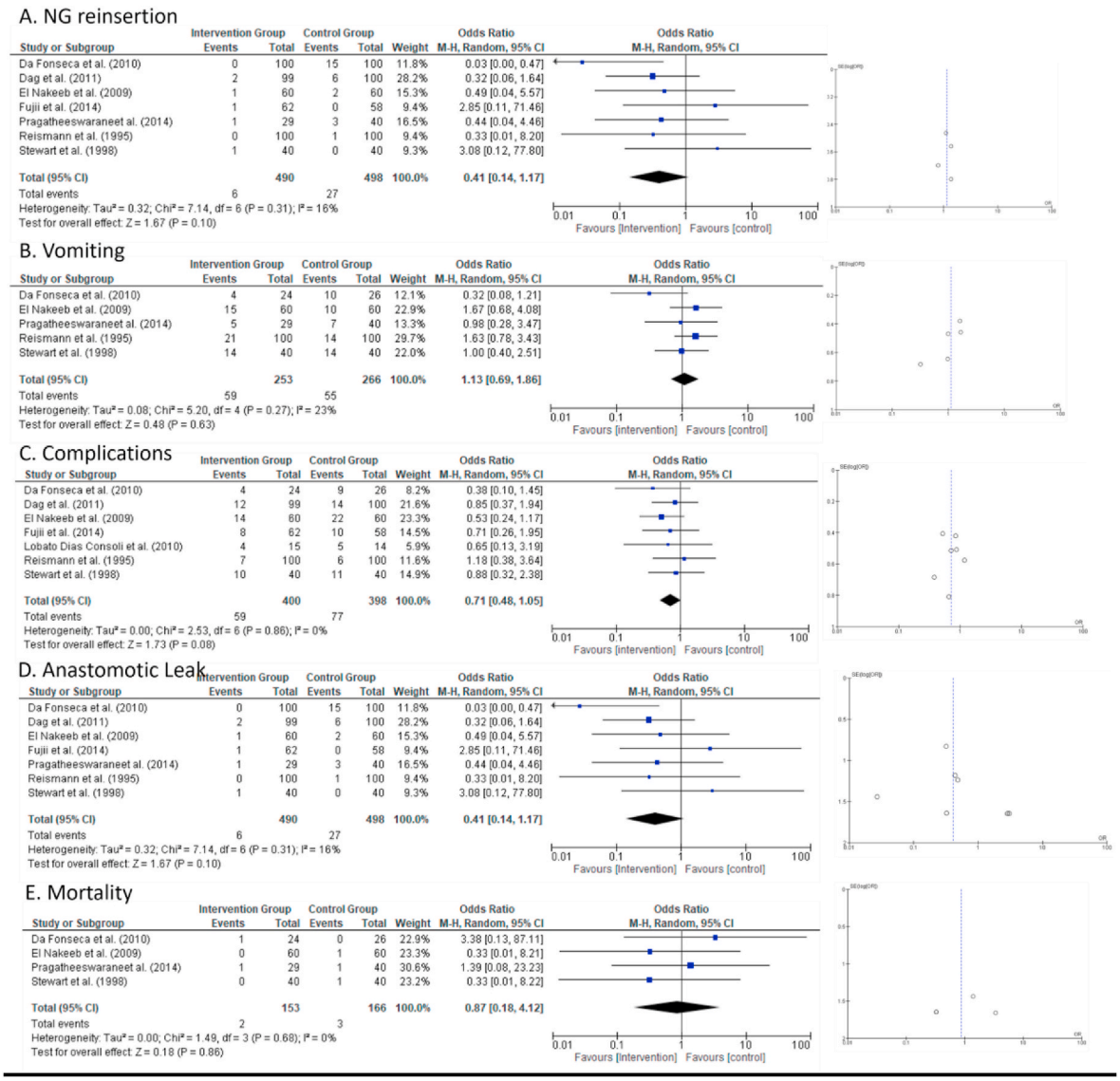

Fig. 5. Secondary Outcome Meta-analysis – a) NG tube reinsertion b) Vomiting episodes, c) Complications d) Anastomotic Leak e) Mortality. Raw data as depicted in Table 5.

study found a statistically significant difference. Table 5 summarises secondary outcomes.

We further pursued to perform a meta-analysis of the available secondary outcome dichotomous data to analyse aggregate heterogeneity and putative statistical significance. Despite acceptable heterogeneity, none of the outcome comparisons between intervention and control groups reached statistical significance (Fig. 5).

3.5. Bias

Bias is summarised in Table 9. Randomization method was unclear in three trials [35,36,39]. Pragatheeswarane *et al.* [40] used permuted block randomization and Da Fonseca *et al.* [37], Dag *et al.* [41], and Stewart *et al.* [38] used a computer programme. None of the studies were blinded which is a significant limitation.

Da Fonseca *et al.* [37] when explaining the protocol to patients gave 'particular attention to details regarding the early feeding protocol and its potential reduction of hospital stay' increasing bias of the participants' views but also instigating detection bias from the assessor/surgeon point of view. Reporting bias can also not be excluded particularly from Reissman *et al.* [39] and Lobato Dias Consoli *et al.* [36] as comorbidities, potentially playing a major role in the operating outcomes and incidence of ileus, were not reported.

In all trials data was collected, assessed and interpreted by the surgical team. Dag *et al.* [41] attempted to decrease bias by using two independent investigators to assess the presence of bowel movements daily. Stewart *et al.* [38] used an independent dietician to assess dietary intake.

El Nakeeb *et al.* [42], Pragatheeswarane *et al.* [40] and Reissman *et al.* [39] said that 'patients were monitored'. Da Fonseca *et al.* [37] reported that 'outcome data was recorded prospectively by just one author,' and Lobato Dias Consoli *et al.* [36] said 'patient follow up was performed daily'. Fujii *et al.* [35] collected data retrospectively. These six trials provided no further details as to how the outcomes were recorded. Some of the figures are objective: e.g., incidence of vomiting and length of hospital stay.

Attrition rate was low across all trials: seven trials had a zero percent attrition rate. Da Fonseca *et al.* [37] reported a rate of 4.0% from the intervention group and 10.3% from the control group. None of the trials reported any conflicts of interest.

Table 9
Bias summary table: Scottish intercollegiate guidelines network (SIGN) critical appraisal comparison.

Internal Validity	Reissman et al. (1995)	Stewart et al. *(1998)*	El Nakeeb et al. *(2009)*	Da Fonseca et al. (2010)	Lobato Dias Consoli et al. (2010)	Dag et al. (2011)	Fujii et al. (2014)	Pragatheeswarane et al. (2014)
The study addresses a focussed and clearly defined question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
The assignment of subjects to treatment groups is randomized?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
An adequate concealment method is used?	Unclear.	Yes – Preoperative computer random number generator.	Yes –sealed envelopes.	Yes –computer programme.	Unclear.	Yes – postoperative computer generated list by independent computer consultant.	Unclear.	Yes – permuted block randomization.
The design keeps subjects and investigators 'blind' about treatment allocation?	No	No	No	No	No	No	No	No
The treatment and control groups are similar at the start of the trial?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
The only difference between groups is the treatment under investigation?	Yes	Yes	Yes	Yes	Yes	No – higher number subtotal colectomy cases in intervention group.	Yes	Yes
All relevant outcomes are measured in a standard, valid and reliable way?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	0%	0%	0%	4% Intervention 10.3% Control	0%	0%	0%	0%
All the subjects are analysed in the groups to which they were randomly allocated? (intention to treat analysis)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Where the study is carried out on more than one site, results are comparable for all sites?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Overall assessment of the study?	Moderate Quality	Moderate Quality	Moderate Quality	Low Quality	Low Quality	Moderate Quality	Low Quality	Low Quality
How well was the study done to minimize bias?	Poor – no blinding	Poor – no blinding	Poor – no blinding	Very Poor – no blinding and clear bias of assessors.	Poor – no blinding	Poor – no blinding	Poor – no blinding	Poor - no blinding
Taking into account clinical considerations, your evaluation of the methodology used and the statistical power of the study are you certain that the overall effect of the study is due to the study intervention?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

4. Discussion

There is a consensus that early postoperative introduction of diet and oral fluids in elective colorectal surgery is safe [5,13–15]. Indeed, the ERAS recommendations state that "an oral ad-libitum" diet is recommended 4 h postoperatively in rectal surgery [14]. Given that all eight studies included in this review had a gradiated introduction to diet in these patients, on closer scrutiny of the included studies, this ERAS recommendation appears to misrepresent the data available. Whilst the data would indicate that general oral intake in terms of ileus, vomiting and mortality is safe, the optimal volume of oral intake in the immediate postoperative period remains unclear.

In the current era where enhanced recovery is effectively ubiquitous, the rate of ileus in postoperative elective surgery remains stubbornly high [3]. Developing an ileus negatively impacts patient recovery, influences the length of hospital stay and is an uncomfortable phenomenon warranting invasive treatments such as NG tubes. Our analysis displays, perhaps surprisingly, that there are only eight RCTs where ileus rates are explored comparing early oral intake is tested against no oral fluid or diet ingestion in the elective colorectal literature.

Whilst we do not interpret these data as reverting to a nil-by-mouth strategy, the available data would suggest that there is room for further investigation in this area. Interestingly, all the trials included in this review had a graded introduction to diet, with commencement of fluids initially followed by solid nutrition in the preceding postoperative days. This is contrary to the current ERAS guidance for patients in the United Kingdom.

It is interesting that the ERAS protocols published there is no specific volume of fluid allowed orally but the IV volume is strictly reviewed [9, 14]. More studies are available on the IV administration of fluid and rates of ileus than the fluid which directly interacts with the bowel – oral [10–12]. Ileus is a multifactorial complication. Patient physiology, co-morbidities, medication used during and after surgery, the nature of the surgery and the postoperative fluid management will all influence ileus rates, therefore it is not as simple as influencing one individual factor [43].

Acknowledging the multifactorial aetiology, this review demonstrates that the impact of oral ingestion on ileus rates has yet to be addressed fully. Some oral ingestion is safe (according to all studies included). What remains unclear is how much. This leads to the potential for a further RCT comparing a liberal intake regimen against a gradiated intake approach and its impact on ileus rates within an ERAS programme. Due to the paucity of data available, the specific components of a restricted intake arm (whether this should be on a restriction in absolute volume or on a mL/kg/hour basis) is not available. Furthermore, due to the multifactorial cause of ileus, such a trial would need to be carefully designed to eliminate the significant potential confounders.

The strengths within this review are the systematic approach to paper assessment and data collection. All attempts have been made to ensure the approach is objective and all relevant papers are included.

There are, however, significant limitations in this work. This review was restricted by the low number of good quality RCTs available; only eight trials were suitable for inclusion. Each had inherent problems with bias (Table 9): all studies were non-blinded. The heterogeneity within the data negated the potential for meta-analysis assessment. All studies have low numbers of participants, in total only 883 patients were included. The inability to control confounding factors and consequent stratification of patients according to the length and nature as well as the indication of the operation conducted imposes another risk in outcome estimation and inherent limitation of this study. There is very little data on concordance with protocols and none of these studies were conducted within an ERAS protocol. The lengthy timeframes between studies also leads to increased confounders. Nonetheless, analysing these limitations imposed by the employed RCTs, one becomes clear, the necessity for well-designed balanced RCTs in order to resolve this important clinical question for the benefit of postoperative patients.

5. Conclusion

In 1994 Binderow *et al.* [17] concluded that 'further investigation is needed to determine the proper diet in the early postoperative period.' In 2022, 28 years later, we have not found evidence that this work has been completed. This review has shown that it is unclear how the oral fluid volume intake postoperatively affects gastrointestinal function and ileus. We are therefore unable to give a specific recommendation to update the current ERAS guidelines. The optimum fluid volume and type of postoperative diet for patients following elective colorectal surgery within an ERAS programme remains an important area for further research.

Ethical approval

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Author contributions

All authors have made substantial contributions to each of the following: 1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; 3) final approval of the version to be submitted. The authors had no writing assistance. All authors have read and complied with the author guidance.

Trial registry number

1. Name of the registry: Prospero
2. Unique Identifying number or registration ID: CRD42020189311
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020189311

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Appendix A. Supplementary data

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