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Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications (Review)

Herbert G, Perry R, Andersen HK, Atkinson C, Penfold C, Lewis SJ, Ness AR, Thomas S

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Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD004080.

DOI: [10.1002/14651858.CD004080.pub4](https://doi.org/10.1002/14651858.CD004080.pub4).

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[Intervention Review]

Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications

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Editorial group: Cochrane Colorectal Group.

Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 7, 2019.

Citation: Herbert G, Perry R, Andersen HK, Atkinson C, Penfold C, Lewis SJ, Ness AR, Thomas S. Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications. *Cochrane Database of Systematic Reviews* 2019, Issue 7. Art. No.: CD004080. DOI: [10.1002/14651858.CD004080.pub4](https://doi.org/10.1002/14651858.CD004080.pub4).

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ABSTRACT

Background

This is an update of the review last published in 2011. It focuses on early postoperative enteral nutrition after lower gastrointestinal surgery. Traditional management consisted of 'nil by mouth', where patients receive fluids followed by solids after bowel function has returned. Although several trials have reported lower incidence of infectious complications and faster wound healing upon early feeding, other trials have shown no effect. The immediate advantage of energy intake (carbohydrates, protein or fat) could enhance recovery with fewer complications, and this warrants a systematic evaluation.

Objectives

To evaluate whether early commencement of postoperative enteral nutrition (within 24 hours), oral intake and any kind of tube feeding (gastric, duodenal or jejunal), compared with traditional management (delayed nutritional supply) is associated with a shorter length of hospital stay (LoS), fewer complications, mortality and adverse events in patients undergoing lower gastrointestinal surgery (distal to the ligament of Treitz).

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL, the Cochrane Library 2017, issue 10), Ovid MEDLINE (1950 to 15 November 2017), Ovid Embase (1974 to 15 November 2017). We also searched for ongoing trials in ClinicalTrials.gov and World Health Organization International Clinical Trials Registry Platform (15 November 2017). We handsearched reference lists of identified studies and previous systematic reviews.

Selection criteria

We included randomised controlled trials (RCT) comparing early commencement of enteral nutrition (within 24 hours) with no feeding in adult participants undergoing lower gastrointestinal surgery.

Data collection and analysis

Two review authors independently assessed study quality using the Cochrane 'Risk of bias' tool tailored to this review and extracted data. Data analyses were conducted according to the Cochrane recommendations.

We rated the quality of evidence according to GRADE.

Primary outcomes were LoS and postoperative complications (wound infections, intraabdominal abscesses, anastomotic dehiscence, pneumonia).

Secondary outcomes were: mortality, adverse events (nausea, vomiting), and quality of life (QoL).

LoS was estimated using mean difference (MD (presented as mean $\pm$ SD). For other outcomes we estimated the common risk ratio (RR) and calculated the associated 95% confidence intervals. For analysis, we used an inverse-variance random-effects model for the primary outcome (LoS) and Mantel-Haenszel random-effects models for the secondary outcomes. We also performed Trial Sequential Analyses (TSA).

Main results

We identified 17 RCTs with 1437 participants undergoing lower gastrointestinal surgery. Most studies were at high or unclear risk of bias in two or more domains. Six studies were judged as having low risk of selection bias for random sequence generation and insufficient details were provided for judgement on allocation concealment in all 17 studies. With regards to performance and deception bias; 14 studies reported no attempt to blind participants and blinding of personnel was not discussed either. Only one study was judged as low risk of bias for blinding of outcome assessor. With regards to incomplete outcome data, three studies were judged to be at high risk because they had more than 10% difference in missing data between groups. For selective reporting, nine studies were judged as unclear as protocols were not provided and eight studies had issues with either missing data or incomplete reporting of results.

LOS was reported in 16 studies (1346 participants). The mean LoS ranged from four days to 16 days in the early feeding groups and from 6.6 days to 23.5 days in the control groups. Mean difference (MD) in LoS was 1.95 (95% CI, -2.99 to -0.91, $P < 0.001$) days shorter in the early feeding group. However, there was substantial heterogeneity between included studies ($I^2 = 81$, %, $\text{Chi}^2 = 78.98$, $P < 0.00001$), thus the overall quality of evidence for LoS is low. These results were confirmed by the TSA showing that the cumulative Z-curve crossed the trial sequential monitoring boundary for benefit.

We found no differences in the incidence of postoperative complications: wound infection (12 studies, 1181 participants, RR 0.99, 95%CI 0.64 to 1.52, very low-quality evidence), intraabdominal abscesses (6 studies, 554 participants, RR 1.00, 95%CI 0.26 to 3.80, low-quality evidence), anastomotic leakage/dehiscence (13 studies, 1232 participants, RR 0.78, 95%CI 0.38 to 1.61, low-quality evidence; number needed to treat for an additional beneficial outcome (NNTB) = 100), and pneumonia (10 studies, 954 participants, RR 0.88, 95%CI 0.32 to 2.42, low-quality evidence; NNTB = 333).

Mortality was reported in 12 studies (1179 participants), and showed no between-group differences (RR = 0.56, 95%CI, 0.21 to 1.52, $P = 0.26$, $I^2 = 0\%$, $\text{Chi}^2 = 3.08$, $P = 0.96$, low-quality evidence). The most commonly reported cause of death was anastomotic leakage, sepsis and acute myocardial infarction.

Seven studies (613 participants) reported vomiting (RR 1.23, 95%CI, 0.96 to 1.58, $P = 0.10$, $I^2 = 0\%$, $\text{Chi}^2 = 4.98$, $P = 0.55$, low-quality evidence; number needed to treat for an additional harmful outcome (NNTH) = 19), and two studies (118 participants) reported nausea (RR 0.95, 0.71 to 1.26, low-quality evidence). Four studies reported combined nausea and vomiting (RR 0.94, 95%CI 0.51 to 1.74, very low-quality evidence). One study reported QoL assessment; the scores did not differ between groups at 30 days after discharge on either QoL scale EORTC QLQ-C30 or EORTC QLQ-OV28 (very low-quality evidence).

Authors' conclusions

This review suggests that early enteral feeding may lead to a reduced postoperative LoS, however cautious interpretation must be taken due to substantial heterogeneity and low-quality evidence. For all other outcomes (postoperative complications, mortality, adverse events, and QoL) the findings are inconclusive, and further trials are justified to enhance the understanding of early feeding for these. In this updated review, only a few additional studies have been included, and these were small and of poor quality.

To improve the evidence, future trials should address quality issues and focus on clearly defining and measuring postoperative complications to allow for better comparison between studies. However due to the introduction of fast track protocols which already include an early feeding component, future trials may be challenging. A more feasible trial may be to investigate the effect of differing postoperative energy intake regimens on relevant outcomes.

PLAIN LANGUAGE SUMMARY

The effect of having nutrition within the first 24 hours after bowel surgery on length of hospital stay and postoperative complications

Review question

To look at whether feeding patients early after surgery (orally or through a tube) can help them to leave hospital sooner with fewer complications.

Background

Traditionally, after gastrointestinal surgery, it was usual for patients not to be given any food until their bowel regained some function (e.g. bowel sounds, passing wind, bowel motion). Studies have looked at whether feeding patients sooner after surgery can help reduce complications (e.g. pneumonia), but there are mixed results. It is important to do this update of the review because the evidence in previous reviews is not extensive. The relevance of early feeding following its incorporation within a programme of patient care (also known as the enhanced recovery after surgery (ERAS)), remains an important question to answer.

Study characteristics

This review found 17 relevant studies that recruited 1437 participants in total who had undergone lower gastrointestinal surgery (distal to the ligament of Treitz).

Key results

We found evidence that patients who received nutrition within the first 24 hours after their surgery were able to leave hospital almost two days sooner than those patients who were not given any nutrition until their bowel activity returned. However, the quality of the evidence is low and therefore early feeding after surgery may not lead to patients leaving hospital sooner. They may also have a reduced risk of dying. However, we found weak evidence that patients who were given nutrition within the first day after their operation were more at risk of vomiting. There were no differences in complication rates (such as wound infection or pneumonia) between patients who were fed early and those that were not.

Quality of the evidence

All studies were of low quality, which may mean their results are less reliable. To explore further early feeding after surgery, more studies are needed which are larger and of better quality.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement

Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement

Patient or population: lower gastrointestinal surgery

Setting: hospital

Intervention: early enteral nutrition

Comparison: later commencement

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk with no calories	Corresponding risk with early enteral nutrition				
Length of hospital stay (days)	The mean LoS of control groups ranged from six to 24 days	MD 1.95 lower (2.99 lower to 0.91 lower)	-	1346 (16 RCTs)	⊕⊕⊕⊕ LOW ¹	Trial Sequential Analysis showed that the boundary for benefit was crossed. This indicates that early feeding seems to decrease the mean length of hospital stay by at least one day if risk of bias and other threats to the validity can be disregarded
Wound infection	91 per 1,000	91 per 1,000 (58 to 138) (33 fewer to 47 more)	RR 0.99 (0.64 to 1.52)	1181 (12 RCTs)	⊕⊕⊕⊕ VERY LOW ²	Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of wound infection by 30% or more
Intraabdominal abscess	29 per 1,000	29 per 1,000 (8 to 110) (21 fewer to 81 more)	RR 1.00 (0.26 to 3.80)	554 (6 RCTs)	⊕⊕⊕⊕ LOW ³	It was not possible to perform Trial Sequential Analysis due to limited data and too few events
Anastomotic leakage/dehiscence	47 per 1,000	37 per 1,000 (18 to 76) (19 fewer to 29 more)	RR 0.78 (0.38 to 1.61)	1232 (13 RCTs)	⊕⊕⊕⊕ LOW ³	Absolute risk reduction: 0.01 Thus, for every 1000 participants receiving early feeding, 10 less anastomotic leakage compared to later commencement. Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of anastomotic leakage/dehiscence by 30% or more

Pneumonia (within hospital stay)	21 per 1,000	18 per 1,000 (7 to 51) (14 fewer to 30 more)	RR 0.88 (0.32 to 2.42)	954 (10 RCTs)	⊕⊕⊕⊕ LOW ³	Absolute risk reduction: 0.003 Thus, for every 1000 participants receiving early feeding, 3 less pneumonia compared to later commencement. Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of pneumonia by 30% or more
Mortality	30 per 1,000	17 per 1,000 (6 to 46) (24 fewer to 16 more)	RR 0.56 (0.21 to 1.52)	1179 (12 RCTs)	⊕⊕⊕⊕ LOW ⁴	Absolute risk reduction: 0.013 Thus, for every 1000 participants receiving early feeding, 13 less mortality compared to later commencement. Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of mortality by 30% or more
Vomiting	231 per 1,000	284 per 1,000 (222 to 365) (9 fewer to 134 more)	RR 1.23 (0.96 to 1.58)	613 (7 RCTs)	⊕⊕⊕⊕ LOW ⁵	Absolute risk reduction: - 0.053 So for every 1000 participants receiving early feeding, 53 more vomiting compared to later commencement. Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of vomiting by 30% or more
Nausea	627 per 1,000	596 per 1,000 (445 to 790) (172 fewer to 163 more)	RR 0.95 (0.71 to 1.26)	118 (2 RCTs)	⊕⊕⊕⊕ LOW ⁵	Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of nausea by 30% or more
Nausea and vomiting	262 per 1,000	241 per 1,000 (157 to 369) (105 fewer to 107 more)	RR 0.92 (0.60 to 1.41)	238 (4 RCTs)	⊕⊕⊕⊕ VERY LOW ⁶	Trial Sequential Analysis showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of nausea and vomiting by 30% or more
Quality of Life	1 study: EORTC OV-28 (global): Traditional feeding 28.6(13.7) versus early feeding 26.5(14.9), P= 0.68. EORTC C-30 (global): Traditional feeding 56.1(22.2) versus early feeding 64.6(17.1), P=0.172.				⊕⊕⊕⊕ LOW ⁷	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Abbreviations: **CI**: Confidence interval; **WMD**: weighted mean differences; **RR**: Risk ratio

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹Downgraded by two levels because of the following: risk of bias (blinding did not occur in any study; random sequence generation and allocation concealment were poorly reported) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I²)

²Downgraded by three levels because of the following: risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment were poorly reported, and selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement), imprecision (confidence intervals are wide) and indirectness (included various definitions e.g. some incorporated pelvic abscesses whilst others did not; unclear definition of outcome)

³Downgraded by two levels because of the following: risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment were poorly reported, selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement) and imprecision (confidence intervals are wide and very few events occurred)

⁴Downgraded by two levels because of the following: indirectness (unclear definition whether mortality occurred prior or after discharge) and imprecision (confidence intervals are wide and very few events occurred)

⁵Downgraded by two levels because of the following: risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment were poorly reported, selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement) and imprecision (confidence intervals are wide)

⁶Downgraded by three levels because of the following: risk of bias (blinding did not occur in any study, allocation concealment was poorly reported, selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement) and imprecision (confidence intervals are wide) and indirectness (included various definitions of nausea and vomiting)

⁷Downgraded by two levels because of the following: risk of bias (blinding did not occur in this study, allocation concealment was poorly reported, selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement) and imprecision (just one study available)

Summary of findings 2. Subgroup and Sensitivity analyses

Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement

Patient or population: lower gastrointestinal surgery

Setting: hospital

Intervention: early enteral nutrition

Comparison: later commencement

Outcomes	Anticipated absolute effects* (95% CI)	Relative effect (95% CI)	No. of participants	Quality of the evidence	Comments
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	Assumed risk with no calories	Corresponding risk with early enteral nutrition		(studies)	(GRADE)
Subgroup 1: Length of hospital stay (days) distal to ligament of Treitz	The mean LoS of control groups ranged from 6 to 17 days	MD 1.77 shorter (2.95 shorter to 0.59 shorter)	-	1156 (13 RCTs)	⊕⊕⊕⊕ LOW ¹
Subgroup 2: Length of hospital stay (days) distal and proximal to ligament of Treitz	The mean LoS of control groups ranged from 9 to 24 days	MD 2.58 days shorter (4.40 days shorter to 0.76 days shorter)	-	190 (3 RCTs)	⊕⊕⊕⊕ LOW ²
Subgroup 3: Length of hospital stay (days) oral feeding only	The mean LoS of control groups ranged from 6 to 17 days.	MD 2.06 days shorter (3.26 days shorter to 0.87 days shorter)	-	1075 (11 RCTs)	⊕⊕⊕⊕ LOW ¹
Subgroup 4: Length of hospital stay (days) tube feeding with/without oral feeding	The mean LoS of control groups ranged from 9 to 24 days.	MD 1.75 days shorter (4.32 days shorter to 0.82 days shorter)	-	271 (5 RCTs)	⊕⊕⊕⊕ VERY LOW ³
Sensitivity analysis 2: Removing studies with imputed results	The mean LoS of control groups ranged from seven to 17 days	MD 2.27 days shorter (3.62 days shorter to 0.92 days shorter)	-	396 (5 RCTs)	⊕⊕⊕⊕ VERY LOW ³
Sensitivity analysis 3: Worst case scenario imputation	The mean LoS of control groups ranged from 6 to 24 days	MD 2.06 days shorter (3.18 days shorter to 0.94 days shorter)	-	235 (3 RCTs)	⊕⊕⊕⊕ LOW ¹
Sensitivity analysis 4: Best case scenario imputation	The mean LoS of control groups ranged from 6 to 24 days	MD 1.80 days shorter (2.61 days shorter to 1.00 day shorter)	-	235 (3 RCTs)	⊕⊕⊕⊕ LOW ¹

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Abbreviations: **CI**: Confidence interval; **WMD**: weighted mean differences; **RR**: Risk ratio

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹Downgraded by two levels because of the following: risk of bias (blinding did not occur in any study; random sequence generation and allocation concealment were poorly reported) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I²)

²Downgraded by two levels because of the following: risk of bias (blinding did not occur in any study and allocation concealment was poorly reported) and imprecision (confidence intervals are wide and only based on 3 studies)

³Downgraded by three levels because of the following: risk of bias (blinding did not occur in any study and allocation concealment was poorly reported) and imprecision (confidence intervals are wide) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I²)

BACKGROUND

Description of the condition

Traditionally, it was standard in many elective surgical practices to keep patients 'nil by mouth' (NBM) from the previous evening (six to 12 hours preoperatively) and postoperatively for several days until resolution of ileus: a period of loss of peristalsis that is often experienced after lower gastrointestinal surgery (Weissenfluh 2006). Evidence of bowel motility (such as the reappearance of bowel sounds and passage of flatus or bowel movement) may (although are poor markers of resolution of ileus), signify resolution of ileus, following which individuals would begin with a clear liquid diet and slowly advance to a regular diet (Warren 2011). This period of bowel rest (Grizas 2008) was considered important to prevent complications such as anastomotic dehiscence, aspiration pneumonia, bowel distension, bowel obstruction and nausea and vomiting (Maessen 2009). Surgical patients in the past were however often malnourished (Hill 1977; Lennard-Jones 1992; McWhirter 1994), which may have caused an increase in morbidity and mortality (Vet's Affairs 1991). In recent years this practice has been challenged as studies have shown that both pre- and postoperative fasting may be periods of unnecessary starvation that result in adverse consequences on patient outcomes (Andersen 2011; Ljungqvist 2009; Viganò 2012). Avoidance of long periods of preoperative fasting, the use of preoperative carbohydrate loading and re-establishment of oral feeding as soon as possible after surgery have been incorporated within the Enhanced Recovery After Surgery (ERAS) programme (Department of Health 2010).

Description of the intervention

Prolonged fasting after surgery may deplete the patient of vital nutrients (McWhirter 1994). A common practice in the postoperative management of patients who undergo gastrointestinal surgery has been to withhold nutrition until bowel function is restored. The fear being that early enteral nutrition may encourage ileus, anastomotic leakage/dehiscence or aspiration pneumonia. It has been suggested that feeding in the postoperative management of patients may actually help reduce postoperative complications and their stay in hospital (da Fonseca 2011).

How the intervention might work

Within 24 hours of starvation, changes in the body's metabolism are evident including increased insulin resistance and reduced muscle function. Experimental data from both humans and animals (Fukuzawa 2007) suggest that providing nutrition in the postoperative period improves wound healing (relevant to the integrity of the intestinal anastomosis), muscle function and reduces sepsis. Furthermore, it has been suggested that early enteral nutrition is useful for recovering gastrointestinal motility and maintaining the nutritional status for patients undergoing gastrointestinal surgery (Kawasaki 2009).

Why it is important to do this review

Studies have shown improved wound healing (Karl 2014; Schroeder 1991), and reduced infectious complications (Moore 1989) with early nutrition. The first randomised study to show jejunal feeding was tolerated within 24 hours of surgery was published in 1979 and showed a reduced length of hospital stay (LoS) in patients fed early (Sagar 1979). Subsequently, there have been further studies

which have explored the safety and benefits of early postoperative feeding (Chatterjee 2012; Dag 2011) with mixed results in terms of benefits in relation to LoS and postoperative complications such as pneumonia, anastomotic dehiscence, abdominal abscess and wound infection. Early postoperative feeding has now been incorporated into the UK ERAS programme. However, the extent to which early postoperative feeding is implemented clinically is unclear, and it is a care practice that is not always carried out. Ahmed and colleagues (Ahmed 2012) conducted a systematic review of 11 studies in a variety of countries reporting compliance to individual ERAS elements in a clinical setting in colorectal surgical patients. In the nine studies which reported relevant data, compliance with early postoperative feeding ranged from 13% to 100%. Another study showed that of the 861 colorectal surgical patients enrolled in an ERAS programme, 65% had 'normal food' but this was on postoperative day two (Maessen 2009). These studies show that early feeding is not consistently implemented. The previous reviews of early postoperative feeding were limited by the available evidence and so an update is warranted. This systematic review summarises the available evidence on early enteral nutrition within the first 24 hours post lower gastrointestinal surgery (distal to the ligament of Treitz) on LoS and complications.

OBJECTIVES

To evaluate whether early commencement of postoperative enteral nutrition (within 24 hours), oral intake and any kind of tube feeding (gastric, duodenal or jejunal), compared with traditional management (delayed nutritional supply) is associated with a shorter length of hospital stay (LoS), fewer complications, mortality and adverse events in patients undergoing lower gastrointestinal surgery (distal to the ligament of Treitz).

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs), including cluster-RCTs, of early enteral nutrition (defined as oral intake or using any kind of tube feeding: gastric, duodenal or jejunal) containing energy (carbohydrate, protein or fat) that commenced within 24 hours postoperatively in patients undergoing either acute or elective lower gastrointestinal surgery (distal to the ligament of Treitz). Trials were considered irrespective of whether blinding or placebo treatment was performed. Studies reporting comparison of treatment between parenteral, enteral nutrition and controls were included only if data could be provided separately for patients in the feeding group and control group. Studies with multiple arms were included if data allowed a clear distinction between each single group. Unpublished studies and abstracts were considered and included if we were able to obtain complete manuscripts from the author(s).

Types of participants

We included studies of adult participants (above 18 years of age and both gender) undergoing lower gastrointestinal surgery, with malignant or benign disease including inflammatory bowel diseases. We defined lower gastrointestinal surgery as where an anastomosis was formed distal to the ligament of Treitz. Studies including participants with surgery distal as well as proximal to the ligament of Treitz were included.

Types of interventions

This review focused on early enteral feeding, regardless of method (oral or tube), defined as nutrition given within the first 24 hours postoperatively to patients undergoing surgery in the lower gastrointestinal tract. The control arm was traditional management, defined as no oral intake or any kind of tube feeding containing energy before bowel function returns. The following were excluded: studies in children (i.e. age less than 18 years); trials comparing different types of enteral nutrition with each other; trials in which patients served as their own controls and cross-over trials; trials reporting only upper gastrointestinal surgery; and trials on parenteral nutrition.

Types of outcome measures

Primary outcomes

1. Length of hospital stay (days)
2. Postoperative complications using the Clavien-Dindo classification for surgical complications (Dindo 2004):
 - a. wound infections (e.g. a standardised criteria to assess wound infection (Buzby II-IV: Buzby 1988))
 - b. intraabdominal abscesses
 - c. anastomotic leakage/dehiscence
 - d. pneumonia (within hospital stay)

Secondary outcomes

1. Mortality
2. Adverse events: nausea, vomiting (within hospital stay)
3. Quality of Life (standardised scale)

Search methods for identification of studies

Electronic searches

We conducted a comprehensive literature search to identify all published and unpublished randomised controlled trials with no language or date of publication restrictions. The following electronic databases were searched:

1. Cochrane Central Register of Controlled Trials (CENTRAL; 2017, issue 10) in the Cochrane Library (15 November 2017) (Appendix 1);
2. Ovid MEDLINE (from 1946 to 15 November 2017) (Appendix 2);
3. Ovid Embase (from 1974 to 15 November 2017) (Appendix 3);
4. US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov; searched 15 November 2017);
5. World Health Organization International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/>; searched 15 November 2017)

6. LILACS (Latin American and Caribbean Health Science Information database) (from 1979 to 20 December 2013) (Appendix 4)

A sensitivity- and precision-maximising search filter (RCT) was applied to the MEDLINE and Embase search strategies as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 6.4.11, Higgins 2011).

We searched for ongoing trials in Clinicaltrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) database (WHO ICTRP database), by using combinations of search terms including "early AND feeding" and "enteral AND nutrition".

We also searched conference abstracts from the most recent gastrointestinal conferences (DDW, ASCO, UEGW).

Searching other resources

We searched Google and Google Scholar, and handsearched reference lists of identified studies, previous reviews and systematic reviews for additional relevant articles.

Data collection and analysis

Selection of studies

Two review authors (CA and SL) independently screened titles and abstracts of all studies identified from searches. Each study was coded as either eligible for inclusion (potentially eligible/unclear) or excluded. The review authors were blinded to each others' codes. We retrieved full-text copies of all eligible and potentially eligible studies, and the same two review authors (CA and SL) independently screened full texts, identified studies for inclusion, and recorded reasons for exclusion of the ineligible studies. Disagreements were resolved through discussion or consultation with a third and fourth author (HA and ST).

We collated multiple reports that related to the same study, so that each study rather than each report was the unit of interest in the review. For any studies reported in multiple publications, we used the reference that provided the most comprehensive information. We contacted authors of studies eligible for inclusion to clarify inclusion/exclusion criteria of their research, where further information was needed. Articles in foreign languages were translated by a person (not in the byline) who could read and write that language, if they matched the inclusion criteria, data were extracted onto the data extraction form (CA and SL). Justification for excluding studies has been reported in the [Characteristics of excluded studies](#).

We have presented the overall selection process in detail in the PRISMA flow diagram (Figure 1).

Figure 1. Study flow diagram.

Figure 1. (Continued)

Data extraction and management

We developed a data extraction form adapted for this review ([Appendix 5](#)) from an original form provided by Cochrane Colorectal Cancer Group and a previous Cochrane review ([Short 2015](#)).

Two review authors (GH and RP) piloted it on two studies selected for inclusion, prior to its use for all studies. The same review authors independently extracted the study characteristics and outcome from the included studies.

Titles and abstracts that were not available in English were translated by a person (not in the byline) who could read and write that language. If a trial in a non-English language matched the inclusion criteria, it was directly extracted onto the data extraction form, confirmed by two review authors (GH and RP). Hereafter, two review authors (GH and RP) transferred all data into the Review Manager 5.3 software ([RevMan 2014](#)). A third review author (ST) checked all the extracted data for accuracy against the trial reports.

For included studies with multiple reports, we extracted data from the report with the most recent data for a specific outcome.

Assessment of risk of bias in included studies

Two review authors (GH and RP) independently assessed risk of bias for each study. The 'Risk of bias' tool that we used was based on the criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 8: [Higgins 2011](#); [Appendix 6](#)) and was tailored to this review (see [Appendix 5](#)). We developed this as data extraction continued. We judged each potential source of bias as high, low or unclear risk, using the criteria provided in [Appendix 6](#) for the following domains.

1. Random sequence generation
2. Allocation concealment
3. Blinding of participants and personnel
4. Blinding of outcome assessment

5. Incomplete outcome data

6. Selective outcome reporting

Two review authors (GH and RP) discussed the risk of bias for all studies to ensure uniformity and agreement. For each outcome we summarised the 'Risk of bias' judgements across different studies for the domains listed. Single studies were categorised as overall low risk of bias if they has low risk across all domains; overall unclear risk of bias with unclear risk in one or more key domains; and overall high risk of bias with high risk in one or more key domains.

For the sensitivity analysis we listed four of the seven standard domains (random sequence generation, allocation concealment, incomplete outcome data and selective outcome reporting), considered the most important for determining the validity of our findings.

For the outcome 'mortality' we judged and categorised lack of blinding of participants as low risk of bias.

Measures of treatment effect

We considered continuous variables (LoS) as weighted mean differences (WMD), and included 95% confidence intervals (95% CIs). We considered frequency of postoperative complications and adverse events related to the intervention, and presented dichotomous data using a risk ratio (RR) with 95% confidence intervals (CIs).

Unit of analysis issues

We found no unit of analysis issues. The individual participant is the unit of analysis in all the included trials. No studies used cluster-randomisation, and as cluster-RCT's do not work well with surgery; this study design is unlikely for future updates of this review.

Dealing with missing data

Regarding trials with incompletely reported outcomes, two review authors (SL and GH) contacted the lead authors of the primary study to request further information (Chapter 16: Higgins 2011). Details of those studies which include results from additional correspondence are included in Table 1. With regards to participants missing from included studies, we have based analyses on intention-to-treat for relevant outcome measures.

Where primary outcome data were not provided in the form of a mean and standard deviation, we derived these from the reported test statistics or estimated them from the reported data if suitable test statistics were not reported. We used the following methods to estimate or impute missing data (see Table 2 for further details).

1. Where LoS results were presented as median and range, we estimated mean and standard deviation using the formulae described by Wan 2014.
2. We imputed missing standard deviations for LoS using the mean of the standard deviations reported by other studies within that treatment arm.
3. Where LoS were presented as Kaplan-Meier graphs, we extracted the following LoS data for each trial arm where available: median (50%), inter-quartile range (25% to 75%) and range (minimum and maximum). Mean LoS and its associated standard deviation were subsequently derived as described above. We did not use results for LoS presented as hazard ratios without further descriptive LoS measures to estimate median LoS, due to potentially high uncertainty in estimation (Cortes 2014).
4. Where complications were reported as percent incidence, we converted this into the number of participants who experienced complications.

Assessment of heterogeneity

We determined clinical heterogeneity on the basis of both the participant demographic data and methodology of the studies. We assessed statistical heterogeneity across studies by visual inspection of the forest plot and using the χ^2 measurement. Heterogeneity is more difficult to detect when sample sizes and number of events are small, so we used a cut off of $P < 0.01$ for the χ^2 measurement to decide if there was statistical evidence of heterogeneity as described in the *Cochrane Handbook for Systematic Reviews of Intervention* (Chapter 9.5, Deeks 2011). As a measure of the variation in intervention effect due to statistical heterogeneity, we also assessed the I^2 statistic. We applied the following thresholds for the interpretation of the I^2 statistic (Deeks 2011).

1. 0% to 40%: might not be important
2. 30% to 60%: may represent moderate heterogeneity
3. 50% to 90%: may represent substantial heterogeneity
4. 75% to 100%: considerable heterogeneity

Clinical heterogeneity was explored through post-hoc subgroup analyses, as described in the [Subgroup analysis and investigation of heterogeneity](#) section.

Assessment of reporting biases

We assessed reporting bias using funnel plot asymmetry of included studies. We did not assess funnel plot asymmetry for outcomes reported in fewer than 10 studies, since it is considered unreliable as described in the *Cochrane Handbook for Systematic Reviews of Intervention* (Chapter 10, Sterne 2011). We visually inspected funnel plots for asymmetry, and for continuous outcomes we used Egger's regression test. There is currently no guidance for testing funnel plot asymmetry for outcomes measured as risk ratios (Sterne 2011). The application of funnel plot asymmetry tests to detect publication bias is considered appropriate and meaningful for outcomes with more than 10 included trial as recommended in the *Cochrane Handbook for Systematic Reviews of Intervention* (Sterne 2011).

Data synthesis

We performed analyses in RevMan 5.3 (RevMan 2014). Analyses comprised only within-study comparisons rather than individual-level data. For analysis, we used an inverse-variance random-effects model for the primary outcome (LoS) and Mantel-Haenszel random-effects models without zero-cell correction (Higgins 2011) for dichotomous outcomes (Bradburn 2007), since the event risks $>1\%$. The effect of a continuity correction (0.5) for trial arms with zero events was assessed in our sensitivity analyses.

We undertook Trial Sequential Analysis (TSA) using TSA software (Thorlund 2011) to calculate the required information size, and to determine whether the cumulative Z-curve of the trial sequential analysis boundaries for benefit, harm, or futility were crossed. The required information size for the primary outcome (LoS) was based on a reduction in mean LoS of one day with an associated variance of nine days, using results from a comparable population of people receiving colorectal surgery (Short 2015). We also used an alpha of 3.3% (accounting for multiple outcomes Jakobsen 2016), a beta of 20%, and the observed diversity in the trials in the meta-analysis (Jakobsen 2014). For postoperative complications and secondary outcomes, which were all dichotomous outcomes, we estimated the required information size based on the proportion of participants in the control group with the outcome, a relative risk reduction of 30%, an alpha of 2.5% (accounting for multiple outcomes Jakobsen 2016), a beta of 20%, and the observed diversity in the trials in the meta-analysis. To maintain approximate consistency with our main data synthesis, we included a continuity correction of 0.001 for the TSA (the TSA software does not allow no zero-cell correction).

We performed the analyses using Review Manager 5 (RevMan 2014), R with the 'meta' package (Schwarzer 2007), and Trial Sequential Analysis (TSA - Trial Sequential Analysis).

Subgroup analysis and investigation of heterogeneity

We conducted two post-hoc subgroup analyses to explore the effect of clinical diversity on LoS. Given that some trials had included patients undergoing surgery either distal or proximal to the ligament of Treitz (but which could not be separated out for analysis), we conducted a post-hoc subgroup analysis for LoS to determine the sensitivity of overall conclusions to the surgical site. We created two subgroups: one which encompassed trials that had only included patients having surgery distal to the ligament of Treitz (this group was termed 'distal to ligament of Treitz'), and the other group, which encompassed trials that had included patients

undergoing surgery either distal or proximal to the ligament of Treitz (this group was termed 'distal and proximal to ligament of Treitz'). We also created two subgroups relating to whether the route of postoperative feeding used in the intervention was 'oral feeding only' or by 'tube feeding with or without oral feeding'. We also planned to conduct two further subgroup analyses; one comparing patients who have elective surgery versus acute surgery and the other comparing patients with cancer versus non-cancerous conditions.

Sensitivity analysis

We conducted sensitivity analyses based on methodological and reporting quality of the studies analysed. We considered the impact of methodological quality by excluding studies of high risk of bias and we assessed how robust our overall results were to the use of estimates for missing data. We therefore conducted the following sensitivity analyses.

1. We repeated meta-analysis of the primary outcome LoS excluding studies found to be at high risk of bias for at least two of the following components: random sequence generation, allocation concealment, incomplete outcome data and selective outcome reporting.
2. In order to determine whether imputation or estimation of missing data biased results, the meta-analysis of LoS was repeated with the following changes:
 - a. we excluded studies with imputed results;

- b. instead of using the mean of the standard deviations reported by other studies, we used the maximum (worst-case scenario) and the minimum (best-case scenario) reported standard deviations.

3. To determine the effect of including trials with zero events in one of the arms, we repeated our analysis of dichotomous outcomes with a continuity correction of 0.5 was added to an arm of a study with zero events. Studies with zero events in both arms were not included in the data synthesis.

'Summary of findings' tables

We assessed the overall quality of evidence of all outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach in 'Summary of findings' tables (Schünemann 2009).

The quality of evidence can be downgraded one level (serious concern) or two levels (very serious concern) for one of the following reasons: study limitations (risk of bias), inconsistency of evidence, indirectness (indirect outcomes, interventions, controls), imprecision (wide confidence interval, small sample size) and publication bias. Judgements about the quality of the evidence (high, moderate, low or very low) were justified, documented and incorporated into the reporting of results for each outcome.

The GRADE system classifies the quality of evidence in one of four grades.

Grade	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence on the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

RESULTS

Description of studies

Results of the search

The original version of this review was published in 2001 (Lewis 2001). It was published as a Cochrane Review in 2006 (Andersen 2006) and updated in 2011 (Andersen 2011), including the following 14 studies: (Beier-Holgersen 1996; Binderow 1994; Carr 1996; Hartsell 1997; Heslin 1997; Lucha 2005; Mulrooney 2004; Ortiz 1996; Reissman 1995; Sagar 1979; Schroeder 1991; Smedley 2004; Stewart 1998; Watters 1997). Three of these studies have been removed from the present update. Two because they were dealing with upper gastrointestinal surgery only (Heslin 1997; Watters 1997), and one study did not have a control group that was nil by mouth (NBM)/received no energy (Smedley 2004). See tables of [Characteristics of included studies](#), [Characteristics of excluded studies](#). Regarding seven trials which did not fully report

on outcomes, we contacted the trial authors and received four usable responses (Dag 2011; Mulrooney 2004; Ortiz 1996; Stewart 1998): three with further information about length of hospital stay (LoS) (Mulrooney 2004; Ortiz 1996; Stewart 1998), and three about both primary and secondary outcomes (Dag 2011; Mulrooney 2004; Stewart 1998). Regarding three trials where it was unclear if they met the inclusion criteria, all authors responded and confirmed they met inclusion criteria (da Fonseca 2011; Nakeeb 2009; Reissman 1995). We contacted first authors for two included studies for additional information, but the correspondence did not provide usable extra information (Beier-Holgersen 1996; Chatterjee 2012).

For this update, the electronic search identified 3956 records of potential relevance to our review. We identified 62 additional records through handsearching (Google and Google Scholar, and scanning reference lists of included studies and relevant systematic reviews). After removal of 1681 duplicates, 2337 records remained. After initial screening of the titles and abstracts, 2193 records

were excluded. We sought full texts for the remaining 144, and upon screening we excluded 117 records with reasons (see [Characteristics of excluded studies](#)).

In total for this review update, we identified 17 RCT's (27 records) for inclusion, comprising 1437 participants.

We provide full details of the search results in the PRISMA flow diagram ([Figure 1](#)).

Included studies

We provide full characteristics of the 17 independent studies in the [Characteristics of included studies](#) table. For five studies reported in multiple publications, we used the reference that provided the most comprehensive information ([Beier-Holgersen 1996](#); [Binderow 1994](#); [Carr 1996](#); [da Fonseca 2011](#); [Ortiz 1996](#)). Published data were available for all 17 studies for one primary outcome measure (LoS). Additional unpublished data were obtained for three studies for further information about LoS ([Mulrooney 2004](#); [Ortiz 1996](#); [Stewart 1998](#)).

All trials included in the review were randomised controlled trials (RCTs). Studies varied in sample size, although the majority of studies were small. The number of participants in the studies ranged from 28 ([Carr 1996](#)) to 199 ([Dag 2011](#)). Studies were conducted in 12 countries; four in the USA ([Binderow 1994](#); [Hartsell 1997](#); [Lucha 2005](#); [Reissman 1995](#)), three in the UK ([Carr 1996](#); [Mulrooney 2004](#); [Sagar 1979](#)), one in Denmark ([Beier-Holgersen 1996](#)), one in India ([Chatterjee 2012](#)), one in Brazil ([da Fonseca 2011](#)), one in Turkey ([Dag 2011](#)), one in Italy ([Minig 2009](#)), one in Egypt ([Nakeeb 2009](#)), one in Spain ([Ortiz 1996](#)), one in New Zealand ([Schroeder 1991](#)), one in Australia ([Stewart 1998](#)), and one in China ([Yang 2013](#)). One of the included studies ([Yang 2013](#)) was published in Chinese.

The studies adopted different feeding regimens in the intervention groups: in three studies ([Binderow 1994](#); [Lucha 2005](#); [Ortiz 1996](#)), participants began on a regular diet; in seven studies ([da Fonseca 2011](#); [Dag 2011](#); [Hartsell 1997](#); [Minig 2009](#); [Nakeeb 2009](#); [Reissman 1995](#); [Stewart 1998](#)), participants began with a liquid diet and progressed to a regular/solid diet; in two studies ([Beier-Holgersen 1996](#); [Yang 2013](#)) participants began on a nutritional supplement and progressed to a regular diet; in five studies ([Carr 1996](#); [Chatterjee 2012](#); [Mulrooney 2004](#); [Sagar 1979](#); [Schroeder 1991](#)), participants were on enteral feed. The routes of feeding within the intervention group were either through a nasoduodenal ([Beier-Holgersen 1996](#)), nasojejunal ([Carr 1996](#); [Mulrooney 2004](#); [Sagar 1979](#); [Schroeder 1991](#)) or nasogastric ([Chatterjee 2012](#)) tube, or oral ([Binderow 1994](#); [da Fonseca 2011](#); [Dag 2011](#); [Hartsell 1997](#); [Lucha 2005](#); [Minig 2009](#); [Nakeeb 2009](#); [Ortiz 1996](#); [Reissman 1995](#); [Stewart 1998](#); [Yang 2013](#)).

The 17 included studies all describe early enteral feeding after elective lower gastrointestinal surgery, but with a wide variety of gastrointestinal conditions ([Table 1](#)). Nine trials reported patients undergoing colorectal surgery, ([da Fonseca 2011](#); [Dag 2011](#); [Hartsell 1997](#); [Lucha 2005](#); [Mulrooney 2004](#); [Nakeeb 2009](#); [Ortiz 1996](#); [Stewart 1998](#); [Yang 2013](#)). Four reported all surgery distal to the ligament of Trietz ([Binderow 1994](#); [Carr 1996](#); [Reissman 1995](#); [Schroeder 1991](#)) and four reported some surgery proximal to the ligament of Trietz as well as distal ([Beier-Holgersen 1996](#); [Chatterjee 2012](#); [Minig 2009](#); [Sagar 1979](#)). Eight studies did not state the underlying pathology of disease of the study participants, whereas nine stated that they included both benign and malignant conditions.

See [Table 1](#) for an overview of study characteristics regarding site of surgery, feed type, route of feeding, feed timing and amount, pathology and outcomes, definitions and time frames, depending on reporting in the individual studies.

Controls received traditional care, which is where no energy is given until bowel activity/resolution of ileus. Of our outcomes, LoS was the most commonly reported, followed by anastomotic leakage, wound infection, mortality, pneumonia, vomiting, intraabdominal abscess, nausea and vomiting (as a combined outcome), and nausea. Quality of life (QoL) was only reported in one study ([Minig 2009](#)). Additional reported outcomes included postoperative complications such as ileus, thrombosis and urinary tract infection (see [Table 3](#)) and adverse events such as readmission and diarrhoea (see [Table 4](#)).

Excluded studies

Of the 146 full texts assessed for eligibility, we excluded 122 records. The most common justifications for exclusion were not being lower gastrointestinal surgery (N = 22) and not having an appropriate control group (N = 18), followed by not a relevant topic (N = 16), feeding started greater than 24 hours after surgery (N = 15), the study was actually a review (N = 17), the study was not an RCT (N = 12), the study used total parenteral nutrition (N = 9), examined multiple variables not just feeding (N = 3), could not be sourced/not readable (N = 3), or was only available as an abstract (N = 5), feeding commenced post-discharge (n = 1) and one study is still awaiting classification (N = 1).

Risk of bias in included studies

Risk of bias for each included study is described in detail in the [Characteristics of included studies](#) section. Details of 'Risk of bias' judgements for each study are presented in [Figure 2](#) and [Figure 3](#).

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Figure 3. (Continued)

	α	α	α	α	α	α	α	α	α	α	α	α	α
Beier-Holgersen 1996	?	?	+	+	+	+	+	+	+	+	+	+	+
Binderow 1994	?	?	-	-	?	?	-	?	?	-	-	+	-
Carr 1996	?	?	-	-	-	?	-	?	+	-	-	+	-
Chatterjee 2012	?	?	-	-	-	?	-	-	+	-	-	+	?
da Fonseca 2011	+	?	-	-	-	?	-	-	+	-	-	+	?
Dag 2011	+	?	-	-	-	?	-	-	+	?	-	?	?
Hartsell 1997	?	?	-	-	-	?	-	-	+	-	-	+	?
Lucha 2005	?	?	-	-	?	?	-	-	?	?	-	?	-
Minig 2009	+	?	-	-	-	-	-	-	+	-	-	-	?
Mulrooney 2004	?	?	?	-	-	-	-	-	+	-	-	-	?
Nakeeb 2009	?	?	-	-	-	?	-	-	+	-	-	+	-
Ortiz 1996	?	?	-	-	-	-	-	-	+	?	-	+	?
Reissman 1995	?	?	-	-	-	-	-	-	+	-	-	+	?
Sagar 1979	+	?	-	-	-	-	?	-	?	?	-	?	-
Schroeder 1991	?	?	-	-	?	?	-	?	?	-	-	?	-
Stewart 1998	+	?	-	-	-	?	-	-	+	-	-	+	?
Yang 2013	+	?	-	-	?	?	?	?	?	-	-	-	?

Allocation

Random sequence generation

We judged six studies to be at low risk of bias for random sequence generation (da Fonseca 2011; Dag 2011; Minig 2009; Sagar 1979; Stewart 1998; Yang 2013). Randomisation was undertaken using a computer-generated random number generator (da Fonseca 2011; Dag 2011; Minig 2009; Stewart 1998), a statistical table (Sagar 1979) or a random number table (Yang 2013). For all other studies (Beier-Holgersen 1996; Binderow 1994; Carr 1996; Chatterjee 2012; Hartsell 1997; Lucha 2005; Mulrooney 2004; Nakeeb 2009; Ortiz 1996; Reissman 1995; Schroeder 1991) insufficient details were provided, resulting in a judgement of unclear risk of bias.

Allocation concealment

Insufficient details were provided in all 17 studies with regards to their allocation concealment methods; we therefore judged all to have an unclear risk of bias. Two studies (Carr 1996; Nakeeb 2009) mentioned using sealed envelopes, however they did not report whether they were sequentially numbered or opaque; they were therefore judged as unclear.

Blinding

Participants

Fourteen of the studies (Binderow 1994; Carr 1996; Chatterjee 2012; Dag 2011; Hartsell 1997; Lucha 2005; Minig 2009; Nakeeb 2009; Ortiz 1996; Reissman 1995; Sagar 1979; Schroeder 1991; Stewart 1998; Yang 2013) reported no attempt to blind participants. They were judged to be at high risk of bias as they were unlikely to be adequately blinded with an intervention of this nature. One study reported that participants were informed of the group to which they were assigned on the first postoperative day (da Fonseca 2011) and was also judged to be at high risk of bias. One study (Mulrooney 2004) reported, through author correspondence, that participants were not aware of group allocation until postoperatively, but insufficient detail was provided on the blinding procedure and the timing postoperatively that blinding was broken; this study was judged to be of unclear risk of bias. One study, (Beier-Holgersen 1996) where the intervention group received a nutrition supplement, was judged to be at low risk of bias for blinding of participants as they used an identical placebo (flavoured orange drink) to blind their control participants.

Personnel

Personnel blinding was not discussed in 14 studies (Binderow 1994; Carr 1996; Chatterjee 2012; Dag 2011; Hartsell 1997; Lucha

2005; Minig 2009; Nakeeb 2009; Ortiz 1996; Reissman 1995; Sagar 1979; Schroeder 1991; Stewart 1998; Yang 2013) and were therefore judged to be at high risk of bias as they are unlikely to be adequately blinded with an intervention of this nature. Two studies (da Fonseca 2011; Mulrooney 2004 author correspondence) insufficiently described methods used to minimise possible bias, and were consequently judged to be at high risk of bias.

Only one study, (Beier-Holgersen 1996) was judged to be at low risk of bias for blinding of personnel.

Outcome assessment

One study (Beier-Holgersen 1996) was judged at low risk of bias as it was reported as double-blind and the randomisation code was not broken until patients had been followed up for 30 days after surgery. In the remaining 16 studies (Binderow 1994; Carr 1996; Chatterjee 2012; da Fonseca 2011; Dag 2011; Hartsell 1997; Lucha 2005; Minig 2009; Mulrooney 2004; Nakeeb 2009; Ortiz 1996; Reissman 1995; Sagar 1979; Schroeder 1991; Stewart 1998; Yang 2013), the blinding of the outcome assessor for wound infection, intraabdominal abscesses, postoperative complications (all complications considered, not just the primary and secondary outcomes of interest), anastomotic leakage/dehiscence, adverse events (all considered) and LoS was not discussed and were judged to be at high risk of bias as they are unlikely to be adequately blinded with an intervention of this nature. Twelve studies (Beier-Holgersen 1996; Carr 1996; Chatterjee 2012; da Fonseca 2011; Dag 2011; Hartsell 1997; Minig 2009; Mulrooney 2004; Nakeeb 2009; Ortiz 1996; Reissman 1995; Stewart 1998) reported mortality data, and were judged to be at low risk of bias for this outcome because the outcome assessor is unlikely to affect this outcome.

Incomplete outcome data

Three studies were judged to be at high risk of bias (Minig 2009; Mulrooney 2004; Yang 2013) because they had greater than 10% difference in missing data between groups. Four trials were judged unclear risk of bias as either information was not provided (Lucha 2005; Sagar 1979; Schroeder 1991) or dropouts after randomisation were not reported (Dag 2011). The remaining 10 studies were judged to be at low risk of bias.

Selective reporting

We judged 10 studies to be at unclear risk of bias as protocols were not available. However seven studies (Beier-Holgersen 1996; Binderow 1994; Carr 1996; Lucha 2005; Nakeeb 2009; Sagar 1979; Schroeder 1991) did have some issues that resulted in bias. Five had missing data for primary or secondary outcomes (Beier-Holgersen 1996; Binderow 1994; Lucha 2005; Nakeeb 2009; Sagar 1979) and

five (Beier-Holgersen 1996; Carr 1996; Lucha 2005; Nakeeb 2009; Schroeder 1991) either reported results that were not stated in the methods or did not report results that had been stated in the methods.

Effects of interventions

See: **Summary of findings for the main comparison** Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement; **Summary of findings 2** Subgroup and Sensitivity analyses

The 17 randomised controlled trials represent a total of 1437 patients, all undergoing lower gastrointestinal surgery but with a wide variety of clinical gastrointestinal conditions.

1. Primary outcomes

1.1 Length of hospital stay

Length of hospital stay (LoS) was reported in all 17 studies, but one was excluded from meta-analysis (Beier-Holgersen 1996) due to not reporting LoS in a compatible format (median only, without range or interquartile range (IQR)). We included estimated results for LoS which differed from the published results in eight of the included studies (Binderow 1994; Lucha 2005; Mulrooney 2004; Nakeeb 2009; Ortiz 1996; Reissman 1995; Sagar 1979; Stewart 1998), details of which are presented in Table 2. The mean LoS ranged from four days to 16 days in early feeding groups and from 6.6 days to 23.5 days in control groups. Mean difference (MD) from the random-effects model in LoS was 1.95 (95% CI, -2.99 to -0.91, $P = 0.0002$) days shorter in the intervention group (Analysis 1.1). However, there was a high level of heterogeneity between studies ($I^2 = 81\%$, $\text{Chi}^2 = 78.98$, $P < 0.00001$) (Table 5; Table 6, and Figure 4). The results from Beier-Holgersen (Beier-Holgersen 1996) (median LoS of eight days in the early feeding and 11.5 days in the control group), support a reduction in LoS with early feeding. These results were confirmed by the Trial Sequential Analysis showing that the cumulative Z-curve crossed the trial sequential monitoring boundary for benefit (Figure 5). Although the required information size to support or reject an *a priori* intervention effect of a reduction in LoS of one day ($\text{var} = 9$ days, α of 3.3% and β of 20%) has not yet been reached, which was 2444 people. The Trial Sequential Analysis-adjusted CI was -3.57 to -0.33 days. Overall, using GRADE criteria, we judged the quality of the evidence to be low. This outcome was downgraded by two levels because of risk of bias (blinding did not occur in any study; random sequence generation and allocation concealment was poorly reported) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, substantial statistical heterogeneity).

Figure 4. Funnel plot of comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.1 Length of hospital stay.

Figure 5. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.1 Length of hospital stay

1.2 Postoperative complications

Wound infection

Wound infection was reported in 12 of the included studies (Beier-Holgersen 1996; Chatterjee 2012; da Fonseca 2011; Dag 2011; Hartsell 1997; Minig 2009; Mulrooney 2004; Nakeeb 2009; Ortiz 1996; Reissman 1995; Sagar 1979; Stewart 1998). Absolute risks ranged from 0% (0/40) to 25% (15/60) in the intervention groups and from 0% (0/29) to 33.3% (10/30) in the control groups. Using the Mantel-Haenszel methods the combined RR was 0.99 (0.64 to 1.52, $P = 0.95$), with some heterogeneity between trials ($I^2 = 5\%$, $\text{Chi}^2 = 10.54$, $P = 0.39$) (Table 7 and Figure 6). The study by Beier-Holgersen (Beier-Holgersen 1996) differs from the 11 other studies by having a considerably higher proportion of patients with wound infection in the control group (33%). Excluding this study (results not presented) resulted in less heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 4.43$, $P = 0.55$) and a RR 1.12 (95% CI, 0.73 to 1.71, $P = 0.62$). TSA showed that the information size was not large enough to rule out that early feeding versus control

reduces the risk ratio of wound infection events by 30% or more (Figure 7). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction (*a priori* estimate) of wound infection (with a control group proportion of 9.1%, an alpha of 3.3%, and a beta of 20%) is 3,388 patients. The TSA-adjusted CI was 0.48 to 2.11. Using GRADE criteria, wound infection was judged as having very low-quality evidence. This outcome was downgraded by three levels because of risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment was poorly reported and selective reporting, (where insufficient information was provided due to lack of protocol or reporting outcomes not mentioned in methods or having to input missing data)), imprecision (confidence intervals are wide) and indirectness (included various definitions e.g. some incorporated pelvic abscesses whilst others did not; unclear definition of outcome).

We tested for publication bias by visual inspection of the funnel plot for wound infection (Figure 8), although this had only nine included trials after excluding those with zero events in one or both arms.

Figure 6. Comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome: 3 Wound infection

Figure 7. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.3 Wound infection.

Figure 8. Funnel plot of comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.3 Wound infection.

Intraabdominal abscess

Intraabdominal abscess was reported in six studies ([Beier-Holgersen 1996](#); [Minig 2009](#); [Mulrooney 2004](#); [Ortiz 1996](#); [Reissman 1995](#); [Sagar 1979](#)). Absolute risks ranged from 0% (0/36) to 13% (2/15) in both the early feeding groups and the control groups. Using a random-effects method, the combined RR for this outcome was 1.00 (95% CI, 0.26 to 3.80, $P = 1.00$), with very little heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 0.97$, $P = 0.91$) ([Table 8](#) and [Figure 9](#)). It was not possible to do TSA for intraabdominal

abscess due to limited data and too few events. We judged the quality of the evidence for intraabdominal abscess to be low. This outcome was downgraded by two levels because of risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment was poorly reported, and selective reporting, (where insufficient information was provided due to lack of protocol or reporting outcomes not mentioned in methods or having to input missing data)) and imprecision (confidence intervals are wide and very few events occurred).

Figure 9. Comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome: 4 Intraabdominal abscess

Anastomotic leakage/dehiscence

Anastomotic leakage/dehiscence was reported in 13 studies (Beier-Holgersen 1996; Chatterjee 2012; da Fonseca 2011; Dag 2011; Hartsell 1997; Lucha 2005; Minig 2009; Mulrooney 2004; Nakeeb 2009; Ortiz 1996; Reissman 1995; Sagar 1979; Stewart 1998). The risk of dehiscence ranged from 0% (0/80) to 8.3% (3/36) in early feeding groups and from 0% (0/40) to 13.3% (4/30) in control groups. The combined RR from the random-effects model was 0.78 (95% CI 0.38 to 1.61, $P = 0.51$), with some evidence of heterogeneity between studies ($I^2 = 0\%$, $\chi^2 = 5.43$, $P = 0.94$) (Table 9 and Figure 10). The absolute risk reduction (ARR) was 0.01. Thus, for every 100 participants receiving early feeding, one less anastomotic leakage compared to 100 participants receiving later commencement of feeding (NNTB).

TSA showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of anastomotic leakage/dehiscence events by 30% or more (Figure 11). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction (*a priori* estimate) of anastomotic leakage/dehiscence (with a control group proportion of 27.6%, an alpha of 3.3%, and a beta of 20%) is 6,824 patients (vertical red dashed line). The TSA-adjusted CI was 0.04 to 14.75. Anastomotic leak/dehiscence was also judged as having low-quality evidence. It was also downgraded by two levels because of risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment was poorly reported and selective reporting, (where insufficient information was provided due to lack of protocol or reporting outcomes not mentioned in methods or having to input missing data)) and imprecision (confidence intervals are wide and very few events occurred).

Figure 10. Comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome: 5 Anastomotic leakage

Figure 11. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.5 Anastomotic leakage.

Pneumonia

Post-surgical pneumonia was reported in 10 studies (Beier-Holgersen 1996; da Fonseca 2011; Dag 2011; Hartsell 1997; Lucha 2005; Mulrooney 2004; Ortiz 1996; Reissman 1995; Schroeder 1991; Stewart 1998). Pneumonia events ranged from none to 6.3% (1/16) in the intervention group and from none to 6.7% (2/30) in the

control group. The combined RR using the random-effects model was 0.88 (95% CI, 0.32 - 2.42, $P = 0.81$) with little evidence of heterogeneity between studies ($I^2 = 0\%$, $\text{Chi}^2 = 0.65$, $P = 1.00$) (Table 10 and Figure 12). The absolute risk reduction (ARR) was 0.003. Thus, for every 1000 participants receiving early feeding, 3 less pneumonia compared to later commencement of feeding (NNTB).

Figure 12. Comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome: 6 Pneumonia

TSA showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of pneumonia by 30% or more (Figure 13). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction (*a priori* estimate) of anastomotic leakage/dehiscence (with a control group proportion of 2.1%, an alpha of 3.3%, and a beta of 20%) is 15,624 patients (vertical red dashed line). The TSA-adjusted CI was 0.01 to 54.17. Using GRADE criteria, we judged the quality of the evidence for pneumonia to be low.

This outcome was downgraded by two levels because of risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment was poorly reported and selective reporting, (where insufficient information was provided due to lack of protocol reporting outcomes not mentioned in methods or having to input missing data)) and imprecision (confidence intervals are wide and very few events occurred).

Figure 13. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.6 Pneumonia.

Other complications

A range of other complications were reported in the included studies, which included pulmonary failure, myocardial infarction, urinary tract infection, toxic hepatitis, deep vein thrombosis, bleeding, pelvic abscess. See [Table 3](#) for full list of other complications.

2. Secondary outcomes

2.1 Mortality

Mortality was reported in 12 studies ([Beier-Holgersen 1996](#); [Carr 1996](#); [Chatterjee 2012](#); [da Fonseca 2011](#); [Dag 2011](#); [Hartzell 1997](#); [Minig 2009](#); [Mulrooney 2004](#); [Nakeeb 2009](#); [Ortiz 1996](#); [Reissman 1995](#); [Stewart 1998](#)). Mortality ranged from none to 6.7% (2/30) in the early feeding groups, and from none to 19% (7/37) in the control groups. Mortality was reported predominantly in the hospital unit during the entire experimental period, except for three studies in which mortality was reported after 30 days ([Beier-Holgersen 1996](#), [da Fonseca 2011](#)) or 60 days ([Mulrooney 2004](#)). The most commonly

reported cause of death was anastomotic leakage/dehiscence, sepsis, and acute myocardial infarction. There was weak evidence of a decrease in the relative risk (RR) of mortality among patients fed early from the random-effects model (RR = 0.56, 95% CI, 0.21 to 1.52, $P = 0.26$), with little statistical heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 3.08$, $P = 0.96$) ([Table 11](#) and [Figure 14](#)). TSA showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of mortality by 30% or more ([Figure 15](#)). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction (*a priori* estimate) of mortality (with a control group proportion of 3.0%, an alpha of 3.3%, and a beta of 20%) is 11,665 patients (vertical red dashed line). The TSA-adjusted CI was 0.01 to 31.66. Overall, using GRADE criteria, this outcome was downgraded by two levels to low quality of evidence because of indirectness (unclear definition whether mortality occurred prior or after discharge) and imprecision (confidence intervals are wide and very few events occurred). We did not consider downgrading for risk of bias issues (i.e. lack of blinding) for this outcome.

Figure 14. Comparison: 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome: 7 Mortality

Figure 15. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.7 Mortality.

2.2 Adverse events: Vomiting, nausea, and combined nausea and vomiting

A total of seven studies described incidence of vomiting (Beier-Holgersen 1996; Binderow 1994; Hartsell 1997; Nakeeb 2009; Reissman 1995; Stewart 1998; Yang 2013), and the absolute risks ranged from 8.6% (3/35) to 50% (15/30) in the early feeding groups and from 2.9% (1/35) to 57% (17/30) in the control groups. There was weak evidence of an increase in the RR of vomiting among patients fed early using a random-effects model (RR = 1.23, 95% CI, 0.96 to 1.58, $P = 0.10$) with little heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 4.98$, $P = 0.55$) (Analysis 1.8). TSA showed that the information size was not large enough to rule out that early feeding

versus control reduces the risk ratio of vomiting events by 30% or more (Figure 16). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction of vomiting (with a control group proportion of 23.1%, an alpha of 3.3%, and a beta of 20%) is 1,250 patients. The TSA-adjusted CI was 0.80 to 1.91. Vomiting was judged as having low-quality evidence. This outcome was downgraded by two levels because of risk of bias (blinding did not occur in any study (except one), random sequence generation and allocation concealment was poorly reported, selective reporting (where insufficient information was provided due to lack of protocol or reporting outcomes not mentioned in methods or having to input missing data)), and imprecision (wide confidence intervals).

Figure 16. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.8 Vomiting.

Two studies with 118 participants reported incidence of nausea (Beier-Holgersen 1996; Hartsell 1997). The risk ratio (RR) was 0.93, 95% CI 0.70 to 1.23, with no statistical heterogeneity ($I^2 = 0\%$). TSA showed that the information size was not large enough to rule out that early feeding versus control reduces the RR of nausea events by 30% or more (Figure 17). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction of nausea (with a control group proportion of 62.7%, an alpha of 3.3%, and a beta of 20%) is 268 patients. Although the threshold for utility has nearly been crossed, which would

indicate that the inclusion of further trials is unlikely to lead to a conclusion of increased or decreased risk of nausea events with early feeding. The TSA-adjusted CI was 0.55 to 1.55. This outcome was downgraded by two levels because of risk of bias (blinding only occurred in one study, random sequence generation and allocation concealment was poorly reported, selective reporting (where insufficient information was provided due to lack of protocol or reporting outcomes not mentioned in methods or having to input missing data)), and imprecision (wide confidence intervals).

Figure 17. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.9 Nausea.

Four studies (Carr 1996; da Fonseca 2011; Chatterjee 2012; Minig 2009) reported incidence of nausea and vomiting as a combined variable, which was included post-hoc as an additional adverse event. There was no evidence of treatment effects for either outcome (nausea RR = 0.95, 95% CI, 0.71 - 1.26, P = 0.70; Analysis 1.9; nausea and vomiting RR = 0.94, 95% CI, 0.51 - 1.74, P = 0.84; Analysis 1.10), with little heterogeneity between trials (nausea $I^2 = 40\%$, $\text{Chi}^2=4.97$, P = 0.17; nausea and vomiting $I^2 = 40\%$, $\text{Chi}^2=4.97$, P = 0.17) although estimates of heterogeneity should be interpreted with caution given the small number of studies. TSA showed that the information size was not large enough to rule out that early feeding versus control reduces the risk ratio of nausea

and vomiting events by 30% or more (Figure 18). The heterogeneity-adjusted required information size to demonstrate or reject a 30% relative risk reduction of nausea and vomiting (with a control group proportion of 26.2%, an alpha of 3.3%, and a beta of 20%) is 2,180 patients. The TSA-adjusted CI was 0.08 to 11.08. This outcome was downgraded by three levels because of risk of bias (blinding did not occur in any study, allocation concealment was poorly reported, selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement)) and imprecision (wide confidence intervals) and indirectness (included various definitions of nausea and vomiting).

Figure 18. Trial sequential analysis of early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: 1.10 Nausea and vomiting.

A number of trials reported other adverse events (Table 4), rare events and not subject for analyses in this review. These included distention, diarrhoea, hypoxemia and small bowel obstruction.

2.3 Quality of Life

Just one study (Minig 2009) assessed QoL using two separate tools. The European Organisation for research and treatment of Cancer (EORTC) is often used to measure overall health status. The authors opted for EORTC QLQ-C30 (Aaronson 1993) which was supplemented by the EORTC QIQ-OV28 (Griemel 1998) questionnaire (specifically for ovarian cancer). They were both administered before surgery and 30 days after discharge. The scores did not differ between groups at 30 days after discharge: EORTC OV-28 (global) traditional feeding (28.6 (13.7) versus early feeding 26.5 (14.9), $P = 0.68$) and EORTC C-30 (Global) traditional feeding (56.1 (22.2) versus early feeding 64.6 (17.1), $P = 0.17$). This outcome was downgraded by two levels because of risk of bias (blinding did not occur in this study, allocation concealment was poorly reported, selective reporting (as some outcomes were reported in methods but not in results/vice versa or no protocol was available to make a judgement) and also downgraded for imprecision.

3. Subgroup analysis

The post-hoc subgroup analysis, using a random-effects model, of studies in patients having surgery distal to the ligament of Treitz (13 studies) compared with studies that included patients having surgery distal or proximal to the ligament of Treitz (three studies) confirmed the main finding. Compared with usual care, in the intervention arm LoS was reduced by 1.77 (95% CI, -2.95 to -0.59, $P = 0.003$) days in patients having surgery distal to the ligament of Treitz and by 2.58 (95% CI, -4.40 to -0.76, $P = 0.005$) days in patients having surgery distal or proximal to the ligament of Treitz (Analysis 1.1, Table 5). Heterogeneity remained high in the 'distal only' subgroup

($I^2 = 84\%$, $\text{Chi}^2 = 74.33$, $P < 0.001$) but was less in the 'distal or proximal' subgroup ($I^2 = 31\%$, $\text{Chi}^2 = 2.90$, $P = 0.23$).

For the subgroup of patients having surgery distal to the ligament of Treitz, using GRADE criteria, we judged the quality of the evidence to be low. This outcome was downgraded by two levels because of risk of bias (blinding did not occur in any study; random sequence generation and allocation concealment was poorly reported) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, substantial statistical heterogeneity). For the subgroup of patients having surgery distal or proximal to the ligament of Treitz, using GRADE criteria, we also judged the quality of the evidence to be low. This outcome was downgraded by two levels because of the following: risk of bias (blinding did not occur in any study and allocation concealment was poorly reported) and imprecision (confidence intervals are wide).

The post-hoc subgroup analysis of studies in which patients in the intervention arm were fed orally only (11 studies) compared with studies in which patients were fed through a tube with or without oral feeding (five studies) found conflicting results for the effectiveness of early feeding on LoS. In studies using only oral feeding in their early feeding arm, compared with usual care, LoS was reduced by 2.06 (95% CI, -3.26 to -0.87, $P = 0.0007$) days (Analysis 1.2, Table 6). However, in studies which used tube feeding (with or without oral feeding) in their early feeding arm, the evidence supporting a reduction in LoS in the early feeding arm compared with usual care by 1.75 (95% CI, -4.32 to 0.82, $P = 0.18$) days was weak. Heterogeneity remained high in both the 'oral feeding only' ($I^2 = 85\%$, $\text{Chi}^2 = 66.53$, $P < 0.00001$) and 'tube feeding +/- oral feeding' ($I^2 = 67\%$, $\text{Chi}^2 = 12.18$, $P = 0.02$) subgroups. The oral feeding only subgroup was judged to be low in terms of quality of evidence. It was downgraded by two levels because of the following: risk of bias (blinding did not occur in any study;

random sequence generation and allocation concealment were poorly reported) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I^2). Whereas the tube feeding with/without oral feeding subgroup was judged to be very low quality. It was downgraded by three levels because of the following: risk of bias (blinding did not occur in any study and allocation concealment was poorly reported) and imprecision (confidence intervals are wide) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I^2).

Given that the clinical populations of only two studies (Nakeeb 2009; Yang 2013) were 100% cancer and the rest were either a mixture of cancer and non-cancer or did not specify, it was deemed impossible to conduct this subgroup analysis.

Only one study (Chatterjee 2012), reported that their population would include patients having either acute or elective surgery, two studies did not specify and the remaining 14 studies were all elective surgery, so it was again deemed impossible to conduct a subgroup analysis.

Subgroup analyses are presented in [Summary of findings 2](#).

4. Sensitivity analysis

We conducted the following sensitivity analyses for the continuous outcomes included in this review and presented these in [Summary of findings 2](#).

4.1 Removing studies with at least two domains with high risk of bias

None of the included studies were classified as having a high risk of bias in two or more of the following components: random sequence generation, allocation concealment, incomplete outcome data or selective outcome reporting. Therefore we were unable to carry out this sensitivity analysis.

4.2a Removing studies with imputed results

Results were estimated or imputed for LoS in five studies (Binderow 1994; Lucha 2005; Nakeeb 2009; Reissman 1995; Sagar 1979). After excluding these results from the meta-analysis of LoS we found an overall reduction in LoS in favour of early feeding of 2.27 days (95% CI, -3.62 to -0.92, $P = 0.001$), with substantial heterogeneity between trials ($I^2 = 80\%$, $\text{Chi}^2 = 49.43$, $P < 0.00001$). Using GRADE criteria this analysis was downgraded by three levels because of the following: risk of bias (blinding did not occur in any study and allocation concealment was poorly reported) and imprecision (confidence intervals are wide) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I^2).

4.2b Worst/best case scenario imputation

Results were imputed for the standard deviations of LoS in three studies (Binderow 1994; Lucha 2005; Nakeeb 2009) using the mean of the standard deviations reported by other studies. Under the worst case scenario (maximum of reported standard deviations) we found an overall reduction in LoS in favour of early feeding of 2.06 days (95% CI, -3.18 to -0.94, $P = 0.0003$), with substantial heterogeneity between trials ($I^2 = 81\%$, $\text{Chi}^2 = 77.59$, $P < 0.00001$). Under the best case scenario (minimum of reported standard deviations) we found an overall reduction in LoS in favour of early

feeding of 1.80 days (95% CI, -2.61 to -1.00, $P < 0.0001$), with substantial heterogeneity between trials ($I^2 = 83\%$, $\text{Chi}^2 = 89.28$, $P < 0.00001$). This analysis was downgraded by two levels because of the following: risk of bias (blinding did not occur in any study; random sequence generation and allocation concealment were poorly reported) and inconsistency (large variation in size of effect, some confidence intervals do not overlap, very high I^2) ([Summary of findings 2](#)).

4.3 Inclusion of continuity correction for zero cell counts

The inclusion of a continuity correction for zero cell counts resulted in narrower confidence intervals around the relative risk estimate for the effect of the intervention on mortality. The combined RR was 0.53 (95% CI 0.25 to 1.13, $P = 0.10$), with no evidence of heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 4.8$, $P = 0.85$). The increased precision provides weak evidence that early feeding may reduce the risk of postoperative mortality. Relative risk estimates for the remaining outcomes were changed only minimally after continuity correction. For wound infection the combined RR was 0.84 (0.51 to 1.39, $P = 0.50$), with some heterogeneity between trials ($I^2 = 25\%$, $\text{Chi}^2 = 13.36$, $P = 0.20$). For intraabdominal abscess the combined RR was 0.65 (0.21 to 2.01, $P = 0.46$), with minimal heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 1.60$, $P = 0.81$). For anastomotic leak the combined RR was 0.74 (0.40 to 1.36, $P = 0.33$), with minimal heterogeneity between trials ($I^2 = 3\%$, $\text{Chi}^2 = 12.42$, $P = 0.41$). For pneumonia the combined RR was 1.12 (0.51 to 2.47, $P = 0.78$), with minimal heterogeneity between trials ($I^2 = 0\%$, $\text{Chi}^2 = 3.85$, $P = 0.92$).

5. Publication bias

We tested for publication bias by visual inspection of the funnel plot for LoS ([Figure 4](#)), which had more than 10 included trials, and wound infection ([Figure 8](#)), although this had only nine included trials after excluding those with zero events in one or both arms. Neither of the presented funnel plots as well as Egger's regression test for LoS ($z = -1.00$, $P = 0.32$) indicate plot asymmetry, thus suggesting that the results are unlikely to be affected by reporting biases (including publication bias). However, these results should be interpreted with caution due to the generally high level of heterogeneity between studies. We did not perform funnel plots for the following outcomes: Intraabdominal abscess, anastomotic leakage, pneumonia, mortality, vomiting, nausea, and nausea and vomiting (reported in combination), due to limited number of included studies (less than 10) for any of the outcomes.

DISCUSSION

Summary of main results

Our review shows that there is evidence for a reduction in length of hospital stay (LoS) with early feeding (reduction of 1.95 days, [Analysis 1.1](#)). However, evidence to support this is of low quality, thus the results should be interpreted with caution. We also found weak evidence of a 23% increase in risk of vomiting, but with confidence intervals which include no effect ([Analysis 1.8](#)). There was no clear difference between early feeding versus control regarding the postoperative complications wound infection ([Analysis 1.3](#)), intraabdominal abscess ([Analysis 1.4](#)), anastomotic leakage ([Analysis 1.5](#)), or pneumonia ([Analysis 1.6](#)). Likewise for mortality and the adverse events nausea ([Analysis 1.9](#)), or nausea and vomiting as a combined variable ([Analysis 1.10](#)). Findings are

summarised in the [Summary of findings for the main comparison](#). Sensitivity analyses for use of estimated data showed no clinically important changes to the findings. Subgroup analysis indicated that LoS did not differ when excluding studies that had participants undergoing surgery proximal to the ligament of Treitz as well as participants having surgery distal to the ligament of Treitz ([Analysis 1.1](#)). One study assessed quality of life (QoL) and no between-group difference was reported at 30 days post-discharge.

Overall completeness and applicability of evidence

We attempted to identify and synthesise all existing research to provide a comprehensive estimate of the effect of early feeding on LoS and postoperative complications. The previous update ([Andersen 2011](#)) search for trials comparing early commencement of postoperative enteral nutrition with traditional management (no nutritional supply before bowel function) included 14 studies representing a total of 1224 patients. The current review updated this with the addition of six trials ([Chatterjee 2012](#); [da Fonseca 2011](#); [Dag 2011](#); [Minig 2009](#); [Nakeeb 2009](#); [Yang 2013](#)) and removal of three ([Heslin 1997](#); [Smedley 2004](#); [Watters 1997](#)), to give 17 studies, involving 1437 participants. Our search strategies however may not have identified all of the existing literature. Additionally, two identified publications could not be located through our library resources, two could only be found in abstract format and so were excluded after attempting to contact authors, and one study was not in a readable format in Chinese ([Characteristics of excluded studies](#)). One study ([Beier-Holgersen 1996](#)) reported LoS in a format that could not be used in the review and so was excluded from the meta-analysis for LoS. However, where possible we estimated and made assumptions about the data, which allowed us to use the majority of identified information ([Table 2](#)).

Surgical and anaesthetic practice has changed dramatically since publication of the first randomised controlled trial in 1979 ([Sagar 1979](#)). Surgery is less 'stressful' especially if done laparoscopically. Patients recover from anaesthetics faster and combined with improved postoperative analgesia enable patients to mobilise and return to usual activities much faster than previously. Thus patients today may be more able to tolerate early enteral feeding than in previous studies. It is also possible that in an era where multi-model programmes such as the Enhanced Recovery After Surgery (ERAS) programme are encouraged, the benefits of early enteral feeding may not be so obvious but may still add to the overall improvements in recovery.

Quality of the evidence

Assessments of quality of evidence for each outcome are presented in the [Summary of findings for the main comparison](#). Overall, using GRADE criteria, there is a low level of evidence that early feeding leads to a shorter period of LoS. There is also a low level of evidence that early feeding reduces the risk of mortality. There is a low level of evidence of a weak increased risk of vomiting in those who are fed early. There are low levels of evidence that early feeding does not reduce the following postoperative outcomes (intraabdominal abscesses, anastomotic dehiscence, pneumonia) or adverse events (nausea) compared to traditional feeding. There is also a very low level of evidence that early feeding does not reduce wound infection compared to traditional feeding.

1. Methodology

Methodological quality and risk of bias were difficult to assess in many studies due to poor reporting. Those with available information were of poor methodological rigour. Randomisation sequence generation was the most reported of all evaluated risk of bias elements, however other elements such as allocation concealment were more poorly reported and there were few reports of attempts to blind patients, outcome assessors and other personnel. Incomplete outcome reporting was mainly low risk but selective reporting was judged to be either high or unclear risk of bias. Overall, the majority of 'Risk of bias' assessments were therefore judged as 'unclear' or 'high' risk.

2. Outcome assessment

LoS was the clinical outcome of interest in this research area. However, it was likely to be influenced by variation in discharge criteria, which may result in differences between studies. Timing of the mortality assessment was also not clearly defined or consistent between studies. For example, nine studies reported mortality within the hospital unit, whilst three used 30-day mortality or mortality within two months. This lack of uniformity across centres will have caused rates of reporting to differ between studies. Furthermore, the definition of some of the other outcomes of interest were not clear and often differed between studies, which may introduce variability among some outcomes. For example, for the wound infection outcome, one study ([Sagar 1979](#)) reported incorporating pelvic abscesses (as well as subphrenic abscesses and anastomotic leak) within its definition, whilst others (e.g. [Chatterjee 2012](#); [Ortiz 1996](#); [Reissman 1995](#); [Stewart 1998](#)) separated pelvic abscess from wound infection. [Carr 1996](#) had an overall outcome of infection which incorporated wound and urinary together so was excluded from the meta-analysis for wound infection because effects on wound infection alone could not be separated out. One study ([Beier-Holgersen 1996](#)), reported using a standardised criteria to assess wound infection (Buzby II-IV), whilst the surgical team decided the definition in another ([Mulrooney 2004](#) - author correspondence). The definition reported in [Beier-Holgersen \(Beier-Holgersen 1996\)](#) may have been more sensitive than in the other studies as they reported a third of controls had experienced a wound infection, whereas in other studies, minimal infection rates were noted. The outcomes nausea and vomiting relied on participants self-report. Postoperative participants may feel unwell or disorientated; hence these self-reported outcomes may be open to misreporting or bias. However, this risk of bias is applicable to all studies reporting nausea and vomiting and cannot be more accurately recorded by any other means. Additionally, blinding of participants and outcome assessors with this intervention is difficult, and an awareness of treatment allocation may result in participants and outcome assessors misreporting the outcomes.

3. Heterogeneity

The 17 randomised trials identified were clinically heterogeneous, which was reflected in the considerable evidence of heterogeneity in one of the primary outcomes, LoS. Combining trials that differ in terms of underlying condition, operation, and intervention may be inappropriate. However, we were interested in the pragmatic comparison of early versus deferred feeding strategies after lower gastrointestinal surgery and not in differences between feed types or specific routes of feeding. Our ability to detect statistical heterogeneity was limited by the small number of trials and by

the often inadequate reporting. The post-hoc subgroup analyses, which compared surgical sites ('distal to the ligament of Treitz only' compared with 'distal and proximal to the ligament of Treitz') and oral feeding route ('oral feeding only' compared with 'nasogastric tube +/- oral feeding') did not explain the observed heterogeneity in LoS.

Potential biases in the review process

The review process may have been biased. Although we believe that our electronic and handsearching strategies identified the majority of relevant trials, it is possible that we may have missed some available literature or unpublished material. We stopped handsearching at the end of December 2017, and in the time period until publication other trials may have been published or made available. These will be incorporated into future updates to this review. We made judgements of risk of bias according to predefined rules, but the information required to make these judgements was infrequently published. Judgements of risk of bias, however, were completed following all data collection, so did not impact on the review process. We may have introduced bias in the review process as we had to make estimations and assumptions using the available data to be able to conduct meta-analyses. We conducted a sensitivity analysis removing all results that had been estimated, and the direction and extent of effect for LoS remained the same, indicating that the quality of our statistical manipulations did not substantially change our findings. We found no evidence of funnel plot asymmetry, but several outcomes (intraabdominal abscess, vomiting, nausea, and nausea and vomiting) were reported in only a small number of trials, which precluded assessment of funnel plot asymmetry for these outcomes. Many of the outcomes were rare events (mortality, wound infection, intraabdominal abscess, anastomotic leak, pneumonia) and the methods for handling these events may have biased the pooled estimates of the effect of early feeding. We conducted sensitivity analyses in which we used a zero-cell continuity correction method and this made a small difference to the findings relating to mortality, but no other clinically meaningful differences. None of the reviewed studies accounted for competing risks, the scenario in which an alternative outcome occurs which prevents or delays the primary outcome from occurring, and may have resulted in biased results. In the reviewed studies wound infections may extend a hospital stay and mortality will mean a patient is not discharged, both of which may lead to biased estimates of intervention effects on LoS.

We made a number of assumptions about the comparability of study methodology, including the control and intervention protocols. The exact timing of feeding and type of feed received in the intervention and control groups was not always clear, and likely differed between studies (Table 1 and Characteristics of included studies). In addition, the experience of the surgeon, the length of the operation, postoperative pain control, the use of antibiotics, and the success of the operation, may have affected outcomes. Control group participants likely began receiving energy at different times as for most studies it was introduced after evidence of return to normal bowel function e.g. bowel sounds, flatus; for some, calories will have been introduced on postoperative day one (the same day as the intervention group) as explicitly reported in one study (da Fonseca 2011).

Agreements and disagreements with other studies or reviews

The key message of this systematic review is that there is no obvious benefit for keeping patients 'nil by mouth' (NBM) after lower gastrointestinal surgery, and confirms the conclusion from our previous reviews (Andersen 2011; Lewis 2001; Lewis 2009). The first review in this area (Lewis 2001) was published in 2001 and included 11 studies. We published subsequent updates in 2009 (Lewis 2009) and 2011 (Andersen 2011) which included 13 and 14 studies, respectively. Other systematic reviews that have looked at early postoperative feeding in gastrointestinal tract resection or colorectal surgery include Osland 2011, Zhuang 2013 and Shu 2016. Osland 2011 included 15 trials involving 1240 patients undergoing gastrointestinal tract resection. Zhuang 2013 included seven trials involving 587 patients undergoing elective colorectal surgery, and Shu 2016 included 11 trials involving 1095 patients undergoing digestive tract surgery.

The present review included 17 studies representing a total of 1437 patients all undergoing lower gastrointestinal surgery. All the outcomes we assessed were clinically relevant in the context of lower gastrointestinal surgery. Compared to previous reviews including ours (Andersen 2011; Lewis 2001; Lewis 2009), and those done by others (Osland 2011; Zhuang 2013), this review showed a greater reduction in LoS in the early feeding group (1.96 days compared to 0.89, 0.89, 0.84, 1.28, and 1.58 days, respectively). The reduction in mortality with early postoperative feeding in this review (RR = 0.56, 95% confidence interval (CI) 0.21 to 1.52, P = 0.26) was similar to that reported in our earliest review (Lewis 2001) and also by Osland 2011 (RR = 0.48, 95% CI 0.18 to 1.29, P = 0.15, and OR = 0.71, 95% CI, 0.32 to 1.56, P = 0.39, respectively). Our previous reviews (Andersen 2011; Lewis 2009), however, found stronger statistical evidence that mortality was reduced with early postoperative feeding (RR = 0.42, 95% CI 0.18 to 0.96, P = 0.03, and RR = 0.41, 95% CI 0.18 to 0.93, P = 0.03, respectively).

Similar to our previous reviews (Andersen 2011; Lewis 2001; Lewis 2009), the current review showed no evidence of treatment effects for mortality or for the following clinical complications: intraabdominal abscess, pneumonia, wound infections or anastomotic leakage. Compared to the most recent version of our review (Andersen 2011), we found a similar effect size for an increased risk of vomiting among those fed early, but a wider confidence interval, suggesting weaker evidence of a treatment effect (RR = 1.27, 95% CI 1.01 to 1.61, P = 0.05 versus RR = 1.23, 95% CI 0.96 to 1.58, P = 0.10, respectively). Although not entirely comparable with our findings (given that we did not look at infectious and non-infectious complications as combined groups) Shu 2016 found that early enteral nutrition in patients with digestive tract surgery was more effective than no early feeding in decreasing the incidence of infectious (RR = 0.50, 95% CI 0.38 to 0.67, P < 0.01) and non-infectious (RR = 0.72, 95% CI 0.43 to 1.22, P < 0.05) complications. In addition, Zhuang 2013 found a reduction in total postoperative complications (RR = 0.70, 95% CI 0.50 to 0.98, P = 0.04).

AUTHORS' CONCLUSIONS

Implications for practice

Traditionally, it has been standard in many elective surgical practices to keep patients 'nil by mouth' postoperatively for

several days. In recent years this practice has been challenged as studies have shown that this may be a period of unnecessary starvation (Andersen 2011). On this evidence, re-establishment of oral feeding as soon as possible after surgery is now encouraged and has been incorporated within the enhanced recovery after surgery (ERAS) programme. This update supports the notion of early commencement of feeding, and the inclusion of early feeding within ERAS programmes for patients undergoing lower gastrointestinal surgery, as there was no evidence that keeping patients nil by mouth is beneficial, except perhaps in terms of reducing vomiting. This review strengthens the evidence that early feeding reduces LoS. Overall, the reduction corresponded to almost two days, which is both clinically and economically important. Postoperative feeding after non-gastrointestinal surgery has also been shown to reduce postoperative inpatient stay (Delmi 1990; Schilder 1997). A reduction in complication rates may help to explain this observation, as might a faster return of gastrointestinal function. Although previous reviews have reported that early feeding leads to a reduction in mortality (Andersen 2011; Lewis 2009), the current review did not support this finding and the earliest version of this review (Lewis 2001) found weaker evidence. Future studies should focus their attention on the reporting of postoperative outcomes. Unfortunately, it was impossible to comment on many factors, which may have influenced the clinical complication endpoints such as the fitness of the patient, experience of the surgeon, whether resections were on the small or large bowel, the operation time, pain control, use of antibiotics and the success of the operation in removing the underlying pathology. Surgical and anaesthetic practice has changed since publication of the first randomised controlled trial (Sagar 1979). Surgery has become less 'stressful' especially if undertaken laparoscopically. Patients recover from anaesthetics faster and when combined with improved postoperative analgesia and attention to fluid balance, patients mobilise and recover more rapidly. Thus, patients today may be more able to tolerate early enteral feeding than was seen in previous studies. It is also possible that the potential benefits of early enteral feeding may not be so obvious as it has been incorporated within the ERAS programme which aims to reduce postoperative complications and LoS through

a multi-modal perioperative care pathway. Challenges to the implementation of ERAS also need to be considered. For example, a recent qualitative investigation in healthcare providers reported a number of potential barriers, such as keeping ERAS visible, gaining the buy-in of relevant stakeholders and spreading the programme (Herbert 2017). Nonetheless, if early postoperative feeding does provide benefit, then the identification and implementation of strategies to improve uptake of this ERAS component should be a priority.

Implications for research

The earliest review conducted in 2001 (Lewis 2001) suggested that an adequately powered clinical trial was required to assess early enteral feeding on appropriate outcomes. This review suggests that we now have sufficient evidence to indicate that early enteral feeding leads to a reduced postoperative length of hospital stay. However, the findings were inconclusive for all other outcomes, and further clinical trials are therefore justified to further understand the effect of early enteral feeding on postoperative complications and other secondary outcomes. This review further suggests that trials should clearly define their outcomes in terms of timeframe and definition to allow for better comparison between studies. However, the examination of the effect of early nutrition alone in the hospital context today would be difficult, due to the nature of surgery changing with fast track surgery protocols, and the incorporation of the recommendation to feed early post-surgery within this. The trials reviewed used different feeding routes and amounts of energy, which make it unclear which is the best approach to consider in clinical practice. Of benefit, would be to investigate if different feeding regimens affect outcomes post-surgery. However, any trial would need to be large and would therefore be expensive.

ACKNOWLEDGEMENTS

We would like to thank Vanessa Er for her support in extracting the studies in Chinese, and the Information Specialist in CCCG for running the searches.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Beier-Holgersen 1996

Methods	Randomised double-blind controlled trial No information provided about duration of study
Participants	60 participants (30 in each group); mainly colorectal surgery (87%) Bowel resection Route of feeding: nasoduodenal Median age: 66.5 years (range 27-93) (intervention group), 61.5 years (range 27-80) (control group) Male:Female 18:12 (intervention group), 20:10 (control group)
Interventions	Intervention group: received a nutrition supplement of Nutridrink (orange flavour) within four hours postoperatively. Nutridrink contained 150 kcal/100 mL and 5 g protein/100 mL. Nutritional supplement given until fourth day. Control group: received placebo (water with orange flavour, no energy, vitamins or trace elements) during same period.
Outcomes	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, postoperative complications (pneumonia, dehiscence, pulmonary failure), LoS, adverse events (nausea, vomiting).
Notes	Country of study: Denmark

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	Low risk	Reported as double-blinded. Use of an identical placebo flavoured orange. Groups received different volume of drink (4000 mL vs. 4700 mL). Unlikely to unblind.
Blinding of personnel (performance bias) All outcomes	Low risk	Reported as double-blinded. Nutridrink or placebo in identical containers was administered by the nursing staff.
Blinding of outcome assessor (detection bias) - wound infections	Low risk	The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.

Beier-Holgersen 1996 (Continued)

Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Low risk	The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	Low risk	The principal investigator saw the patients every day during their stay in the ward, and all complications (pneumonia, dehiscence, pulmonary failure, myocardial infarction) were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	Low risk	The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.
Blinding of outcome assessor (detection bias) - mortality	Low risk	The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	Low risk	(Nausea, vomiting) The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.
Blinding of outcome assessor (detection bias) - length of hospital stay	Low risk	The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data.
Selective reporting (reporting bias)	High risk	No protocol available. The outcome LoS was reported in results but not explicitly stated as an outcome of interest in methods (just PO course).

Binderow 1994

Methods	Randomised controlled trial Between July 1st 1992 and October 31st 1992
Participants	64 participants (32 in each group). Elective laparotomy with either a colonic or ileal resection. Route of feeding: oral.

Binderow 1994 (Continued)

Mean age: 52 years (range 15-81) (intervention group), 52 years (range 15-87) (control group)

Male:Female 14:18 (intervention group), 18:14 (control group)

Interventions	Intervention group: received "regular solid food diet" on first postoperative morning. Control group: received a maximum of 8 oz of ice chips per day until return of bowel activity. Patients then begun on diet of clear liquids and if tolerated for 24 hours advanced to a regular diet.
Outcomes	LoS, vomiting. For LoS outcome standard deviations not reported
Notes	Country of study: USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Ileus) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - mortality	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdomi-	High risk	(Vomiting) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.

Binderow 1994 (Continued)

nal distention, aspiration,
tube blockage and any
other adverse events

Blinding of outcome as- sessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data
Selective reporting (re- porting bias)	High risk	No protocol available. All outcomes listed in methods were reported in the re- sults.

Carr 1996

Methods	Randomised controlled trial No information provided about duration of study
Participants	30 participants. 2 participants did not proceed to resection, and their data were not included. 28 partic- ipants (14 in each group). Elective gastrointestinal resection Route of feeding: nasojejunal tube Mean (SD) age: 60.1 years (7.5) (intervention group), 51.1 years (8.2) (control group) Male:Female 9:5 (intervention group), 8:6 (control group)
Interventions	Intervention group: feeding started on return from operating theatre by using standard isocaloric feed (Fresubin, Fresenius, Cheshire). Energy and water requirements were calculated from the weight of the patient, and a mixture of Fresubin and water provided the full basic fluid requirements. Initially feeding was at 25 mL an hour and was increased by 25 mL four-hourly until the target volume was reached, at which point intravenous fluids were stopped. Control group: received intravenous fluids with NBM until passage of flatus. Oral fluids started on pas- sage of flatus and increased to normal diet over 48 hours. Intravenous fluids and enteral feeding were stopped with introduction of diet.
Outcomes	Mortality, LoS, nausea and vomiting
Notes	Country of study: UK

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence genera- tion (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	Patients were randomly allocated by closed envelope. Not reported if sequen- tially numbered or opaque.

Carr 1996 (Continued)

Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Bleeding duodenal ulcer, infection) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Nausea and vomiting, distension, diarrhoea) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data
Selective reporting (reporting bias)	High risk	No protocol available. Some outcomes were reported in methods but not in results (sepsis) and there was a very general statement of clinical outcomes in the methods section (but more detail of complications, adverse events, LoS given in results)

Chatterjee 2012

Methods	Randomised controlled trial
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Chatterjee 2012 (Continued)

Study conducted April 2008 to March 2010

Participants	<p>120 participants (60 in each group).</p> <p>Gastric, small bowel, large bowel and uncomplicated simple biliary-enteric anastomosis.</p> <p>Route of feeding: oral</p> <p>Mean age (SD): 38.18 (11.9) (intervention group), 36.23 (12.88) (control group)</p> <p>Sex ratio (M:F): 42:18 (intervention group), 46:14 (control group)</p>
Interventions	<p>Intervention group: oral liquids (25 mL/hour) started within 24 hours of operation with clamping the NGT and the feed was increased by 25 mL/hour at 12-hour intervals. When patient tolerated liquid diet, NGT removed and semi-solid diet and then normal oral diet were started to reach nutritional goal (25 kcal/kg/day).</p> <p>Control group: kept NBM and were then fed 48-72 hours after or more following enteric anastomosis depending upon return of full peristaltic sounds. NGT removed when output was less than 20 mL to 30 mL/day and there was no paralytic ileus. Gradually shifted to semi-solid and then to solid normal diet.</p>
Outcomes	Wound infection, anastomotic leakage, mortality, LoS, nausea and vomiting
Notes	Country of study: India

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA - not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Respiratory tract infection, urinary tract infection, incidence of re-exploration) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) -	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.

Chatterjee 2012 (Continued)

anastomotic leakage/dehiscence

Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Vomiting and nausea) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data.
Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.

da Fonseca 2011

Methods	Randomised controlled trial Study conducted May 2006 to February 2009
Participants	50 participants: intervention (n = 24), control (n = 26) Elective colonic resections. Route of feeding: oral Mean age (SD): 57.4 years (16.3) (intervention group), 51.7 years (13.3) (control group) Sex: (M:F) 8:16 (intervention group), 10:16 (control group)
Interventions	Intervention group: On postoperative day (POD) 1 patients received an oral liquid diet (approximately 500 cm ³) and were advanced to a regular diet within the next 24 hours. Control group: patients NBM until elimination of the first flatus and then received an oral liquid diet, followed by a regular diet within the next 24 hours.
Outcomes	Wound infection, anastomotic leakage, mortality, LoS, pneumonia, nausea and vomiting
Notes	Country of study: Brazil
Risk of bias	
Bias	Authors' judgement Support for judgement

da Fonseca 2011 (Continued)

Random sequence generation (selection bias)	Low risk	Patients were randomly assigned to groups by a computer program.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants (performance bias) All outcomes	High risk	Not blinded. All participants were informed of the group to which they were assigned on first POD, when the oral diet was offered to certain participants.
Blinding of personnel (performance bias) All outcomes	High risk	Reported the difficulty of having a physician blinded to the groups. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Reported the difficulty of having a physician blinded to the groups. To minimise possible bias, outcome data for both groups were recorded prospectively by just one author (LMF).
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA - not assessed.
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Aspiration pneumonia, angina pectoris, prolonged ileus, catheter sepsis, deep vein thrombosis, pancreatitis). Reported the difficulty of having a physician blinded to the groups. To minimise possible bias, outcome data for both groups were recorded prospectively by just one author (LMF).
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Reported the difficulty of having a physician blinded to the groups. To minimise possible bias, outcome data for both groups were recorded prospectively by just one author (LMF).
Blinding of outcome assessor (detection bias) - mortality	Low risk	Reported the difficulty of having a physician blinded to the groups. To minimise possible bias, outcome data for both groups were recorded prospectively by just one author (LMF). Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Nausea and vomiting, hyporexia, readmission). Reported the difficulty of having a physician blinded to the groups. To minimise possible bias, outcome data for both groups were recorded prospectively by just one author.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Reported the difficulty of having a physician blinded to the groups. To minimise possible bias, outcome data for both groups were recorded prospectively by just one author (LMF).
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data.
Selective reporting (reporting bias)	Unclear risk	No protocol available.

Dag 2011

Methods	Randomised controlled trial Study conducted August 2007 to September 2009
Participants	199 participants: intervention (n = 99), control (n = 100) Elective open colorectal surgery Route of feeding: oral Mean age (range): 62 years (35-85) (intervention group), 61 years (17-89) (control group) Sex (M:F) 52:47 (intervention group), 61:39 (control group)
Interventions	Intervention group: oral feeding commenced approximately 12 hours after operation with a fluid diet; this was gradually increased to a solid diet as tolerated by the patient. Control group: fasted until passage of flatus or stool.
Outcomes	Wound infection, anastomotic leakage, pneumonia, mortality, LoS.
Notes	Country of study: Turkey

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was performed according to a computer generated list immediately after surgery by an independent computer consultant.
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA- not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Pneumonia, toxic hepatitis, sepsis, evisceration, cerebral infarct) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) -	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.

Dag 2011 (Continued)

anastomotic leakage/de-
hiscence

Blinding of outcome as- sessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to af- fect this outcome.
Blinding of outcome as- sessor (detection bias) - adverse events (e.g. nau- sea, vomiting, abdomi- nal distention, aspiration, tube blockage and any other adverse events	Unclear risk	NA- not assessed
Blinding of outcome as- sessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts after randomisation not reported.
Selective reporting (re- porting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the re- sults.

Hartsell 1997

Methods	Randomised controlled trial Study conducted between May 1 st 1995 and February 1 st 1996
Participants	58 participants (29 in each group). Elective colorectal surgery Route of feeding: oral Mean age: 66 years (range 40-83) (intervention group), 68 years (40-83) (control group)
Interventions	Intervention group: began a full liquid diet on postoperative day 1. If the patient consumed 1000 mL or more in a 24-hour period, they were advanced to regular diet the next day. Control group: began a liquid diet after evidence of return to normal bowel function. These patients were advanced to a regular diet when they consumed 1000mL or more in a 24-hour period.
Outcomes	Wound infection, anastomotic leakage, mortality, pneumonia, LoS, nausea, vomiting.
Notes	Country of study: USA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence genera- tion (selection bias)	Unclear risk	No information provided

Hartsell 1997 (Continued)

Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA - not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Pneumonia) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Nausea, vomiting) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data less than 10%.
Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.

Lucha 2005

Methods	Randomised controlled trial Study conducted July 1999 to December 2001
Participants	51 participants Elective open gastrointestinal surgery, Route of feeding: oral Age: both groups were similar with an average age of 51 (range, 22 to 74 years old). Sex: 65% males
Interventions	Intervention group: bowel rest for 8 hours after completion of surgery followed by a regular diet. Control group: bowel rest until passage of flatus, followed by 24 hours of clear liquids and advancement to a regular diet.
Outcomes	Anastomotic leakage, pneumonia, LoS. For LoS outcome standard deviations not reported.
Notes	Country of study: USA The RCT also focused on tolerance of diet

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA – not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Pneumonia) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) -	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.

Lucha 2005 (Continued)

anastomotic leakage/de-
hiscence

Blinding of outcome as- essor (detection bias) - mortality	Unclear risk	NA – not assessed
Blinding of outcome as- essor (detection bias) - adverse events (e.g. nau- sea, vomiting, abdomi- nal distention, aspiration, tube blockage and any other adverse events	Unclear risk	NA – not assessed
Blinding of outcome as- essor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information reported
Selective reporting (re- porting bias)	High risk	No protocol available. One outcome was reported in the results but not stated in methods (complications)

Minig 2009

Methods	Randomised controlled trial Study conducted January 1 st 2007 to March 15 th 2008
Participants	51 participants: intervention (n = 27), control (n = 24) Gynaecologic oncology patients undergoing laparotomy with associated intestinal resection Route of feeding: oral Median age (range): 54 (42, 62) (intervention group), 58 (47, 66) (control group) Female
Interventions	Intervention group: offered liquids: mineral water (no gas), tea, chamomile infusion or apple juice, during the first 24 PO hours (day 0). If well tolerated, as evidenced by absence of nausea and vomiting, they were then fed a regular diet of boiled or grilled beef, chicken or fish starting on day 1 and for the entire duration of hospital stay. Control group: NBM awaiting resolution of PO ileus. After resumption of normal bowel function, as expressed by presence of bowel sound and passage of flatus, and if patients did not have nausea and emesis, they were switched to oral liquid diet for 24 hours. If tolerated, they were placed on semi-solid diet of rice or pasta, vegetable soup, boiled potatoes or bread for 1 day. Regular diet was finally pre-scribed provided the semisolid diet had been well tolerated.
Outcomes	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, LoS, nausea and vomiting.
Notes	Country of study: Italy

Minig 2009 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients were randomised using the web-based TENALEA randomisation system (https://it.tenalea.net/ieo).
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Infectious complications, intestinal complications, ileus, bleeding, pleural effusion, thromboembolic complications, pneumothorax) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Nausea and vomiting, diarrhoea, readmission) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	High risk	Greater than 10% missing data

Minig 2009 (Continued)

Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.
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Mulrooney 2004

Methods	Randomised controlled trial No information provided about duration of study
Participants	73 participants, intervention (n = 37), control (n = 36) Colonic resection Route of feeding: nasojejunal
Interventions	Intervention group: uniform feeding regimen, until oral intake met at least half of the nutritional requirements. Control group: NBM and intravenous fluids
Outcomes	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, pneumonia, LoS.
Notes	Country of study: UK

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	Unclear risk	Participants were not aware of group allocation until postoperatively (author correspondence), but insufficient detail was provided on the blinding procedure and the timing postoperatively that blinding was broken
Blinding of personnel (performance bias) All outcomes	High risk	Surgeon not aware of group allocation until surgery (author correspondence); surgeon therefore not blinded at time of surgery. Other personnel unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature. (Correspondance regarding this outcome from author.)
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature. (Correspondance regarding this outcome from author.)
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Pneumonia, urinary tract infection) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature. (Correspondance regarding this outcome from author.)

Mulrooney 2004 (Continued)

Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature. (Correspondence regarding these outcomes from author.)
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	Vomiting information collected via a log, however group numbers are not reported (author correspondence). Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	High risk	61% of the 64 patients assessed for nausea or vomiting reported no symptoms. However 73 participants were randomised.
Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.

Nakeeb 2009

Methods	Randomised controlled trial Study conducted June 2005 to April 2008
Participants	120 participants (60 in each group) Elective open colorectal surgery Route of feeding: oral Mean age (SD, range): 52.3 (12.5, 21-70) (intervention group), 56.3 (11.6, 25-69) (control group) Sex ratio (M:F): 39:21 (intervention group), 42:18 (control group)
Interventions	Intervention group: Began fluids on the first POD and advanced to a regular diet within the next 24 to 48 hours, as tolerated (indicated by an absence of vomiting or abdominal distension). Control group: Managed in traditional way: NMB until resolution of ileus, then a fluid diet, followed by a regular diet.
Outcomes	Wound infection, anastomotic leakage, mortality, LoS, vomiting.
Notes	Country of study: Egypt

Risk of bias

Bias	Authors' judgement	Support for judgement
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Nakeeb 2009 (Continued)

Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes. Did not report being sequentially numbered or opaque
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA - not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Burst abdomen, abnormal serum electrolyte, pulmonary infection) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Vomiting, readmission) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data
Selective reporting (reporting bias)	High risk	No protocol available. Some outcomes were reported in the results but not stated in methods (patient satisfaction, readmission rates)

Nakeeb 2009 (Continued)

Standard deviations appear to be from paired t tests – should be unpaired (identified by statistician, CP)

Ortiz 1996

Methods	Randomised controlled trial No information provided about duration of study
Participants	190 participants: intervention (95 in each group). Elective colorectal surgery. Diagnosed with either neoplasm (165), inflammatory bowel disease (21) or diverticular disease (4) Route of feeding: oral Mean age: 65.54 years (range 22-90) (intervention group), 65.07 years (range 39-88) (control group) Male: Female 57:38 (intervention group), 55:40 (control group)
Interventions	Intervention group: on postoperative evening were allowed ad libitum clear liquids, which continued to first postoperative day and progressed to a regular diet as desired. Control group: after resolution of ileus patients were started on a clear liquid diet if this was tolerated for 24 hours they were advanced to a regular diet (traditional way).
Outcomes	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, pneumonia, LoS.
Notes	Country of Study: Spain

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - postoperative complications	High risk	(Haemorrhage, pneumonia, venous thrombosis, urinary infection, intestinal obstruction, ileostomy necrosis) Blinding of outcome assessor not discussed.

Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications (Review)

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Ortiz 1996 (Continued)

tions e.g. acute myocardial infarction, thrombosis or pneumonia		Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	Unclear risk	NA - not assessed
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature. (Correspondance regarding this outcome from author.)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data
Selective reporting (reporting bias)	Unclear risk	No protocol available. LoS was not listed as an outcome of interest nor was it reported. We accessed this information through author correspondence.

Reissman 1995

Methods	Randomised controlled trial Study conducted November 1992 to April 1994
Participants	161 participants: intervention (n = 80), control (n = 81). Elective laparotomy with bowel resection of colon or small bowel. Route of feeding: oral Mean age: 51 years (range 16-82) (intervention group), 56 years (range 20-90) (control group) Male: Female 34:46 (intervention group), 43:38 (control group)
Interventions	Intervention group: began a clear liquid diet on first postoperative day and advanced to a regular diet within next 24-48 hours. Control group: were nil by mouth until resolution of ileus. Then a clear liquid diet followed by a regular diet (traditional way).
Outcomes	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, pneumonia, LoS, vomiting.
Notes	Country of Study : USA

Reissman 1995 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Pneumonia, intestinal obstruction, urinary tract infection, pelvic abscess) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - mortality	Low risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Vomiting) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomised participants are included in the results (author correspondence).

Reissman 1995 (Continued)

Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.
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Sagar 1979

Methods	Randomised controlled trial No information provided about duration of study
Participants	30 participants (15 in each group) Gastrointestinal surgery (oesophago-gastrectomy, gastrectomy, colectomy, anterior resection, abdominoperineal resection) Route of feeding: nasojejun tube Mean age (years) $\pm$ SE: 54.8 $\pm$ 2.9 (intervention group), 54.5 $\pm$ 2.8 (control group) Male:Female 8:7 (intervention group), 9:6 (control group)
Interventions	Intervention group: Flexical was infused through the feeding channel, beginning on the first POD. For the first 24 hours a half strength solution was infused at 25 mL/hour. Thereafter, undiluted Flexical was infused at 25 mL/hour on the second POD, 50 mL/hour on the third POD, and 100 mL/hour on the fourth and fifth days. If there were no complications the double lumen tube was removed on the sixth day and the patient given as much Flexical as they could take by mouth on the sixth and seventh days. In addition all patients given 2 L dextrose (5% w/v) and 1 L saline (0.9% w/v) intravenously from the first to third POD. Control group: patient given 1 L saline (0.9%) and 2 L dextrose (5%) intravenously and were NBM for two days. On third POD they were given a 30 mL drink of water if there were no contraindications. Thereafter, oral intake was gradually increased until by the fifth day the patients could take as much fluid as desired. IV fluids stopped on the fifth POD, and light diet introduced on sixth and seventh days.
Outcomes	Wound infection, intraabdominal abscess, anastomotic leakage, LoS.
Notes	Country of study: UK

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Prospective randomised study from statistical tables
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.

Sagar 1979 (Continued)

Blinding of outcome assessor (detection bias) - wound infections	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - mortality	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided
Selective reporting (reporting bias)	High risk	No protocol available. All outcomes listed in methods were reported in the results. Missing standard deviations for LoS (imputed by statistician, CP).

Schroeder 1991

Methods	Randomised controlled trial No information provided about duration of study
Participants	32 participants; 16 in each group. Small or large bowel resection with reanastomosis. Route of feeding: Nasojejun tube Mean age: 51±18 years (intervention group), 53 ± 22 years (control group)

Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications (Review)

Schroeder 1991 (Continued)

Male:Female 8:8 (intervention group), 9:7 (control group)

Interventions	Intervention: full strength <i>Osmolite</i> solution for 56 hours. On morning of 3rd PO day tubes removed and reintroduction of diet. Control: hypo-caloric fluids and gradual reintroduction of diet.
Outcomes	Pneumonia, LoS.
Notes	Country of study: New Zealand

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Myocardial infarction, pneumonia, atelectasis) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - mortality	Unclear risk	N/A -not assessed
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration,	High risk	(Diarrhea, small bowel obstruction) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.

Schroeder 1991 (Continued)

tube blockage and any
other adverse events

Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided
Selective reporting (reporting bias)	High risk	No protocol available. Some outcomes were reported in the results, without being stated in methods (LoS and time to flatus)

Stewart 1998

Methods	Randomised controlled trial No information provided about duration of study
Participants	80 participants (40 in each group) Elective intraperitoneal colorectal resections without stoma formation (Ileocolic resection (10); hemicolectomy (right or left) (35); subtotal colectomy (11); anterior resection (24)) Route of feeding: oral Mean age (range): 58 (25-89) (intervention group), 59 (17-88) (control group) Sex ratio (M:F): 19/21 (intervention group), 18/22 (control group)
Interventions	Intervention group: allowed free fluids from 4 hours after operation and progressed to a solid diet from the first POD at their own discretion. Control group: remained fasting until passage of flatus or bowel motion, and were then commenced on clear fluids and progressed to a solid diet over 24 to 48 hours at the surgeon's discretion.
Outcomes	Wound infection, anastomotic leakage, mortality, pneumonia, LoS, vomiting.
Notes	Country of study: Australia

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Patients randomly assigned according to a computer number generator to one of two groups.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.

Stewart 1998 (Continued)

Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	High risk	Assessors were not blinded.
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	NA - not assessed.
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	High risk	(Respiratory complications, cardiovascular complications, urinary tract infection, pneumonia) Assessors were not blinded.
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	High risk	Assessors were not blinded.
Blinding of outcome assessor (detection bias) - mortality	Low risk	Assessors were not blinded. Outcome assessor unlikely to affect this outcome.
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Vomiting). Assessors were not blinded.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Assessors were not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Less than 10% missing data.
Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.

Yang 2013

Methods	Randomised controlled trial
	Study conducted May to December 2008
Participants	70 participants (35 in each group)
	Colorectal cancer

Yang 2013 (Continued)

Route of feeding: oral (nutritional drinks)

Mean age (SD): 57.2 (11.7) (intervention group), 59.5 (12.1) (control group)

Sex ratio (M:F): 20:12 (intervention group), 23:7 (control group)

Interventions	Intervention group: oral intake of 30 mL to 50 mL Ensure (US Abbott; 4.184 kJ energy) 6 to 12 hours post-surgery at 1- to 2-hour intervals. Amount adjusted based on participant's tolerance. Participants also provided with IV fluid. Most participants stopped having IV fluid 3-4 days PO. Control group: food/drink intake commenced after first flatus. Started with liquid diet and gradually changed to normal diet.
Outcomes	LoS, vomiting.
Notes	Country of study: China Article directly extracted from Chinese

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Calculator generated random number table
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants (performance bias) All outcomes	High risk	No reports of attempts to blind participants. Participants are unlikely to be adequately blinded with an intervention of this nature.
Blinding of personnel (performance bias) All outcomes	High risk	No reports of attempts to blind personnel. Personnel are unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - wound infections	Unclear risk	N/A - not assessed
Blinding of outcome assessor (detection bias) - intraabdominal abscesses	Unclear risk	N/A - not assessed
Blinding of outcome assessor (detection bias) - postoperative complications e.g. acute myocardial infarction, thrombosis or pneumonia	Unclear risk	N/A - not assessed
Blinding of outcome assessor (detection bias) - anastomotic leakage/dehiscence	Unclear risk	N/A - not assessed

Yang 2013 (Continued)

Blinding of outcome assessor (detection bias) - mortality	Unclear risk	N/A - not assessed
Blinding of outcome assessor (detection bias) - adverse events (e.g. nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events)	High risk	(Vomiting, stomach distension) Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Blinding of outcome assessor (detection bias) - length of hospital stay	High risk	Blinding of outcome assessor not discussed. Outcome assessor unlikely to be adequately blinded with an intervention of this nature.
Incomplete outcome data (attrition bias) All outcomes	High risk	Greater than 10% missing data
Selective reporting (reporting bias)	Unclear risk	No protocol available. All outcomes listed in methods were reported in the results.

IV: intravenous
LoS: length of hospital stay
NBM: nil by mouth
NGT: nasogastric tube
POD: postoperative day
RCT: randomised controlled trial
SD: standard deviation
SE: standard error
w/v: weight/volume

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Abela 2017	Narrative review
Barletta 2011	Not an RCT or feeding
Barlow 2011	Not lower GI surgery; upper GI surgery
Beati 1998	Abstract only
Beattie 2000	Feeding did not start until a mean of 6.5 days after GI surgery, and the trial compared normal diet versus normal diet plus supplement
Behrns 2000	Both groups received calories
Bernardes 2008	Upper GI surgery
Beyer 1991	Total parenteral nutrition
Bickel 1992	Nutrition began greater than 24 hours postoperatively

Study	Reason for exclusion
Bisgaard 2002	Review
Boelens 2014	Compared enteral with parenteral nutrition
Buchmann 1996	An abstract. Results presented in the 1998 reference
Buchmann 1998	Not randomised on early enteral feeding. The comparisons focus on post enteral nutrition for two surgical techniques, whether there is any difference between open and minimal invasive procedures with respect to the start of oral intake.
Bufo 1994	Not a randomised trial
Choudhry 1996	Variety of indications for placement of a PEG tube
Dardai 1985	Total parenteral nutrition
de Aguilar-Nascimento 2002	Both comparison groups start feeding more than 24 hours after surgery.
Delaney 2003	This is a well performed RCT, but reported multiple variables not just diet.
Feo 2004	Both treatment groups were allowed liquid diet, therefore no control group to early enteral feeding
Gianotti 2011	Not RCT (early feeding group compared with historical controls)
Gustafsson 2011	Review
Gómez Sánchez 2010	Compares two types of fluids (immunonutrition and 'conventional')
Gómez Sánchez 2011	Immunonutrition and does not specifically state that it is looking at early postoperative feeding versus NBM
Han-Geurts 2001	Patients undergoing colonic and vascular surgery were randomly allocated to choose when they wanted to start an oral diet (patient-controlled group) or a fixed-feeding regimen where diet was introduced on postoperative day four
Han-Geurts 2007	It is not clear if some or all patients are common to the 2001 publication, but reason for exclusion the same: atients undergoing colonic and vascular surgery were randomly allocated to choose when they wanted to start an oral diet (patient-controlled group) or a fixed-feeding regimen where diet was introduced on postoperative day four
Hedberg 1999	Not randomised
Henriksen 2002	All patients received the same nutrition (the comparison was in regards to other factors)
Heslin 1997	Includes only upper GI
Holst 2015	Review
Hoover 1980	Patients receiving enteral nutrition compared with a control group, receiving intravenous nutrition. Main outcome is cumulative 10-day nitrogen balance.
Hyltander 2005	Upper GI and total parental nutrition
Kaur 2005	Non-traumatic GI perforation. 44% had DU's, 39% ileal (TB or typhoid). Closure was direct, no resections and GI anastamosis formed. Feeding was started 24 hours after surgery.

Study	Reason for exclusion
Keele 1997	Not dealing with early enteral feeding, rather whether oral diet supplements have an effect or not.
Kemen 1995	Both comparison groups receives early postoperative enteral nutrition. One with arginine-omega-3 fatty acids and ribonucleic acid-supplemented diet versus placebo.
Klappenbach 2013	Not lower GI surgery: Appendectomy where there is no anastomosis.
Klek 2011	Gastrectomy and pancreas. All groups received some form of nutrition – no control group.
Kompan 1999	Study on trauma patients, admitted in shock and stabilised in 6 hours.
Kong 2017	Feeding started after hospital discharge
Lau 2014	Two types of calorie-containing diets compared
Le Guen 2014	Review
Lee 2010	Early feeding and early mobilisation versus traditional care
Lee 2014	Not lower GI surgery
Li 2015 (a)	Not lower GI surgery
Li 2014	Article cannot be sourced
Li 2015	Not lower GI surgery
Lidder 2013	All groups were allowed calories postoperatively, so there can not be a comparison of calories versus no calories
Liu 2013	Not lower GI surgery
Liu 2014	Review
Mahla 2016	Surgery does not involve a GI resection with re-anastomosis
Mahmoodzadeh 2015	Not lower GI surgery
Malhotra 2004	GI perforation also feeding > 48 hours
Mari 2011	Multi-modal intervention: unable to separate effects of feeding alone
Maňásek 2016	Not an RCT
McCarter 1998	No control group was used, as the comparisons groups begin tube feedings at 4 hours (group A) or at 24 hours (group B) after intervention
Mirea 2015	Compared enteral with parenteral nutrition
Moore 1991	Review on multisystem trauma, a decade perspective
Moss 1981	Not able to determine if the study was randomised
Murchan 1995	Can only obtain abstract but does not state that comparison is early versus traditional nutrition

Study	Reason for exclusion
Nakajima 2009	Not relevant
Neri 2001	Total parental nutrition
Nessim 1999	This is a study examining the benefits of bowel confinement where the interventional group received clear liquids with high dose loperamide and codeine with the control group of patients started a regular dietary intake on the day of surgery
Nguyen 2009	Not relevant
Niu 2015	Compared enteral with parenteral nutrition
Osland 2011	Review
Palmer 1998	Both groups receive calorie-containing diets. Compares supplement with no supplement.
Pappa 2011	Does not look at early feeding
Peng 2014	Not lower GI surgery
Pragatheeswarane 2014	The provision of fluids was not within 24 hours postsurgery: it was given "at the 24th hour". The 'clear liquid diet' was water, coconut water, clear vegetable soup etc (author correspondence). For those who were initially given water, their fluids would not have contained any calories.
Rosales 2009	Gastrectomy
Ryan 1981	All three groups undergoing elective partial colectomy received early feeding, randomised to receive either jejunal feeding of elemental diet (ED) or isotonic intravenous infusions of dextrose (IV).
Schwenk 1998	A comparison of laparoscopic or conventional resection of colorectal tumours. Major endpoints were the postoperative time to the first bowel movement and the time until oral feeding without parenteral alimentation was tolerated.
Seenu 1995	No method stated. Individual protocol for commencement of postoperative feeding.
Seri 1984	Both groups received early postoperative feeding
Sharma 2013	Two types of calorie-containing diets compared
Shen 2013	Review
Shoar 2013	Not lower GI surgery
Shrikhande 2009	Review
Shu 2013	Review
Shu 2016	Systematic review
Singh 1998	Patients in the early feeding group did not start receiving 'feed' until after 24 hours (before 24 hours they received saline/dextrose). Our study criteria is that patients receive enteral feed within 24 hours of surgery.
Smedley 2004	No control group that was NBM/received no calories

Study	Reason for exclusion
Smeets 2017	Systematic review
Smith 2002	Pseudo randomised on an intention to treat. Decision on treatment group was determined individually
Soliani 2001	Comparison of three different methods of feeding administration
Stein 2002	Not GI surgery; PEG feeding
Takala 1985	Not a randomised study
Tong 2006	Article could not be located
Ugarte 2000	Not RCT
Vaithiswaran 2008	Feeding started via NJ tube 12 to 24 hours saline & 5% dextrose then 24 to 48 hours 1L and half strength feed at 50 mL/hour. Thus patients were not fed within 24 hours of surgery
Velez 1997	Not a randomised study
Vlug 2009	Not analysed as an RCT; ERAS study
Wallström 2014	Review
Wang 2013	Nutrition began greater than 24 hours postoperatively
Wang 2014	Nutrition began greater than 24 hours postoperatively
Watters 1997	Includes only upper GI
Weber 1999	Not relevant
Weinstein 1993	Caesarean section
Wiedeck 1984	Comparison between enteral and parenteral nutrition.
Wiren 2002	This study evaluates the feasibility of alpha-ketoglutarate enrichment of enteral feeding and the effect on protein metabolism (nitrogen balance).
Wong 1995	Trial of growth hormone
Wu 1996	Chinese - article not in readable format
Wu 2000	Chinese - not clear if feeding started within 24 hours post surgery
Wu 2004	Gastric cancer – not relevant
Wu 2007	Chinese - not clear if feeding started within 24 hours post surgery.
Yu 2013	Not lower GI surgery
Yuanlong 1999	Compared enteral with parenteral nutrition
Zaidi 2016	Mixed upper and lower GI, no definition of early oral feeding

Study	Reason for exclusion
Zhang 2014	Nutrition began greater than 24 hours postoperatively
Zhang 2017	Systematic review
Zhao 2014	Not lower GI surgery
Zhou 2006	Compares early versus late removal of naso-gastric tubes after colorectal surgery
Zhuang 2013	Systematic review
Zitta 2012	Unclear what "conventional postoperative treatment" is, and involved mechanical bowel preparation

DU: duodenal Ulcer
 ED: elemental diet
 ERAS: enhanced recovery after surgery GI: gastrointestinal
 GI: gastrointestinal
 IV: intravenous
 NBM: 'nil by mouth'
 NJ: nasojejunal
 PEG: percutaneous endoscopic gastrostomy
 RCT: randomised controlled trial
 TB: tuberculosis

Characteristics of studies awaiting assessment *[ordered by study ID]*

[Fanaie 2005](#)

Methods	Randomised controlled trial Duration of study: August 2003 and November 2004
Participants	110 participants (55 in each group) Route of feeding: oral Sex ratio (M:F): 31/24 (intervention group), 38/17 (control group)
Interventions	Intervention group: early feeding beginning with liquid diet, 8 hours postoperatively. Control group: given a regular diet with normal bowel sounds.
Outcomes	Postoperative complications: wound infection, leakage of anastomosis, obstruction, mesenteric emboli, upper gastrointestinal bleeding, wound dehiscence, prolonged ileus and mortality.
Notes	Country of study: Iran

GI: gastrointestinal

DATA AND ANALYSES

Comparison 1. Early enteral nutrition versus later commencement after gastrointestinal surgery

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Length of hospital stay	16	1346	Mean Difference (IV, Random, 95% CI)	-1.95 [-2.99, -0.91]
1.1 Surgical site distal to ligament of Treitz	13	1156	Mean Difference (IV, Random, 95% CI)	-1.77 [-2.95, -0.59]
1.2 Surgical site distal and proximal to ligament of Treitz	3	190	Mean Difference (IV, Random, 95% CI)	-2.58 [-4.40, -0.76]
2 Length of hospital stay	16	1346	Mean Difference (IV, Random, 95% CI)	-1.95 [-2.99, -0.91]
2.1 Oral feeding only	11	1075	Mean Difference (IV, Random, 95% CI)	-2.06 [-3.26, -0.87]
2.2 Tube +/- oral feeding	5	271	Mean Difference (IV, Random, 95% CI)	-1.75 [-4.32, 0.82]
3 Wound infection	12	1181	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.51, 1.39]
4 Intraabdominal abscess	6	554	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.21, 2.01]
5 Anastomotic leakage	13	1232	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.40, 1.36]
6 Pneumonia	10	954	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.51, 2.47]
7 Mortality	12	1179	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.25, 1.13]
8 Vomiting	7	613	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.96, 1.58]
9 Nausea	2	118	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.70, 1.23]
10 Nausea and vomiting	4	238	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.51, 1.74]

Analysis 1.1. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 1 Length of hospital stay.

Analysis 1.2. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 2 Length of hospital stay.

Analysis 1.3. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 3 Wound infection.

Analysis 1.4. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 4 Intraabdominal abscess.

Analysis 1.5. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 5 Anastomotic leakage.

Analysis 1.6. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 6 Pneumonia.

Analysis 1.7. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 7 Mortality.

Analysis 1.8. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 8 Vomiting.

Analysis 1.9. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 9 Nausea.

Analysis 1.10. Comparison 1 Early enteral nutrition versus later commencement after gastrointestinal surgery, Outcome 10 Nausea and vomiting.

ADDITIONAL TABLES

Table 1. Characteristics of the seventeen included trials of early enteral feeding

Study	Site of surgery	Elective or acute surgery	Feed type	Route of feeding	Feed timing and amount in intervention group	Pathology	Outcomes	Additional data
Beier Holgersen (1996)	Lower GI (87%), Upper GI (13%)	Elective surgery	Nutritional supplement (Nutridrink, Nutricia)	Nasoduodenal tube (2nd and 3rd part of duodenum) and oral	Intervention: Nutritional supplement (Nutridrink, Nutricia) within four hours postoperatively. POD 1 = 1000ml nutrition (median); POD 2 = 1200 mL (median) nutrition; POD 3 = 1000mL (median) nutrition; POD 4 = 1000mL nutrition. Normal diet from 5th POD.	65% Malignant; 35% Benign	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, postoperative complications (pneumonia, dehiscence, pulmonary failure, myocardial infarction), LoS, adverse events (nausea, vomiting). Patients were seen every day and all complications were recorded using Buzby's classification.	Yes (data set provided)
Binderow (1994)	27% small bowel, 73% large bowel	Elective surgery	Regular diet	Oral	Intervention: Patients told to eat as much of the diet as they wanted.	Not reported	LoS, postoperative complications (ileus), adverse events (vomiting). Patients completed a daily symptom log, in addition to a daily interview, examination and review of nursing records.	No
Carr (1996)	Intestinal only	Elective surgery	Enteral feed (Fresubin, Fresenius). Oral fluids started on passage of flatus and progressed to regular diet over 48 hours.	Double lumen Nasojejunal tube and oral	Feeding was started two to three hours after surgery and continued until normal diet was possible. Energy and water requirements were calculated from the weight of the patient, and a mixture of Fresubin and water provided the full basic fluid requirements (35 mL/kg body weight/day). Initially feeding was at 25 mL an hour and was increased by 25 mL four hourly until the target volume was reached, at which point intravenous fluids were stopped.	Not reported	Mortality, LoS, postoperative complications (bleeding duodenal ulcer, infection), adverse events (nausea and vomiting, distension, diarrhoea)	No

Table 1. Characteristics of the seventeen included trials of early enteral feeding (Continued)

Chatterjee (2012)	Large bowel, small bowel, gastric, and biliary	Emergency or elective surgery	Enteral feed progressed to regular diet	Nasogastric tube - progressed to oral	Oral liquids (25 mL/hour) were started within 24 hours of operation with clamping the NGT and the feed was increased by 25 mL/hour at 12 hours interval. When the patients started tolerating the liquid diet, NGT was removed and the semisolid diet and then normal oral diet were started to reach the nutritional goal (25 kcal/ kg/ day) as soon as possible.	38% Malignant, 62% Benign	Wound infection, wound dehiscence, anastomotic leakage (detected by clinical examination of septicaemia, distention of abdomen, change in character and measure of drain output/0 and radiological investigations (USG, CT scan), mortality, LoS, postoperative complications (respiratory tract infection, urinary tract infection, incidence of re-exploration) adverse events (nausea and vomiting)	Yes (half data set provided)
Da Fonseca (2011)	Lower GI (100%) -	Elective surgery	Liquid diet progressed to regular diet	Oral	POD 1 patients received an oral liquid diet (approximately 500 cm ³) and were advanced to a regular diet within the next 24 hours)	88% Malignant, 12% Benign	Wound infection, anastomotic leak, mortality, LoS, postoperative complications (aspiration pneumonia, angina pectoris, prolonged ileus, catheter sepsis, deep vein thrombosis, pancreatitis), adverse events (nausea and vomiting, hyporexia, readmission)	Yes (confirmed study met inclusion criteria)
Dag (2011)	Lower GI (100%) - elective open colorectal surgery	Elective surgery	Fluid diet gradually increased to a solid diet	Oral	Fluid diet (12 hours after surgery)	Not reported	Wound infection, anastomotic leakage, postoperative complications (pneumonia, toxic hepatitis, sepsis, evisceration, cerebral infarct), LoS	Yes (provided mortality data)
Hartzell (1997)	Lower GI (100%)	Elective surgery	Liquid diet progressed to regular diet	Oral	Full liquid diet on POD 1. If patient consumed 1000 mL or more in a 24-hour period, they were advanced to a regular diet next day.	64% Malignant, 36% Benign	Wound infection, anastomotic leakage, mortality, postoperative complications (pneumonia), LoS, adverse events (nausea, vomiting)	No
Lucha (2005)	Lower GI (100%)	Elective surgery	Regular diet	Oral	Not reported	Not reported	Anastomotic leakage, postoperative complications (pneumonia), LoS	No

Table 1. Characteristics of the seventeen included trials of early enteral feeding (Continued)

Minig (2009)	Gynaecological patients with malignancy. 37/40 had either rectosigmoid or rectosigmoid and small bowel resection. 3/40 had small bowel resection	Elective surgery	Liquids, mineral water (no gas), tea, chamomile infusion or apple juice. Progressed to regular diet of boiled or grilled beef, chicken or fish on POD1.	Oral	Liquids, mineral water (no gas), tea, chamomile infusion or apple juice during first 24 hours. Progressed to regular diet of boiled or grilled beef, chicken or fish on POD1.	Malignant (100%)	Wound infection, intraabdominal abscesses, anastomotic leakage, mortality, postoperative complications (infectious complications, intestinal complications, ileus, bleeding, pleural effusion, thromboembolic complications, pneumothorax), LoS, adverse events (nausea and vomiting, diarrhoea, readmission), QoL (EORTC QLQ-C30 and EORTC QLQ-QV28).	No
Mulrooney 2004	Lower GI (100%)	NR	Enteral feed (Nutrison Standard by Nutricia Clinical Care)	Nasojejunal tube and oral	Jejunal feeding was started within 24 hours from the end of the operation at 25 mL/hour. This rose to 50 mL/hour on day 2 and 75 mL/hour on day 3 etc. The feed ran continuously with no break. The nutritional goal (final feeding rate) was calculated using the dietetic department guidelines at DRI. The feed was stopped once oral feeding recovery was adequate (nutritional intake meets at least half of the calorie and protein requirement).	73% malignant and 27% benign	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, postoperative complication (pneumonia, urinary tract infection), LoS	Yes (provided data on outcomes of interest)
Nakeeb (2009)	Lower GI (100%)	Elective surgery	Fluids POD1 progressed to regular diet within next 24 to 48 hours	Oral	Not reported	100% cancer	Wound infection, anastomotic leakage (diagnosis was from symptoms such as fever and leakage of intestinal contents), mortality, LoS, postoperative complications (burst abdomen, abnormal serum electrolyte, pulmonary infection), adverse events (vomiting, readmission).	Yes (confirmed study met inclusion criteria)

Table 1. Characteristics of the seventeen included trials of early enteral feeding (Continued)

Follow up occurred 10-14 days postoperatively in the form of clinical, lab and radiological evaluations.								
Ortiz (1996)	Lower GI (100%)	Elective surgery	Regular diet	Oral	On postoperative evening patients allowed ab libitum intake of clear liquids; this continued until POD 1 at which time they progressed to a regular diet as desired.	87% Malignant, 13% Benign	Wound infection, anastomotic leakage, intraabdominal abscess, mortality, postoperative complication (haemorrhage, pneumonia, venous thrombosis, urinary infection, intestinal obstruction, ileostomy necrosis), LoS	Yes (LoS provided)
Reissman (1995)	Lower GI (100%)	Elective surgery	Clear liquid diet	Oral	Clear liquid diet on POD 1 and advanced to a regular diet within the next 24 to 48 hours, as tolerated.	Not reported	Wound infection, intraabdominal abscess, anastomotic leakage, mortality, postoperative complications (recorded daily) (pneumonia, intestinal obstruction, urinary tract infection, pelvic abscess), LoS, adverse events (vomiting) (recorded daily)	Yes (confirmed study met inclusion criteria)
Sagar (1979)	Lower GI (73%), Upper GI (27%)	NR	Enteral feed (elemental, Flexical Mead Johnson Laboratories)	Nasojejunal tube and oral	For the first 24 hours a half strength solution was infused at 25 mL/hour. Thereafter, undiluted. Flexical was infused at 25 mL/hour on POD 2, 50 mL/hour on POD 3, and 100 mL/hour on POD 4 and 5. If there were no complications the double lumen tube was removed on the sixth day and the patient given as much Flexical as they could take by mouth on POD 6 and 7. Patients given 2 L dextrose (50, w/v) and 1 L saline (0.9% w/v) intravenously from POD 1 -3.	Not reported	Wound infection (inspected on the 10th day or earlier if infection was suspected), anastomotic leakage, intraabdominal abscess, LoS	No
Schroeder (1991)	30/32 had colonic re-	NR	Enteral feed (Osmolite,	Nasojejunal tube	Immediate infusion with full-strength Osmolite at	Not reported	Postoperative complications (pneumonia, intestinal ob-	No

Table 1. Characteristics of the seventeen included trials of early enteral feeding *(Continued)*

	section and 2/32 had small bowel resection		Ross Labo- ratories)		a rate of 50 mL/hour via a continuous infusion pump. Patient encouraged to drink water. If absorption was oc- curring with no problems, the infusion rate was then increased to 80 mL/hour and the iv rate decreased accordingly. On the morn- ing of POD 3 (i.e., either 72 or 67 hours after com- mencement of operation) both tubes were removed and the patient allowed to take whatever they liked by mouth.		struction, urinary tract infec- tion, pelvic abscess), LoS, ad- verse events (diarrhoea, small bowel obstruction)	
Stewart (1998)	Lower GI (100%)	Elective surgery	Free fluids progressed to a solid di- et.	Oral	Free fluids from 4 hours af- ter the operation and pro- gressed to a solid diet from POD 1 at their own discre- tion.	Not report- ed	Wound infection, anastomot- ic leakage, mortality, postop- erative complications (res- piratory complications, car- diovascular complications, urinary tract infection, pneu- monia), LoS, adverse events (vomiting)	Yes (data set provid- ed, LoS and pneumonia extracted)
Yang (2013)	Lower GI (100%)	Elective surgery	Nutritional supplement (Ensure, Ab- bott) pro- gressed to regular diet	Oral	Nutritional supplement (En- sure, Abbott) progressed to regular diet within 12 hours. 30 mL to 50 mL Ensure 6 to 12 hours post-surgery at 1- to 2-hour intervals. POD 2, 100 mL to 200 mL Ensure at - to 3-hour intervals.	100% can- cer	LoS, adverse events (vomit- ing, stomach distension)	No

Table 2. Estimated results and assumptions for length of hospital stay outcome

Study	Estimated result
Binderow (1994)	SD not reported, SD imputed using mean SD of other studies (by treatment arm)
Lucha (2005)	SD not reported, SD imputed using mean SD of other studies (by treatment arm)
Mulrooney (2004)	Results extracted from additional correspondence - thesis
Nakeeb (2009)	SD appear to be from paired t-tests, SD imputed using mean SD of other studies (by treatment arm)
Ortiz (1996)	Results provided from additional correspondence
Reissman (1995)	SEMs converted to SD
Sagar (1979)	Estimated mean LoS and SDs using Wan et al (2014)
Stewart (1998)	Results calculated from additional correspondence

Table 3. Other postoperative complications

Study	Complication	Intervention group	Control group
Beier-Holgersen (1996)	Dehiscence	3	0
	Pulmonary failure (ARDS)	0	1
	Myocardial infarction	1	0
Binderow (1994)	Ileus (duration in days)	3.6	4
Carr (1996)	Bleeding duodenal ulcer	0	1
	Infection (wound, urinary)	0	3
Chatterjee (2012)	Respiratory tract infection	10	5
	Urinary tract infection	5	8
	Incidence of re-exploration	4	1
Dag (2011)	Toxic hepatitis	1	0
	Sepsis	1	2
	Evisceration	0	1
	Cerebral infarct	0	1
Da Fonseca (2011)	Angina pectoris	0	1
	Prolonged ileus	0	2

Table 3. Other postoperative complications (Continued)

	Catheter sepsis	0	1
	Deep vein thrombosis	0	1
	Pancreatitis	1	0
Hartsell (1997)	Sepsis (anastomotic leak, death)	0	1
Minig (2009)	Ileus	0	0
	Intestinal complications	0	3
	Infectious complications	0	3
	Bleeding	6	7
	Bleeding requiring surgical reexploration	1	1
	Pleural effusion	1	3
	Thromboembolic complications	1	2
	Pneumothorax	0	3
Mulrooney (2004)	Urinary tract infection	0	1
Nakeeb (2009)	Burst abdomen	1	2
	Abnormal serum electrolyte	5	6
	Pulmonary infection	2	7
Ortiz (1996)	Haemorrhage	2	2
	Venous thrombosis	2	2
	Urinary infection	0	1
	Intestinal obstruction	2	0
	Ileostomy necrosis	1	0
Reissman (1995)	Intestinal obstruction	1	0
	Urinary tract infection	2	1
	Pelvic abscess	1	1
Schroeder (1991)	Myocardial infarction	1	1
	Atelectasis	2	2
Stewart (1998)	Respiratory complications	4	3
	Cardiovascular complications	4	3

Table 3. Other postoperative complications *(Continued)*

Urinary tract infection	1	2
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Table 4. Other adverse effects

Study	Adverse event	Intervention	Control
Carr (1996)	Distension (n)	2	4
	Diarrhoea (n)	0	1
Da Fonseca (2011)	Hyporexia (n)	1	1
	Readmission (n)	0	4
Minig (2009)	Diarrhoea (mean, EORTC C-30)	13.9	6.7
	Readmission (n)	0	1
Nakeeb (2009)	Readmission (n)	3	4
Schroeder (1991)	Diarrhoea (n)	1	0
	Small bowel obstruction (n)	0	4
Yang (2013)	Stomach distension (n)	6	11

Table 5. Early enteral nutrition versus later commencement after gastrointestinal surgery, surgical site, outcome: 1.1 Length of hospital stay.

Study or subgroup	Experimental			Control			Weight	Mean difference IV, Random, 95%CI	
	Mean	SD	N	Mean	SD	N			
1.1.1 Surgical site distal to ligament of Treitz									
Binderow 1994	6.7	3.7	32	8.0	5.5	32	6.3%	-1.30 [-3.60, 1.00]	
Carr 1996	9.8	6.6	14	9.3	2.8	14	4.2%	0.50 [-3.26, 4.26]	
Da Fonseca 2011	4.0	3.7	24	7.6	8.1	26	4.6%	-3.60 [-7.05, -0.15]	
Dag 2011	5.55	2.35	99	9.0	6.5	100	7.9%	-3.45 [-4.81, -2.09]	
Hartsell 1997	7.2	3.3	29	8.1	2.3	29	7.7%	-0.90 [-2.36, 0.56]	
Lucha 2005	6.3	3.7	26	6.6	5.5	25	5.8%	-0.30 [-2.88, 2.28]	
Mulrooney 2004	11.79	4.46	32	10.57	4.64	29	6.3%	1.22 [-1.07, 3.51]	
Nakeeb 2009	6.2	3.7	60	6.9	5.5	60	7.4%	-0.70 [-2.38, 0.98]	
Ortiz 1996	13.13	4.23	95	16.57	9.23	95	6.8%	-3.44 [-5.48, -1.40]	
Reissman 1995	6.2	1.8	80	6.8	1.8	81	8.9%	-0.60 [-1.16, -0.04]	
Schroeder 1991	10.0	4.0	16	15.0	10.0	16	2.7%	-5.00 [-10.28, 0.28]	
Stewart 1998	9.36	4.11	36	10.08	2.55	36	7.5%	-0.72 [-2.30, 0.86]	
Yang 2013	6.0	1.0	35	11.7	3.8	35	8.0%	-5.70 [-7.00, -4.40]	
Subtotal (95% CI)			578				578	84.2%	-1.77 [-2.95, -0.59]
Heterogeneity: Tau ² = 3.41; Chi ² = 74.33, df = 12 (P < 0.00001); I ² = 84%									
Test for overall effect: Z = 2.95 (P = 0.003)									
1.1.2 Surgical site distal and proximal to ligament of Treitz									

Table 5. Early enteral nutrition versus later commencement after gastrointestinal surgery, surgical site, outcome: 1.1 Length of hospital stay. (Continued)

Chatterjee 2012	8.45	5.14	60	10.53	4.95	60	7.2%	-2.08 [-3.89, -0.27]
Minig 2009	6.9	2.6	18	9.1	4.5	22	6.4%	-2.20 [-4.43, 0.03]
Sagar 1979	16.0	4.8	15	23.5	10.9	15	2.2%	-7.50 [-13.53, -1.47]
Subtotal (95% CI)			93			97	15.8%	-2.58 [-4.40, -0.76]
Heterogeneity: $\tau^2 = 0.83$; $\chi^2 = 2.90$, $df = 2$ ($P = 0.23$); $I^2 = 31\%$								
Test for overall effect: $Z = 2.78$ ($P = 0.005$)								
Total (95% CI)			671			675	100.0%	-1.95 [-2.99, -0.91]
Heterogeneity: $\tau^2 = 3.08$; $\chi^2 = 78.98$, $df = 15$ ($P < 0.00001$); $I^2 = 81\%$								
Test for overall effect: $Z = 3.68$ ($P = 0.0002$)								
Test for subgroup differences: $\chi^2 = 0.54$, $df = 1$ ($P = 0.46$), $I^2 = 0\%$								

Table 6. Early enteral nutrition versus later commencement after gastrointestinal surgery, feeding route, outcome: 1.2 Length of hospital stay.

Study or subgroup	Experimental			Control			Weight	Mean difference IV, Random, 95%CI
	Mean	SD	N	Mean	SD	N		
1.2.1 Oral feeding only								
Binderow 1994	6.7	3.7	32	8.0	5.5	32	6.3%	-1.30 [-3.60, 1.00]
Da Fonseca 2011	4.0	3.7	24	7.6	8.1	26	4.6%	-3.60 [-7.05, -0.15]
Dag 2011	5.55	2.35	99	9.0	6.5	100	7.9%	-3.45 [-4.81, -2.09]
Hartsell 1997	7.2	3.3	29	8.1	2.3	29	7.7%	-0.90 [-2.36, 0.56]
Lucha 2005	6.3	3.7	26	6.6	5.5	25	5.8%	-0.30 [-2.88, 2.28]

Table 6. Early enteral nutrition versus later commencement after gastrointestinal surgery, feeding route, outcome: 1.2 Length of hospital stay. (Continued)

Ming 2009	6.9	2.6	18	9.1	4.5	22	6.4%	-2.20 [-4.43, 0.03]
Nakeeb 2009	6.2	3.7	60	6.9	5.5	60	7.4%	-0.70 [-2.38, 0.98]
Ortiz 1996	13.13	4.23	95	16.57	9.23	95	6.8%	-3.44 [-5.48, -1.40]
Reissman 1995	6.2	1.8	80	6.8	1.8	81	8.9%	-0.60 [-1.16, -0.04]
Stewart 1998	9.36	4.11	36	10.08	2.55	36	7.5%	-0.72 [-2.30, 0.86]
Yang 2013	6.0	1.0	35	11.7	3.8	35	8.0%	-5.70 [-7.00, -4.40]
Subtotal (95% CI)			534			541	77.4%	-2.06 [-3.26, -0.87]
Heterogeneity: $\tau^2 = 5.14$; $\chi^2 = 12.18$, $df = 10$ ($P < 0.00001$); $I^2 = 85\%$								
Test for overall effect: $Z = 3.38$ ($P = 0.00073$)								
1.2.2 Tube +/- oral feeding								
Carr 1996	9.8	6.6	14	9.3	2.8	14	4.2%	0.50 [-3.26, 4.26]
Chatterjee 2012	8.45	5.14	60	10.53	4.95	60	7.2%	-2.08 [-3.89, -0.27]
Mulrooney 2004	11.79	4.46	32	10.57	4.64	29	6.3%	1.22 [-1.07, 3.51]
Sagar 1979	16.0	4.8	15	23.5	10.9	15	2.2%	-7.50 [-13.53, -1.47]
Schroeder 1991	10.0	4.0	16	15.0	10.0	16	2.7%	-5.00 [-10.28, 0.28]
Subtotal (95% CI)			137			134	22.6%	-1.75 [-4.32, 0.82]
Heterogeneity: $\tau^2 = 5.14$; $\chi^2 = 12.18$, $df = 4$ ($P = 0.02$); $I^2 = 67\%$								
Test for overall effect: $Z = 1.34$ ($P = 0.18$)								
Total (95% CI)			671			675	100.0%	-1.95 [-2.99, -0.91]

Table 6. Early enteral nutrition versus later commencement after gastrointestinal surgery, feeding route, outcome: 1.2 Length of hospital stay. *(Continued)*
Heterogeneity: $\tau^2 = 3.08$; $\chi^2 = 78.98$, $df = 15$ ($P < 0.00001$); $I^2 = 81\%$

Test for overall effect: $Z = 3.68$ ($P = 0.0002$)
Test for subgroup differences: $\chi^2 = 0.54$, $df = 1$ ($P = 0.46$), $I^2 = 0\%$

Table 7. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: Wound infection

Study	Experimental		Control		Weight	Risk Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Beier-Holgersen 1996	1	30	10	30	4.7%	0.10 [0.01; 0.73]
Chatterjee 2012	15	60	8	60	26.5%	1.88 [0.86; 4.09]
Da Fonseca 2011	2	24	2	26	5.2%	1.08 [0.17; 7.10]
Dag 2011	5	99	7	100	14.1%	0.72 [0.24; 2.20]
Hartsell 1997	0	29	0	29	0.0%	
Minig 2009	0	18	3	22	0.05	0.00
Mulrooney 2004	4	36	3	37	8.9%	1.37 [0.33; 5.70]
Nakeeb 2009	5	60	5	60	12.5%	1.00 [0.31; 3.28]
Ortiz 1996	5	95	6	95	13.2%	0.83 [0.26; 2.64]
Reissman 1995	2	80	1	81	3.3%	2.03 [0.19; 21.89]
Sagar 1979	3	15	5	15	11.6%	0.60 [0.17; 2.07]
Stewart 1998	0	40	4	40	0.0%	0.00
Total (95% CI)	42	586	54	595	100.0%	0.99 [0.64; 1.52]
Heterogeneity: $\tau^2 = 0.0290$; $\chi^2 = 10.54$, $df = 10$ ($P = 0.39$); $I^2 = 5\%$						
Test for overall effect: $Z = -0.07$ ($P = 0.95$)						

Table 8. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: Intraabdominal abscess

Study	Experimental		Control		Weight	Risk Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Beier-Holgersen 1996	0	30	2	30	0.0%	0.00
Minig 2009	0	18	2	22	0.0%	0.00
Mulrooney 2004	0	36	0	37	0.0%	
Ortiz 1996	1	95	1	95	23.3%	1.00 [0.06; 15.76]
Reissman 1995	1	80	1	81	23.4%	1.01 [0.06; 15.91]

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Table 8. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: Intraabdominal abscess (Continued)

Sagar 1979	2	15	2	15	53.3%	1.00 [0.16; 6.20]
<hr/>						
Total (95% CI)	4	274	8	280	100.0%	1.00 [0.26; 3.80]
<hr/>						
Heterogeneity: $\tau^2 = 0$; $\chi^2 = 0.97$, $df = 4$ ($P = 0.91$); $I^2 = 0\%$						
<hr/>						
Test for overall effect: $Z = 0.00$ ($P = 1.00$)						
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Table 9. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: Anastomotic leakage

Study	Experimental		Control		Weight	Risk Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Beier-Holgersen 1996	2	30	4	30	19.7%	0.50 [0.10; 2.53]
Chatterjee 2012	8	60	3	60	31.7%	2.67 [0.74; 9.57]
Da Fonseca 2011	0	24	4	26	0.0%	0.00
Dag 2011	2	99	6	100	20.9%	0.34 [0.07; 1.63]
Hartsell 1997	0	29	1	29	0.0%	0.00
Lucha 2005	1	26	0	25	0.0%	Inf
Minig 2009	0	18	3	22	0.0%	0.00
Mulrooney 2004	3	36	0	37	0.0%	Inf
Nakeeb 2009	1	60	2	60	9.2%	0.50 [0.05; 5.37]
Ortiz 1996	2	95	4	95	18.5%	0.50 [0.09; 2.67]
Reissman 1995	0	80	1	81	0.0%	0.00
Sagar 1979	0	15	1	15	0.0%	0.00
Stewart 1998	1	40	0	40	0.0%	Inf
<hr/>						
Total (95% CI)	20	612	29	620	100.0%	0.78 [0.38; 1.61]
<hr/>						
Heterogeneity: $\tau^2 = 0$; $\chi^2 = 5.43$, $df = 12$ ($P = 0.94$); $I^2 = 0\%$						
<hr/>						
Test for overall effect: $Z = -0.67$ ($P = 0.51$)						
<hr/>						

Table 10. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: Pneumonia

Study	Experimental		Control		Weight	Risk Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Beier-Holgersen 1996	1	30	2	30	18.5%	0.50 [0.05; 5.22]
Da Fonseca 2011	1	24	0	26	0.0%	Inf
Dag 2011	3	99	3	100	40.9%	1.01 [0.21; 4.88]
Hartsell 1997	1	29	0	29	0.0%	Inf
Lucha 2005	0	26	1	25	0.0%	0.00
Mulrooney 2004	2	36	0	37	0.0%	Inf
Ortiz 1996	2	95	2	95	27.0%	1.00 [0.14; 6.95]
Reissman 1995	0	80	1	81	0.0%	0.00
Schroeder 1991	1	16	0	16	0.0%	Inf
Stewart 1998	1	40	1	40	13.6%	1.00 [0.06; 15.44]
Total (95% CI)	12	475	10	479	100.0%	0.88 [0.32; 2.42]
Heterogeneity: $\tau^2 = 0$; $\chi^2 = 0.65$, $df = 9$ ($P = 1.00$); $I^2 = 0\%$						
Test for overall effect: $Z = -0.24$ ($P = 0.81$)						

Table 11. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome: Mortality

Study	Experimental		Control		Weight	Risk Ratio MH, Random, 95% CI
	Events	Total	Events	Total		
Beier-Holgersen 1996	2	30	4	30	37.2%	0.50 [0.10; 2.53]
Carr 1996	0	14	1	14	0.0%	0.00
Chatterjee 2012	3	60	1	60	19.6%	3.00 [0.32; 28.03]
Da Fonseca 2011	1	24	0	26	0.0%	Inf
Dag 2011	0	99	1	100	0.0%	0.00
Hartsell 1997	0	29	1	29	0.0%	0.00
Minig 2009	0	18	1	22	0.0%	0.00
Mulrooney 2004	2	36	7	37	43.2%	0.29 [0.07; 1.32]

Table 11. Early enteral nutrition versus later commencement after gastrointestinal surgery, outcome:

Mortality <i>(Continued)</i> Nakeeb 2009	0	60	1	60	0.0%	0.00
Ortiz 1996	0	95	0	95	0.0%	
Reissman 1995	0	80	0	81	0.0%	
Stewart 1998	0	40	1	40	0.0%	0.00
Total (95% CI)	8	585	18	594	100.0%	0.56 [0.21; 1.52]
Heterogeneity: Tau ² = 0; Chi ² = 3.08, df = 9 (P = 0.96); I ² = 0%						
Test for overall effect: Z = -1.14 (P = 0.26)						

APPENDICES

Appendix 1. CENTRAL

#1 MeSH descriptor: [Gastrointestinal Tract] explode all trees

#2 MeSH descriptor: [Lower Gastrointestinal Tract] explode all trees

#3 MeSH descriptor: [Intestines] explode all trees

#4 MeSH descriptor: [Gastrointestinal Diseases] explode all trees

#5 MeSH descriptor: [Intestinal Diseases] explode all trees

#6 #1 or #2 or #3 or #4 or #5

#7 (surgery or surgical* or operat* or postoperativ* or perioperativ* or resect*):ti,ab

#8 #6 and #7

#9 MeSH descriptor: [Digestive System Surgical Procedures] explode all trees

#10 MeSH descriptor: [Colectomy] explode all trees

#11 MeSH descriptor: [Colorectal Surgery] explode all trees

#12 MeSH descriptor: [Ileostomy] explode all trees

#13 MeSH descriptor: [Colostomy] explode all trees

#14 ((colorectal* or colon* or rectal* or rectum or abdomin* or gastrointestin* or intestin* or bowel*) near/5 (surgery or surgical* or operat* or postoperativ* or perioperativ* or resect*)):ti,ab

#15 colectom*:ti,ab

#16 colostom* or ileostom*:ti,ab

#17 #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16

#18 MeSH descriptor: [Enteral Nutrition] explode all trees

#19 MeSH descriptor: [Feeding Methods] explode all trees

#20 ((tube or tubes or sip or sips or oral or orally or enteral*) near/5 (nutrition* or feed* or nutrient*)):ti,ab

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#21 MeSH descriptor: [Nutritional Support] explode all trees

#22 MeSH descriptor: [Diet Therapy] explode all trees

#23 MeSH descriptor: [Nutrition Therapy] explode all trees

#24 MeSH descriptor: [Dietary Supplements] explode all trees

#25 nutrition* next support*

#26 ((postoperativ* or post-operativ* or perioperativ* or peri-operativ*) near/1 (nutrition* or feed* or nutrient*)):ti,ab

#27 (early near/2 (nutrition* or feed* or nutrient* or intake))

#28 "enhanced recovery" :ti,ab

#29 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28

#30 #17 and #29

Appendix 2. MEDLINE

1 Gastrointestinal Tract/
2 exp Lower Gastrointestinal Tract/
3 exp Intestines/
4 Gastrointestinal Diseases/
5 exp intestinal diseases/
6 or/1-5
7 su.fs.
8 (surgery or surgical\$ or operat\$ or post-operativ\$ or postoperativ\$ or resect\$).tw.
9 7 or 8
10 6 and 9
11 digestive system surgical procedures/
12 exp Colectomy/
13 Colorectal Surgery/
14 ileostomy/
15 colostomy/
16 ((colorectal\$ or colon\$ or rectal\$ or rectum or abdomin\$) adj5 (surgery or surgical\$ or operat\$ or postoperativ\$ or perioperativ\$ or resect\$)).tw.
17 ((gastrointestin\$ or intestin\$ or bowel\$) adj5 (surgery or surgical\$ or operat\$ or perioperativ\$ or postoperativ\$ or resect\$)).tw.
18 colectom\$.tw.
19 (colostom\$ or ileostom\$).tw.
20 or/10-19
21 Enteral Nutrition/
22 Feeding Methods/
23 ((tube or tubes or sip or sips) adj5 (nutrition\$ or feed\$ or nutrient\$)).tw.

24 ((oral or orally) adj5 (nutrition\$ or feed\$ or nutrient\$)).tw.

25 (enteral\$ adj5 (nutrition\$ or feed\$ or nutrient\$)).tw.

26 Nutritional Support/

27 Diet Therapy/

28 Nutrition Therapy/

29 exp Dietary Supplements/

30 nutrition\$ support\$.tw.

31 ((postoperativ\$ or post-operativ\$ or perioperativ\$ or peri-operativ\$) adj1 (nutrition\$ or feed\$ or nutrient\$)).tw.

32 (early adj2 (nutrition\$ or feed\$ or nutrient\$ or intake)).tw.

33 enhanced recovery.tw.

34 or/21-33

35 20 and 34

36 randomized controlled trial.pt.

37 controlled clinical trial.pt.

38 randomized.ab.

39 placebo.ab.

40 clinical trials as topic.sh.

41 randomly.ab.

42 trial.ti.

43 or/36-42

44 exp animals/ not humans.sh.

45 43 not 44

47 35 and 45

Appendix 3. Embase

1 Gastrointestinal Tract/

2 gastrointestinal tumor/

3 exp Intestines/

4 Gastrointestinal Diseases/

5 exp enteropathy/

6 or/1-5

7 su.fs.

8 (surgery or surgical\$ or operat\$ or post-operativ\$ or postoperativ\$ or resect\$).tw.

9 7 or 8

10 6 and 9

11 abdominal surgery/

12 gastrointestinal surgery/

13 exp intestine surgery/

14 ((colorectal\$ or colon\$ or rectal\$ or rectum or abdomin\$ or gastrointestin\$ or intestin\$ or bowel\$) adj5 (surgery or surgical\$ or operat\$ or postoperativ\$ or perioperativ\$ or resect\$)).tw.

15 colectom\$.tw.

16 (colostom\$ or ileostom\$).tw.

17 or/10-16

18 enteric feeding/

19 food intake/

20 ((tube or tubes or sip or sips or oral or orally or enteral\$) adj5 (nutrition\$ or feed\$ or nutrient\$)).tw.

21 nutritional support/

22 Diet Therapy/

23 diet supplementation/

24 nutrition\$ support\$.tw.

25 ((postoperativ\$ or post-operativ\$ or perioperativ\$ or peri-operativ\$) adj1 (nutrition\$ or feed\$ or nutrient\$)).tw.

26 (early adj2 (nutrition\$ or feed\$ or nutrient\$ or intake)).tw.

27 enhanced recovery.tw.

28 or/18-27

29 17 and 28

30 CROSSOVER PROCEDURE.sh.

31 DOUBLE-BLIND PROCEDURE.sh.

32 SINGLE-BLIND PROCEDURE.sh.

33 (crossover* or cross over*).ti,ab.

34 placebo*.ti,ab.

35 (doubl* adj blind*).ti,ab.

36 allocat*.ti,ab.

37 trial.ti.

38 RANDOMIZED CONTROLLED TRIAL.sh.

39 random*.ti,ab.

40 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39

41 (exp animal/ or exp invertebrate/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans or man or men or wom?n).ti.

42 40 not 41

43 29 and 42

Appendix 4. LILACS (Bireme)

"enhanced recovery" or "enteral nutrition" or (early and (nutrition\$ or feed\$ or nutrient\$ or intake)) [Words]

and

random\$ or trial or placebo or double-blind or single-blind [Words]

and

COLORECT\$ or COLON or RECTAL or ABDOMINAL\$ or post-operativ\$ or post operativ\$ or surgery [Words]

Appendix 5. Data extraction form

Data collection form

Study ID (*surname of first author and year first full report of study was published e.g. Smith 2001*)

1. General Information

Date form completed

Name/ID of person extracting data

Report title

Report author contact details

Publication type

(*e.g. full report, abstract, letter*)

Study funding sources

(*including role of funders*)

Possible conflicts of interest

(*for study authors*)

Notes:

2. Study Eligibility

Study Characteristics	Eligibility criteria	Yes	No	Unclear	Location in text
Type of study	Randomised controlled trial				
	Cluster-randomised trial				
	Completed study				

(Continued)

Participants	<p>Adults (<i>Studies solely on paediatric patients (i.e. age less than 18 years) will be excluded.</i>)</p> <p>Patients undergoing colorectal surgery, both males and female, with malignant and benign disease including inflammatory bowel diseases.</p>
Types of intervention	<p>- Trials comparing feeding patients retrospectively</p> <p>pair-matched with a contemporary group of patients not receiving feeding are excluded.</p> <p>- Trials comparing different types of enteral nutrition with each other are excluded.</p> <p>- Trials in which patients served as their own controls are excluded, and cross-over trials are excluded.</p>
Included: Patients undergoing surgery in the gastrointestinal tract; Early enteral nutrition is defined as all oral intakes (i.e. registered oral intake, supplemented oral feeding) and any kind of tube feeding (gastric, duodenal or jejunal) containing caloric content commenced within 24 hours postoperatively.)	Postoperative enteral nutrition: <hr/> Parenteral nutrition given: <hr/> Colorectal surgery: <hr/> Colon surgery alone: <hr/> Rectal surgery alone: <hr/> Upper gastrointestinal surgery: <hr/> Nutrition initiated < 24 hours: <hr/>
No feeding is traditional management, defined as none caloric oral intake or any kind of tube feeding before bowel function. The definition 'no nutrition' includes non caloric placebo and water.	Nutrition initiated > 24 hours <hr/>
	Route of feeding: <hr/> - Oral - Nasojejunal tube - Nasoduodenal tube - Nasogastric tube - Jejunostomy <hr/>
	Feed type: <hr/> - Normal diet <hr/>

(Continued)

- Polymeric
- Polymeric supplements

Nutrition given pr. days (mL, calories, other)

Additional information on nutrition:

Information on BMI, weight loss or other information

INCLUDE
EXCLUDE
Reason for exclusion
Notes:
3. Participants and setting

	Description	Location in text
Participants		
<i>(total number randomised, and for each group)</i>		
Site of surgery e.g. small bowel, large bowel, both		
Pathology e.g. 10% malignant 90% benign		
Setting/Location		
Inclusion criteria		
Exclusion criteria		
Baseline imbalances		
Were the groups treated identical except for the named interventions?		
Withdrawals and exclusions		
Age (median, interquartile range)		
Sex		
Male:Female		
Race/Ethnicity		
Specific surgery types		
Severity of illness		F

(Continued)

Dukes(A-D) TNM
Co-morbidities
(e.g. diabetes mellitus)
Subgroups reported
(e.g. laparoscopic vs. open surgery)
Study groups not included in review comparison (e.g. placebo groups, alternate treatment groups)
Sample size/Power calculations
Study start date to end date
Primary outcome e.g. length of hospital stay
ERAS protocol used?

Number of NG tube reinserted

Ethics
Notes:
4. Intervention groups
Intervention Group

	Description as stated in report/paper	Location in text
Group name		
Intervention Description		
<i>(e.g. type of gum, frequency of chewing gum, how long gum chewed for each time)</i>		
Duration of treatment period		
<i>(e.g. when started chewing gum, how long for)</i>		
Providers		
<i>(e.g. profession)</i>		
Study groups included in the overall intervention group (e.g. different types of gum)		
Notes:		

Control Group

	Description as stated in report/paper	Location in text
Group name		
Description (include sufficient detail for replication, e.g. content, dose, components)		
Notes:		

5. Results

Number of Wound infections Investigated in study (Y/N):

	Description as stated in report/paper	Location in text																
Outcome																		
Method of reporting (e.g. medical records, patients asked to tell clinicians)																		
Unit of measurement (days/hrs)																		
Results	<table border="1"> <thead> <tr> <th colspan="2">Intervention</th> <th colspan="2">Comparison</th> </tr> </thead> <tbody> <tr> <td>Mean</td> <td>SD or SE (delete one)</td> <td>Mean</td> <td>SD or SE (delete one)</td> </tr> <tr> <td>Median</td> <td>Range or IQR (delete one)</td> <td>Median</td> <td>Range or IQR (delete one)</td> </tr> <tr> <td colspan="4">P value =</td> </tr> </tbody> </table>	Intervention		Comparison		Mean	SD or SE (delete one)	Mean	SD or SE (delete one)	Median	Range or IQR (delete one)	Median	Range or IQR (delete one)	P value =				
Intervention		Comparison																
Mean	SD or SE (delete one)	Mean	SD or SE (delete one)															
Median	Range or IQR (delete one)	Median	Range or IQR (delete one)															
P value =																		
Statistical methods used and appropriateness of these methods (e.g. adjustment for correlation)																		

Number of Intraabdominal abscesses Investigated in study (Y/N):

	Description as stated in report/paper	Location in text

(Continued)

Outcome

Method of reporting

(e.g. medical records, patients asked to tell clinicians)

Unit of measurement (days/hrs)

Results

Intervention

Comparison

Mean

SD or SE
(delete one)

Mean

SD or SE
(delete one)

Median

Range or IQR
(delete one)

Median

Range or IQR
(delete one)

P value =

Statistical methods used and appropriateness of these methods (e.g. adjustment for correlation)

Anastomotic leakage (dehiscence) Investigated in study (Y/N):

Description as stated in report/paper

Location in text

Outcome

Method of reporting

(e.g. medical records, patients asked to tell clinicians)

Unit of measurement

(days/hrs)

Results

Intervention

Comparison

Mean

SD or SE
(delete one)

Mean

SD or SE
(delete one)

Median

Range or IQR
(delete one)

Median

Range or IQR
(delete one)

(Continued)

P value =

Statistical methods used and appropriateness of these methods (e.g. adjustment for correlation)

Mortality (within 30 days PO) Investigated in study (Y/N):

Description as stated in report/paper		Location in text		
Outcome	(or other description)			
Method of reporting				
(e.g. medical records, patients asked to tell clinicians)				
Unit of measurement (days/hrs)				
Results	Intervention		Comparison	
	Mean	SD or SE (delete one)	Mean	SD or SE (delete one)
	Median	Range or IQR (delete one)	Median	Range or IQR (delete one)
P value				

Statistical methods used and appropriateness of these methods (e.g. adjustment for correlation)

Length of hospital stay Investigated in study (Y/N):

Description as stated in report/paper		Location in text
Outcome		
Method of reporting		
(e.g. medical records, patients asked to tell clinicians)		

(Continued)

Unit of measurement (*days/hrs*)

Results	Intervention		Comparison	
	Mean	SD or SE (delete one)	Mean	SD or SE (delete one)
	Median	Range or IQR (delete one)	Median	Range or IQR (delete one)
P value =				
Statistical methods used and appropriateness of these methods (e.g. adjustment for correlation)				

POST OP COMPLICATIONS (*e.g. acute myocardial infarction, postoperative thrombosis or pneumonia*) Investigated in study (Y/N):

Intervention result (unit)	Control result (unit)	Statistical result

Notes:
ADVERSE EVENTS (*e.g. nausea, vomiting, abdominal distension, aspiration, tube blockage*) Investigated in study (Y/N):

Intervention result (unit)	Control result (unit)	Statistical result

(Continued)

Notes:

Economic effect Investigated in study (Y/N):

	Description as stated in report/paper	Location in text
Outcome	Economic effect <i>(or other description)</i>	
Method of reporting		
Description		
Notes:		

Quality of Life Investigated in study (Y/N):

	Description as stated in report/paper	Location in text
Outcome	<i>(or other description)</i>	
Method of reporting		
Description		
Notes:		

6. 'Risk of bias' assessment

Domain	Risk of bias			Support for judgement	Location in text
	Low risk	High risk	Unclear		
Random sequence generation <i>(selection bias)</i>					
Allocation concealment <i>(selection bias)</i>					
Blinding of patients					

(Continued)

(performance bias) All outcomes

Blinding of personnel (performance bias) All outcomes

Blinding of outcome assessor (detection bias) – 1. wound infections

Blinding of outcome assessor (detection bias) – 2.intraabdominal abscesses

Blinding of outcome assessor (detection bias) – 3. postoperative complications e.g. acute myocardial infarction, postop thrombosis or pneumonia

Blinding of outcome assessor(detection bias) – 4. anastomotic leakage/dehiscence

Blinding of outcome assessor (detection bias) – 5. mortality within 30 days postop

Blinding of outcome assessor (detection bias) – 6. adverse events such as nausea, vomiting, abdominal distention, aspiration, tube blockage and any other adverse events

Blinding of outcome assessor

7. (Length of Hospital Stay)

Incomplete outcome data

(attrition bias, intention to treat and as-treated analysis)

Selective outcome reporting? (reporting bias)

Other bias
Notes:

7. Applicability

Have important populations been excluded from the study?
(disadvantaged populations etc.)

Yes No Unclear

Justification:
Does the study directly address the review question?

Yes No Unclear

Justification

(issues of partial/indirect applicability)

Notes:

8. Other information

Key conclusions of study authors

References to other RCTS for inclusion

Key general information references

Notes:

Appendix 6. 'Risk of bias' tool

RANDOM SEQUENCE GENERATION

LOW RISK

The investigators describe a random component in the sequence generation process such as:

- Referring to a random number table
- Using a computer random number generator
- Coin tossing
- Shuffling cards or envelopes
- Throwing dice
- Drawing of lots/slips

HIGH RISK

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example:

- Sequence generated by odd or even date of birth
- Sequence generated by some rule based on date (or day) of admission
- Sequence generated by some rule based on hospital or clinic record number.
- Allocation by judgement of the clinician
- Allocation by preference of the participant
- Allocation based on the results of a laboratory test or a series of tests
- Allocation by availability of the intervention

UNCLEAR RISK

Insufficient information about the sequence generation process to permit judgement of 'Yes' or 'No'.

ALLOCATION CONCEALMENT

LOW RISK

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation:

- Central allocation (including telephone, web-based, and pharmacy-controlled, randomisation)
- Sequentially numbered drug containers of identical appearance
- Sequentially numbered, opaque, sealed envelopes - all 3 features of the envelopes must be described

HIGH RISK

(Continued)

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on:

- Using an open random allocation schedule (e.g. a list of random numbers)
- Assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered)
- Alternation or rotation
- Date of birth
- Case record number
- Any other explicitly unconcealed procedure

UNCLEAR RISK

Insufficient information to permit judgement of 'Yes' or 'No'. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement - for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

BLINDING OF PARTICIPANTS AND PERSONNEL

LOW RISK

- Methods of blinding of participants and personnel described sufficiently and deemed adequate

e.g. "The patients in group I received a nutrition supplement of Nutridrink (orange flavour), Nutricia, the Netherlands within four hours postoperatively. Patients in group II received placebo (water with orange flavour, no energy, vitamins or trace elements) during the same period. Nutridrink or placebo in identical containers was administered by the nursing staff."

HIGH RISK

Any one of the following:

- Methods of blinding of outcome assessors described sufficiently but deemed inadequate
 - No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding
- e.g. "This study was limited by small number of cases and the absence of blinding, placebo arm"

UNCLEAR RISK

- Insufficient information to permit judgement of 'Yes' or 'No'

BLINDING OF OUTCOME ASSESSORS

LOW RISK

- Methods of blinding of outcome assessors described sufficiently and deemed adequate

e.g. "The principal investigator saw the patients every day during their stay in the ward, and all complications were recorded by the same investigator. The randomisation code was not broken until all results were available and all patients had been followed up for 30 days after surgery and all complications classified."

HIGH RISK

Any one of the following:

- Methods of blinding of outcome assessors described sufficiently but deemed inadequate

(Continued)

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding
e.g. “This study was limited by small number of cases and the absence of blinding, placebo arm”

UNCLEAR RISK

- Insufficient information to permit judgement of ‘Yes’ or ‘No’
-

INCOMPLETE OUTCOME DATA

LOW RISK

Any one of the following:

- No missing outcome data
 - Missing outcome data less than 10% of the total randomised population
 - Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias)
 - Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups
 - For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate
 - For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size
-

HIGH RISK

Any one of the following:

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups
 - Difference in missing data between the groups greater than 10%
 - Overall missing data greater than 10% of the total randomised population
 - Stated as ‘intention-to-treat analysis’ but does not use this
 - For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate
 - For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size
 - ‘As-treated’ analysis done with substantial departure of the intervention received from that assigned at randomisation
 - Potentially inappropriate application of simple imputation
-

UNCLEAR RISK

Any one of the following:

- Insufficient reporting of attrition/exclusions to permit judgement of ‘Yes’ or ‘No’ (e.g. number randomised not stated, no reasons for missing data provided)
 - Dropouts not mentioned
-

SELECTIVE OUTCOME REPORTING

Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications (Review)

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LOW RISK

The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way

HIGH RISK

Any one of the following:

- Not all of the study's pre-specified primary outcomes have been reported
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis, or any data excluded from the analysis despite the data being available
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study

UNCLEAR RISK

Insufficient information to permit judgement of 'Yes' or 'No'.

- No protocol is available

WHAT'S NEW

Date	Event	Description
4 July 2019	Amended	Minor changes to plain language summary
10 October 2018	New citation required and conclusions have changed	<ol style="list-style-type: none"> 1. New searches performed. 2. Authorship has changed. 3. Primary outcomes: length of hospital stay and postoperative complications. 4. Re-defined the population of interest as lower gastrointestinal surgery. 5. Title changed to reflect above edits. 6. Six new studies included in this update giving a total of 17 included studies
9 October 2018	New search has been performed	<ol style="list-style-type: none"> 1. New searches performed. 2. Authorship has changed. 3. Primary outcomes: length of hospital stay and postoperative complications. 4. Re-defined the population of interest as lower gastrointestinal surgery. 5. Title changed to reflect above edits. 6. Six new studies included in this update giving a total of 17 included studies.

HISTORY

Protocol first published: Issue 1, 2003

Review first published: Issue 4, 2006

Date	Event	Description
5 January 2011	New search has been performed	Updated review with one more included study
21 August 2006	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Search strategies were developed by Henning Keinke Andersen (HKA) and Stephen John Lewis (SJL). Charlotte Atkinson (CA) and SJL screened the titles and abstracts of all studies identified by the updated search. Georgia Herbert (GH) and Rachel Perry (RP) designed the data extraction form and extracted full texts of the included studies. Steven Thomas (ST) checked the extracted data for accuracy against the trial reports. Christopher Penfold (CP) carried out the statistical analyses. GH drafted the update of the review and all authors (HKA, CA, SJL, AN, CP, RP, ST) added valuable comments and participated in the revision of the draft review.

DECLARATIONS OF INTEREST

All authors: none known

SOURCES OF SUPPORT

Internal sources

- RegionH, Copenhagen, Denmark, Denmark.
- NIHR Biomedical Research Unit in Nutrition, Diet and Lifestyle, Bristol, UK.

This research was funded by the National Institute for Health Research (NIHR) Bristol Nutrition Biomedical Research Unit. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health

External sources

- Danish Institute for Health Technology Assessment, Denmark.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have made the following changes from the last update of this review ([Andersen 2011](#)):

1. Authorship has changed from: Andersen HK, Lewis SJ, Thomas S in the last update to: Herbert G, Perry R, Andersen HK, Atkinson C, Penfold C, Lewis SJ, Ness, A, Thomas S
2. Length of hospital stay and postoperative complications were designated as primary outcomes.
3. We included secondary outcomes that had been meta-analysed in the previous review. We also included data for other postoperative complications and adverse events.
4. Studies reporting only upper gastrointestinal surgery were excluded as the review update focus on lower gastrointestinal surgery.
5. Clearly defined population of interest: instead of 'colorectal' or 'gastrointestinal', we define the group of interest as lower gastrointestinal surgery (distal to the ligament of Treitz)
6. To reflect the above changes, the title changed from: *Early enteral nutrition within 24h of colorectal surgery versus later commencement of feeding for postoperative complications* to: *Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications*.
7. Previous review mentioned subgroup analysis comparing malnourished and well-nourished patients but no analysis was conducted. We decided not to follow this up in this review.
8. Previous review mentioned subgroup analysis comparing studies with adequate allocation concealment and inadequate allocation concealment. We extended this to include high risk of bias in two of the following components: random sequence generation, allocation concealment, incomplete outcome data or selective outcome reporting. We conducted this as a sensitivity analysis.
9. We conducted two post-hoc subgroup analyses to explore the effect of clinical diversity on length of hospital stay (LoS). We created two subgroups: one which encompassed trials that had only included patients having surgery distal to the ligament of Treitz (this group was termed 'distal to ligament of Treitz'), and the other which encompassed trials that had included patients undergoing surgery either distal or proximal to the ligament of Treitz (this group was termed 'distal and proximal to ligament of Treitz'). We also created two subgroups relating to whether the route of postoperative feeding used in the intervention was 'oral feeding only' or by 'tube feeding with or without oral feeding'. We also planned to conduct two further subgroup analyses; one comparing patients that have elective surgery versus acute surgery and the other comparing patients with cancer versus non-cancerous conditions.

10. Revised methods including Trial Sequential Analyses (TSA) and no zero-cell continuity correction.

INDEX TERMS

Medical Subject Headings (MeSH)

*Digestive System Surgical Procedures; *Length of Stay; Enteral Nutrition [*methods]; Postoperative Complications [*prevention & control]; Randomized Controlled Trials as Topic; Time Factors

MeSH check words

Humans