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Preoperative carbohydrate treatment for enhancing recovery after elective surgery (Review)

Smith MD, McCall J, Plank L, Herbison GP, Soop M, Nygren J

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[Intervention Review]

Preoperative carbohydrate treatment for enhancing recovery after elective surgery

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ABSTRACT

Background

Preoperative carbohydrate treatments have been widely adopted as part of enhanced recovery after surgery (ERAS) or fast-track surgery protocols. Although fast-track surgery protocols have been widely investigated and have been shown to be associated with improved postoperative outcomes, some individual constituents of these protocols, including preoperative carbohydrate treatment, have not been subject to such robust analysis.

Objectives

To assess the effects of preoperative carbohydrate treatment, compared with placebo or preoperative fasting, on postoperative recovery and insulin resistance in adult patients undergoing elective surgery.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 3), MEDLINE (January 1946 to March 2014), EMBASE (January 1947 to March 2014), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (January 1980 to March 2014) and Web of Science (January 1900 to March 2014) databases. We did not apply language restrictions in the literature search. We searched reference lists of relevant articles and contacted known authors in the field to identify unpublished data.

Selection criteria

We included all randomized controlled trials of preoperative carbohydrate treatment compared with placebo or traditional preoperative fasting in adult study participants undergoing elective surgery. Treatment groups needed to receive at least 45 g of carbohydrates within four hours before surgery or anaesthesia start time.

Data collection and analysis

Data were abstracted independently by at least two review authors, with discrepancies resolved by consensus. Data were abstracted and documented pro forma and were entered into RevMan 5.2 for analysis. Quality assessment was performed independently by two review authors according to the standard methodological procedures expected by The Cochrane Collaboration. When available data were

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insufficient for quality assessment or data analysis, trial authors were contacted to request needed information. We collected trial data on complication rates and aspiration pneumonitis.

Main results

We included 27 trials involving 1976 participants Trials were conducted in Europe, China, Brazil, Canada and New Zealand and involved patients undergoing elective abdominal surgery (18), orthopaedic surgery (4), cardiac surgery (4) and thyroidectomy (1). Twelve studies were limited to participants with an American Society of Anaesthesiologists grade of I-II or I-III.

A total of 17 trials contained at least one domain judged to be at high risk of bias, and only two studies were judged to be at low risk of bias across all domains. Of greatest concern was the risk of bias associated with inadequate blinding, as most of the outcomes assessed by this review were subjective. Only six trials were judged to be at low risk of bias because of blinding.

In 19 trials including 1351 participants, preoperative carbohydrate treatment was associated with shortened length of hospital stay compared with placebo or fasting (by 0.30 days; 95% confidence interval (CI) 0.56 to 0.04; very low-quality evidence). No significant effect on length of stay was noted when preoperative carbohydrate treatment was compared with placebo (14 trials including 867 participants; mean difference -0.13 days; 95% CI -0.38 to 0.12). Based on two trials including 86 participants, preoperative carbohydrate treatment was also associated with shortened time to passage of flatus when compared with placebo or fasting (by 0.39 days; 95% CI 0.70 to 0.07), as well as increased postoperative peripheral insulin sensitivity (three trials including 41 participants; mean increase in glucose infusion rate measured by hyperinsulinaemic euglycaemic clamp of 0.76 mg/kg/min; 95% CI 0.24 to 1.29; high-quality evidence).

As reported by 14 trials involving 913 participants, preoperative carbohydrate treatment was not associated with an increase or a decrease in the risk of postoperative complications compared with placebo or fasting (risk ratio of complications 0.98, 95% CI 0.86 to 1.11; low-quality evidence). Aspiration pneumonitis was not reported in any patients, regardless of treatment group allocation.

Authors' conclusions

Preoperative carbohydrate treatment was associated with a small reduction in length of hospital stay when compared with placebo or fasting in adult patients undergoing elective surgery. It was found that preoperative carbohydrate treatment did not increase or decrease postoperative complication rates when compared with placebo or fasting. Lack of adequate blinding in many studies may have contributed to observed treatment effects for these subjective outcomes, which are subject to possible biases.

PLAIN LANGUAGE SUMMARY

Does giving patients carbohydrate supplements before planned surgery lead to improved recovery?

Review question

We reviewed the evidence on effects of carbohydrate supplements on the recovery of people undergoing planned surgical procedures. We found 27 studies investigating this question.

Background

Carbohydrate (sugar-containing) nutritional supplements have become a routine part of the package of care for people undergoing planned surgical procedures. We wanted to discover whether carbohydrate supplements are a useful part of care packages used by doctors to improve recovery after planned surgical procedures.

Study characteristics

The evidence is current up to March 2014. We identified 27 studies and included the outcomes of 1976 participants. Studies investigated the outcomes of patients undergoing planned surgical procedures on the abdomen (18), the bones or joints (4), the heart (4) or the thyroid gland (1).

Eighteen studies compared carbohydrate supplements versus an identical appearing placebo drink that did not contain carbohydrates; in six of these studies, an additional group of patients had nothing to eat or drink for at least six hours before surgery. In nine studies, taking carbohydrate supplements was compared with having nothing to eat or drink for six hours before surgery.

The primary outcomes of length of hospital stay and complication rate were reported by 19 and 14 studies, respectively.

Key results

Patients given carbohydrates before planned surgical procedures went home between 0.04 and 0.56 days sooner than those receiving a placebo drink or having nothing to eat or drink before surgery. Carbohydrate supplements had little or no effect on complication rate or on how people feel in-hospital during recovery from surgery.

Quality of the evidence

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The overall quality of the evidence varied from very low to high. The quality of evidence in support of carbohydrate supplements resulting in a shorter hospital stay was very low because the included studies had important flaws in their design, a very wide range of results was described and evidence revealed that studies showing no differences in length of hospital stay may not have been published. When we looked only at well-conducted studies, we found that carbohydrate supplements had little or no effect on length of hospital stay.

The quality of evidence to support the effects of carbohydrate supplements on complication rate was low because issues with study design were identified and results were not similar across studies.

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SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Preoperative carbohydrates compared with placebo or fasting for people undergoing elective surgery

Patient or population: adult patients undergoing elective surgery

Settings: hospitals providing elective surgery

Intervention: preoperative carbohydrate supplementation[a]

Comparison: placebo drink or traditional preoperative fasting

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Fasting or placebo	Preoperative carbohydrates				
Complication rate	**Low-risk population[b]**		**RR 0.98** (0.86 to 1.11)	913 (14 studies)	⊕⊕⊖⊖ **low[c]**	Evidence is insufficient to support the hypothesis that preoperative carbohydrate drinks reduce postoperative complication rates
	4 per 100	**4 per 100** (3 to 4)				
	Medium-risk population[b]					
	18 per 100	**17 per 100** (15 to 19)				
	High-risk population[b]					
	39 per 100	**38 per 100** (34 to 43)				
Length of hospital stay (days)	Mean length of hospital stay ranged across control groups from 1 to 16 days	Mean length of hospital stay in the intervention groups was 0.30 days lower (0.56 days lower to 0.04 days lower)		1351 (19 studies)	⊕⊖⊖⊖ **very low[d]**	High degree of heterogeneity across all studies and all subgroups. Evidence of publication bias noted on sensitivity analysis[d]
Postoperative well-being	Mean well-being score ranged	Mean well-being score in the intervention groups was		310 (4 studies)	⊕⊕⊕⊖ **moderate[f]**	As the confidence intervals include no effect, evidence is insufficient to show

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by visual analogue scale or by standardized questionnaire	across control groups from 25 to 63 mm	0 mm different (5.18 mm lower to 5.41 mm higher)[e]				whether perioperative carbohydrate drinks increase or decrease postoperative well-being
Postoperative nausea by visual analogue scale at 24 hours postop	Mean nausea score ranged across control groups from 10 to 16 mm	Mean nausea score in the intervention groups was 1.69 mm lower (4.12 mm lower to 0.74 mm higher)		292 (2 studies)	⊕⊕⊕⊖ **moderate**[g]	As the confidence intervals include no effect, evidence is insufficient to show whether perioperative carbohydrate drinks increase or decrease postoperative nausea
Postoperative vomiting	**Medium-risk population**[h]		**RR 1.25** (0.77 to 2.04)	407 (4 studies)	⊕⊕⊖⊖ **low**[i]	As the confidence intervals include no effect, evidence is insufficient to show whether perioperative carbohydrate drinks increase or decrease postoperative vomiting
	12 per 100	**15 per 100** (9 to 24)				
Postoperative fatigue by visual analogue scale or by 10-point ordinal scale	Mean fatigue score ranged across control groups from 28 to 30.6 mm	Mean fatigue score in the intervention groups was 1.77 mm higher (6.77 mm lower to 10.31 mm higher)[j]		576 (6 studies)	⊕⊕⊕⊖ **moderate**[k]	As the confidence intervals include no effect, evidence is insufficient to show whether perioperative carbohydrate drinks increase or decrease postoperative fatigue
Postop insulin sensitivity (clamp) measured as standardized glucose infusion rate (mg/kg/min)[l]	Mean glucose infusion rate ranged across control groups from 1.4 to 2.41 mg/kg/min	Mean glucose infusion rate in the intervention groups was 0.76 mg/kg/min higher (0.24 mg/kg/min higher to 1.29 mg/kg/min higher)		41 (3 studies)	⊕⊕⊕⊕ **high**	Glucose infusion rate is a measure of total body glucose utilization during the hyperinsulinaemic euglycaemic clamp

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (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).
CI = confidence interval; **RR** = risk ratio.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

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[a]All studies included in this review examined a preoperative dose of at least 45 g of carbohydrate administered within 4 hours of induction of anaesthesia or surgery start time. Most studies administered a dose of 50 g of carbohydrate in the form of an oral beverage, but 2 included studies administered preoperative carbohydrates in intravenous form.

[b]Low-, intermediate- and high-risk populations were taken as first quartile, median and third quartile, respectively, of reported complication rates in the control groups of included studies.

[c]The quality of evidence was graded as low because of limitations of primary studies and imprecision of effect estimates. Note that the summary effect estimate crosses the line of no effect, meaning that a small increase or reduction in the complication rate cannot be excluded.

[d]The quality of evidence was graded as very low because of the quality limitations of the primary studies, imprecision of effect estimates, heterogeneity and evidence of publication bias. It is important to note that both sensitivity analyses restricting analysis to well-blinded studies and 'trim and fill' analysis to explore the effects of publication bias reduced the magnitude of the effect of carbohydrate treatment to the point where the 95% confidence intervals crossed the line of no effect.

[e]The standardized mean difference was converted back to millimetres of a visual analogue scale by using the median of the standard deviation from the control groups of 3 studies reporting data from a visual analogue scale.

[f]The quality of evidence was graded as moderate because of the imprecision of effect estimates from included studies. Note that the summary effect estimate includes the line of no effect; however a small increase or decrease in postoperative well-being cannot be excluded.

[g]The quality of evidence was graded as moderate because of the imprecision of effect estimates from included studies. Note that the summary effect estimate includes the line of no effect; however a small increase or decrease in postoperative nausea cannot be excluded.

[h]The medium-risk population was taken as the median of the reported postoperative vomiting rates in the control groups of included studies. As only 4 studies reported these data, no attempt was made to define low- and high-risk populations.

[i]The quality of evidence was graded as low because of the limitations of the primary studies and the imprecision of the effect estimates. Note that the summary effect estimate includes the line of no effect; however a small increase or decrease in postoperative vomiting cannot be excluded.

[j]The standardized mean difference was converted back to mm of visual analogue scale by using the median of the standard deviation from the control groups of 3 studies reporting data from a visual analogue scale.

[k]The quality of evidence was graded as moderate because of the heterogeneity of the primary studies. Note that the summary effect estimate includes the line of no effect; however a small increase or decrease in postoperative fatigue cannot be excluded.

[l]Glucose infusion rate is a standardized measure of total body glucose utilization during the hyperinsulinaemic euglycaemic clamp. A higher value corresponds with greater insulin sensitivity.

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BACKGROUND

Description of the condition

Humans and other mammals respond to surgery and trauma with multiple neuroendocrine changes leading to catabolism of stored body fuels and retention of salt and water (Desborough 2000; Kehlet 1997). This surgical stress response was first described by Cuthbertson (Wilmore 2002) in the late 1920s, as noted among patients admitted to hospital with long bone fractures. Cuthbertson discovered dramatic increases in nitrogen, potassium, phosphorus, sulphur and creatine urinary losses and concluded that these represented a systemic breakdown in skeletal muscle. Later experimental studies showed increased levels of adrenal cortical hormones in response to injury. Furthermore, severing afferent nerve pathways from the site of injury diminished this response.

Modern understanding of the surgical stress response is that it involves activation of the sympathetic nervous system, secretion of catabolic hormones and local cytokine responses to tissue injury (Desborough 2000). This response is usually proportional to the degree of surgical trauma or injury incurred (Kehlet 1997). The endocrine component includes activation of the hypothalamic-pituitary-adrenal axis with increased cortisol secretion, increased secretion of vasopressin and increased pancreatic secretion of glucagon (Desborough 2000); this response leads to a net increase in peripheral insulin resistance and catabolism of skeletal muscle. The degree of peripheral insulin resistance has been linked to the magnitude of the catabolic response (Nygren 2006).

The stress response to surgery has likely developed as an evolutionary response, allowing injured animals to survive without food and with healing of their wounds (Desborough 2000). However, in the current highly controlled surgical environment, this response is associated with several deleterious effects (Kehlet 1997), including organ dysfunction, hypercoagulation, immunosuppression, catabolism and impaired wound healing. Peripheral insulin resistance in particular is associated with hyperglycaemia—a possible cause of postoperative complications and an independent predictor of length of hospital stay (Nygren 2006).

Description of the intervention

In an attempt to improve surgical outcomes, excessive and undesirable features of the surgical stress response are now routinely targeted by multi-modal therapies, known as 'fast-track surgery' or 'enhanced recovery after surgery' (ERAS).

A common feature of fast-track surgical protocols is that interventions are aimed at reducing the degree of postoperative insulin resistance. These interventions include preoperative administration of oral or intravenous carbohydrates up to two hours before surgery, in contrast to a traditional preoperative fast (Ljungqvist 2003; Nygren 2006).

Reported studies have mainly investigated a clear liquid beverage containing 12.5 g of carbohydrates per 100 mL (Nutricia preOp®, Numico, Zoetermeer, The Netherlands) (Bisgaard 2004; Mathur 2010; Wang 2010). This drink contains polymers of carbohydrates that reduce osmotic load and do not delay gastric emptying. It contains 50 kcal per 100 mL, 290 mOsm/kg, and has a pH of 5.0. Gastric emptying studies have shown that when up to 400 mLis consumed by patients at least two hours before they are given opiate-containing analgesia, residual gastric volume is equivalent to overnight fasting (Ljungqvist 2003). This beverage is indistinguishable in appearance and taste from a placebo beverage containing flavoured sweetened water (0 kcal per 100 mL, 107 mOsm/kg) (Bisgaard 2004).

How the intervention might work

Preoperative carbohydrate treatment aims to replicate normal metabolic responses to eating breakfast (Ljungqvist 2003). This treatment stimulates an endogenous insulin release, which switches off the overnight fasting metabolic state and is given to decrease the extent of peripheral insulin resistance while ameliorating the surgical stress response.

Studies in rodents demonstrate that fasted animals respond to trauma with increased catabolism, poorer muscle strength and greater bacterial translocation than do fed animals (Ljungqvist 2003). Animals in the metabolic 'fed' state fared better than fasted animals.

Animal studies have been followed by studies in patients undergoing elective surgery (Ljungqvist 2003; Nygren 2006). Intravenous glucose infusion has been compared with overnight fasting in participants undergoing upper abdominal surgery or arthroplasty. Both studies showed a reduction in postoperative insulin resistance among participants given intravenous glucose. Preoperative oral carbohydrate treatment was also shown to reduce insulin resistance compared with overnight fasting in participants undergoing colorectal surgery or arthroplasty.

Why it is important to do this review

Because of its effect in reducing the postoperative development of insulin resistance, preoperative carbohydrate treatment is commonly advocated as part of multi-modal fast-track surgery or ERAS pathways. These pathways frequently include routine neuraxial blockade, reduced use of nasogastric tubes and surgical drains and early postoperative ambulation and enteral feeding (Kehlet 1997). Fast-track surgery protocols have been widely studied, and reduced hospital stays and decreased rates of complication have been demonstrated (Desborough 2000; Gouvas 2009).

In contrast to the traditional preoperative fast, administration of preoperative oral carbohydrate drinks has been shown to improve patient comfort before surgery. A randomized trial comparing oral carbohydrates with placebo or overnight fasting showed that oral carbohydrate treatment was associated with reduced anxiety and thirst before surgery (Hausel 2001). Carbohydrate beverages were as effective in reducing preoperative thirst as placebo beverages when compared with fasting in this study. A systematic review of the effects of preoperative fasting on perioperative complications (Brady 2003) noted that study participants given an oral carbohydrate beverage reported reduced anxiety compared with those who followed traditional fasting procedures.

On the other hand, evidence to support improvement in postoperative outcomes following preoperative administration of carbohydrates is less robust. A randomized trial of preoperative intravenous carbohydrates in patients undergoing cholecystectomy showed decreased insulin resistance in the treatment group but no difference in clinical outcomes (Ljungqvist

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1994). A 2004 study on oral carbohydrate treatment in participants undergoing laparoscopic cholecystectomy found no meaningful differences in a variety of clinical outcomes, including pain, nausea and vomiting, fatigue and general well-being (Bisgaard 2004). Another study on participants undergoing laparoscopic cholecystectomy showed a reduction in postoperative nausea and vomiting but no difference in mean hospital stay or non-discharge at 24 hours (Hausel 2005). A larger, single-centre, randomized trial on elective colorectal and liver resections found that oral carbohydrate drinks offered no improvement in postoperative fatigue and no reduction in hospital stay (Mathur 2010). The study authors were not able to identify any systematic reviews addressing the independent effects of preoperative carbohydrate treatment among patients undergoing elective surgery at the time of writing of the protocol for this review.

OBJECTIVES

To assess the effects of preoperative carbohydrate treatment, compared with placebo or preoperative fasting, on postoperative recovery and insulin resistance in adult patients undergoing elective surgery.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomized controlled trials (RCTs) that compared the effects on postoperative recovery and well-being when preoperative carbohydrate treatment was used versus placebo or preoperative fasting.

We included studies irrespective of language and publication status.

We excluded non-randomized studies such as cohort studies because of the increased potential for bias. We also excluded cross-over trials, as this methodology is not suitable for evaluating an intervention that must be given at a specific time point.

We included a single trial known to be quasi-randomized (Ljungqvist 1994), but this was subject to a sensitivity analysis.

Types of participants

We included adult patients (18 years of age or older) undergoing any type of elective surgical procedure while under general, spinal or epidural anaesthesia. We included patients who underwent spinal or epidural blockade in addition to general anaesthesia.

We excluded patients who required urgent or emergency surgery (cases in which surgery is required within 24 hours after the first physician contact for a potentially life-threatening condition).

Types of interventions

The intervention group included all participants who were given at least 45 g of carbohydrate by oral beverage or by the intravenous route. To be included, studies must have planned to administer the carbohydrates within four hours of surgery start time, or induction of anaesthesia. Co-intervention with other oral substances in the four hours before surgery was permitted so long as the dose of carbohydrate was at least 45 g.

The intervention group was compared with a control group consisting of participants who received less than 45 g of carbohydrate in the four hours before anaesthesia. Control participants may have received a placebo drink containing less than 45 g of carbohydrate, clear liquids or nothing by mouth during this time. The control group may have received intravenous fluid therapy during the four hours before surgery start time, so long as the total combined dose of carbohydrates given by oral and intravenous routes remained less than 45 g.

Types of outcome measures

Primary outcomes

1. Length of hospital stay: measured in days.
2. Postoperative complication rate: as defined by trial authors.

We included all trials reporting length of hospital stay or complication rate following elective surgery.

Secondary outcomes

We included all trials with the following secondary outcomes, measured postoperatively.

1. Aspiration pneumonitis rate: defined as observed regurgitation or vomiting in association with abnormal chest radiography or gas exchange.
2. Insulin resistance or sensitivity: measured by hyperinsulinaemic euglycaemic clamp or Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Because of differences in estimates made by these two instruments, we combined the data from each separately in the meta-analysis.
3. Fatigue: measured by such instruments as ordinal or visual analogue scales.
4. General well-being: measured by such instruments as ordinal, visual analogue or composite scales.
5. Nausea 24 hours postoperatively: measured by such instruments as ordinal, visual analogue or composite scales.
6. Vomiting within 24 hours postoperatively: measured as an incidence rate.
7. Return of intestinal function: defined as time in days from operation to first passage of flatus, and to first bowel movement.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 3), MEDLINE (January 1946 to March 2014), EMBASE (January 1947 to March 2014), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (January 1980 to March 2014) and Web of Science (January 1900 to March 2014).

We applied no language restrictions.

We used the sensitivity maximizing search strategies described in Section 6.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to search MEDLINE and EMBASE for RCTs. We also used the free-text and associated exploded medical subject heading (MeSH) terms found in Appendix 1, in combination with sensitivity maximizing RCT search strategies.

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We searched CENTRAL using the search terms provided in Appendix 2. We modified our MEDLINE search strategy (Appendix 3) to reflect subject headings found in the thesauri used by EMBASE (Appendix 4), CINAHL (Appendix 5) and Web of Science (Appendix 6).

Searching other resources

For ongoing trials, we searched the WHO international clinical trials registry platform. This includes clinicaltrials.gov, the *meta*Register of Controlled Trials (mRCT) and other national trial registries.

We used free-text terms in all databases and subject headings in combination when thesauri were components of a database.

We reviewed the related articles feature of PubMed to look for eligible trials and reviews and screened the reference lists of those identified.

We contacted experts in this field in an effort to identify unpublished research and trials still under way.

Data collection and analysis

Selection of studies

The results of the searches described above were combined, and duplicate records were excluded. Two review authors (MDS and JM) independently screened all titles and abstracts for eligibility. We were not blinded to any details of the published trials. Review authors independently recorded the reason for exclusion for each excluded trial. (See Appendix 7 for a copy of the study selection form.)

We first sought to resolve disagreements between review authors on trial selection by discussion. If consensus could not be reached, we consulted with a third review author (PH), who arbitrated on trial inclusion. If further information was required before a decision could be made about trial inclusion, we (MDS) contacted the first author of the relevant trial.

We compiled a list of all eligible trials. (See Appendix 8 for a copy of the form for eligible trials.)

Data extraction and management

Two review authors (MDS and LP) independently extracted and collected data on a paper data extraction form. (A copy of this form is provided in Appendix 9.) We resolved discrepancies between data extracted by discussion. If we were unable to reach a consensus, we consulted with a third review author (PH). If further information from the trial authors was needed, MDS contacted the first author of the relevant trial.

Assessment of risk of bias in included studies

Two review authors (MDS and LP) independently assessed the methodological quality of eligible trials. We resolved disagreements by discussion, and if we could not reach consensus, a third review author (PH) arbitrated.

We performed risk of bias assessment using the 'Risk of bias' tool described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). (A copy of the form we used to do this is provided in Appendix 10.)

We assessed each trial according to the quality domains of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other potential threats to validity.

We considered a trial as having low risk of bias if all domains were assessed as adequate. We considered a trial as having high risk of bias if one or more domains were assessed as inadequate or unclear. We conducted sensitivity analyses to determine whether excluding studies at high risk of bias might have affected the results of the meta-analysis.

We provided the 'Risk of bias' table under Characteristics of included studies and presented a 'Risk of bias summary,' which details all judgements made for all studies included in the review (Figure 1).

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Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

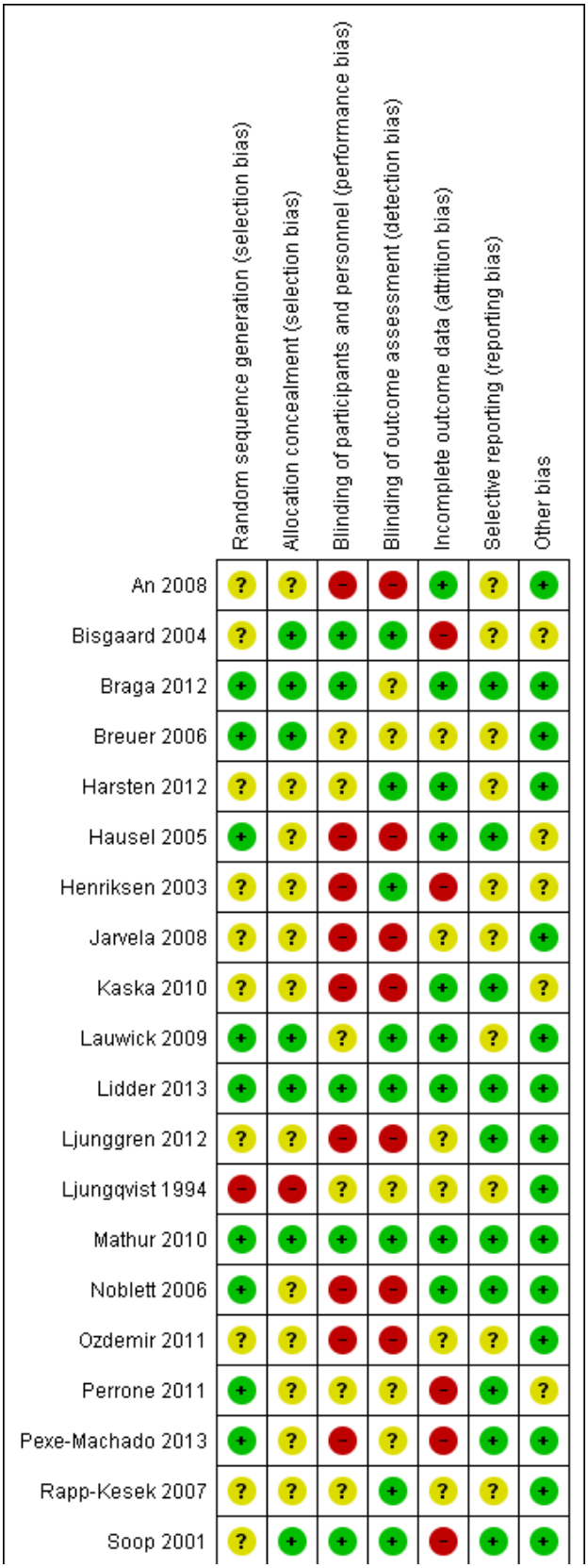

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Figure 1. (Continued)

Measures of treatment effect

We present categorical data as risk ratios (RRs). We present continuous data as mean differences (MDs) or as standardized mean differences (SMDs), as appropriate.

Unit of analysis issues

We combined control groups of placebo drink and preoperative fasting when trials compared carbohydrate drink versus placebo drink and preoperative fasting. For one study conducted as a 2 × 2 factorial design (Lidder 2013), we combined data from the two carbohydrate groups and the two placebo groups according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

We (LP) contacted the first author of included trials to obtain missing data necessary for meta-analysis. We calculated missing standard deviations from standard errors or confidence intervals, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), or from ranges or interquartile ranges, as provided by Hozo et al (Hozo 2005). When standard deviations could not be calculated, we imputed these using the median of reported standard deviations from other similar trials.

We address the impact of missing data in the discussion section of the review.

Assessment of heterogeneity

We assessed the clinical heterogeneity of the included studies according to their clinical diversity (e.g. different surgical procedures, different participant characteristics, different doses, timing of preoperative carbohydrate) and methodological diversity (risk of bias assessment).

We addressed clinical heterogeneity by performing subgroup and sensitivity analyses.

We assessed statistical heterogeneity by performing visual inspection of the forest plot, the I^2 statistic (Higgins 2011) and the Chi^2 test. We considered an I^2 statistic greater than 50% along with a P value less than 0.10 in the Chi^2 test to be indicative of the need for further examination of heterogeneity.

Assessment of reporting biases

We assessed publication bias and other small-study effects in a qualitative manner using a funnel plot. We tested for funnel plot asymmetry by using weighted linear regression of effect estimates on their standard error (Egger 1997) for comparisons and outcomes in which more than 10 trials were included.

Data synthesis

If the degree of clinical heterogeneity was not excessive, we generated a quantitative summary by meta-analysis. We performed the meta-analysis using Review Manager software (RevMan 5.1). We performed both fixed-effect model and random-effects model meta-analyses and explored differences between these two estimates.

Subgroup analysis and investigation of heterogeneity

We performed subgroup analyses for subgroups of participants and interventions. We compared subgroups by using an interaction term when appropriate.

Subgroups of participants

Subgroup analysis according to type of surgery focused on the following.

1. Participants undergoing major abdominal surgery.
2. Participants undergoing minor abdominal surgery.
3. Participants undergoing cardiac surgery.
4. Participants undergoing orthopaedic surgery.

Subgroups of interventions

These analyses examined the following.

1. Preoperative carbohydrate drink versus preoperative fasting.
2. Preoperative carbohydrate drink versus placebo drink.
3. Preoperative carbohydrate administered by intravenous route versus preoperative fasting or placebo drink.

Sensitivity analysis

We performed sensitivity analyses to exclude trials at high risk of bias, such as known quasi-randomized trials. We compared random-effects and fixed-effect estimates of each outcome

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variable. If publication bias was suspected, we performed a 'trim and fill' sensitivity analysis of the primary outcomes. To assess trial influence, we performed sensitivity analyses by sequentially excluding each trial. We used R 2.13.2 (R 2.13.2) using package meta to perform sensitivity analyses not available in RevMan.

Summary of findings

We used the principles of the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) system (Guyatt 2008) in our review to assess the quality of the body of evidence associated with specific outcomes such as length of hospital stay, complication rate, insulin resistance (hyperinsulinaemic euglycaemic clamp), fatigue, well-being and nausea and vomiting and constructed a 'Summary of findings' (SoF) table.

The GRADE approach is used to assess the quality of a body of evidence based on the extent to which one can be confident that an estimate of effect or association reflects the item being assessed. Assessment of the quality of a body of evidence considers study methodological quality, directness of the evidence, heterogeneity of the data, precision of the effect estimates and risk of publication bias.

RESULTS

Description of studies

Results of the search

Electronic searches began on 27 October 2011 and were repeated on 10 July 2013 and 14 March 2014. Electronic searches identified a total of 7074 articles across four databases (Figure 2). An additional 51 studies were identified through handsearching of reference lists of included papers and through contact with experts in the field. After duplicate papers had been excluded, the titles and abstracts of 5890 studies were reviewed by JM and MS. This process led to the exclusion of 5011 studies on review of titles and a further 768 studies on review of abstracts that were obviously not relevant to this review, leaving 111 papers for full retrieval.

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Figure 2. Study flow diagram.

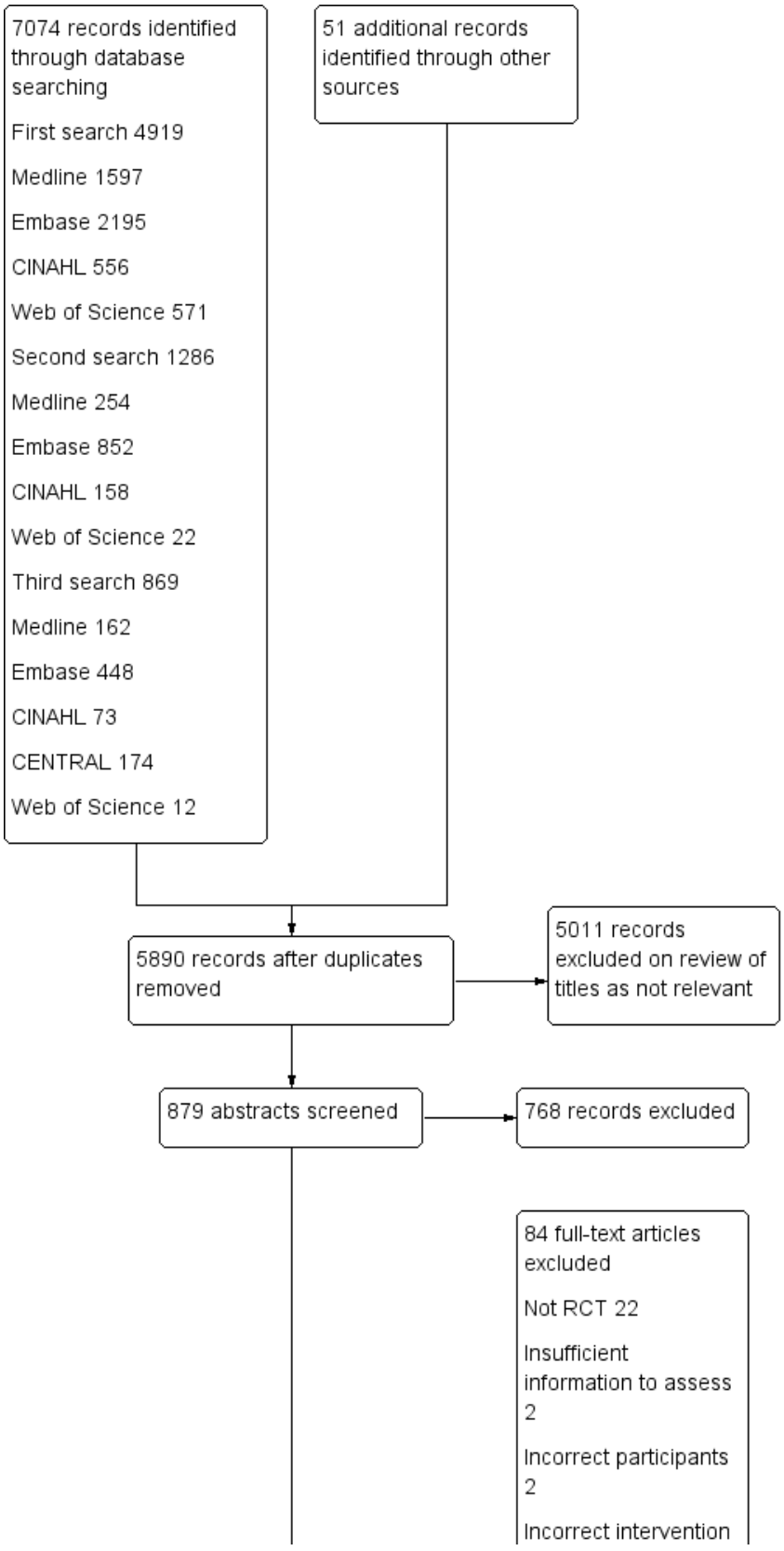

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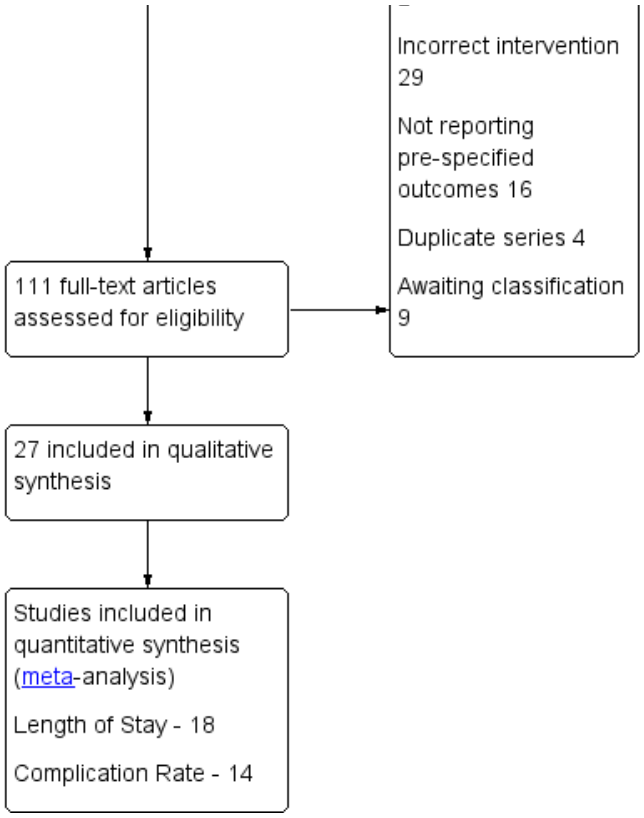
Figure 2. (Continued)



Of the papers reviewed in full, 27 were included in the review and 75 were excluded for various reasons.

We contacted nine study authors (Braga 2012; Breuer 2006; Kaska 2010; Lidder 2013; Mathur 2010; Perrone 2011; Soop 2001; Soop 2004; Yang 2012) to obtain further information about their papers; five responded (Breuer 2006; Lidder 2013; Mathur 2010; Soop 2001; Soop 2004).

Included studies

We included 27 studies in this review. These studies are described in detail under Characteristics of included studies. In total, these studies included 1976 participants, of whom 935 received carbohydrate, 595 received placebo and 446 were fasted preoperatively. Studies were published between 1994 and 2013. Seven studies were conducted in Sweden (Harsten 2012; Hausel 2005; Ljunggren 2012; Ljungqvist 1994; Rapp-Kesek 2007; Soop 2001; Soop 2004), and 13 were conducted elsewhere in Europe (Bisgaard 2004; Braga 2012; Breuer 2006; Henriksen 2003; Jarvela 2008; Kaska 2010; Lauwick 2009; Lidder 2013; Noblett 2006; Ozdemir 2011; Yildiz 2013; Yuill 2005; Zelic 2012), three in China (An 2008; Wang 2010; Yang 2012), two in Brazil (Perrone 2011; Pexe-Machado 2013) and one each in Canada (Tran 2013) and New Zealand (Mathur 2010).

Most of the identified studies involved study participants undergoing elective abdominal surgery (18) (An 2008; Bisgaard 2004; Braga 2012; Hausel 2005; Henriksen 2003; Kaska 2010; Lidder 2013; Ljungqvist 1994; Mathur 2010; Noblett 2006; Ozdemir 2011; Perrone 2011; Pexe-Machado 2013; Wang 2010; Yang 2012; Yildiz 2013; Yuill 2005; Zelic 2012), with four examining orthopaedic surgery (Harsten 2012; Ljunggren 2012; Soop 2001; Soop 2004), three cardiac surgery (Breuer 2006; Jarvela 2008; Rapp-Kesek 2007), one cardiac or spinal surgery (Tran 2013) and one thyroidectomy (Lauwick 2009). Specific inclusion criteria for American Society of Anaesthesiologists (ASA) grading were reported in 13 studies, with eight limiting participants to those with an ASA of I-II (Bisgaard 2004; Hausel 2005; Kaska 2010; Lauwick 2009; Ozdemir 2011; Perrone 2011; Soop 2004; Zelic 2012), four to those with an ASA of I-III (Harsten 2012; Ljunggren 2012; Mathur 2010; Pexe-Machado 2013) and only one study specifically including only ASA III-IV participants (Breuer 2006).

Twenty-five studies (An 2008; Bisgaard 2004; Braga 2012; Breuer 2006; Harsten 2012; Hausel 2005; Henriksen 2003; Jarvela 2008; Lauwick 2009; Lidder 2013; Ljunggren 2012; Mathur 2010; Noblett 2006; Ozdemir 2011; Perrone 2011; Pexe-Machado 2013; Rapp-Kesek 2007; Soop 2001; Soop 2004; Tran 2013; Wang 2010; Yang 2012; Yildiz 2013; Yuill 2005; Zelic 2012) administered the preoperative carbohydrates as an oral beverage, one via the intravenous route (Ljungqvist 1994) and one by both oral and intravenous routes (Kaska 2010). Eighteen studies used a placebo as a control (Bisgaard 2004; Braga 2012; Breuer 2006; Harsten 2012; Hausel 2005; Lauwick 2009; Lidder 2013; Ljunggren 2012; Mathur 2010; Noblett 2006; Ozdemir 2011; Perrone 2011; Pexe-Machado 2013; Soop 2001; Soop 2004; Wang 2010; Yang 2012; Yuill 2005), with six of these including an additional fasting participant group (Breuer 2006; Hausel 2005; Ljunggren 2012; Noblett 2006; Ozdemir 2011; Wang 2010) and nine studies comparing carbohydrates in an unblinded fashion versus fasting alone (An 2008; Henriksen 2003; Jarvela 2008; Kaska 2010; Ljungqvist 1994; Rapp-Kesek 2007; Tran 2013; Yildiz 2013; Zelic 2012).

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The primary outcomes of length of hospital stay and complication rate were reported by 19 (An 2008; Braga 2012; Breuer 2006; Harsten 2012; Hausel 2005; Kaska 2010; Lidder 2013; Ljunggren 2012; Mathur 2010; Noblett 2006; Ozdemir 2011; Perrone 2011; Pexe-Machado 2013; Soop 2001; Soop 2004; Tran 2013; Yang 2012; Yildiz 2013; Yuill 2005) and 14 studies (Braga 2012; Hausel 2005; Kaska 2010; Lidder 2013; Mathur 2010; Noblett 2006; Perrone 2011; Pexe-Machado 2013; Soop 2001; Soop 2004; Tran 2013; Yang 2012; Yuill 2005; Zelic 2012), respectively. Mean and standard deviation were reported (or provided by study authors) in nine studies (An 2008; Harsten 2012; Hausel 2005; Mathur 2010; Ozdemir 2011; Soop 2001; Soop 2004; Yang 2012; Yildiz 2013) and were calculated from the median and range or interquartile range in nine studies (Breuer 2006; Kaska 2010; Lidder 2013; Ljunggren 2012; Noblett 2006; Perrone 2011; Pexe-Machado 2013; Tran 2013; Yuill 2005) by using the techniques described by Hozo 2005; standard deviation was imputed from similar studies in two instances (Braga 2012; Yildiz 2013). Sensitivity analyses excluding these two trials with imputed data did not significantly change analysis outcomes in any case. A single study (Lidder 2013), which was conducted in a 2 × 2 factorial design, required that data from the two carbohydrate groups and the two placebo groups be combined according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Insulin resistance was reported with the HOMA-IR in seven studies (Mathur 2010; Perrone 2011; Pexe-Machado 2013; Rapp-Kesek 2007; Tran 2013; Wang 2010; Yang 2012), and insulin sensitivity by a hyperinsulinaemic euglycaemic clamp in three studies (Ljungqvist 1994; Soop 2001; Soop 2004). A further three studies (Breuer 2006; Kaska 2010; Ljunggren 2012) reported other measures of insulin sensitivity or resistance. Because of the high degree of heterogeneity observed, these additional measures did not contribute to the quantitative analysis.

Excluded studies

It was determined that 74 studies did not meet the inclusion criteria for this review for various reasons, which are summarized in Figure 2 and are detailed in full under Characteristics of excluded studies and Characteristics of studies awaiting classification. Twenty-one studies were not randomized controlled trials (ASAC 2011; Awad 2011; Bisgaard 2006; Brady 2009; Burden 2012; Goodwin 1991; Jones 2011; Lassen 2010; Lin 1997; Ljungqvist 1991; Ljungqvist 2000; Ljungqvist 2001; Ljungqvist 2010; Longarela 2005; Maltby 1991; Maltby 2006; Nygren 1998; Power 2004; Smith 2011; Soop 2000; Stuart 2006), in two studies participants did not undergo surgery (Awad 2011a; Awad 2011b) and in 26 studies the participants did not receive at least 45 g of carbohydrates within four hours of surgery (Adanir 2008; Aronsson 2009; Bopp 2011; Breitman 2011; Dock-Nascimento 2011; Dock-Nascimento 2012; Faria 2009; Helminen 2009; Hendry 2010; Hubner 2010; Itou 2012; Maltby 2004; McCaul 2003; Meisner 2008; Muehling 2009; Phillips 1993; Protic 2010; Protic 2010a; Serclova 2009; Tanabe 1996; Taniguchi 2009; Vincent 1991; Wendel 2013a; Wilson 1999; Zargar-Shoshtari 2009; Zhang 2010). In 16 studies the interventions were correct, but none of the prespecified outcomes of this review were reported (Awad 2010; Awad 2012; Crowe 1984; Enoki 1992; Hausel 2001; Hutchinson 1988; Korusic 2009; Maltby 1988; Melis 2006; Nygren 1995; Okabayashi 2010; Okabayashi 2011; Schricker 2008; Svanfeldt 2007; Thorell 1996; Yagci 2008). An additional four duplicate patient series were identified (Kaska 2006; Ljungqvist 1998; Noblett 2004; Nygren 1999), in which only the most recent and complete data were retained; in two studies information was insufficient to permit assessment of whether review criteria were met (Hausel 1999; Jones 2012).

Studies awaiting classification

A further eight studies, recently published in abstract form, are awaiting sufficient information to allow classification (Aguilar-Nascimento 2012; Asakura 2013; Forde 2012; Jodlowski 2011; Ozer 2013; Tsutsumi 2011; Zelic 2013; Zhao 2013); one trial was identified during the peer review process and will be incorporated into the next version of this review (Yilmaz 2013).

Risk of bias in included studies

Risk of bias of the included studies is detailed under Characteristics of included studies and is summarized in Figure 1 and Figure 3 Most studies were assessed as having unclear or high risk of bias across at least some of the seven domains. Only two studies were assessed as having low risk of bias across all seven domains (Lidder 2013; Mathur 2010).

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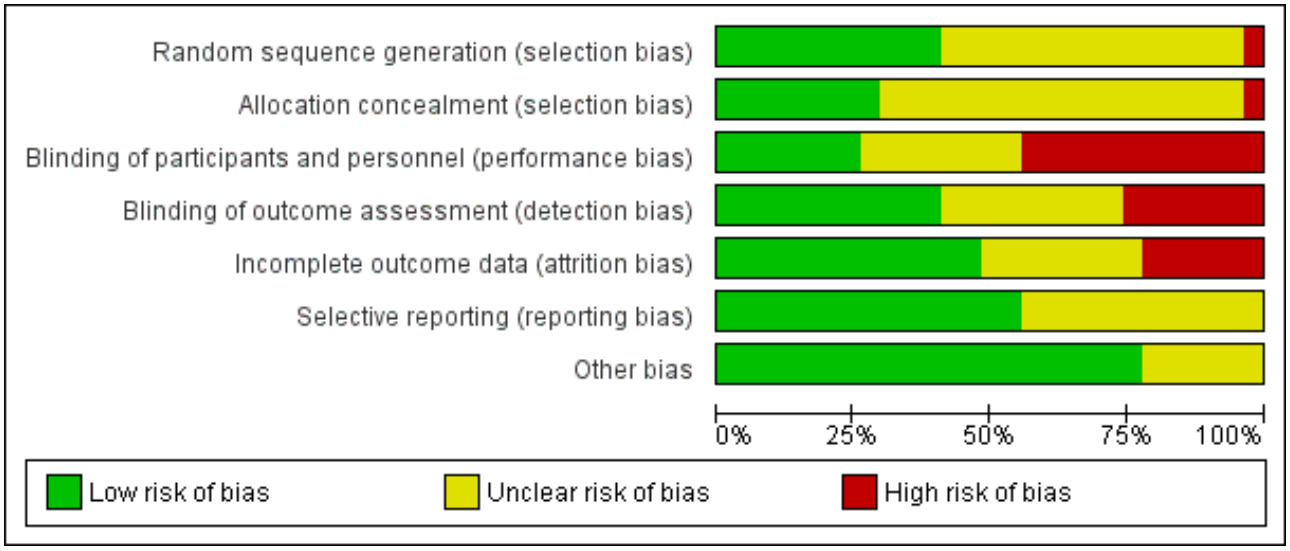
Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

The method of sequence generation was assessed as being at low risk of bias in 11 studies (Braga 2012; Breuer 2006; Hausel 2005; Lauwick 2009; Lidder 2013; Mathur 2010; Noblett 2006; Perrone 2011; Pexe-Machado 2013; Tran 2013; Yildiz 2013). Low-risk methods of sequence generation included computer random number generation in nine studies, a random number table in another study and random number allocation in another study. In one study, quasi-randomization by date of birth was used for allocation (Ljungqvist 1994), and in the remainder, the methods of sequence generation were not adequately reported.

Allocation concealment was assessed as being at low risk of bias in eight studies (Bisgaard 2004; Braga 2012; Breuer 2006; Lauwick 2009; Lidder 2013; Mathur 2010; Soop 2001; Soop 2004). In seven of these, central randomization was used and the study centres were supplied with identical (coded) packages of carbohydrate and placebo drinks (Bisgaard 2004; Braga 2012; Breuer 2006; Lauwick 2009; Mathur 2010; Soop 2001; Soop 2004). One study specifically described using opaque, sealed envelopes for allocation concealment (Lidder 2013). In the quasi-randomized study, participant allocation could not have been concealed from the investigators (Ljungqvist 1994), and in the remaining studies, details of allocation concealment were not reported.

Blinding

Overall, details of blinding were poorly reported by the included studies. By definition, only studies in which a placebo drink was used were capable of adequate blinding; however only six studies were assessed as being at low risk of both performance and detection bias (Bisgaard 2004; Lidder 2013; Mathur 2010; Soop 2001; Soop 2004; Yuill 2005). Adequate blinding has a much greater effect on the results of subjective outcomes than of objective outcomes; however both of the primary outcome measures for this review were subjective. In unblinded studies, participants or treating clinicians may have assessed intervention group participants as being ready for discharge sooner (performance bias). Also, complications may have been recorded at a lower threshold in the control group. Bias associated with incomplete blinding may have affected assessment of well-being, time to passage of flatus and bowel movements, fatigue and nausea. Insulin sensitivity is unlikely to be affected by performance or detection bias.

Incomplete outcome data

In 13 studies, no withdrawals were reported post randomization or all withdrawals were described, balanced between groups and deemed unlikely to affect reported outcomes (An 2008; Braga 2012; Harsten 2012; Hausel 2005; Kaska 2010; Lauwick 2009; Lidder 2013; Mathur 2010; Noblett 2006; Tran 2013; Wang 2010; Yildiz 2013; Zelic 2012). In six studies, the numbers of participants excluded post randomization could have been sufficient to affect reported outcomes (Bisgaard 2004; Henriksen 2003; Perrone 2011; Pexe-Machado 2013; Soop 2001; Soop 2004).

Selective reporting

Fifteen studies were assessed as being at low risk of selective reporting bias (Braga 2012; Hausel 2005; Kaska 2010; Lidder 2013; Ljunggren 2012; Mathur 2010; Noblett 2006; Perrone 2011; Pexe-Machado 2013; Soop 2001; Soop 2004; Tran 2013; Wang 2010; Yang 2012; Yuill 2005). In six of these, the trial protocol was obtained and all registered outcomes were reported in the final publication (Braga 2012; Mathur 2010; Perrone 2011; Pexe-Machado 2013; Tran 2013; Wang 2010). In the remaining eight studies, no protocol could be identified; however all end points that were likely to have been measured were reported by the study authors (Hausel 2005; Kaska 2010; Lidder 2013; Noblett 2006; Soop 2001; Soop 2004; Yang 2012; Yuill 2005). In one study (Ljunggren 2012), additional outcomes were reported in the final publication, as compared with the registered protocol; however again it is likely that all measured outcomes were reported.

Other potential sources of bias

In two studies participants with postoperative complications or mortality were excluded from the analysis, potentially biasing the reported length of hospital stay, as well as complication

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rate (Bisgaard 2004; Henriksen 2003). Another two studies did not report baseline characteristics of participants (Kaska 2010) or described a significant difference between groups (Perrone 2011). This may potentially lead to differences in measured outcomes for reasons other than the intervention. It may also reflect bias in the randomization or allocation process. In Hausel 2005 only a small proportion of potentially eligible patients participated in this study, raising questions about the generalizability of its results. Finally, in Tran 2013, both patients undergoing spinal surgery and those undergoing cardiac surgery were included. It is unclear what effect on outcome resulted from combining the heterogeneous groups of participants.

None of the above potential sources of bias were judged to place the studies at high risk of bias.

Effects of interventions

See: **Summary of findings for the main comparison**

1 Carbohydrates (CHO) versus placebo

The first comparison analysed CHO versus placebo and included 18 studies and 1191 participants.

Length of hospital stay (Analysis 1.1)

The outcome 'length of hospital stay' included 14 studies (867 participants) of four subgroups: major abdominal surgery (mean length of stay greater than two days) (Braga 2012; Lidder 2013; Mathur 2010; Noblett 2006; Ozdemir 2011; Yang 2012; Yuill 2005), minor abdominal surgery (mean length of stay less than two days) (Hausel 2005; Ozdemir 2011; Perrone 2011), orthopaedic surgery (Harsten 2012; Ljunggren 2012; Soop 2001; Soop 2004) and cardiac surgery (Breuer 2006). Evidence of heterogeneity was high in all subgroups, except for those undergoing minor abdominal surgery, as was heterogeneity for the overall treatment effect (I^2 = 57%). No evidence showed of an effect of preoperative carbohydrates on length of hospital stay (overall MD -0.13 days, 95% confidence interval (CI) -0.38 to 0.12). Nor was any significant evidence of treatment effect observed in any of the four subgroups.

Postoperative complication rate (Analysis 1.2)

The outcome of complication rate involved analysis of 10 studies (Braga 2012; Hausel 2005; Lidder 2013; Mathur 2010; Noblett 2006; Perrone 2011; Soop 2001; Soop 2004; Yang 2012; Yuill 2005) and 594 participants. Heterogeneity was low (I^2 = 0%), but three studies in which no complications were reported could not contribute to the meta-analysis (Hausel 2005; Perrone 2011; Soop 2001). No evidence was found of effects of preoperative carbohydrates on postoperative complication rate(RR 0.92, 95% CI 0.73 to 1.16).

Aspiration pneumonitis

The secondary outcome of aspiration pneumonitis was reported in 10 studies (Bisgaard 2004; Lidder 2013; Mathur 2010; Noblett 2006; Perrone 2011; Soop 2001; Soop 2004; Wang 2010; Yang 2012; Yuill 2005), including 562 participants. However, no study reported any events of aspiration pneumonitis, so no meta-analysis could be performed.

Insulin resistance (HOMA-IR) (Analysis 1.3)

Postoperative insulin resistance using the HOMA-IR measure was reported in four studies (Mathur 2010; Perrone 2011; Wang 2010; Yang 2012), including 179 participants. A high degree of heterogeneity was observed (I^2 = 90%), and no evidence of treatment effect was found (MD -4.00, 95% CI -8.19 to 0.18).

Insulin sensitivity (clamp) (Analysis 1.4)

An alternative approach was taken in two studies (Soop 2001; Soop 2004) (29 participants) that measured postoperative insulin sensitivity using a hyperinsulinaemic euglycaemic clamp technique. This approach reports insulin sensitivity by the standardized steady state glucose infusion rate—a measure of whole body glucose utilization. In these studies, preoperative carbohydrates were associated with increased postoperative insulin sensitivity (MD 0.70, 95% CI 0.14 to 1.26).

Postoperative fatigue (Analysis 1.5)

Postoperative fatigue was reported by four studies including 468 participants. In three studies it was measured on a visual analogue scale (Harsten 2012; Lauwick 2009; Mathur 2010), and in one study it was measured on a 10-point ordinal scale (Bisgaard 2004). A high degree of heterogeneity was noted between studies (I^2 = 78%), and no evidence of treatment effect was found (SMD 0.13, 95% CI -0.27 to 0.54).

Postoperative well-being (Analysis 1.6)

Postoperative well-being was reported using different measures of effect, with two studies using a visual analogue scale (VAS) (Bisgaard 2004; Mathur 2010) and one (Ljunggren 2012) using the well-being questionnaire (W-BQ12) (Pouwer 2000). In total, these studies included 242 participants, and no evidence of treatment effect was found (SMD 0.00, 95% CI -0.25 to 0.25).

Postoperative nausea at 24 hours (Analysis 1.7)

Postoperative nausea at 24 hours (by 100 mm VAS) was reported in two studies (Hausel 2005; Mathur 2010) (234 participants) with no heterogeneity (I^2 = 0%) and no evidence of treatment effect (MD -1.71, 95% CI -4.06 to 0.64).

Postoperative vomiting (Analysis 1.8)

Postoperative vomiting was reported as an event rate by three studies (248 participants) (Bisgaard 2004; Hausel 2005; Yang 2012). No evidence of a treatment effect from preoperative carbohydrates was found (RR 1.18, 95% CI 0.65 to 2.12).

Return of intestinal function (Analysis 1.9)

Return of intestinal function was reported as time to passage of flatus by a single study (Noblett 2006) including 33 participants, and no evidence showed of a treatment effect of preoperative carbohydrates. Time to first bowel movement in days was reported in two studies (Noblett 2006; Ozdemir 2011) (83 participants). A high degree of heterogeneity was noted between studies (I^2 = 69%), and no evidence of a treatment effect was found (MD -0.34, 95% CI -0.74 to 0.05).

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2 CHO versus fasting

The second comparison looked at CHO versus fasting and included 15 studies and 973 participants. All of the same outcomes were analysed for this comparison as for comparison one.

Length of hospital stay (Analysis 2.1)

The primary outcome of length of hospital stay was reported by 10 studies (656 participants) and was analysed as four subgroups (major abdominal surgery (An 2008; Kaska 2010; Noblett 2006; Ozdemir 2011; Pexe-Machado 2013), minor abdominal surgery (Hausel 2005; Ozdemir 2011; Yildiz 2013), orthopaedic surgery (Ljunggren 2012) and cardiac surgery (Breuer 2006)). Although heterogeneity remained high (I^2 = 80%), preoperative carbohydrate treatment was associated with a reduced mean length of stay of 0.42 days (95% CI -0.79 to -0.06 days) in the overall analysis. Reduced length of stay was also found in the subgroup of orthopaedic surgery (MD -1.00, 95% CI -1.73 to -0.27), although this contained only a single study (Ljunggren 2012). No evidence of effect of carbohydrates was seen in any of the other subgroups —major abdominal surgery (MD -2.02, 95% CI -4.13 to 0.08), minor abdominal surgery (MD -0.07, 95% CI -0.18 to 0.03) and cardiac surgery (MD 1.00, 95% CI -0.90 to 2.90).

Postoperative complication rate (Analysis 2.2)

Postoperative complication rates were reported by six studies (Hausel 2005; Kaska 2010; Noblett 2006; Pexe-Machado 2013; Tran 2013; Zelic 2012) (386 participants). Heterogeneity was low (I^2 = 0%), and no effect of preoperative carbohydrate drinks on postoperative complication rate was found (RR 1.00, 95% CI 0.87 to 1.16). Notably, the study by Tran 2013 was heavily weighted in this analysis because of the high event rate in both groups. Excluding this study from the analysis did not change the overall effect however (RR 1.05, 95% CI 0.59 to 1.87).

Aspiration pneumonitis.

Again, although aspiration pneumonitis was mentioned by five studies (Jarvela 2008; Noblett 2006; Tran 2013; Wang 2010; Yildiz 2013) (255 participants), no events were reported, precluding meta-analysis.

Insulin resistance (HOMA-IR) (Analysis 2.3)

Insulin resistance was reported with the use of HOMA-IR in four studies (Pexe-Machado 2013; Rapp-Kesek 2007; Tran 2013; Wang 2010) (110 participants) with high heterogeneity (I^2 = 87%); no treatment effect was identified (MD -1.33, 95% CI -4.12 to 1.47).

Insulin sensitivity (clamp)

The alternative of determining insulin sensitivity according to a hyperinsulinaemic euglycaemic clamp was reported by only a single study (Ljungqvist 1994), which found no evidence of effect of preoperative carbohydrate treatment.

Postoperative fatigue (Analysis 2.4)

Postoperative fatigue was reported by two trials (Henriksen 2003; Yildiz 2013) with low heterogeneity (I^2 = 0%). No evidence of a treatment effect of preoperative carbohydrate administration was identified (SMD -0.08, 95% CI -0.47 to 0.31).

Postoperative well-being (Analysis 2.5)

Postoperative well-being was reported by two studies (Henriksen 2003; Ljunggren 2012), which used different instruments (100-mm VAS and W-BQ12). These studies included 87 participants, but no evidence of a treatment effect was found (SMD 0.04, 95% CI -0.40 to 0.47).

Postoperative nausea at 24 hours

Postoperative nausea at 24 hours (by 100-mm VAS) was also reported by only a single study (Hausel 2005), which showed no evidence of a treatment effect (MD -2.00 mm, 95% CI -5.52 to 1.52).

Postoperative vomiting (Analysis 2.6)

Two trials (Hausel 2005; Jarvela 2008) including 214 participants reported postoperative vomiting as count data. Heterogeneity was low (I^2 = 0%), but no effect of preoperative carbohydrate treatment was shown (RR 1.24, 95% CI 0.58 to 2.63).

Return of intestinal function (Analysis 2.7; Analysis 2.8)

Postoperative time to passage of flatus was reported by two studies (An 2008; Noblett 2006), which included 75 participants. In this analysis, participants receiving preoperative carbohydrate treatment reported passage of flatus a mean of 0.39 days earlier (95% CI -0.70 to -0.07) than those fasted preoperatively. Heterogeneity was low (I^2 = 0%), although the results of this analysis were strongly influenced by An 2008, which was weighted at 97%.

Postoperative time to first bowel movement was reported in two studies (Noblett 2006; Ozdemir 2011) incorporating a total of 84 participants. One of these (Ozdemir 2011) reported separately on the outcomes of participants undergoing major and minor abdominal surgery. When the outcomes of all three participant groups were combined, reduced time to first bowel movement was found (MD -0.18 days, 95% CI -0.29 to -0.07); however this analysis heavily weighted the outcomes of the group receiving minor abdominal surgery at 92.1% because of the reduced variability of this outcome. When sensitivity analysis was undertaken, restricting this analysis to only those undergoing major abdominal surgery, the precision of this effect was reduced, leaving the confidence intervals crossing the line of no effect (MD -0.48 days, 95% CI -1.62 to 0.66).

3 CHO versus placebo or fasting

For the final comparison, all studies were included, regardless of whether preoperative carbohydrates were compared with placebo or fasting. When studies contained both placebo and fasting arms, these were combined as described in Table 7.7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Overall this comparison included 27 studies and 1976 participants. Because of the larger numbers of studies and participants, this comparison was used to conduct sensitivity analyses. The Summary of findings for the main comparison was also constructed with the outcomes of this comparison.

Length of hospital stay (Analysis 3.1)

This analysis includes 19 studies and 1351 participants. Four subgroups were constructed: major abdominal surgery (with mean

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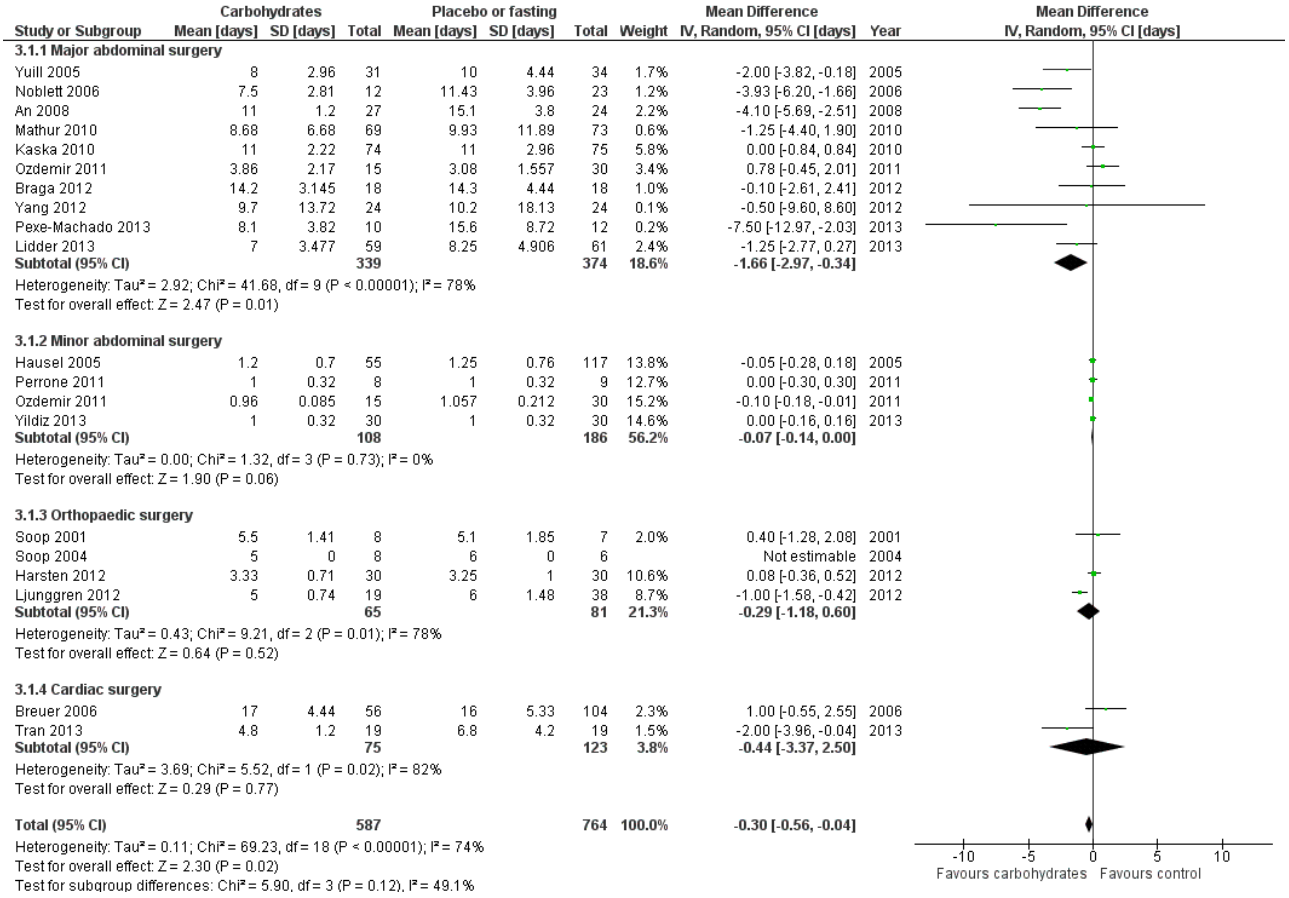
length of stay greater than two days) (An 2008; Braga 2012; Kaska 2010; Lidder 2013; Mathur 2010; Noblett 2006; Ozdemir 2011; Pexe-Machado 2013; Yang 2012; Yuill 2005), minor abdominal surgery (mean length of stay less than two days) (Hausel 2005; Ozdemir 2011; Perrone 2011; Yildiz 2013), orthopaedic surgery (Harsten 2012; Ljunggren 2012; Soop 2001; Soop 2004) and cardiac surgery (Breuer 2006; Tran 2013). One study that included participants undergoing both cardiac surgery and spinal surgery (Tran 2013) was placed into the cardiac surgery subgroup, as this is the procedure that most of the participants underwent. Sensitivity analysis performed by moving this study to the orthopaedic subgroup did not affect subgroup outcomes.

Overall administration of preoperative carbohydrate was associated with a modest reduction in hospital stay (MD -0.30 days, 95% CI -0.56 to -0.04) compared with the placebo or fasting group. This analysis is illustrated in Figure 4.

Figure 4. Forest plot of comparison: 3 CHO versus placebo or fasting, outcome: 3.1 Length of hospital stay [days].



It should also be noted that overall heterogeneity is high (I^2 = 74%), as is heterogeneity in all subgroups except that of minor abdominal surgery. The low heterogeneity in the minor abdominal surgery subgroup is to be expected, as all participants undergoing these operations would be expected to stay in hospital for no longer than 24 hours.

No difference was seen in the relative effects of carbohydrate across subgroups (P value 0.12). Patients undergoing major abdominal surgery have a longer average length of stay, hence a larger absolute decrease in average length of stay was seen in this subgroup (MD -1.66 days, 95% CI -2.97 to -0.34). Caution is needed in interpreting these findings because of the degree of heterogeneity observed in average lengths of stay in the major abdominal surgery subgroup, and because of variation in study quality.

A funnel plot of this analysis is presented in Figure 5. Weighted linear regression of effect estimates on their standard error (Egger 1997) revealed evidence of publication bias or other small-study effects in this analysis (t = -2.19, degrees of freedom (df) = 17, P value 0.04). A sensitivity analysis was then conducted using the 'trim and fill' method, resulting in a reduced and non-significant effect estimate (MD -0.13 days, 95% CI -0.43 to 0.18).

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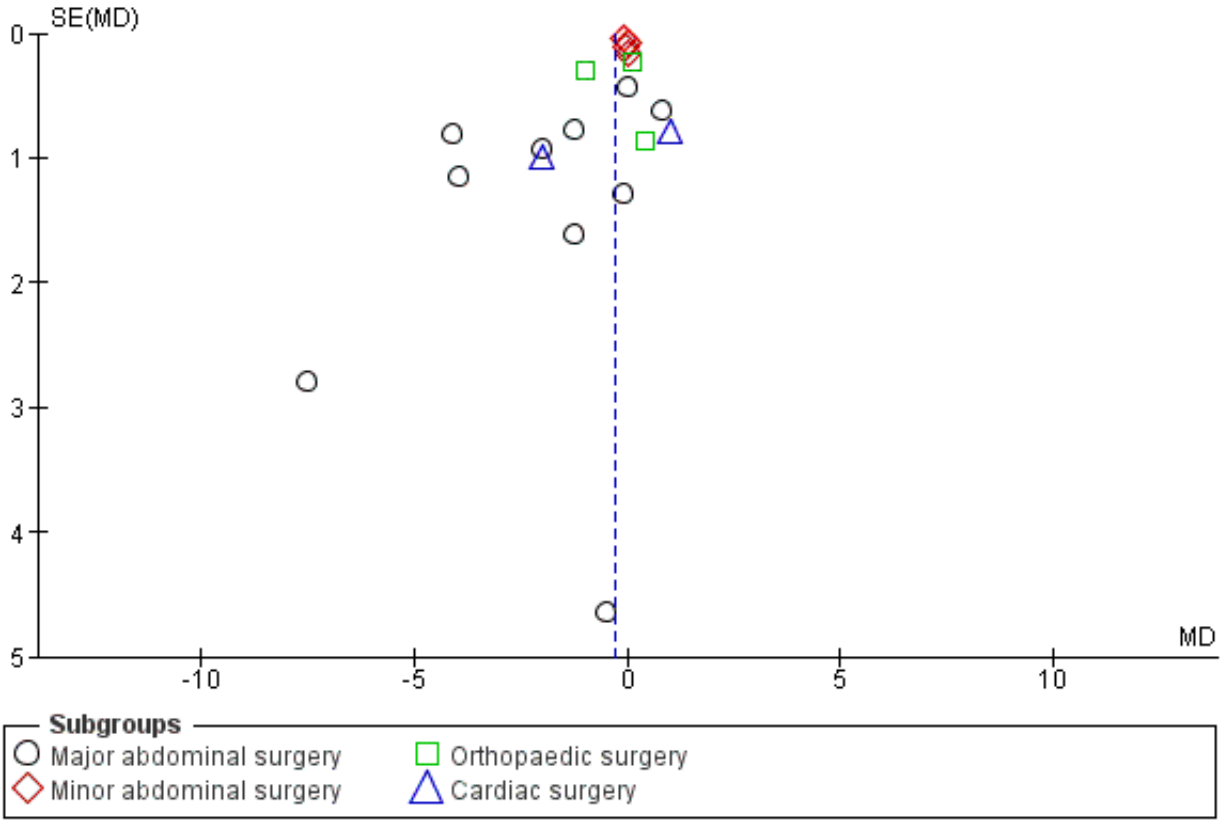
Figure 5. Funnel plot of comparison: 3 CHO versus placebo or fasting, outcome: 3.1 Length of hospital stay [days].



Through a sensitivity analysis, the outcome of length of hospital stay was reanalysed with subgroups of adequate blinding versus unclear or inadequate blinding (Analysis 3.2). Among the four studies judged to have adequate blinding of participants, treating clinicians and outcome assessors (Lidder 2013; Mathur 2010; Soop 2001; Soop 2004), no evidence of treatment effect of preoperative carbohydrates was found (MD -0.59, 95% CI -1.73 to 0.55) and heterogeneity was low (I^2 = 10%).

The 15 remaining studies, in which blinding was at unclear or high risk of bias, showed evidence of treatment effect (MD -0.29, 95% CI -0.55 to -0.02) and increased heterogeneity (I^2 = 77%).

Postoperative complication rate (Analysis 3.3)

This analysis includes 14 studies (Braga 2012; Hausel 2005; Kaska 2010; Lidder 2013; Mathur 2010; Noblett 2006; Perrone 2011; Pexe-Machado 2013; Soop 2001; Soop 2004; Tran 2013; Yang 2012; Yuill 2005; Zelic 2012) and 913 participants, although three studies in which no complications were reported did not contribute to the meta-analysis (Hausel 2005; Perrone 2011; Soop 2004). Heterogenity was low (I^2 = 0%), and no evidence of effect of preoperative carbohydrate treatment on postoperative complication rate was found (RR 0.98, 95% CI 0.86 to 1.11). One study with a high event rate (Tran 2013) contributed 67.5% of the weighting of this analysis; however exclusion of this study, or any of the other studies sequentially, did not alter the results of this analysis. This analysis is presented as a funnel plot for investigation of small-study effects in Figure 6. No evidence of publication bias was identified using weighted linear regression (t = 0.3217, df = 9, P value 0.76).

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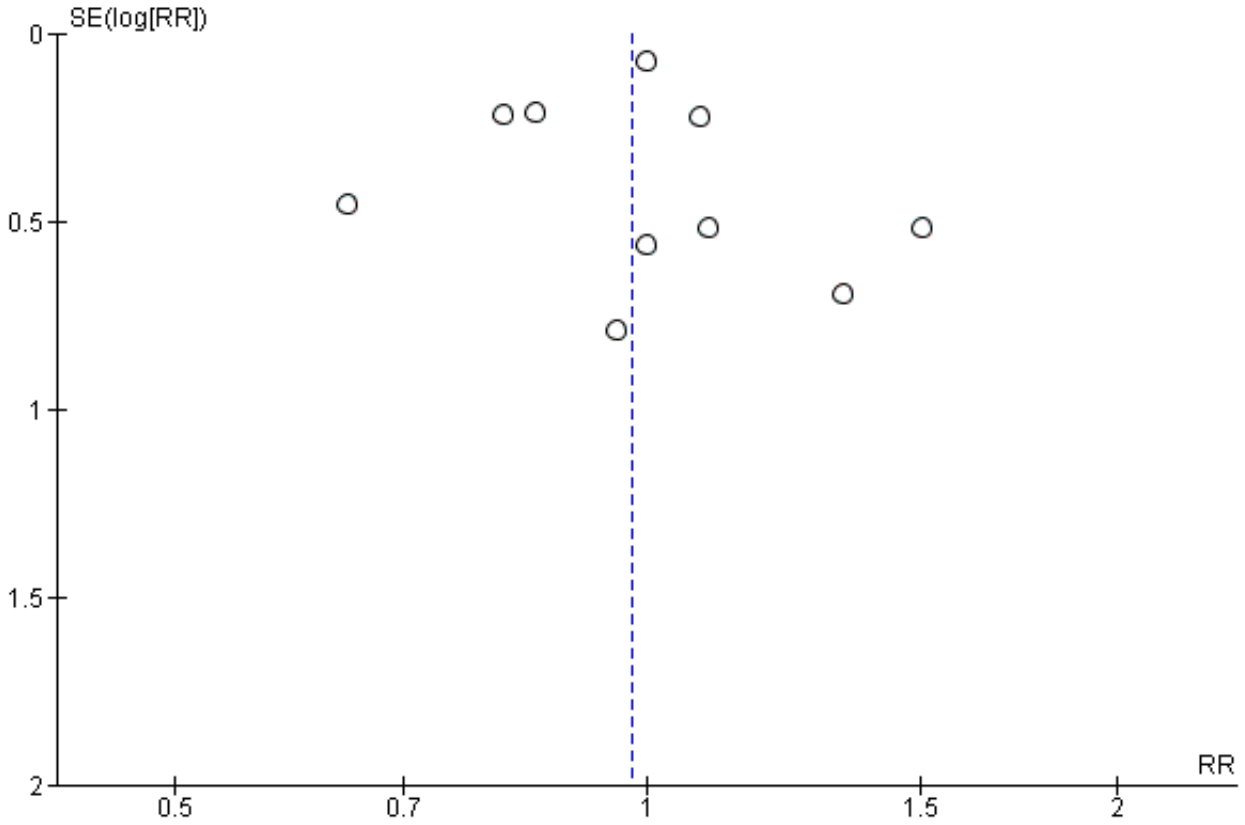
Figure 6. Funnel plot of comparison: 3 CHO versus placebo or fasting, outcome: 3.3 Complication rate.



Aspiration pneumonitis

Thirteen studies (Bisgaard 2004; Jarvela 2008; Lidder 2013; Mathur 2010; Noblett 2006; Perrone 2011; Soop 2001; Soop 2004; Tran 2013; Wang 2010; Yang 2012; Yildiz 2013; Yuill 2005) involving 789 participants reported on the outcome of aspiration pneumonitis; however no cases of this were described. Therefore it was not possible to undertake meta-analysis of this outcome.

Insulin resistance (HOMA-IR) (Analysis 3.4)

This outcome was reported in seven studies (Mathur 2010; Perrone 2011; Pexe-Machado 2013; Rapp-Kesek 2007; Tran 2013; Wang 2010; Zelic 2012) that included 273 participants. Overall heterogeneity was again high (I^2 = 86%), and no evidence of treatment effect was found (MD -1.59, 95% CI -3.35 to 0.17). Influential analysis performed by excluding studies in turn found that exclusion of Wang 2010 reduced heterogeneity to an I^2 of 57%, as well as reducing the magnitude of the effect estimate (MD -0.05, 95% CI -1.06 to 0.97). No obvious explanation for this could be identified. Excluding other studies had no significant effect on the results, and in no case did exclusion of a single study lead to evidence of treatment effect within 95% confidence intervals.

Insulin sensitivity (clamp) (Analysis 3.5)

Postoperative insulin sensitivity was determined by hyperinsulinaemic euglycaemic clamp in three studies (Ljungqvist 1994; Soop 2001; Soop 2004) incorporating 41 participants. Results are presented as a standardized glucose infusion rate in mg/kg/min, with higher figures showing increased peripheral glucose utilization and therefore increased insulin sensitivity. Meta-analysis showed that preoperative carbohydrate treatment was associated with postoperative increased insulin sensitivity (MD 0.76 mL/kg/min, 95% CI 0.24 to 1.29). Heterogeneity was low (I^2 = 0%), although influential analysis found that by excluding Soop 2004, the precision of the effect estimate was reduced and the 95% confidence intervals crossed the line of no effect (MD 0.59 mL/kg/min, 95% CI -0.34 to 1.52).

Postoperative fatigue (Analysis 3.6)

Postoperative fatigue was reported by six studies incorporating 576 participants. Five studies measured fatigue using a VAS (Harsten 2012; Henriksen 2003; Lauwick 2009; Mathur 2010; Yildiz 2013); one measured fatigue using a 10-point ordinal scale (Bisgaard 2004). Combining this outcome by using standardized mean differences yielded high heterogeneity (I^2 = 64%) and no evidence of treatment effect (SMD 0.06, 95% CI -0.23 to 0.35). Influential analysis found that exclusion of any study did not result in a significant treatment effect; however exclusion of Harsten 2012 did reduce heterogeneity (I^2 = 0%).

Postoperative well-being (Analysis 3.7)

Postoperative well-being was reported by four studies, which included 310 participants. Three studies measured well-being on a VAS (Bisgaard 2004; Henriksen 2003; Mathur 2010), and one used a 12-question W-BQ12 (Ljunggren 2012). Heterogenity between studies was low (I^2 = 0%), and no evidence of a treatment effect was

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found (SMD 0.00, 95% CI -0.22 to 0.23). Influential analysis found that exclusion of any study did not yield evidence of a treatment effect.

Postoperative nausea at 24 hours (Analysis 3.8)

This outcome was reported by only two studies (Hausel 2005; Mathur 2010), which included in total 292 participants. Both studies measured nausea using a 100-mm VAS. Combining these studies did not reveal evidence of a treatment effect (MD -1.69, 95% CI -4.12 to 0.74).

Postoperative vomiting (Analysis 3.9)

Postoperative vomiting was reported by four studies (Bisgaard 2004; Hausel 2005; Jarvela 2008; Yang 2012), which included 407 participants. Meta-analysis yielded no evidence of a treatment effect from preoperative carbohydrates (RR 1.25, 95% CI 0.77 to 2.04). Heterogeneity was low (I^2 = 0%), and influential analysis found that exclusion of any individual study did not alter findings of the meta-analysis.

Return of intestinal function (Analysis 3.10; Analysis 3.11)

Time to passage of first flatus was reported by two studies including 86 participants. Overall, preoperative carbohydrate treatment was associated with a reduction in mean time to passage of flatus of 0.39 days (95% CI -0.70 to -0.07). This analysis was heavily weighted (97.2%) toward the study by An 2008, which reported a statistically significant reduction in time to passage of flatus on its own. The remaining study (Noblett 2006) found no evidence of a treatment effect with preoperative carbohydrates.

Time to first bowel motion after surgery was reported by two studies (Noblett 2006; Ozdemir 2011) including 125 participants. One study (Ozdemir 2011) separately reported the outcomes of subgroups of participants undergoing major or minor abdominal surgery. Overall comparison revealed moderate heterogeneity (I^2 = 63%) and no evidence of treatment effect (MD -0.28 days, 95% CI -0.62 to 0.05). Influential analysis was not performed, as only two studies were included in this analysis.

DISCUSSION

Summary of main results

This review reports that patients undergoing elective surgery who receive preoperative carbohydrate treatment have a small overall reduction in length of hospital stay (0.30 days shorter, 95% CI -0.56 to -0.04) compared with those receiving placebo or subject to traditional preoperative fasting. However, no difference in length of stay was seen in studies that compared preoperative carbohydrate treatment with placebo (MD -0.13 days, 95% CI -0.38 to 0.12).

Preoperative carbohydrate treatment was not associated with any decrease or increase in postoperative complication rate when compared with placebo or fasting.

When secondary outcomes were considered, no evidence of effect was found for preoperative carbohydrate treatment when compared with placebo or fasting for the postoperative outcome of insulin resistance (HOMA-IR), fatigue, well-being, nausea, vomiting or time to first bowel movement. Preoperative carbohydrate treatment when compared with placebo or fasting was associated with a small increase in the return of intestinal function when measured as time to passage of flatus (MD -0.39 days, 95% CI -0.70 to -0.07). Preoperative carbohydrate treatment was also associated with an increase in postoperative insulin sensitivity when measured by a hyperinsulinaemic euglycaemic clamp (MD 0.76 mg/kg/min, 95% CI 0.24 to 1.29).

These main findings of the review are presented in Summary of findings for the main comparison.

Overall completeness and applicability of evidence

This review examined data from 27 studies including 1976 participants undergoing a range of elective surgical procedures. Most participants received an oral carbohydrate drink, with only two studies examining the effect of intravenously administered carbohydrates. The limited number of included studies examining carbohydrates administered via the intravenous route precluded separate analysis of this subgroup and limited the ability of this review to draw conclusions regarding this method of administration.

Overall the range of elective operations studied in this review was broad; however little evidence was found that specifically addressed patients undergoing minimally invasive surgery. The only minimally invasive surgical technique for which outcomes were specifically reported was laparoscopic cholecystectomy, with all other studies specifically excluding participants undergoing minimally invasive surgery or including their results with those of participants undergoing open surgical techniques.

It is important to note that many studies limited participation to patients with an ASA rating of I-II or I-III. Only one study was specifically limited to participants with an ASA of III or IV undergoing cardiac surgery (Breuer 2006). Even studies that included ASA III and IV participants generally reported smaller numbers, as these patients are less likely to undergo elective surgical procedures. This limits generalizability of the findings of this review to higher-risk patients undergoing elective surgery.

Length of hospital stay was the most commonly reported outcome, followed by complication rate. Secondary outcomes were reported much more infrequently, with insulin resistance (HOMA-IR), sensitivity (clamp), fatigue, well-being, nausea, vomiting and return of intestinal function reported by six, three, five, four, two, four and three studies, respectively. This limited the ability of this review to perform subgroup analyses of these outcomes across participants undergoing different operations and, consequently, hinders the generalizability of these findings.

Although aspiration pneumonitis as a specific complication was mentioned by 13 studies (Soop 2001; Soop 2004; Bisgaard 2004; Yuill 2005; Noblett 2006; Jarvela 2008; Wang 2010; Mathur 2010; Perrone 2011; Yang 2012; Tran 2013; Yildiz 2013; Lidder 2013), no incidents of this admittedly rare complication were reported. This review is unable to present any conclusions with respect to this outcome.

It is important to note that all three studies (Ljungqvist 1994; Soop 2001; Soop 2004) reporting insulin sensitivity using the hyperinsulinaemic euglycaemic clamp technique were conducted in Sweden—two by the same author and the other by a colleague at the same institution. Two of these studies (Soop 2001; Soop 2004) included participants undergoing total hip joint replacement,

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and the other, open cholecystectomy (Ljungqvist 1994). This may limit the generalizability of this outcome to other populations and contexts.

It is also important to consider the outcome of insulin resistance when measured by HOMA-IR, for which no significant effects of preoperative carbohydrate were found. This fact may be due to differences between these two measures, that is, HOMA-IR measures basal (essentially hepatic) insulin resistance, and the hyperinsulinaemic euglycaemic clamp measures peripheral insulin sensitivity at active levels of insulin production (Muniyappa 2008).

Geographically, although overall reasonable variability was noted, seven (Harsten 2012; Hausel 2005; Ljunggren 2012; Ljungqvist 1994; Rapp-Kesek 2007; Soop 2001; Soop 2004) of the 27 included studies were conducted in Sweden and only one in North America (Canada) (Tran 2013). This may limit the applicability of these results to other countries with different models of health care delivery.

Quality of the evidence

The 27 studies and 1976 participants that form the basis of this review certainly provide a considerable body of evidence. The overall methodological quality of the included studies was moderate, with most studies assessed as having one or more domains of unclear or high risk of bias. In light of the subjective nature of most of the outcomes of this review, perhaps of greatest concern is the lack of adequate blinding resulting from lack of identical placebo, or other potential risks to adequate blinding.

The main significant clinical effect of preoperative carbohydrate treatment compared with control was a reduction in hospital stay. That this reduction in stay was limited to comparisons of preoperative carbohydrate versus fasting and preoperative carbohydrate versus placebo or fasting, but was not found in the meta-analysis of preoperative carbohydrate versus placebo, raises concerns that performance bias may be contributing to this finding. The subgroup analysis comparing studies with low risk of performance bias versus those with unclear or high risk would also support this assumption, given that reduced length of stay was not found in the low risk of performance bias subgroup.

Potential biases in the review process

This review was conducted according to procedures specified in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We rigorously searched multiple electronic databases, personal libraries and reference lists without language restriction with the goal of identifying studies. This review group consists of several authors with expertise in this field, who have published some of the studies that make up this review (JM, JN, LP, MS) and are in contact with those continuing to undertake research in this field. Titles, abstracts and papers were reviewed by at least two review authors independently. Thus we can be confident that all relevant studies have been included.

Data abstraction and quality assessment were also performed by at least two review authors, reducing the chances of error. Unfortunately, the published report did not always provide enough information to allow review authors to abstract the data or to be certain about the quality assessment. When possible, we contacted study authors, but some information is still outstanding as of the publication date of this review. In particular, four studies published in abstract form only, which were identified at the time of the second literature search, have provided insufficient information to allow review authors to determine their eligibility for this review (Aguilar-Nascimento 2012; Forde 2012; Jodlowski 2011; Tsutsumi 2011).

We also note that 16 studies were excluded because they did not report any of the prespecified outcomes. It is possible that some of these trials did examine our prespecified outcomes but did not report the findings; this is known as reporting bias and is difficult to identify because to do so requires cross-referencing of published trial protocols or making contact with the authors of excluded trials. We did not attempt to contact the authors of these trials and could identify protocols for only four (Awad 2010; Awad 2012; Okabayashi 2011; Schricker 2008).

It is significant to note that when the data for evidence of publication bias were examined, weighted linear regression of effect estimates on their standard error (Egger 1997) revealed evidence of publication bias or another small-study effect. Reporting bias might have contributed to this finding. Sensitivity 'trim and fill' analysis resulted in attenuation and reduction in precision of the observed treatment effect. No other evidence of publication bias was identified in this review.

For several studies, the central tendency of the data was reported as a median rather than as a mean, and the spread was reported as a range or interquartile range. These data were approximated to mean and standard deviation by using the techniques described in Hozo 2005; however it is important to note that these approximations may differ from the reported mean and standard deviation statistics. Two studies (Braga 2012; Yildiz 2013) also required standard deviations for length of hospital stay and postoperative fatigue to be imputed from the median of the reported standard deviations of other similar studies. Sensitivity analysis performed to exclude these studies did not significantly alter any of the outcomes.

Agreements and disagreements with other studies or reviews

The authors of this review could not identify any other systematic reviews addressing this question at the time of submission of our protocol (Smith 2011), although three were subsequently published. In 2011 Jones 2011 published a narrative review that was based on a systematic literature search of three electronic databases. The search was limited to articles published in the English language over the previous 10 years. These review authors specifically restricted their search to papers relevant to colorectal surgery, and it is unclear whether the search was limited to randomized controlled trials.

These review authors retrieved a total of 20 papers and included 11 in their review (Jones 2011). They did not undertake a quantitative synthesis of the results by meta-analysis but concluded that preoperative carbohydrate treatment was both safe and effective. Lack of formal study quality assessment, lack of quantitative synthesis and more limited study inclusion criteria by Jones et al make it difficult to compare their results with those of the present review.

The next review was published by Li et al in 2012 (Li 2012) and consisted of a systematic literature search of multiple electronic databases without language restrictions. Inclusion

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criteria were randomized controlled trials evaluating preoperative carbohydrate administration in surgical patients. Data were abstracted by multiple reviewers and quality was graded according to recommendations provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This review identified 22 studies and measured a variety of outcomes, including multiple other measures of insulin sensitivity and resistance. The main findings of this study were that preoperative carbohydrate administration was associated with greater insulin sensitivity when measured by various instruments. This study did not find an association between preoperative carbohydrate treatment and reduced length of hospital stay, potentially because of the fewer included studies.

Finally, another systematic review published in 2013 addressed the effects of preoperative carbohydrate treatment on length of hospital stay, insulin resistance, complication rate and nausea and vomiting (Awad 2013). This review was conducted in a systematic manner and specifically stated that standard methods recommended by The Cochrane Collaboration were used. A comprehensive search was conducted of multiple electronic databases between January 1980 and April 2012. Inclusion criteria included prospective randomized trials of adult patients undergoing elective surgery for whom preoperative carbohydrate treatment of at least 50 g was administered before surgery, and participants were compared with a control arm.

Awad et al identified 21 studies for inclusion in the qualitative synthesis, and length of hospital stay was determined on the basis of 12 studies and 1198 participants (Awad 2013). Similar to the present review, Awad et al found that preoperative carbohydrate treatment was associated with a reduction in length of stay after major abdominal surgery, but not after minor surgery or orthopaedic surgery. Awad et al also found no evidence of a treatment effect of preoperative carbohydrates on complication rate and an increase in insulin sensitivity when measured by hyperinsulinaemic euglycaemic clamp.

It is not surprising that the authors of Awad 2013 reported findings similar to those of the present review, given that the search strategy and the methodology used were almost identical. However the more up-to-date search and the greater number of included papers in the present review have improved its precision and external validity in comparison.

AUTHORS' CONCLUSIONS

Implications for practice

Preoperative carbohydrate loading already forms an integral part of many enhanced recovery or fast-track surgery protocols. Results of the present review provide very low-quality evidence on the efficacy of preoperative oral carbohydrate drinks as part of fast-track surgical protocols in reducing hospital stay, possibly mediated in part through reduced postoperative insulin resistance and faster return of intestinal function. However overall reduction in hospital stay was modest and of uncertain clinical significance (0.30 days, 95% CI -0.56 to -0.04 days), and no evidence of effect of preoperative carbohydrate treatment was demonstrated for complication rate or other important clinical outcomes. With this in mind, the potential benefits with respect to hospital stay need to be balanced against the costs of this intervention, as well as patient preferences, when fast-track protocols are designed.

Implications for research

The strength of the evidence found to support preoperative carbohydrate treatment in reducing hospital stay could be improved if a treatment effect could be demonstrated by well-designed, blinded, placebo-controlled trials, and across different types of surgery. Additional well-conducted studies in major abdominal surgery, minimally invasive surgery, orthopaedic surgery and cardiac surgery could contribute usefully to the literature and to future meta-analyses. Studies need to be well blinded and should aim to measure as many patient-relevant outcomes as possible by using standardized instruments such as visual analogues scales. Further studies reporting insulin sensitivity by hyperinsulinaemic euglycaemic clamp and studies conducted in North America would be particularly valuable.

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Dr Jonas Nygren commented on the first draft of this protocol. He was then asked to collaborate with us and became an author of the protocol and of the subsequent review. Dr Nygren's contribution to the review is described in the Contributions of authors section.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

An 2008

Methods	Randomized controlled trial
	January 2006 to January 2007
Participants	Patients with histologically confirmed colon cancer undergoing elective resection
	Participants randomized: 51 (27 CHO, 24 fasting)
	Participants analysed: 51 (27 CHO, 24 fasting)

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An 2008 *(Continued)*

	Exclusions: diabetes mellitus, medication use that might affect insulin sensitivity, renal or hepatic insufficiency, inflammation
Interventions	Carbohydrates: oral beverage containing 50 g of carbohydrates in 200 mL administered 3 hours before anaesthesia Fasting: nil by mouth for 6 hours for solids and 2 hours for liquids before surgery
Outcomes	Length of hospital stay, postop time to passage of flatus
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Details of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded; this may affect subjective outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Participants and personnel were not blinded; this may affect subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No postrandomization withdrawals reported in this study
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published, and not all important outcomes were reported
Other bias	Low risk	No other important threats to validity have been identified in this study; however limited information is available in the text

Bisgaard 2004

Methods	Double-blind randomized controlled trial October 1999 to March 2001
Participants	Patients undergoing elective laparoscopic cholecystectomy. Participants randomized: 94 Participants analysed: 86 (43 CHO:43 placebo) Age, years: inclusion range 18-75, median age 42 CHO and 44 placebo ASA: I-II only

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Bisgaard 2004 *(Continued)*

	Exclusions: previous endoscopic retrograde cholangiopancreatography with papillotomy within 1 month before surgery, diabetes, gastric disease or previous gastric surgery, chronic pain, expected poor compliance, receiving opioids or tranquillizers for longer than 1 week before surgery, protocol violations, postoperative complications
Interventions	Carbohydrate: oral carbohydrate drink (containing 50 g carbohydrates in 400 mL administered 2 hours before surgery) Placebo: placebo drink of 400 mL given 2 hours before surgery
Outcomes	Postop fatigue by visual analogue scale, postop well-being by visual analogue scale, postop vomiting
Notes	Participants suffering postop complications were specifically excluded from this study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Central randomization by product manufacturer; method of sequence generation not described
Allocation concealment (selection bias)	Low risk	Central randomization with supply of identically coded tetra packs
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants, clinical team and study observers all blinded to intervention group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants, clinical team and study observers all blinded to intervention group
Incomplete outcome data (attrition bias) All outcomes	High risk	Participants with postoperative complications were excluded post randomization; numbers excluded post randomization were not reported
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not prepublished, and not all potentially relevant outcomes were reported
Other bias	Unclear risk	Exclusion of participants with postop complications

Braga 2012

Methods	Double-blind randomized controlled trial September 2007 to May 2008
Participants	Patients undergoing elective pancreaticoduodenectomy for pancreatic cancer or periampullary cancer Patients randomized: 36 (18 CHO, 18 placebo) Participants analysed: 36 (18 CHO, 18 placebo) Age, years: Inclusion range 18-80, mean 64.1 Exclusions: severe malnutrition, impaired gastric emptying, uncontrolled diabetes mellitus, renal failure, cardiovascular dysfunction, ongoing infection, low plasma neutrophil level, psychiatric disease,

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Braga 2012 *(Continued)*

	epilepsy, suspicion of drug abuse, severe alcohol abuse, pregnancy, breast-feeding or fertile women refusing to use contraceptives, allergy to any component of the investigational product, inability to cooperate adequately, enrolment in other studies
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g carbohydrate, glutamine and antioxidants in 250 mL given 3 hours before induction of anaesthesia Placebo: low-energy product containing orange juice concentrate, starch, sodium saccharin and colours in 250 mL given 3 hours before induction of anaesthesia
Outcomes	Length of hospital stay, complication rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Concealed random number generation by computer
Allocation concealment (selection bias)	Low risk	Concealed random number generation by computer
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identically packaged intervention and control drinks, described as double-blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Study described as double-blind; however it is not reported whether assessors and data collectors were blind to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals post randomization were reported
Selective reporting (reporting bias)	Low risk	Study protocol was registered online, and all protocol end points were reported
Other bias	Low risk	No other deficiencies were identified

Breuer 2006

Methods	3-Arm parallel-group randomized trial
Participants	Adults undergoing elective coronary artery bypass grafting or valve replacement Patients randomized: 188 Participants analysed: 160 (56 CHO, 44 placebo, 60 fasting) Age, years: patients 18 or older, median 64 ASA: III-IV only

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Breuer 2006 *(Continued)*

	Exclusions: conditions likely to impair gastrointestinal motility or to enhance gastro-oesophageal reflux, potentially difficult airway management, non-elective surgery, presence of infection, pregnancy, maltose or fructose intolerance, type 1 diabetes
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g carbohydrates in 400 mL administered 2 hours before induction of anaesthesia Placebo: oral 400 mL placebo drink administered 2 hours before induction of anaesthesia Fasting: from midnight before surgery
Outcomes	Length of hospital stay, insulin resistance by postoperative insulin requirement
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-based randomization in blocks of 6
Allocation concealment (selection bias)	Low risk	Computer-based central randomization
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Uniform bottles of carbohydrate versus placebo drink; however fasting group not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Uniform bottles of carbohydrate versus placebo drink; however fasting group not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Distribution of exclusions and withdrawals post randomization not reported
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published, and not all relevant end points were reported (such as complication rate)
Other bias	Low risk	No other risks of bias were identified

Harsten 2012

Methods	Double-blind randomized controlled trial September 2009 to April 2011
Participants	Patients undergoing elective total hip replacement under spinal anaesthesia Patients randomized: 60 (30 CHO, 30 placebo) Participants analysed: 60 (30 CHO, 30 placebo) Age, years: inclusion range 50-80, mean 69 treatment, 71 placebo ASA: I-III

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Harsten 2012 *(Continued)*

	BMI: less than or equal to 35 kg/m^2 Exclusions: diabetes mellitus, prior hip surgery on same hip, ongoing infection, immunological deficiency
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g CHO in 400 mL administered 90 minutes before induction and again 2 hours post surgery Placebo: oral flavoured water 400 mL administered 90 minutes before induction and again 2 hours post surgery
Outcomes	Length of hospital stay, postop fatigue
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not given
Allocation concealment (selection bias)	Unclear risk	Allocation by sealed envelopes, not known whether these were opaque or sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Nurse administering intervention drink was not blinded as to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All other care providers were blinded as to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts post randomization
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not registered, and not all relevant outcomes were reported (such as complication rate)
Other bias	Low risk	No other potential sources of significant bias were identified

Hausel 2005

Methods	3-Arm parallel-group randomized trial
Participants	Patients undergoing elective laparoscopic cholecystectomy Participants randomized: 174 Participants analysed: 172 (55 CHO, 59 placebo, 58 fasting) Age, years: "adults," mean 48.3 CHO, 48.0 fasting, 46.8 placebo ASA: I-II only

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Hausel 2005 *(Continued)*

	Exclusions: conditions that may impair gastrointestinal motility, gastro-oesophageal reflux, potentially difficult airways, diabetes mellitus, suspected or documented choledocholithiasis, participants scheduled for afternoon surgery
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g in 400 mL delivered at least 2 hours before premedication Placebo: oral 400 mL placebo drink at least 2 hours before premedication Fasting: from midnight before surgery
Outcomes	Length of hospital stay, total complications, postoperative vomiting
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization list
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Fasting from midnight group was not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Fasting from midnight group was not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only two withdrawals post randomization out of 174 participants
Selective reporting (reporting bias)	Low risk	Trial protocol was not published, but all relevant and likely end points were reported
Other bias	Unclear risk	Only 22% of available laparoscopic cholecystectomy patients participated in this study, thus limiting generalizability of its findings

Henriksen 2003

Methods	3-Arm parallel-group randomized trial
Participants	Patients undergoing elective bowel resection Participants randomized: 58 Participants analysed: 48 (17 CHO, 15 CHO + protein, 16 fasting) Age, years: mean 64 for CHO, 63 for CHO + protein, 64 for fasting

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Henriksen 2003 *(Continued)*

	Exclusions: inflammatory bowel disease, disseminated malignant disease, previous treatment for intra-abdominal cancer, serious cardiovascular disease (NYHA angina class III and IV), diabetes mellitus, disabling mental disease, dementia; history of alcohol, medicine or drug abuse
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g CHO in 400 mL administered 3 hours before surgery Carbohydrate + protein: oral carbohydrate + protein drink containing 50 g CHO and 3.5% soy protein in 400 mL delivered 3 hours before surgery Fasting: preoperative fasting for 3 hours before surgery
Outcomes	Postoperative fatigue and well-being
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization described by "closed envelope technique"; however method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	1 study author was aware of allocation but did not have input into data collection
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded to fasting versus active treatment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Unblinded investigator was not involved in data collection
Incomplete outcome data (attrition bias) All outcomes	High risk	Distribution and effect of participants excluded post randomization was not clear
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published, and not all important end points were reported (length of stay, complication rate)
Other bias	Unclear risk	One postoperative death excluded from analysis

Jarvela 2008

Methods	2-Arm parallel-group randomized controlled trial November 2004 to June 2005
Participants	Patients undergoing elective coronary artery bypass grafting Participants randomized: 101 (CHO 50, fasting 51) Participants analysed: 101 (CHO 50, fasting 51) Age, years: inclusion criteria not stated; mean 64 CHO, 66.8 placebo

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Jarvela 2008 *(Continued)*

	Exclusions: diagnosed diabetes, any cause of delayed gastric emptying
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g in 400 mL administered 2 hours before surgery Fasting: overnight fasting the night before surgery
Outcomes	Postoperative aspiration pneumonitis, postoperative vomiting
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization with consecutively sealed envelopes, method of sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Unclear whether consecutively sealed envelopes were opaque or numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Operating room staff were blinded to treatment group; however participants were not blinded because of trial design
Blinding of outcome assessment (detection bias) All outcomes	High risk	Participants were not blinded because of trial design
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Exclusions post randomization were not reported
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published, and not all important end points were reported
Other bias	Low risk	No other risks of bias were identified

Kaska 2010

Methods	Randomized trial involving 3 parallel treatment groups
Participants	221 patients undergoing colorectal surgery Participants randomized: 221 (oral CHO 74, IV CHO 72, fasting 75) Participants analysed: 221 (oral CHO 74, IV CHO 72, fasting 75) Age, years: inclusion range 35-75, mean 60.4 ASA: I-II BMI: 20-30 kg/m^2 as inclusion criterion Exclusions: metabolic disease, systolic cardiac dysfunction, atrial fibrillation, moderate to severe valvular disease
Interventions	Oral carbohydrate: Nutricia preop (50 g CHO/400 mL) up to 2 hours before surgery

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Kaska 2010 *(Continued)*

	IV carbohydrate: 500 mL 10% glucose delivered between 6 and 2 hours before surgery Fasting: from midnight the night before surgery
Outcomes	Length of hospital stay, total complications, insulin resistance by quantitative insulin sensitivity check index (QUICKI)
Notes	IV CHO group only received 25 g of carbohydrate during the 4 hours directly before surgery and therefore were not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Allocation concealment by "envelope method," details not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study described as "blinded," but no placebo was used for interventions
Blinding of outcome assessment (detection bias) All outcomes	High risk	Study described as "blinded," but no placebo was used for interventions
Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusions post randomization were reported
Selective reporting (reporting bias)	Low risk	Trial protocol was not published, but all relevant end points were likely reported
Other bias	Unclear risk	Baseline clinical characteristics of participants were not reported

Lauwick 2009

Methods	Double-blind 2-parallel-arm randomized controlled trial January 2004 to July 2006
Participants	Adult women undergoing elective thyroidectomy Participants randomized: 208 (105 CHO, 103 placebo) Participants analysed: 200 (100 CHO, 100 placebo) Age, years: inclusion range 19-70, mean 45 CHO and 46 placebo ASA: I-II only BMI: less than 35 kg/m^2 as inclusion criterion Exclusions: men, diabetes mellitus, gastro-oesophageal reflux, preoperative vomiting and antiemetic therapy, steroid treatment, history of motion sickness or postoperative nausea and vomiting

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Lauwick 2009 *(Continued)*

Interventions	Carbohydrate: oral carbohydrate drink containing 50 g of carbohydrates in 400 mL administered 2 hours before transfer to the operating room Placebo: drink of 100 mL water administered 2 hours before transfer to the operating room
Outcomes	Postop fatigue
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization online
Allocation concealment (selection bias)	Low risk	Computer-generated randomization online
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Surgeons and clinical personnel were blinded, but intervention drinks were of different volumes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Surgeons and clinical personnel were blinded, but intervention drinks were of different volumes
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusions post randomization were reported and were unlikely to affect outcome
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published, and many clinically significant end points were not reported
Other bias	Low risk	No other potential sources of bias were identified

Lidder 2013

Methods	Prospective 4-arm (2 × 2 factorial) double-blind randomized trial
Participants	Patients having a planned curative resection with primary anastomosis of histologically confirmed colorectal cancer Participants randomized: 120 Participants analysed: 120 Age, years: 18 or older Exclusions: inability to consent, frailty, pregnancy, diabetes, fasting plasma glucose greater than 7 mmol/L, use of steroids or immunosuppressants, abnormal gastric emptying, intestinal obstruction, use of enteral or parenteral nutrition
Interventions	Group A: oral placebo drink (400 mL) administered 2 hours before surgery, and oral placebo drink 600 mL per day on each postoperative day in hospital

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Lidder 2013 *(Continued)*

	Group B: oral carbohydrate drink (50 g in 400 mL) administered 2 hours before surgery, and oral placebo drink 600 mL per day on each postoperative day in hospital Group C: oral placebo drink (400 mL) administered 2 hours before surgery, and oral polymeric nutritional supplement drink 900 kcal and 600 mL per day on each postoperative day in hospital Group D: oral carbohydrate drink (50 g in 400 mL) administered 2 hours before surgery, and oral polymeric nutritional supplement drink 900 kcal and 600 mL per day on each postoperative day in hospital
Outcomes	Length of hospital stay, total complications, aspiration pneumonitis, insulin resistance (HOMA-IR)
Notes	4-Arm randomized trial (2 independent binary random treatment allocations) involving postoperative nutritional supplementation, as well as preoperative carbohydrate supplementation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization
Allocation concealment (selection bias)	Low risk	Opaque sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identically packaged intervention and placebo products produced centrally
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Codes to unblind interventions not released until database was locked
Incomplete outcome data (attrition bias) All outcomes	Low risk	No postrandomization withdrawals
Selective reporting (reporting bias)	Low risk	Trial protocol was not published, but all relevant end points were likely reported
Other bias	Low risk	No other potential sources of significant bias were identified

Ljunggren 2012

Methods	Open-label randomized clinical trial with 3 parallel treatment groups May 2008 to September 2009
Participants	Patients undergoing elective total hip joint replacement under spinal anaesthesia Participants randomized: 60 (20 CHO, 20 placebo, 20 fasting) Participants analysed: 57 (19 CHO, 18 placebo, 20 fasting) Age, years: range 44-89, mean 69 ASA: I 9, II 37, III 11

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Ljunggren 2012 *(Continued)*

	Exclusion: endocrine disorders including diabetes and treatment with cortisone
Interventions	Carbohydrate: oral carbohydrate drink (50 g CHO/400 mL) administered 2 hours before entry into OR Placebo: oral tap water 800 mL administered 2 hours before entry into OR Fasting: from midnight the night before surgery
Outcomes	Length of hospital stay, insulin resistance (IV glucose tolerance test and quantitative insulin sensitivity check index (QUICKI)), postop well-being
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation unclear
Allocation concealment (selection bias)	Unclear risk	Sealed envelope method mixed in large batches. Unclear whether envelopes were opaque or sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label study with no blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear how postrandomization withdrawals might affect results, although numbers of exclusions post randomization were small
Selective reporting (reporting bias)	Low risk	Trial protocol was published, but some reported outcomes were not prespecified in the protocol; however it is likely that all relevant outcomes were reported
Other bias	Low risk	No other significant risks of bias were identified

Ljungqvist 1994

Methods	Quasi-randomized controlled trial
Participants	Patients undergoing elective open cholecystectomy Participants analysed: 12 (6 CHO, 6 fasting) Age, years: mean 45 CHO and 42 fasting Exclusions: taking regular medications, history of metabolic disease or history of metabolic disease in first-degree relatives, fasting blood glucose greater than 6 mmol/L, signs of previous unknown disease or alcohol abuse

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Ljungqvist 1994 *(Continued)*

Interventions	Carbohydrate: intravenous glucose infusion (5 mg/kg/min) from 1 hour after the last extensive meal on the day before operation until 30-60 minutes before the beginning of anaesthesia Fasting: preoperative fasting from 6 pm the night before surgery, without intravenous infusions
Outcomes	Insulin sensitivity by hyperinsulinaemic euglycaemic clamp
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasi-randomization by date of birth
Allocation concealment (selection bias)	High risk	Quasi-randomization by date of birth
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Intervention was not blinded; however it is unclear how this might affect the objective outcome of insulin sensitivity
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Intervention was not blinded; however it is unclear how this might affect the objective outcome of insulin sensitivity
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Exclusions and dropouts were not reported
Selective reporting (reporting bias)	Unclear risk	Protocol was not published, and not all relevant outcomes were reported
Other bias	Low risk	No other sources of potential bias were identified

Mathur 2010

Methods	Double-blind randomized controlled trial July 2004 to December 2005
Participants	Patients undergoing major elective colorectal (n = 97) or liver resection (n = 45) Participants randomized: 162 (80 CHO, 82 placebo) Participants analysed: 142 (69 CHO, 73 placebo) Age, years: inclusion range 18-80, median 60 CHO and 65 placebo ASA: inclusion range I-III (n = 19:93:30) Exclusions: pregnancy, inability to consumer clear fluids, gastrointestinal obstruction, diabetes mellitus, liver cirrhosis, corticosteroid treatment exceeding 5 mg/d

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Mathur 2010 *(Continued)*

Interventions	Carbohydrate: oral carbohydrate drink containing 50 g CHO in 400 mL administered 2 hours before anaesthesia Placebo: oral 400 mL placebo drink administered 2 hours before anaesthesia
Outcomes	Length of hospital stay, insulin resistance by HOMA-IR, postoperative fatigue
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated variable block size central randomization, stratified by type of surgery
Allocation concealment (selection bias)	Low risk	Central randomization using opaque sealed envelopes. Placebo and active drinks identically packaged
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identical coded tetra packs provided by study sponsor
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Identical coded tetra packs provided by study sponsor
Incomplete outcome data (attrition bias) All outcomes	Low risk	Missing data were described and balanced between groups, unlikely to affect outcomes
Selective reporting (reporting bias)	Low risk	Trial protocol was published, and all planned outcomes were reported
Other bias	Low risk	No other source of potential bias was identified

Noblett 2006

Methods	3-Arm parallel-group randomized trial
Participants	Patients undergoing elective colorectal surgery Participants randomized: 36 (12 CHO, 12 placebo, 12 fasting) Participants analysed: 35 (CHO 12, placebo 11, fasting 12) Age, years: mean 58 CHO, 59 placebo, 55 fasting ASA: median II in all groups Exclusions: diabetes mellitus, gastro-oesophageal reflux, disorders of gastric emptying
Interventions	Carbohydrate: oral carbohydrate drink containing 47.5 g CHO in 400 mL administered 3 hours before surgery Placebo: oral 400 mL water administered 3 hours before surgery

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Noblett 2006 *(Continued)*

	Fasting: from midnight before surgery
Outcomes	Length of hospital stay, time to passage of flatus and bowel movement, postop complications, postop aspiration pneumonitis
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence generation is described as by "random number allocation"
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes opened by researcher, not clear whether these were opaque or sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Taste of intervention drinks different, and fasting group not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Taste of intervention drinks different, and fasting group not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusion post randomization only because of cancellation of surgery
Selective reporting (reporting bias)	Low risk	Study protocol was not published, but all likely important outcomes were reported in this study
Other bias	Low risk	No other threats to validity were identified

Ozdemir 2011

Methods	3-Arm parallel-group randomized trial
Participants	Patients undergoing elective major (abdominal hysterectomy) or minor (inguinal hernia) surgery Participants randomized: 90 (45 major, 45 minor; each group randomly assigned 15:15:15 to CHO, placebo and fasting) Age, years: inclusion criteria 30-70, mean major: 45.66 CHO, 51.53 placebo, 47.66 fasting; minor: 45.80 CHO, 48.06 placebo, 45.40 fasting ASA: inclusion range I-II only
Interventions	Carbohydrates: oral carbohydrate beverage (50 g/400 mL) given 2 hours before surgery Placebo: oral water (400 mL) given 2 hours before surgery Fasting: from the night before surgery
Outcomes	Length of hospital stay, time to first bowel movement

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Ozdemir 2011 *(Continued)*

Notes	Postop nausea + vomiting and fatigue were described as categorical outcomes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Placebo drink of water was not indistinguishable from carbohydrate drink; therefore blinding was unlikely to be complete
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding was unlikely to be complete, and subjective outcomes were included
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Presence or absence of dropouts or withdrawals was not reported
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published in advance, and not all relevant outcomes were reported
Other bias	Low risk	No other sources of potential bias was identified

Perrone 2011

Methods	Double-blind randomized controlled trial
Participants	Patients undergoing elective cholecystectomy (open or laparoscopic) or unilateral inguinal hernia repair Participants randomized: 26 (14 treatment, 12 placebo) Participants analysed: 17 (8 treatment, 9 placebo) Age, years: inclusion range 18-65, mean 35 treatment, 41 placebo ASA: I-II BMI: less than or equal to 35 kg/m^2 Exclusions: acute cholecystitis, type 2 diabetes mellitus, chronic liver or kidney disease, gastro-oesophageal reflux, gastroparesis, intestinal obstruction, prolonged operations, "significant intraoperative occurrences"
Interventions	Carbohydrate + protein: oral carbohydrate + protein drink (54 g CHO, 9 g protein, 237 mL) administered 3 hours before surgery Placebo: oral 237 mL water drink 3 hours before surgery
Outcomes	Length of hospital stay, insulin resistance (HOMA-IR), total complications

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Perrone 2011 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Study described as blinded but details not reported. Water may not be suitable as placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	As above
Incomplete outcome data (attrition bias) All outcomes	High risk	Proportionally high numbers of postrandomization withdrawals, reasons not reported
Selective reporting (reporting bias)	Low risk	Trial protocol was published with primary outcomes reported as per protocol
Other bias	Unclear risk	Significant difference in preoperative ASA distribution between treatment groups

Pexe-Machado 2013

Methods	Single-blind randomized controlled trial
Participants	Patients undergoing elective laparotomy for gastrointestinal malignancy (subtotal gastrectomy, hemicolectomy, anterior resection of the rectum) Participants randomized: 30 (15 CHO, 15 control) Participants analysed: 22 (10 CHO, 12 control) Age, years: inclusion range 18-65, mean 48 CHO and 49 control ASA: inclusion range I-III (I 6, II 13, III 3) Exclusions: diabetes mellitus, chronic kidney failure, chronic liver disease, serum bilirubin > 2 mg/dL, BMI > 35 kg/m^2, gastro-oesophageal reflux, gastroparesis, intestinal obstruction, non-compliance with study protocol, severe intraoperative complications, operation time longer than 6 hours
Interventions	CHO: oral carbohydrate drink containing 67 g of carbohydrate and 8 g of protein in 200 mL administered 3 hours before surgery Control: fasting 6-8 hours before surgery
Outcomes	Length of hospital stay, Insulin resistance (HOMA-IR), total complications

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Pexe-Machado 2013 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were unblinded, and treating clinicians might have been blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Study was described as single-blind; however it is not reported whether treating clinicians or data collection personnel were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	8 out of 30 participants were excluded post randomization, including 2 for intraoperative complications; this may have affected study outcomes
Selective reporting (reporting bias)	Low risk	Study protocol was registered and published. No selective outcome reporting was identified
Other bias	Low risk	No other specific risks were identified

Rapp-Kesek 2007

Methods	2-Arm parallel-group randomized controlled trial
Participants	Patients over 65 years of age scheduled to undergo elective coronary artery bypass grafting Participants randomized: 18 (9 CHO, 9 fasting) Participants analysed: 18 (9 CHO, 9 fasting) Age, years: older than 65. Mean age, 71 CHO and 73 fasting Exclusions: diabetes mellitus, other metabolic disease; severely impaired respiratory, circulatory or renal function
Interventions	CHO: oral carbohydrate drink containing 50 g of carbohydrate in 400 mL administered 3-5 hours before induction of anaesthesia Fasting: from 8 PM the evening before surgery
Outcomes	Insulin resistance (HOMA-IR)
Notes	

Risk of bias

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Rapp-Kesek 2007 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	This study is not blinded, but it is unclear how this would affect an objective measurement such as insulin resistance
Blinding of outcome assessment (detection bias) All outcomes	Low risk	This study is not blinded, but it is unlikely that lack of blinding will affect measurement of insulin resistance
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Dropouts and withdrawals were not described
Selective reporting (reporting bias)	Unclear risk	Protocol was not published, and not all likely relevant outcomes were reported
Other bias	Low risk	None were identified

Soop 2001

Methods	Double-blind randomized controlled trial
Participants	Patients undergoing elective total hip joint replacement surgery under regional anaesthesia Participants randomized: 19 Participants analysed: 15 (CHO 8, placebo 7) Age, years: inclusion range 18-80, mean 66 CHO and 58 placebo BMI: 18-28 kg/m^2 Exclusions: medications known to affect gastric emptying or intermediary metabolism; signs or symptoms of metabolic, renal, hepatic or gastric disease; abnormal fasting glucose, creatinine, C-reactive protein or liver function tests
Interventions	Carbohydrate: oral drink containing 50 g of carbohydrates in 400 mL administered 2 hours before epidural anaesthesia Placebo: 400 mL placebo drink administered 2 hours before epidural anaesthesia
Outcomes	Length of hospital stay, insulin resistance by hyperinsulinaemic euglycaemic clamp, total complications
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

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Soop 2001 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Central randomization but method of sequence generation not described
Allocation concealment (selection bias)	Low risk	Central randomization with identical coded tetra packs supplied by manufacturer
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Identical coded tetra packs supplied by manufacturer
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Identical coded tetra packs supplied by manufacturer
Incomplete outcome data (attrition bias) All outcomes	High risk	4 (out of 19) participants were excluded post randomization; treatment assignment of excluded participants was not reported
Selective reporting (reporting bias)	Low risk	Trial protocol was not published, but all likely relevant outcomes were reported
Other bias	Low risk	

Soop 2004

Methods	Double-blind randomized controlled trial
Participants	Patients undergoing elective total hip joint replacement under epidural anaesthesia Participants randomized: 15 (8 CHO, 7 placebo) Participants analysed: 14 (8 CHO, 6 placebo) Age, years: inclusion range 18-80, mean 59 CHO versus 66 placebo ASA: I-II only BMI: 18-28 kg/m^2 Exclusions: conditions or medications known to affect insulin sensitivity, upper gastrointestinal disease, fasting glucose, C-reactive protein, liver function tests or creatinine outside reference range, intolerance to non-steroidal anti-inflammatory drugs or epidural anaesthesia, major complications that could affect metabolic or clinical recovery
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g CHO in 400 mL delivered 150 minutes before surgery Placebo: 400 mL oral placebo drink delivered 150 minutes before surgery
Outcomes	Length of hospital stay, insulin resistance by hyperinsulinaemic euglycaemic clamp, complication rate
Notes	Participants with major complications were excluded from the study

Risk of bias

Bias	Authors' judgement	Support for judgement

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Soop 2004 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Described as "randomized and double-blinded," details not given
Allocation concealment (selection bias)	Low risk	Central allocation of intervention
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded and centrally allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded and centrally allocated
Incomplete outcome data (attrition bias) All outcomes	High risk	One participant receiving placebo was excluded post randomization
Selective reporting (reporting bias)	Low risk	Published protocol was not available, but all likely relevant outcomes were reported
Other bias	Low risk	No other potential source of bias was identified

Tran 2013

Methods	Open-label randomized controlled trial April 2008 to February 2009
Participants	Adult patients undergoing elective coronary artery bypass grafting or spinal surgery with fusion Participants randomized: 38 (26 CABG (13 CHO, 13 fasting), 12 spine (6 CHO, 6 fasting)) Participants analysed: 38 (19 CHO, 19 fasting) Age, years: median 59 (CHO and fasting) BMI: only included participants with BMI < 40 kg/m^2, median 26.9 kg/m^2 CHO and 25.6 kg/m^2 fasting Exclusions: gastrointestinal motility or reflux issues, existing type 1 or type 2 diabetes, inability to speak English, urgent or emergency surgery, entry into surgery more than 5 hours after ingestion of morning drink
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g carbohydrates in 400 mL administered 2 hours before surgery Fasting: from 8 PM the night before surgery
Outcomes	Length of hospital stay, insulin resistance (HOMA-IR), postoperative complication rate
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

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Tran 2013 *(Continued)*

Random sequence generation (selection bias)	Low risk	Randomization was described as being conducted in permuted blocks of 6
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants was undertaken
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No blinding of participants was undertaken, and blinding of assessors was not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomized participants are accounted for
Selective reporting (reporting bias)	Low risk	Protocol was published, and all proposed outcomes were reported
Other bias	Unclear risk	Mix of included operations was heterogeneous and unusual; unclear how this may affect results

Wang 2010

Methods	3-Arm parallel-group randomized trial
Participants	Adult patients undergoing open surgery for colorectal cancer Participants randomized: 52 (18 CHO, 17 placebo, 17 fasting) Participants analysed: 48 (16 CHO, 16 placebo, 16 fasting) Age, years: inclusion range 25-75, median 66 CHO, 62 placebo, 63 fasting Exclusions: diabetes or impaired glucose tolerance, medication affecting insulin sensitivity, greater than 10% body weight loss during previous 6 months, presence of distant metastases, renal or hepatic insufficiency, gastro-oesophageal reflux, gastrointestinal obstruction or conditions known to affect gastric emptying rate
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g in 400 mL administered between 3 hours and 1 hour before induction of anaesthesia Placebo: oral placebo beverage of 400 mL volume administered between 3 hours and 1 hour before induction of anaesthesia Fasting: overnight the night before surgery
Outcomes	Insulin resistance (HOMA-IR), aspiration pneumonitis
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

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Wang 2010 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Participants described as randomly assigned, but details not given
Allocation concealment (selection bias)	Unclear risk	Participants described as randomly assigned, but details not given
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants assigned to fasting were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors blinded; blinding unlikely to affect HOMA-IR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusions post randomization balanced and unlikely to affect outcome
Selective reporting (reporting bias)	Low risk	Trial protocol was published, and all relevant outcomes were reported
Other bias	Low risk	No other sources of potential bias were identified

Yang 2012

Methods	Double-blind randomized controlled trial
Participants	Patients undergoing open radical distal gastrectomy for gastric cancer Participants randomized: 60 Participants analysed: 48 (CHO 24, placebo 24) Age, years: mean 63.4 CHO versus 62.6 placebo Exclusions: emergency or laparoscopic surgery; pre-existing nausea, vomiting, pyloric obstruction or delayed gastric emptying; metabolic disease including diabetes mellitus or impaired glucose tolerance; chemotherapy or radiotherapy before surgery; presence of distal metastases on CT; weight loss greater than 10% in 6 months; medications affecting insulin sensitivity; renal or hepatic insufficiency
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g of carbohydrates in 500 mL administered 2-3 hours before induction of anaesthesia Placebo: 500 mL fluid containing (carbohydrate-free) sweetener administered 2-3 hours before induction of anaesthesia
Outcomes	Length of hospital stay, Insulin resistance (HOMA-IR), total complications, aspiration pneumonitis, postoperative vomiting
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

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Yang 2012 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not described in text
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Study described as double-blind, but method of blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Study described as double-blind, but method of blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Postrandomization withdrawal of 12 participants, balanced between groups, but reasons for withdrawals incompletely described
Selective reporting (reporting bias)	Low risk	Study protocol was not registered or published online, but all likely relevant outcomes were reported
Other bias	Low risk	No other potential threats to validity were identified

Yildiz 2013

Methods	Single-blind randomized controlled trial
Participants	Patients undergoing elective laparoscopic cholecystectomy under general anaesthesia Participants randomized: 60 (30 CHO, 30 fasting) Age, years: inclusion criteria 25-65, mean 47.63 CHO and 43.56 fasting ASA: I-II only by inclusion criteria Exclusions: gastro-oesophageal reflux, gastrointestinal motility disorders, diabetes mellitus, cardiac disease, mental retardation or dementia, allergy history, use of sedating or antidepressive medications, use of alcohol, anticipated difficult airways, those who could not understand pain scoring system
Interventions	Carbohydrate: oral carbohydrate drink (50 g/400 mL) given 2-3 hours preoperatively Fasting: for 8 hours preop
Outcomes	Length of hospital stay, aspiration pneumonitis, postop nausea, postop fatigue
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table used for generation of randomization sequence

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Yildiz 2013 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not described, other than "Randomized in a single blind fashion"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of intervention was undertaken with participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Described as "Randomized in a single blind fashion"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts/withdrawals were reported
Selective reporting (reporting bias)	Unclear risk	Protocol was not published, and not all potentially relevant outcomes were reported (such as total complication rate)
Other bias	Low risk	No other source of potential bias was identified

Yuill 2005

Methods	Double-blind randomized placebo-controlled trial August 1999 to March 2001
Participants	Patients undergoing elective major abdominal surgery via open approach Participants randomized: 72 Participants analysed: 65 (31 CHO, 34 placebo) Age, years: mean 52.8 CHO and 52.1 placebo BMI: mean 25.2 kg/m^2 CHO and 25.1 kg/m^2 placebo Exclusions: impaired renal function, liver cirrhosis, diabetes, metabolic abnormalities, gastric stasis or obstruction, emergency or laparoscopic procedures
Interventions	Carbohydrate: oral carbohydrate drink containing 50.4 g carbohydrates in 400 mL administered 2-3 hours before anaesthesia Placebo: 400 mL oral placebo electrolyte drink administered 2-3 hours before anaesthesia
Outcomes	Length of hospital stay, total complications
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Trial described as "Double-blind, randomized, placebo controlled trial," details not reported

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Yuill 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Trial described as "Double-blind, randomized, placebo controlled trial," details not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Trial described as double-blind; placebo drink was used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Trial described as double;blind; placebo drink was used
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Reasons for withdrawal or exclusion were not reported. Split between intervention and control groups was not described
Selective reporting (reporting bias)	Low risk	Trial protocol was not published, but all likely relevant outcomes were reported
Other bias	Low risk	No other risks were identified

Zelic 2012

Methods	Observer-blinded randomized controlled trial
Participants	Patients undergoing surgery for colon, upper rectal or rectosigmoid cancer Participants randomized: 40 Participants analysed: 40 (20 CHO, 20 fasting) Age, years: inclusion range not specified, mean 70.2 for treatment and 68.6 for fasting ASA: I-II BMI: less than or equal to 30 kg/m^2 Exclusions: previous operations, metastatic disease, diabetes mellitus, conditions that might impair gastrointestinal motility, gastro-oesophageal reflux, potential for a difficult airway
Interventions	Carbohydrate: oral carbohydrate drink containing 50 g CHO in 400 mL given 2 hours before induction of anaesthesia Fasting: from the evening before surgery
Outcomes	Time to first passage of flatus, time to first bowel movement, total complications
Notes	Trial was described as "double blind"; however no placebo was given, and 2 investigators were aware of participant allocation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of sequence allocation not described

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Zelic 2012 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Closed envelope technique, unclear whether envelopes were opaque or sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Observers were blinded as to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No postrandomization withdrawals were reported
Selective reporting (reporting bias)	Unclear risk	Trial protocol was not published, and not all relevant outcomes were reported
Other bias	Low risk	No other significant sources of potential bias were identified

Abbreviations:
ASA = American Society of Anesthesiologists physical classification score.
BMI = body mass index.
CABG = coronary artery bypass graft.
CHO = carbohydrates.
CT = computed tomography.
HOMA-IR = Homeostatic Model Assessment of Insulin Resistance.
IV = intravenous.
OR = operating room.
QUICKI = quantitative insulin sensitivity check index.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Adanir 2008	Intervention group did not receive carbohydrates
Aronsson 2009	Insufficient dose of carbohydrate administered in intervention group
ASAC 2011	Review article, not randomized controlled trial
Awad 2010	None of the prespecified outcomes were reported in this study
Awad 2011	Review article, not a randomized controlled trial
Awad 2011a	Participants did not undergo surgery
Awad 2011b	Participants did not undergo surgery
Awad 2012	None of the prespecified end points for this review were reported
Bisgaard 2006	Letter to the editor, not a randomized controlled trial
Bopp 2011	Intervention group received only 25 g of carbohydrates preoperatively

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Study	Reason for exclusion
Brady 2009	Review article, not a randomized controlled trial
Breitman 2011	Participants received an insufficient dose of carbohydrate, which was administered postoperatively
Burden 2012	Review article, not a randomized controlled trial
Crowe 1984	None of the prespecified outcomes were reported by this trial
Dock-Nascimento 2011	Insufficient dose of carbohydrate was administered preoperatively
Dock-Nascimento 2012	Only 25 g of carbohydrates was administered within 2 hours of surgery
Enoki 1992	None of the prespecified outcomes were reported by this trial
Faria 2009	Insufficient dose of carbohydrate was administered preoperatively
Goodwin 1991	Non-randomized assignment to treatment groups; unclear as to whether the intervention group (orange juice) received sufficient carbohydrates
Hausel 1999	Number of participants randomly assigned to each group was not reported
Hausel 2001	None of the prespecified outcomes were reported by this trial
Helminen 2009	Intervention group was not planned to receive carbohydrates within 4 hours of induction of anaesthesia
Hendry 2010	This was a study of a multi-modal enhanced recovery protocol with multiple co-interventions
Hubner 2010	This was a study of a multi-modal enhanced recovery protocol with multiple co-interventions
Hutchinson 1988	None of the prespecified outcomes were reported by this trial
Itou 2012	Only 25 g of carbohydrates was administered within 2 hours of surgery
Jones 2011	Review article, not a randomized controlled trial
Jones 2012	Conference proceedings with insufficient information to include in the review
Kaska 2006	Duplicate patient series
Korusic 2009	None of the prespecified outcomes were reported by this trial
Lassen 2010	Letter to the editor, not a randomized controlled trial
Lin 1997	Non-randomized assignment to treatment and control groups
Ljungqvist 1991	Non-randomized assignment to treatment and control groups
Ljungqvist 1998	Duplicate patient series
Ljungqvist 2000	Review article, not a randomized controlled trial
Ljungqvist 2001	Review article, not a randomized controlled trial

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Study	Reason for exclusion
Ljungqvist 2010	Letter to the editor, not a randomized controlled trial
Longarela 2005	Letter to the editor, not a randomized controlled trial
Maltby 1988	None of the prespecified outcomes were reported by this trial
Maltby 1991	Non-randomized assignment to treatment and control groups
Maltby 2004	Non-standardized administration of carbohydrate intervention
Maltby 2006	Review article, not a randomized controlled trial
McCaul 2003	Insufficient dose of carbohydrates in the intervention group
Meisner 2008	Insufficient dose of carbohydrates administered to the intervention group
Melis 2006	None of the prespecified outcomes were reported by this trial
Muehling 2009	Studied intervention was multi-modal enhanced recovery protocol; unclear whether this included any carbohydrate intervention
Noblett 2004	Duplicate patient series
Nygren 1995	None of the prespecified outcomes were reported by this trial
Nygren 1998	Non-randomized assignment to intervention and control groups
Nygren 1999	Duplicate patient series
Okabayashi 2010	None of the prespecified outcomes were reported by this trial
Okabayashi 2011	None of the prespecified outcomes were reported by this trial
Phillips 1993	Non-standardized drink as intervention
Power 2004	Review article, not a randomized controlled trial
Protic 2010	Insufficient dose of carbohydrates was administered to intervention group
Protic 2010a	Insufficient dose of carbohydrates was administered to intervention group
Schricker 2008	None of the prespecified outcomes were reported by this trial
Serclova 2009	This was a study of a multi-modal enhanced recovery protocol with multiple co-interventions
Smith 2011	Review article, not a randomized controlled trial
Soop 2000	Review article, not a randomized controlled trial
Stuart 2006	Review article, not a randomized controlled trial
Svanfeldt 2007	None of the prespecified outcomes were reported by this trial
Tanabe 1996	Intervention group received an insufficient dose of carbohydrates

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Study	Reason for exclusion
Taniguchi 2009	Intervention group received an insufficient dose of carbohydrates
Thorell 1996	None of the prespecified outcomes were reported by this trial
Vincent 1991	Intervention group received an insufficient dose of carbohydrates
Wendel 2013	Intervention group received an insufficient dose of carbohydrates
Wilson 1999	Intervention group received an insufficient dose of carbohydrates
Yagci 2008	None of the prespecified outcomes were reported by this trial
Zargar-Shoshtari 2009	This was a study of a multi-modal enhanced recovery protocol with multiple co-interventions
Zhang 2010	Intervention group received an insufficient dose of carbohydrates

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

Aguilar-Nascimento 2012

Methods	Parallel-group randomized controlled trial
Participants	Adult patients undergoing major operations for gastrointestinal cancer Participants analysed: 22 (10 CHO, 12 fasting)
Interventions	Carbohydrate: oral beverage 200 mL containing 11% protein and 89% carbohydrate administered 3 hours before surgery Fasting: for 6 to 8 hours before surgery
Outcomes	Length of hospital stay
Notes	Published as recent conference proceedings with insufficient information to determine whether inclusion criteria for this review are met

Asakura 2013

Methods	3-Arm parallel-group randomized controlled trial
Participants	Patients undergoing surgery of the body surface Age, years: inclusion range 20-79 ASA: I-II only
Interventions	Carbohydrate: OS-1 1000 mL from 20:00 the evening before surgery until 2 hours before anaesthesia Arginaid water: 250 mL of oral arginaid water at 0600 the morning of surgery Fasting: from midnight the night before surgery

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Asakura 2013 *(Continued)*

Outcomes	Quality of recovery score
Notes	Although unlikely to meet the inclusion criteria for this review, this trial is published in abstract form as conference proceedings, and information is insufficient at present to show whether inclusion criteria for this review are met

Forde 2012

Methods	Double-blind parallel-group randomized controlled trial
Participants	Patients undergoing curative colorectal cancer surgery
Interventions	Carbohydrate: oral beverage containing 48 g of carbohydrates in 400 mL administered 3 hours before anaesthesia Placebo: details not reported in conference proceedings
Outcomes	Length of hospital stay, postoperative well-being
Notes	Published as recent conference proceedings with insufficient information to show whether inclusion criteria for this review are met.

Jodlowski 2011

Methods	Parallel-group randomized controlled trial
Participants	Patients undergoing elective colorectal surgery Participants randomized: 48
Interventions	Carbohydrate: details not reported in conference proceedings Fasting: details not reported in conference proceedings
Outcomes	Length of hospital stay, complication rate, insulin resistance, postoperative return of gut function, postoperative well-being
Notes	Published as recent conference proceedings with insufficient information to show whether inclusion criteria for this review are met

Ozer 2013

Methods	2-Arm parallel-group randomized controlled trial
Participants	Female patients undergoing general anaesthesia
Interventions	Carbohydrate: 400 mL oral carbohydrate beverage administered 2 hours before surgery Fasting: for 8 hours before surgery
Outcomes	Postoperative body temperature and vasoconstriction threshold

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Ozer 2013 *(Continued)*

Notes	Although unlikely to meet the inclusion criteria for this review, this trial is published in abstract form as conference proceedings, and information is insufficient at present to show whether inclusion criteria for this review are met

Tsutsumi 2011

Methods	3-Arm parallel-group randomized controlled trial
Participants	Patients receiving surgery Participants randomized: 60 Other details not reported in conference proceedings
Interventions	High carbohydrate: 50 g carbohydrates given between 19:00 hours the day before surgery and 2 hours before surgery Low carbohydrate: 25 g carbohydrates given between 19:00 hours the day before surgery and 2 hours before surgery No carbohydrate: 0 g carbohydrates given between 19:00 hours the day before surgery and 2 hours before surgery
Outcomes	Oxygen consumption, carbon dioxide production and respiratory quotient
Notes	Published as recent conference proceedings with insufficient information to show whether inclusion criteria for this review are met

Yilmaz 2013

Methods	2-Arm parallel-group randomized controlled trial December 2008 to March 2009
Participants	Adult patients scheduled to undergo elective laparoscopic cholecystectomy Participants randomized: 40 (20 CHO, 20 fasting) Age, years: inclusion range 18-60, mean 42.6 for carbohydrate group and 45.7 for fasting group ASA: I-II BMI: less than 30 kg/m^2 Exclusions: conditions that may impair gastrointestinal motility including gastro-oesophageal reflux, potential for a difficult airway, history of motion sickness, diabetes mellitus, severe hepatic or renal failure, any endocrine disorder, allergy to study medications, pregnancy
Interventions	Carbohydrate: oral beverage containing 50 g of carbohydrates in 400 mL administered 2 hours before surgery Fasting: for 8 hours before surgery
Outcomes	Complication rate, postoperative nausea and vomiting

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Yilmaz 2013 *(Continued)*

Notes	This study likely meets the inclusion criteria for this review; however it was identified at the time of the third and final literature search and will be incorporated into the next version of this review. Given that no participants in this study were reported as suffering from complications, inclusion will not affect either of the primary outcomes reported in this review

Zelic 2013

Methods	2-Arm parallel-group randomized controlled trial
Participants	Patients undergoing elective laparoscopic cholecystectomy
Interventions	Carbohydrate: carbohydrate-rich beverage given before surgery Fasting: from the evening before surgery
Outcomes	Stress response following surgery measured by serum cortisol and C-reactive protein
Notes	Although unlikely to meet the inclusion criteria for this review, information is insufficient at present to show whether inclusion criteria for this review are met

Zhao 2013

Methods	2-Arm parallel-group randomized controlled trial November 2009 to March 2011
Participants	Oesophageal cancer patients receiving radical operation Participants randomized: 68 (34 fast-track surgery, 34 control)
Interventions	Interventions were not described in the abstract of the conference proceedings
Outcomes	Length of hospital stay, complication rate, return of gastrointestinal function, insulin resistance
Notes	Although unlikely to meet the inclusion criteria for this review, this trial is published in abstract form as conference proceedings, and information is insufficient at present to show whether inclusion criteria for this review are met

ASA: American Society of Anesthesiologists physical classification score.
BMI: body mass index.
CHO: carbohydrate.

DATA AND ANALYSES

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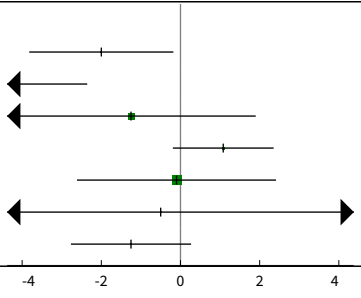
Comparison 1. CHO versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Length of hospital stay	14	867	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.38, 0.12]
1.1 Major abdominal surgery	7	464	Mean Difference (IV, Random, 95% CI)	-1.23 [-2.79, 0.33]
1.2 Minor abdominal surgery	3	161	Mean Difference (IV, Random, 95% CI)	-0.05 [-0.12, 0.02]
1.3 Orthopaedic surgery	4	126	Mean Difference (IV, Random, 95% CI)	-0.26 [-1.11, 0.58]
1.4 Cardiac surgery	1	116	Mean Difference (IV, Random, 95% CI)	1.0 [-0.90, 2.90]
2 Complication rate	10	594	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.73, 1.16]
3 Postop insulin resistance (HOMA-IR)	4	179	Mean Difference (IV, Random, 95% CI)	-4.00 [-8.19, 0.18]
4 Postop insulin sensitivity (clamp)	2	29	Mean Difference (IV, Random, 95% CI)	0.70 [0.14, 1.26]
5 Postop fatigue	4	468	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.27, 0.54]
6 Postop well-being	3	242	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.25, 0.25]
7 Postop nausea at 24 hours	2	234	Mean Difference (IV, Random, 95% CI)	-1.71 [-4.06, 0.64]
8 Postop vomiting	3	248	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.65, 2.12]
9 Postop time to first bowel motion	2	83	Mean Difference (IV, Random, 95% CI)	-0.34 [-0.74, 0.05]

Analysis 1.1. Comparison 1 CHO versus placebo, Outcome 1 Length of hospital stay.

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Major abdominal surgery							
Yuill 2005	31	8 (3)	34	10 (4.4)		1.81%	-2[-3.82,-0.18]
Noblett 2006	12	7.5 (2.8)	11	13 (4.6)		0.64%	-5.5[-8.64,-2.36]
Mathur 2010	69	8.7 (6.7)	73	9.9 (11.9)		0.63%	-1.25[-4.4,1.9]
Ozdemir 2011	15	3.9 (2.2)	15	2.8 (1.3)		3.44%	1.08[-0.19,2.35]
Braga 2012	18	14.2 (3.1)	18	14.3 (4.4)		0.98%	-0.1[-2.61,2.41]
Yang 2012	24	9.7 (13.7)	24	10.2 (18.1)		0.08%	-0.5[-9.6,8.6]
Lidder 2013	59	7 (3.5)	61	8.3 (4.9)		2.52%	-1.25[-2.77,0.27]



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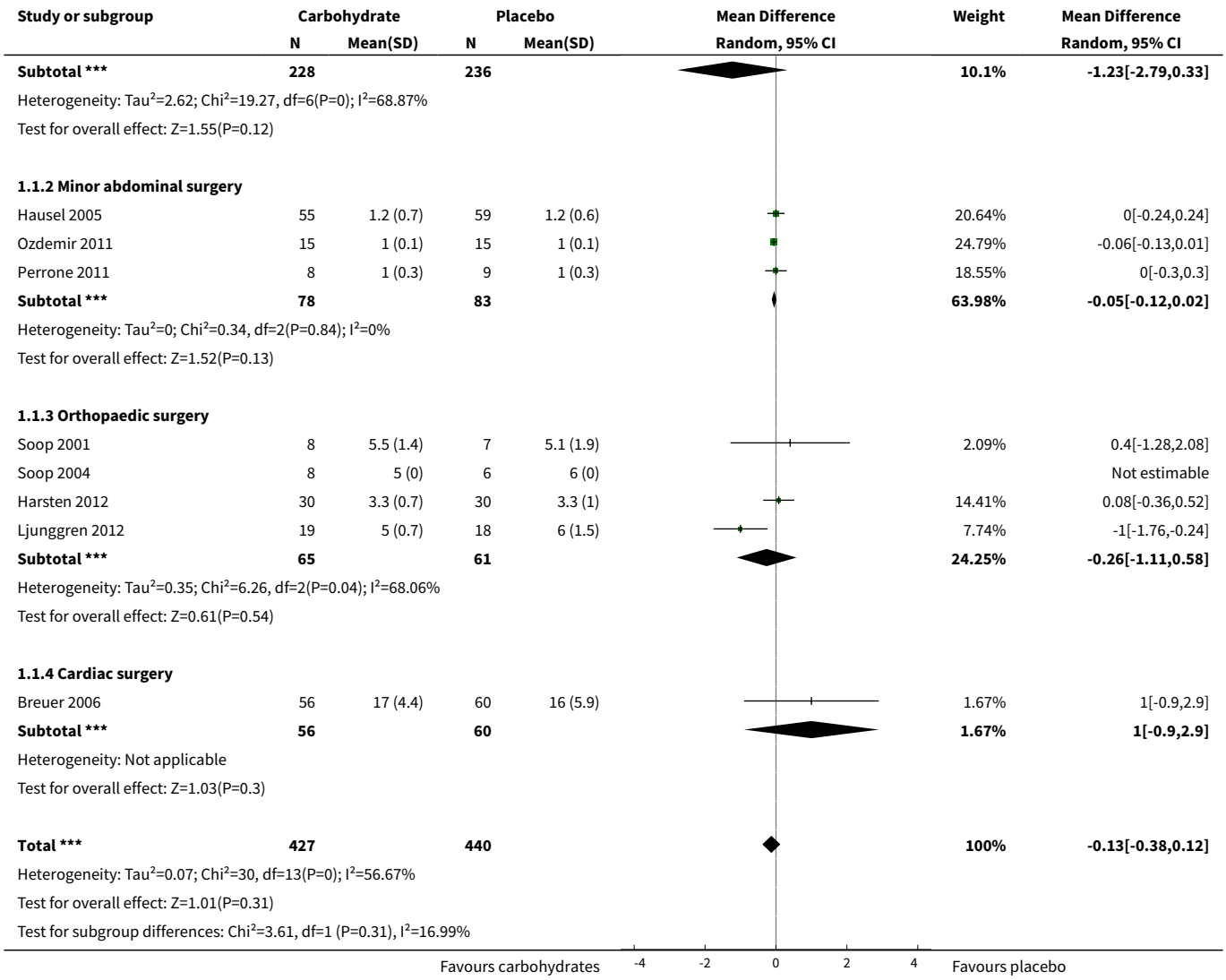
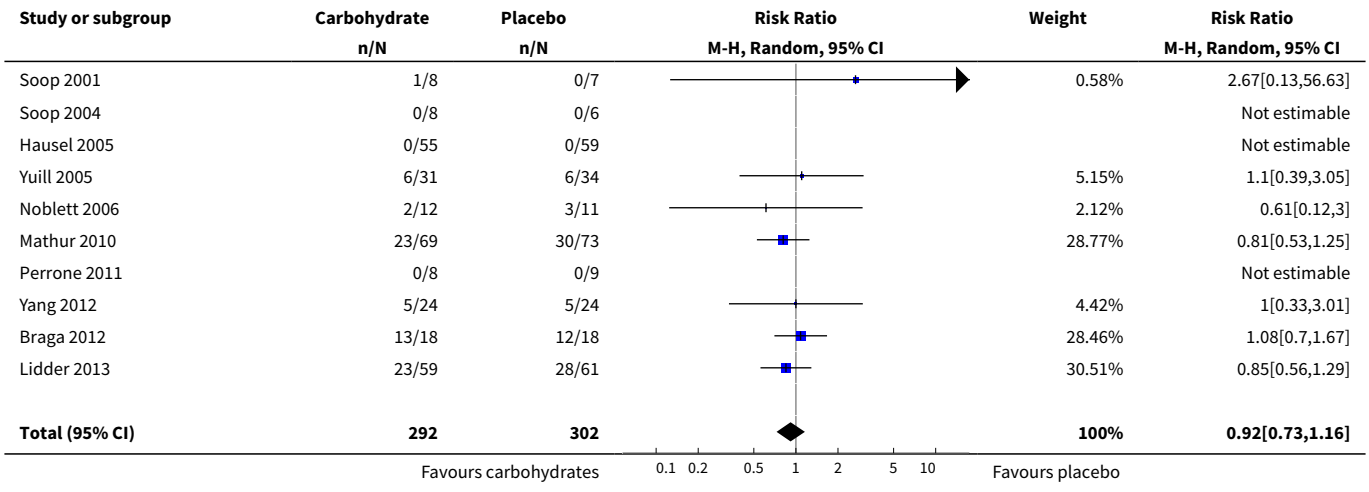


Analysis 1.2. Comparison 1 CHO versus placebo, Outcome 2 Complication rate.



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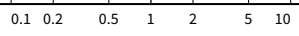
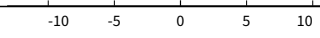
Study or subgroup	Carbohydrate n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 73 (Carbohydrate), 84 (Placebo)					
Heterogeneity: Tau^2=0; Chi^2=1.89, df=6(P=0.93); I^2=0%					
Test for overall effect: Z=0.74(P=0.46)					



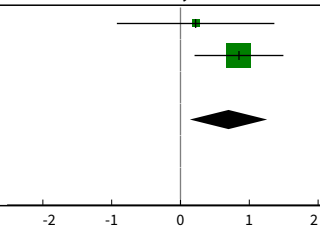
Analysis 1.3. Comparison 1 CHO versus placebo, Outcome 3 Postop insulin resistance (HOMA-IR).

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Mathur 2010	37	1.6 (1.5)	45	1.4 (1.5)		30.28%	0.15[-0.5,0.8]
Wang 2010	16	17 (4.4)	16	25 (5.2)		25.53%	-8[-11.35,-4.65]
Perrone 2011	8	2.8 (2)	9	5.7 (3.5)		27.12%	-2.99[-5.67,-0.31]
Yang 2012	24	5.7 (6.9)	24	12.7 (15.3)		17.08%	-7.01[-13.73,-0.29]
Total * **	**85**		**94**			**100%**	**-4[-8.19,0.18]**
Heterogeneity: Tau^2=14.96; Chi^2=29.83, df=3(P<0.0001); I^2=89.94%							
Test for overall effect: Z=1.87(P=0.06)							



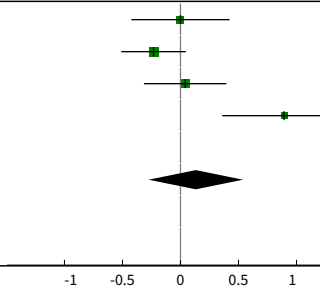
Analysis 1.4. Comparison 1 CHO versus placebo, Outcome 4 Postop insulin sensitivity (clamp).

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Soop 2001	8	2.6 (0.5)	7	2.4 (1.5)		24.13%	0.22[-0.92,1.36]
Soop 2004	8	2.3 (0.7)	6	1.4 (0.5)		75.87%	0.85[0.2,1.5]
Total * **	**16**		**13**			**100%**	**0.7[0.14,1.26]**
Heterogeneity: Tau^2=0; Chi^2=0.88, df=1(P=0.35); I^2=0%							
Test for overall effect: Z=2.43(P=0.01)							



Analysis 1.5. Comparison 1 CHO versus placebo, Outcome 5 Postop fatigue.

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Placebo N	Placebo Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Bisgaard 2004	43	6 (2.3)	43	6 (2)		24.25%	0[-0.42,0.42]
Lauwick 2009	100	37 (30)	100	44 (30)		28.47%	-0.23[-0.51,0.05]
Mathur 2010	58	44.6 (28.3)	64	43.4 (30.6)		26.26%	0.04[-0.31,0.4]
Harsten 2012	30	39 (25)	30	15 (28)		21.02%	0.89[0.36,1.42]
Total * **	**231**		**237**			**100%**	**0.13[-0.27,0.54]**
Heterogeneity: Tau^2=0.13; Chi^2=13.5, df=3(P=0); I^2=77.78%							
Test for overall effect: Z=0.64(P=0.52)							



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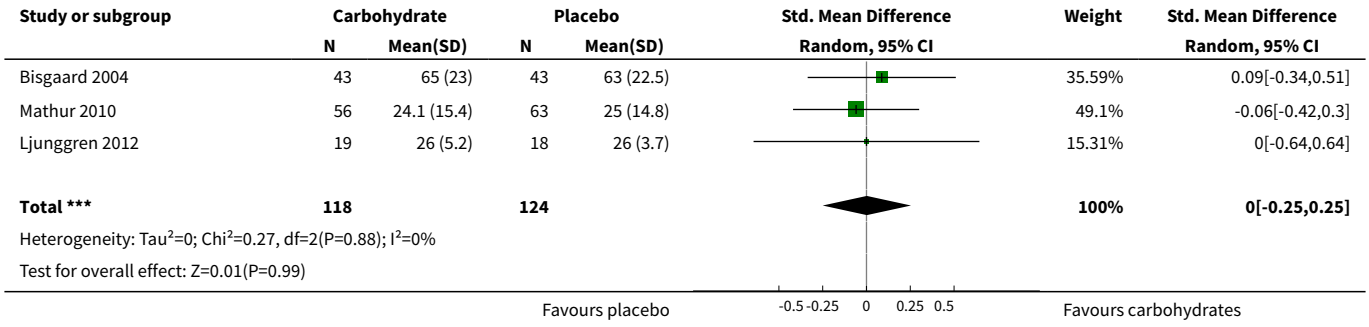
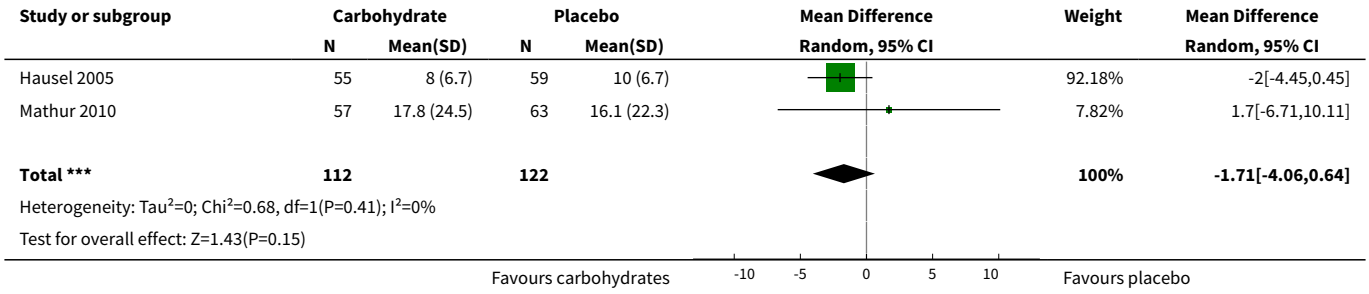
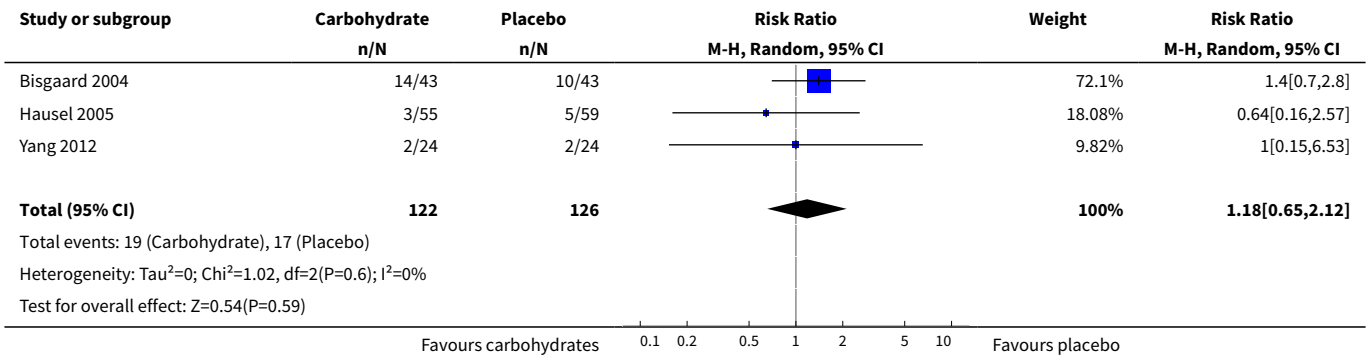
Analysis 1.6. Comparison 1 CHO versus placebo, Outcome 6 Postop well-being.



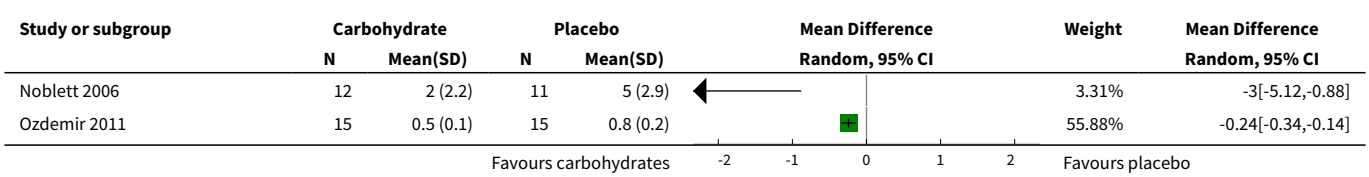
Analysis 1.7. Comparison 1 CHO versus placebo, Outcome 7 Postop nausea at 24 hours.



Analysis 1.8. Comparison 1 CHO versus placebo, Outcome 8 Postop vomiting.



Analysis 1.9. Comparison 1 CHO versus placebo, Outcome 9 Postop time to first bowel motion.



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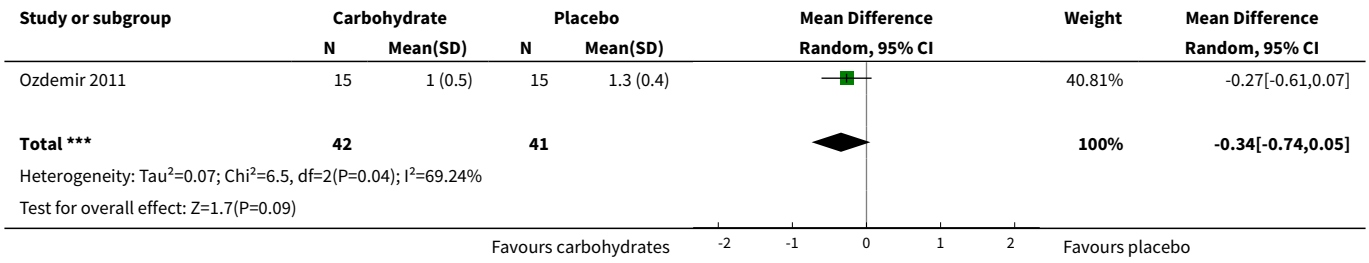

Comparison 2. CHO versus fasting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Length of hospital stay	10	656	Mean Difference (IV, Random, 95% CI)	-0.42 [-0.79, -0.06]
1.1 Major abdominal surgery	5	276	Mean Difference (IV, Random, 95% CI)	-2.02 [-4.13, 0.08]
1.2 Minor abdominal surgery	3	203	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.18, 0.03]
1.3 Orthopaedic surgery	1	39	Mean Difference (IV, Random, 95% CI)	-1.0 [-1.73, -0.27]
1.4 Cardiac surgery	2	138	Mean Difference (IV, Random, 95% CI)	-0.47 [-3.41, 2.47]
2 Complication rate	6	386	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.87, 1.16]
3 Postop insulin resistance (HOMA-IR)	4	110	Mean Difference (IV, Random, 95% CI)	-1.33 [-4.12, 1.47]
4 Postop fatigue	2	108	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.47, 0.31]
5 Postop well-being	2	87	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.40, 0.47]
6 Postop vomiting	2	214	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.58, 2.63]
7 Postop time to passage of first flatus	2	75	Mean Difference (IV, Random, 95% CI)	-0.39 [-0.70, -0.07]
8 Postop time to first bowel movement	2	84	Mean Difference (IV, Random, 95% CI)	-0.18 [-0.29, -0.07]

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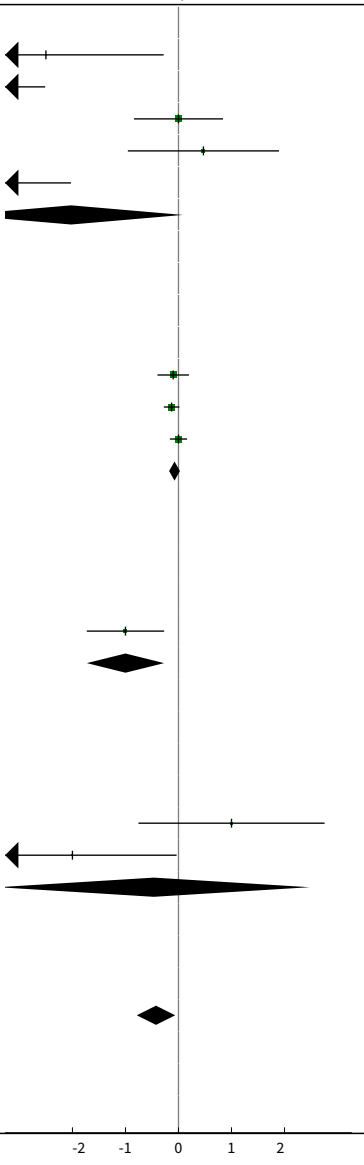
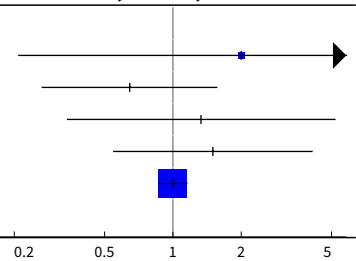
Analysis 2.1. Comparison 2 CHO versus fasting, Outcome 1 Length of hospital stay.

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Fasting N	Fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.1.1 Major abdominal surgery							
Noblett 2006	12	7.5 (2.8)	12	10 (2.7)		2.37%	-2.5[-4.72,-0.28]
An 2008	27	11 (1.2)	24	15.1 (3.8)		4.2%	-4.1[-5.69,-2.51]
Kaska 2010	74	11 (2.2)	75	11 (3)		9.98%	0[-0.84,0.84]
Ozdemir 2011	15	3.9 (2.2)	15	3.4 (1.8)		4.97%	0.47[-0.96,1.9]
Pexe-Machado 2013	10	8.1 (3.8)	12	15.6 (8.7)		0.43%	-7.5[-12.97,-2.03]
Subtotal ***	**138**		**138**			**21.95%**	**-2.02[-4.13,0.08]**
Heterogeneity: Tau^2=4.47; Chi^2=31.15, df=4(P<0.0001); I^2=87.16%							
Test for overall effect: Z=1.88(P=0.06)							
2.1.2 Minor abdominal surgery							
Hausel 2005	55	1.2 (0.7)	58	1.3 (0.9)		18.76%	-0.1[-0.4,0.2]
Ozdemir 2011	15	1 (0.1)	15	1.1 (0.3)		20.73%	-0.13[-0.28,0.02]
Yildiz 2013	30	1 (0.3)	30	1 (0.3)		20.57%	0[-0.16,0.16]
Subtotal ***	**100**		**103**			**60.07%**	**-0.07[-0.18,0.03]**
Heterogeneity: Tau^2=0; Chi^2=1.39, df=2(P=0.5); I^2=0%							
Test for overall effect: Z=1.44(P=0.15)							
2.1.3 Orthopaedic surgery							
Ljunggren 2012	19	5 (0.7)	20	6 (1.5)		11.49%	-1[-1.73,-0.27]
Subtotal ***	**19**		**20**			**11.49%**	**-1[-1.73,-0.27]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.69(P=0.01)							
2.1.4 Cardiac surgery							
Breuer 2006	56	17 (4.4)	44	16 (4.4)		3.56%	1[-0.75,2.75]
Tran 2013	19	4.8 (1.2)	19	6.8 (4.2)		2.94%	-2[-3.96,-0.04]
Subtotal ***	**75**		**63**			**6.5%**	**-0.47[-3.41,2.47]**
Heterogeneity: Tau^2=3.6; Chi^2=4.98, df=1(P=0.03); I^2=79.94%							
Test for overall effect: Z=0.31(P=0.76)							
Total ***	**332**		**324**			**100%**	**-0.42[-0.79,-0.06]**
Heterogeneity: Tau^2=0.16; Chi^2=49.13, df=10(P<0.0001); I^2=79.64%							
Test for overall effect: Z=2.29(P=0.02)							
Test for subgroup differences: Chi^2=9.35, df=1 (P=0.02), I^2=67.91%							



Analysis 2.2. Comparison 2 CHO versus fasting, Outcome 2 Complication rate.

Study or subgroup	Carbohydrate n/N	Fasting n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Hausel 2005	0/55	0/58			Not estimable
Noblett 2006	2/12	1/12		0.41%	2[0.21,19.23]
Kaska 2010	7/74	11/75		2.65%	0.64[0.26,1.57]
Zelic 2012	4/20	3/20		1.13%	1.33[0.34,5.21]
Pexe-Machado 2013	5/10	4/12		2.06%	1.5[0.55,4.13]
Tran 2013	18/19	18/19		93.75%	1[0.86,1.16]



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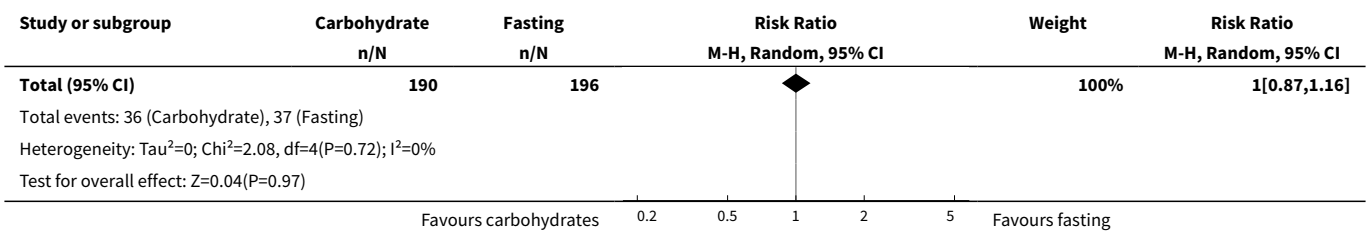
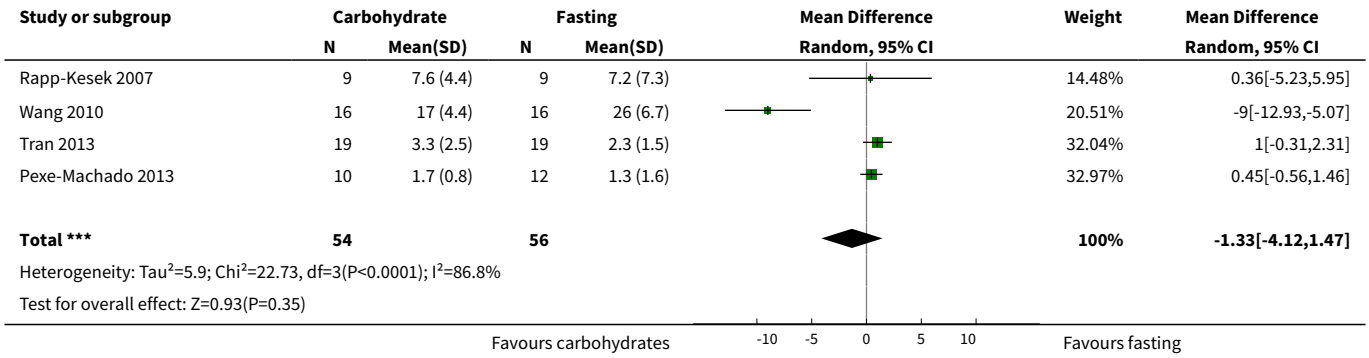
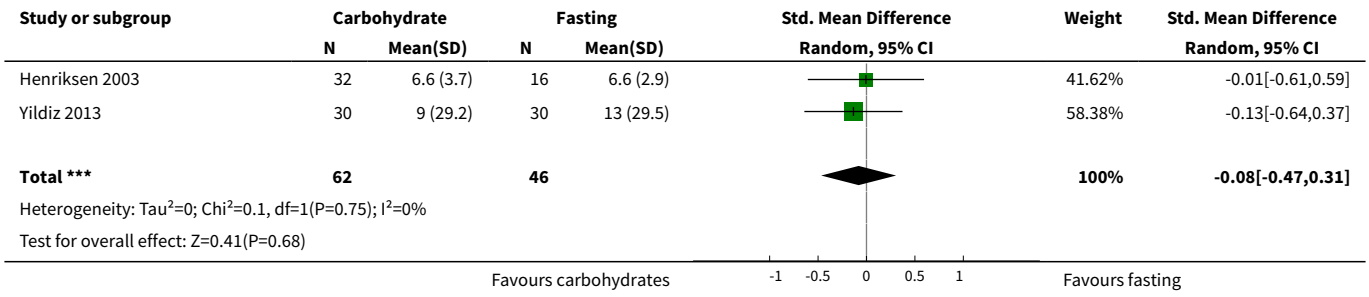


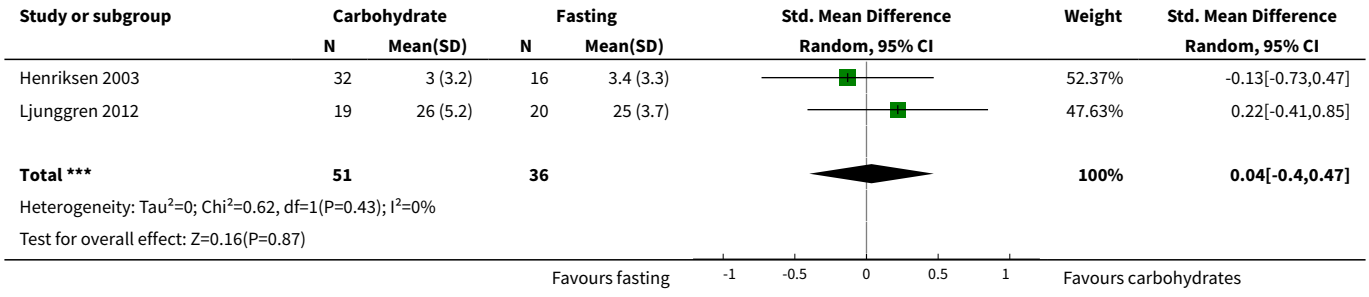
Analysis 2.3. Comparison 2 CHO versus fasting, Outcome 3 Postop insulin resistance (HOMA-IR).



Analysis 2.4. Comparison 2 CHO versus fasting, Outcome 4 Postop fatigue.



Analysis 2.5. Comparison 2 CHO versus fasting, Outcome 5 Postop well-being.



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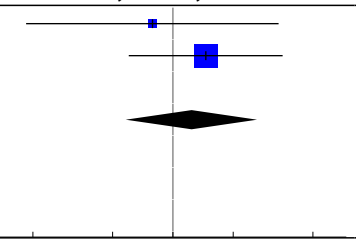
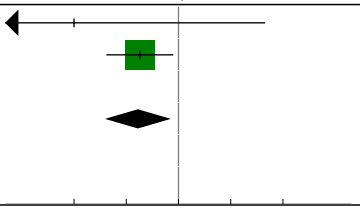
Analysis 2.6. Comparison 2 CHO versus fasting, Outcome 6 Postop vomiting.

Study or subgroup	Carbohydrate n/N	Fasting n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Hausel 2005	3/55	4/58		27.06%	0.79[0.19,3.37]
Jarvela 2008	10/50	7/51		72.94%	1.46[0.6,3.53]
Total (95% CI)	**105**	**109**		**100%**	**1.24[0.58,2.63]**
Total events: 13 (Carbohydrate), 11 (Fasting)					
Heterogeneity: Tau^2=0; Chi^2=0.5, df=1(P=0.48); I^2=0%					
Test for overall effect: Z=0.55(P=0.58)					



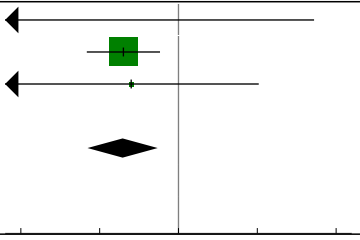
Analysis 2.7. Comparison 2 CHO versus fasting, Outcome 7 Postop time to passage of first flatus.

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Fasting N	Fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Noblett 2006	12	2 (3)	12	3 (1.3)		2.98%	-1[-2.83,0.83]
An 2008	27	3.2 (0.6)	24	3.6 (0.5)		97.02%	-0.37[-0.69,-0.05]
Total ***	**39**		**36**			**100%**	**-0.39[-0.7,-0.07]**
Heterogeneity: Tau^2=0; Chi^2=0.44, df=1(P=0.51); I^2=0%							
Test for overall effect: Z=2.41(P=0.02)							



Analysis 2.8. Comparison 2 CHO versus fasting, Outcome 8 Postop time to first bowel movement.

Study or subgroup	Carbohydrate N	Carbohydrate Mean(SD)	Fasting N	Fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Noblett 2006	12	2 (2.2)	12	3.5 (2.6)		0.33%	-1.5[-3.43,0.43]
Ozdemir 2011	15	0.5 (0.1)	15	0.7 (0.2)		92.09%	-0.17[-0.29,-0.06]
Ozdemir 2011	15	1 (0.5)	15	1.2 (0.6)		7.58%	-0.15[-0.55,0.25]
Total ***	**42**		**42**			**100%**	**-0.18[-0.29,-0.07]**
Heterogeneity: Tau^2=0; Chi^2=1.82, df=2(P=0.4); I^2=0%							
Test for overall effect: Z=3.12(P=0)							



Comparison 3. CHO versus placebo or fasting

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Length of hospital stay	19	1351	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.56, -0.04]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Major abdominal surgery	10	713	Mean Difference (IV, Random, 95% CI)	-1.66 [-2.97, -0.34]
1.2 Minor abdominal surgery	4	294	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.14, 0.00]
1.3 Orthopaedic surgery	4	146	Mean Difference (IV, Random, 95% CI)	-0.29 [-1.18, 0.60]
1.4 Cardiac surgery	2	198	Mean Difference (IV, Random, 95% CI)	-0.44 [-3.37, 2.50]
2 Length of hospital stay	19		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Adequate blinding	4	291	Mean Difference (IV, Random, 95% CI)	-0.59 [-1.73, 0.55]
2.2 Unclear/inadequate blinding	15	1060	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.55, -0.02]
3 Complication rate	14	913	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.86, 1.11]
4 Postop insulin resistance (HOMA-IR)	7	273	Mean Difference (IV, Random, 95% CI)	-1.59 [-3.35, 0.17]
5 Postop insulin sensitivity (clamp)	3	41	Mean Difference (IV, Random, 95% CI)	0.76 [0.24, 1.29]
6 Postop fatigue	6	576	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.23, 0.35]
7 Postop well-being	4	310	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.22, 0.23]
8 Postop nausea at 24 hours	2	292	Mean Difference (IV, Random, 95% CI)	-1.69 [-4.12, 0.74]
9 Postop vomiting	4	407	Risk Ratio (M-H, Random, 95% CI)	1.25 [0.77, 2.04]
10 Postop time to passage of first flatus	2	86	Mean Difference (IV, Random, 95% CI)	-0.39 [-0.70, -0.07]
11 Postop time to first bowel movement	2	125	Mean Difference (IV, Random, 95% CI)	-0.28 [-0.62, 0.05]

Analysis 3.1. Comparison 3 CHO versus placebo or fasting, Outcome 1 Length of hospital stay.

Study or subgroup	Carbohydrates N	Carbohydrates Mean(SD)	Placebo or fasting N	Placebo or fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.1.1 Major abdominal surgery							

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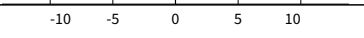
Study or subgroup	Carbohydrates N	Carbohydrates Mean(SD)	Placebo or fasting N	Placebo or fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Yuill 2005	31	8 (3)	34	10 (4.4)		1.75%	-2[-3.82,-0.18]
Noblett 2006	12	7.5 (2.8)	23	11.4 (4)		1.17%	-3.93[-6.2,-1.66]
An 2008	27	11 (1.2)	24	15.1 (3.8)		2.22%	-4.1[-5.69,-2.51]
Mathur 2010	69	8.7 (6.7)	73	9.9 (11.9)		0.63%	-1.25[-4.4,1.9]
Kaska 2010	74	11 (2.2)	75	11 (3)		5.8%	0[-0.84,0.84]
Ozdemir 2011	15	3.9 (2.2)	30	3.1 (1.6)		3.37%	0.78[-0.45,2.01]
Braga 2012	18	14.2 (3.1)	18	14.3 (4.4)		0.97%	-0.1[-2.61,2.41]
Yang 2012	24	9.7 (13.7)	24	10.2 (18.1)		0.08%	-0.5[-9.6,8.6]
Pexe-Machado 2013	10	8.1 (3.8)	12	15.6 (8.7)		0.22%	-7.5[-12.97,-2.03]
Lidder 2013	59	7 (3.5)	61	8.3 (4.9)		2.4%	-1.25[-2.77,0.27]
Subtotal * **	**339**		**374**			**18.62%**	**-1.66[-2.97,-0.34]**
Heterogeneity: Tau²=2.92; Chi²=41.68, df=9(P<0.0001); I²=78.41%							
Test for overall effect: Z=2.47(P=0.01)							
3.1.2 Minor abdominal surgery							
Hausel 2005	55	1.2 (0.7)	117	1.3 (0.8)		13.75%	-0.05[-0.28,0.18]
Perrone 2011	8	1 (0.3)	9	1 (0.3)		12.69%	0[-0.3,0.3]
Ozdemir 2011	15	1 (0.1)	30	1.1 (0.2)		15.21%	-0.1[-0.18,-0.01]
Yildiz 2013	30	1 (0.3)	30	1 (0.3)		14.58%	0[-0.16,0.16]
Subtotal * **	**108**		**186**			**56.24%**	**-0.07[-0.14,0]**
Heterogeneity: Tau²=0; Chi²=1.32, df=3(P=0.73); I²=0%							
Test for overall effect: Z=1.9(P=0.06)							
3.1.3 Orthopaedic surgery							
Soop 2001	8	5.5 (1.4)	7	5.1 (1.9)		2.01%	0.4[-1.28,2.08]
Soop 2004	8	5 (0)	6	6 (0)			Not estimable
Harsten 2012	30	3.3 (0.7)	30	3.3 (1)		10.63%	0.08[-0.36,0.52]
Ljunggren 2012	19	5 (0.7)	38	6 (1.5)		8.67%	-1[-1.58,-0.42]
Subtotal * **	**65**		**81**			**21.31%**	**-0.29[-1.18,0.6]**
Heterogeneity: Tau²=0.43; Chi²=9.21, df=2(P=0.01); I²=78.28%							
Test for overall effect: Z=0.64(P=0.52)							
3.1.4 Cardiac surgery							
Breuer 2006	56	17 (4.4)	104	16 (5.3)		2.31%	1[-0.55,2.55]
Tran 2013	19	4.8 (1.2)	19	6.8 (4.2)		1.53%	-2[-3.96,-0.04]
Subtotal * **	**75**		**123**			**3.84%**	**-0.44[-3.37,2.5]**
Heterogeneity: Tau²=3.69; Chi²=5.52, df=1(P=0.02); I²=81.9%							
Test for overall effect: Z=0.29(P=0.77)							
Total * **	**587**		**764**			**100%**	**-0.3[-0.56,-0.04]**
Heterogeneity: Tau²=0.11; Chi²=69.23, df=18(P<0.0001); I²=74%							
Test for overall effect: Z=2.3(P=0.02)							
Test for subgroup differences: Chi²=5.9, df=1 (P=0.12), I²=49.11%							



Favours carbohydrates

Favours control

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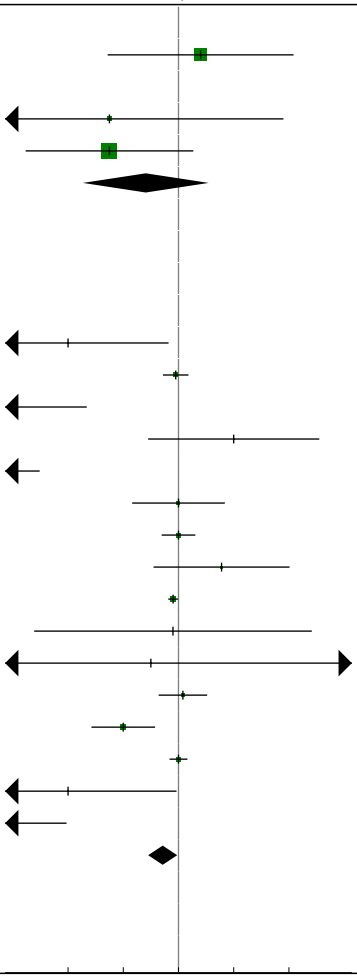
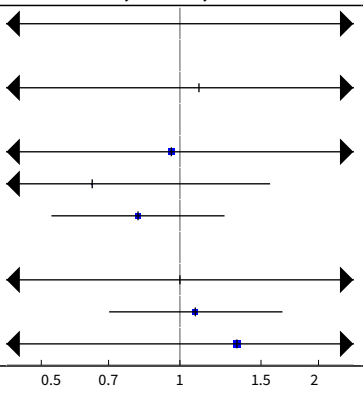
Analysis 3.2. Comparison 3 CHO versus placebo or fasting, Outcome 2 Length of hospital stay.

Study or subgroup	Carbohydrates N	Carbohydrates Mean(SD)	Placebo or fasting N	Placebo or fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.2.1 Adequate blinding							
Soop 2001	8	5.5 (1.4)	7	5.1 (1.9)		39.86%	0.4[-1.28,2.08]
Soop 2004	8	5 (0)	6	6 (0)			Not estimable
Mathur 2010	69	8.7 (6.7)	73	9.9 (11.9)		12.55%	-1.25[-4.4,1.9]
Lidder 2013	59	7 (3.5)	61	8.3 (4.9)		47.59%	-1.25[-2.77,0.27]
Subtotal ***	**144**		**147**			**100%**	**-0.59[-1.73,0.55]**
Heterogeneity: Tau²=0.11; Chi²=2.22, df=2(P=0.33); I²=10.08%							
Test for overall effect: Z=1.02(P=0.31)							
3.2.2 Unclear/inadequate blinding							
Yuill 2005	31	8 (3)	34	10 (4.4)		1.85%	-2[-3.82,-0.18]
Hausel 2005	55	1.2 (0.7)	117	1.3 (0.8)		14.46%	-0.05[-0.28,0.18]
Noblett 2006	12	7.5 (2.8)	23	11.4 (4)		1.24%	-3.93[-6.2,-1.66]
Breuer 2006	56	17 (4.4)	104	16 (5.3)		2.45%	1[-0.55,2.55]
An 2008	27	11 (1.2)	24	15.1 (3.8)		2.35%	-4.1[-5.69,-2.51]
Kaska 2010	74	11 (2.2)	75	11 (3)		6.13%	0[-0.84,0.84]
Perrone 2011	8	1 (0.3)	9	1 (0.3)		13.35%	0[-0.3,0.3]
Ozdemir 2011	15	3.9 (2.2)	30	3.1 (1.6)		3.57%	0.78[-0.45,2.01]
Ozdemir 2011	15	1 (0.1)	30	1.1 (0.2)		15.98%	-0.1[-0.18,-0.01]
Braga 2012	18	14.2 (3.1)	18	14.3 (4.4)		1.03%	-0.1[-2.61,2.41]
Yang 2012	24	9.7 (13.7)	24	10.2 (18.1)		0.08%	-0.5[-9.6,8.6]
Harsten 2012	30	3.3 (0.7)	30	3.3 (1)		11.2%	0.08[-0.36,0.52]
Ljunggren 2012	19	5 (0.7)	38	6 (1.5)		9.14%	-1[-1.58,-0.42]
Yildiz 2013	30	1 (0.3)	30	1 (0.3)		15.32%	0[-0.16,0.16]
Tran 2013	19	4.8 (1.2)	19	6.8 (4.2)		1.62%	-2[-3.96,-0.04]
Pexe-Machado 2013	10	8.1 (3.8)	12	15.6 (8.7)		0.23%	-7.5[-12.97,-2.03]
Subtotal ***	**443**		**617**			**100%**	**-0.29[-0.55,-0.02]**
Heterogeneity: Tau²=0.11; Chi²=66.15, df=15(P<0.0001); I²=77.32%							
Test for overall effect: Z=2.13(P=0.03)							
Test for subgroup differences: Chi²=0.26, df=1 (P=0.61), I²=0%							



Analysis 3.3. Comparison 3 CHO versus placebo or fasting, Outcome 3 Complication rate.

Study or subgroup	Carbohydrates n/N	Placebo or fasting n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Soop 2001	1/8	0/7		0.16%	2.67[0.13,56.63]
Soop 2004	0/8	0/6			Not estimable
Yuill 2005	6/31	6/34		1.45%	1.1[0.39,3.05]
Hausel 2005	0/55	0/117			Not estimable
Noblett 2006	2/12	4/23		0.63%	0.96[0.2,4.5]
Kaska 2010	7/74	11/75		1.91%	0.64[0.26,1.57]
Mathur 2010	23/69	30/73		8.12%	0.81[0.53,1.25]
Perrone 2011	0/8	0/9			Not estimable
Yang 2012	5/24	5/24		1.25%	1[0.33,3.01]
Braga 2012	13/18	12/18		8.04%	1.08[0.7,1.67]
Zelic 2012	4/20	3/20		0.82%	1.33[0.34,5.21]



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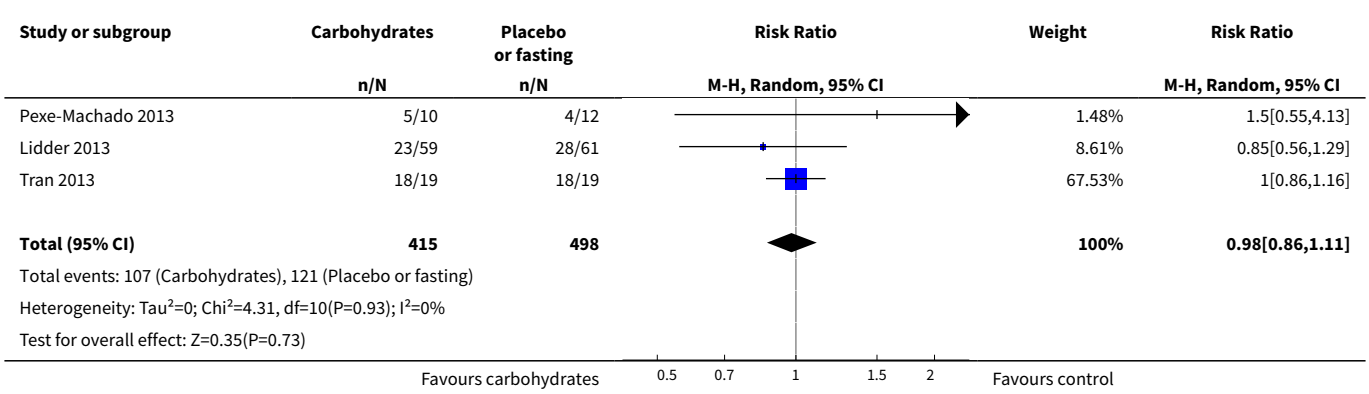
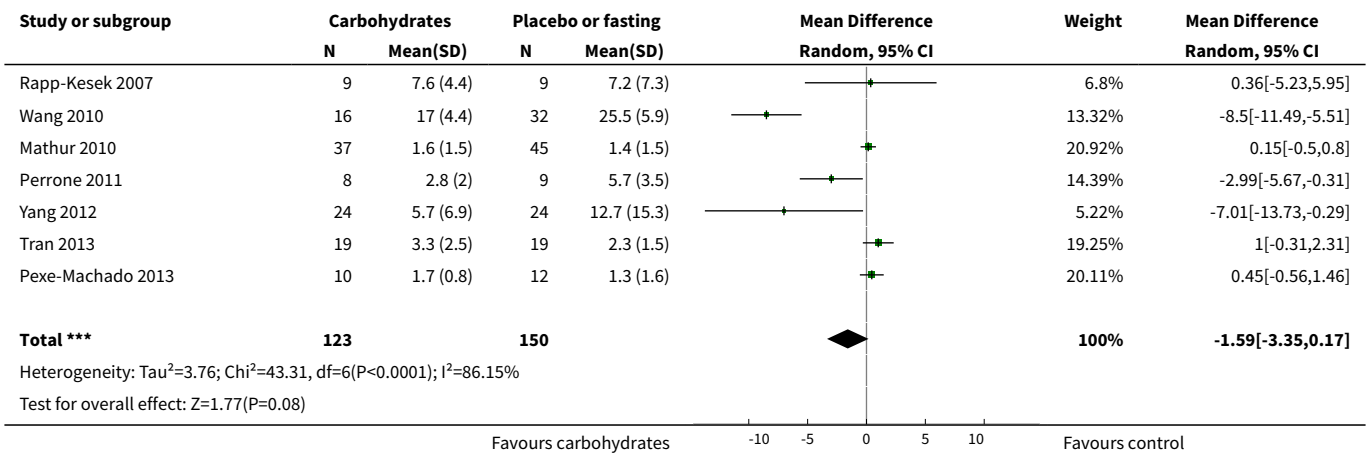
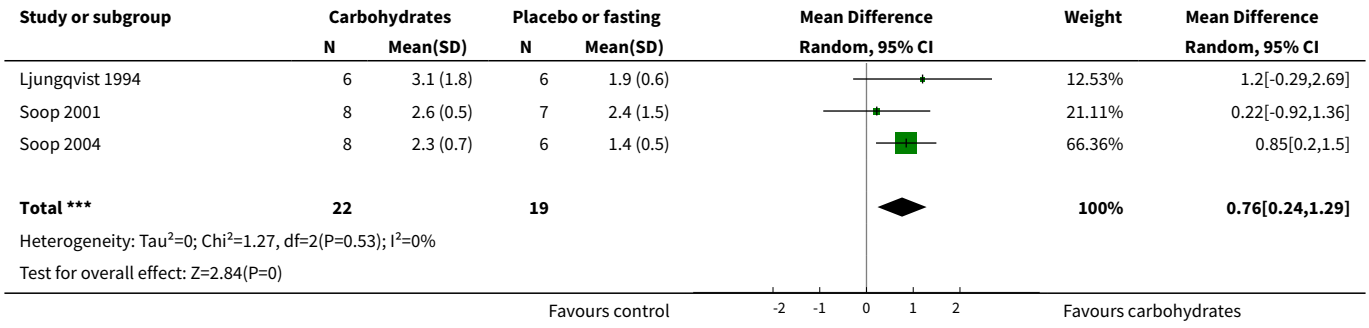


Analysis 3.4. Comparison 3 CHO versus placebo or fasting, Outcome 4 Postop insulin resistance (HOMA-IR).



Analysis 3.5. Comparison 3 CHO versus placebo or fasting, Outcome 5 Postop insulin sensitivity (clamp).



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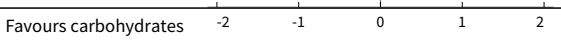
Analysis 3.6. Comparison 3 CHO versus placebo or fasting, Outcome 6 Postop fatigue.

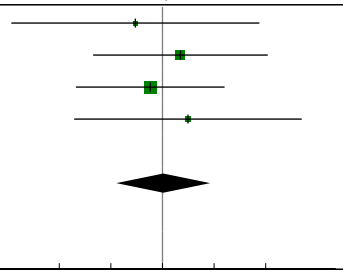
Study or subgroup	Carbohydrates N	Carbohydrates Mean(SD)	Placebo or fasting N	Placebo or fasting Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Henriksen 2003	32	6.6 (3.7)	16	6.6 (2.9)		12.57%	-0.01[-0.61,0.59]
Bisgaard 2004	43	6 (2.3)	43	6 (2)		17.25%	0[-0.42,0.42]
Lauwick 2009	100	37 (30)	100	44 (30)		21.78%	-0.23[-0.51,0.05]
Mathur 2010	58	44.6 (28.3)	64	43.4 (30.6)		19.33%	0.04[-0.31,0.4]
Harsten 2012	30	39 (25)	30	15 (28)		14.2%	0.89[0.36,1.42]
Yildiz 2013	30	9 (29.2)	30	13 (29.5)		14.87%	-0.13[-0.64,0.37]
Total ***	**293**		**283**			**100%**	**0.06[-0.23,0.35]**
Heterogeneity: Tau^2=0.08; Chi^2=13.8, df=5(P=0.02); I^2=63.77%							
Test for overall effect: Z=0.43(P=0.67)							



Favours carbohydrates — Favours control

Analysis 3.7. Comparison 3 CHO versus placebo or fasting, Outcome 7 Postop well-being.

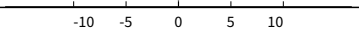
Study or subgroup	Carbohydrates N	Carbohydrates Mean(SD)	Placebo or fasting N	Placebo or fasting Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Henriksen 2003	32	3 (3.2)	16	3.4 (3.3)		14.31%	-0.13[-0.73,0.47]
Bisgaard 2004	43	65 (23)	43	63 (22.5)		28.87%	0.09[-0.34,0.51]
Mathur 2010	56	24.1 (15.4)	63	25 (14.8)		39.83%	-0.06[-0.42,0.3]
Ljunggren 2012	19	26 (5.2)	38	25.5 (3.7)		16.99%	0.12[-0.43,0.67]
Total ***	**150**		**160**			**100%**	**0[-0.22,0.23]**
Heterogeneity: Tau^2=0; Chi^2=0.64, df=3(P=0.89); I^2=0%							
Test for overall effect: Z=0.03(P=0.97)							



Favours control — Favours carbohydrates

Analysis 3.8. Comparison 3 CHO versus placebo or fasting, Outcome 8 Postop nausea at 24 hours.

Study or subgroup	Carbohydrates N	Carbohydrates Mean(SD)	Placebo or fasting N	Placebo or fasting Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Hausel 2005	55	8 (6.7)	117	10 (10.1)		91.63%	-2[-4.54,0.54]
Mathur 2010	57	17.8 (24.5)	63	16.1 (22.3)		8.37%	1.7[-6.71,10.11]
Total ***	**112**		**180**			**100%**	**-1.69[-4.12,0.74]**
Heterogeneity: Tau^2=0; Chi^2=0.68, df=1(P=0.41); I^2=0%							
Test for overall effect: Z=1.36(P=0.17)							



Favours carbohydrates — Favours control

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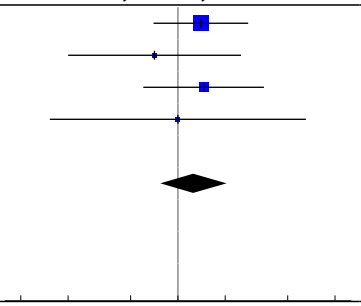
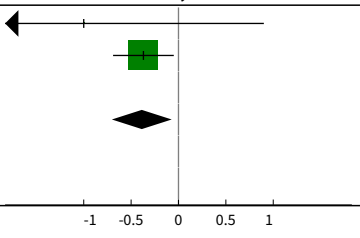
Analysis 3.9. Comparison 3 CHO versus placebo or fasting, Outcome 9 Postop vomiting.

Study or subgroup	Carbohydrates n/N	Placebo or fasting n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bisgaard 2004	14/43	10/43		48.78%	1.4[0.7,2.8]
Hausel 2005	3/55	9/117		14.59%	0.71[0.2,2.52]
Jarvela 2008	10/50	7/51		29.98%	1.46[0.6,3.53]
Yang 2012	2/24	2/24		6.65%	1[0.15,6.53]
Total (95% CI)	**172**	**235**		**100%**	**1.25[0.77,2.04]**
Total events: 29 (Carbohydrates), 28 (Placebo or fasting)					
Heterogeneity: Tau^2=0; Chi^2=1.05, df=3(P=0.79); I^2=0%					
Test for overall effect: Z=0.92(P=0.36)					



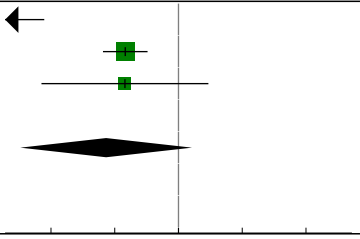
Analysis 3.10. Comparison 3 CHO versus placebo or fasting, Outcome 10 Postop time to passage of first flatus.

Study or subgroup	Carbohydrates N	Mean(SD)	Placebo or fasting N	Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Noblett 2006	12	2 (3)	23	3 (2.2)		2.76%	-1[-2.9,0.9]
An 2008	27	3.2 (0.6)	24	3.6 (0.5)		97.24%	-0.37[-0.69,-0.05]
Total ***	**39**		**47**			**100%**	**-0.39[-0.7,-0.07]**
Heterogeneity: Tau^2=0; Chi^2=0.41, df=1(P=0.52); I^2=0%							
Test for overall effect: Z=2.4(P=0.02)							



Analysis 3.11. Comparison 3 CHO versus placebo or fasting, Outcome 11 Postop time to first bowel movement.

Study or subgroup	Carbohydrates N	Mean(SD)	Placebo or fasting N	Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Noblett 2006	12	2 (2.2)	23	4.2 (2.8)		3.71%	-2.22[-3.91,-0.53]
Ozdemir 2011	15	0.5 (0.1)	30	0.7 (0.2)		57.89%	-0.21[-0.3,-0.12]
Ozdemir 2011	15	1 (0.5)	30	1.2 (0.5)		38.4%	-0.21[-0.54,0.12]
Total ***	**42**		**83**			**100%**	**-0.28[-0.62,0.05]**
Heterogeneity: Tau^2=0.05; Chi^2=5.4, df=2(P=0.07); I^2=62.99%							
Test for overall effect: Z=1.65(P=0.1)							



APPENDICES

Appendix 1. Free-text terms and associated exploded MeSH terms

1. Surcial Procedures, Operative
2. Surgical Procedures, Elective
3. Surgical

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4. Surgery
5. Elective surgery
6. Abdominal surgery
7. Carbohydrates
8. Carbohydrate
9. CHO
10. Nutricia
11. Maltodextrin
12. Oral
13. Drink
14. Placebo
15. Fasting
16. Preoperative
17. Postoperative Care
18. Postoperative Period
19. Postoperative Complications
20. Insulin resistance
21. Pain, Postoperative
22. Recovery
23. Nausea
24. Vomiting
25. Fatigue
26. Clinical trials
27. Controlled-clinical trials
28. Randomized-controlled trials

Appendix 2. CENTRAL search

#1 MeSH descriptor Carbohydrates explode all trees
#2 ((carbohydrat* or CHO) near (oral or load* or treatment or drink* or fluid* or administrat* or rich))
#3 (oral fluid* or CHO or fasting):ti,ab
#4 nutricia* or maltodextrin
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Postoperative Care, this term only
#7 MeSH descriptor Postoperative Period, this term only
#8 MeSH descriptor Insulin Resistance, this term only
#9 MeSH descriptor Surgical Procedures, Elective, this term only
#10 MeSH descriptor Postoperative Complications, this term only
#11 MeSH descriptor Cholecystectomy, Laparoscopic, this term only
#12 MeSH descriptor Pain, Postoperative, this term only
#13 pre?op*:ti,ab
#14 (postoperative near (recovery or pain or nausea or vomiting or fatigue)):ti,ab
#15 (insulin near resistance):ti,ab
#16 (surgery near (elective or abdominal)):ti,ab
#17 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)
#18 (#5 AND #17)

Appendix 3. MEDLINE search

1. ((carbohydrat* or CHO) adj3 (oral or load* or treatment or drink* or fluid* or administrat* or rich)).mp. or (oral fluid* or CHO or fasting).ti,ab. or (nutricia* or maltodextrin).mp. or Carbohydrates/
2. Postoperative Care/ or Postoperative Period/ or Insulin Resistance/ or Surgical Procedures, Elective/ or Postoperative Complications/ or Cholecystectomy, Laparoscopic/ or Pain, Postoperative/ or pre?op*.ti,ab. or (post?operative adj3 (recovery or pain or nausea or vomiting or fatigue)).ti,ab. or (insulin adj3 resistance).ti,ab. or (surgery adj3 (elective or abdominal)).ti,ab.
3. 1 and 2
4. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (animals not (humans and animals)).sh.
5. 3 and 4

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Appendix 4. EMBASE search

1. ((carbohydrat* or CHO) adj3 (oral or load* or treatment or drink* or fluid* or administrat* or rich)).mp. or (oral fluid* or CHO or fasting).ti,ab. or (nutricia* or maltodextrin).mp. or carbohydrate/
2. pre?op*.ti,ab. or (post?operative adj3 (recovery or pain or nausea or vomiting or fatigue)).ti,ab. or (insulin adj3 resistance).ti,ab. or (surgery adj3 (elective or abdominal)).ti,ab. or postoperative care/ or postoperative period/ or postoperative pain/ or insulin resistance/ or elective surgery/ or postoperative complication/ or cholecystectomy/
3. (placebo.sh. or controlled study.ab. or random*.ti,ab. or trial*.ti,ab.) not (animals.sh not (humans.sh and animals.sh))
4. 3 and 2 and 1

Appendix 5. CINAHL search

S1 TX (carbohydrat* or CHO) and AB (oral or load* or treatment or drink* or fluid* or administrat* or rich)
S2 AB oral fluid* or CHO or fasting
S3 TX nutricia* or maltodextrin
S4 (MM "Carbohydrates")
S5 S1 or S2 or S3 or S4
S6 (MH "Postoperative Pain") OR (MH "Postoperative Period") OR (MH "Postoperative Care") OR (MH "Postoperative Complications") OR (MH "Insulin Resistance") OR (MH "Surgery, Elective") OR (MH "Cholecystectomy, Laparoscopic")
S7 TI pre?op* or AB pre?op*
S8 AB postoperative and AB (recovery or pain or nausea or vomiting or fatigue)
S9 AB insulin and AB resistance
S10 AB surgery and AB (elective or abdominal)
S11 S6 or S7 or S8 or S9 or S10
S12 S5 and S11
S13 (random* or placebo or trial*) or (((single or double or triple or treble) and (mask* or blind*))) or (multicenter* or prospective)
S14 (MH "Random Assignment") OR (MH "Clinical Trials") OR (MH "Placebos") OR (MH "Double-Blind Studies") OR (MH "Single-Blind Studies") OR (MH "Triple-Blind Studies") OR (MH "Prospective Studies") OR (MH "Multicenter Studies")
S15 S13 or S14
S16 S12 and S15

Appendix 6. Web of Science search

1. TS=((carbohydrat* or CHO) same (oral or load or treatment or drink* or fluid* or administrat* or rich)) or TS=(oral fluid* or CHO or fasting) or TS=(nutricia* or maltodextrin)
2. TS=(post$op* same (care or period or complications or pain or recovery or nausea or vomiting or fatigue)) or TS=(pre$op*) or TS=((cholecystectomy or surgery or surgical) same (elective or abdominal or laparoscopic)) or TS=(insulin same resistance)
3. #1 AND #2

Appendix 7. Study selection form

Preoperative oral carbohydrate loading for enhancing recovery after elective surgery

Study selection form

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ISDN	First author	Journal/Conference, etc.	Year	Reviewer	Title reviewed	Abstract reviewed	Full text reviewed
					Yes/No	Yes/No	Yes/No

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Study selection guidelines

RCT	Relevant participants (elective surgical procedure) (aged 18 years or older)	Relevant interventions (preop administration of greater than 45 g of carbohydrate between 2 and 4 hours before induction of anaesthesia) (control group of fasting for 4 hours before induction of anaesthesia *or* placebo containing less than 45 g of carbohydrate)	Relevant outcomes (length of hospital stay, complication rate) (postoperative insulin resistance, aspiration, fatigue, well-being, return of intestinal function, nausea and vomiting)	Duplicate patient series
Yes/No/Unclear	Yes/No/Unclear	Yes/No/Unclear	Yes/No/Unclear	Yes/No/Unclear

Do not proceed if any of the above answers is 'No.' If study is to be included in the 'Excluded studies' section of the review, record the reason for exclusion below
Outcome: Include/Exclude
If excluded:
Record in 'Excluded studies'—Yes/No
Reason for exclusion
If included:
Unique ID

Appendix 8. Eligible trials form

Preoperative oral carbohydrate loading for enhancing recovery after elective surgery

Eligible trials form

Unique ID	ISDN	Author(s)	Journal/Conference proceedings, etc.	Year
1				
2				
3				
...				

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Appendix 9. Data extraction form

Preoperative oral carbohydrate loading for enhancing recovery after elective surgery

Data extraction form

Unique ID	ISDN	First author	Year	Reviewer	Date reviewed

Notes

Study methods and details

Trial characteristics	Details
Study site(s)	
Country/countries	
How was participant eligibility defined?	
Mean or median age of participants	
Risk breakdown of participants (ASA where defined)	
Surgery type/number	
Number receiving: * Epidural anaesthesia * Spinal anaesthesia * General anaesthesia	
Number undergoing laparoscopic/minimally invasive surgery	
How many participants were randomized?	
Number of participants allocated to: * Carbohydrate * Placebo * Fasting	
Number of participants analysed: * Carbohydrate * Placebo * Fasting	

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(Continued)

Carbohydrate group: * Preparation * Time administered * Route administered * Volume of drink * Carbohydrate dose * Co-intervention
Placebo group: * Details of placebo * Time administered * Amount of drink * Carbohydrate dose
Fasting group: * Duration of preop fast—solids * Duration of preop fast—liquids * Duration of preop fast—carbohydrate

References to other trials

Did this report include any references to published or unpublished trials potentially eligible for this review?	**Yes/No**

First author	**Journal/Conference**	**Title**	**Year of publication/presentation**	**Contact details**

Outcomes—Complete a separate copy for each relevant subgroup

Subgroup	**n**

For continuous data

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Outcome	Unit of measurement	Carbohydrate group			Placebo group			Fasting group			Details
		n	Mean	SD	n	Mean	SD	n	Mean	SD	
Primary outcome—Length of hospital stay											
Insulin resistance (HOMA-IR)											
Insulin resistance (clamp)											
Postop fatigue											
Postop well-being											
Postop nausea at 24 hours											
Postop vomiting in the first 24 hours											
Postop time to passage of flatus											
Postop time to first bowel movement											

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For dichotomous data

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Outcome	Carbohydrate group		Placebo group		Fasting group		Details
	Number with event	Number without event	Number with event	Number without event	Number with event	Number without event	
Primary outcome—Total complications							
Aspiration pneumonitis							
Postop vomiting 1 or more episodes							

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Appendix 10. Quality assessment of eligible trials form

Preoperative oral carbohydrate loading for enhancing recovery after elective surgery

Quality assessment form

Unique ID	ISDN	First author	Journal/Conference, etc.	Year	Reviewer

Domain	Describe	Reviewer's judgement—Risk of bias
1. Adequate sequence generation		Low/Unclear/High
2. Allocation concealment		Low/Unclear/High
3. Blinding—Subjective		Low/Unclear/High/NA
Blinding—Objective		Low/Unclear/High/NA
4. Incomplete outcome data—Length of stay		Low/Unclear/High/NA
Incomplete outcome data—Complication rate		Low/Unclear/High/NA
Incomplete outcome data—Secondary end points		Low/Unclear/High/NA
5. Selective outcome reporting		Low/Unclear/High
6. Other potential threats to validity		Low/Unclear/High

WHAT'S NEW

Date	Event	Description
15 August 2014	Amended	Typo corrected, footnote D, Summary of findings table.

CONTRIBUTIONS OF AUTHORS

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Conceiving of the review: JM, LP, MS, JN.

Designing the review: MDS, JM.

Co-ordinating the review: MDS.

Undertaking manual searches: MDS.

Screening search results: MDS.

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Organizing retrieval of papers: MDS, MS.

Screening retrieved papers against inclusion criteria: MDS, JM, PH.

Appraising quality of papers: MDS, LP, PH.

Abstracting data from papers: MDS, LP, PH.

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Providing additional data about papers: LP, JN.

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Analysing RevMan statistical data: MDS, PH.

Performing other statistical analysis not using RevMan: MDS.

Completing double entry of data: (data entered by person one: MDS; data entered by person two: LP).

Interpreting data: MDS, PH, JM, LP, MS, JN.

Making statistical inferences: MDS, PH.

Writing the review: MDS, JM, LP, PH, MS, JN.

Providing guidance on the review: JM, PH, JN.

Securing funding for the review: N/A.

Performing previous work that served as the foundation of the present study: JM, LP, JN, MS.

Serving as guarantor for the review (one review author): MDS.

Taking responsibility for reading and checking the review before submission: MDS.

DECLARATIONS OF INTEREST

Mark D Smith (MDS), John McCall (JM), Lindsay Plank (LP), G Peter Herbison (PH), Mattias Soop (MS), Jonas Nygren (JN)

JM and LP were involved in the design, conduct and publication of a study that was included in this review (Mathur 2010). Funding support for this study was provided by Nutricia (NZ) Ltd. They have no pecuniary interest in the product used in any of the studies.

MDS and PH have no known conflicts of interest to declare.

MS and JN have conducted and published studies on preoperative oral carbohydrate treatment. They are not receiving funding in relation to this review.

To avoid the risk of bias, initial study selection and quality appraisal were performed by at least one review author without a declared interest (MDS), as was arbitration in cases of disagreement between review authors (PH).

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The subgroup analyses conducted differ between the protocol (Smith 2011) and this review. With regards to subgroup analysis according to type of surgery, we planned to split the subgroup of participants undergoing abdominal surgery into those undergoing open surgery and those undergoing laparoscopic surgery. The only laparoscopic surgery for which outcome data were reported separately was laparoscopic cholecystectomy; other outcome data reported for laparoscopic or minimally invasive techniques were scant, as were data that were reported in combination with those of open surgery.

Instead we reported the outcomes of major versus minor abdominal surgery separately, both to ensure consistency with the published review by Awad et al (Awad 2013) and to explore the differential effects of preoperative carbohydrate treatment on study participants undergoing abdominal operations with a short expected hospital stay versus those with a more prolonged hospital stay.

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Subgroup analysis was not performed according to type of anaesthesia, again because this detail was not well described in the included trials, and because outcome data often were not reported separately for participants undergoing neuraxial anaesthesia.

For subgroups of the intervention, only two trials were identified in which carbohydrate was administered via the intravenous route, precluding meaningful subgroup analysis. Instead outcomes of participants receiving a placebo drink were combined with those of participants undergoing traditional fasting in a separate analysis, to increase statistical power and increase precision.

Sensitivity analysis to exclude trials at high risk of bias was confined to trials with unclear or high risk of bias across the two domains of blinding. As only two trials were judged to be at low risk of bias across all domains, this was considered to preclude meaningful meta-analysis.

Finally, sensitivity analyses were conducted by using the software package 'R' (R 2.13.2) instead of Stata because of the primary review author's (MDS) familiarity with this software package. Also, the open source licence of this software makes it easier for other researchers to confirm the analyses contained in this review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Elective Surgical Procedures; *Length of Stay; Beverages; Carbohydrates [*administration & dosage]; Fatigue [prevention & control]; Flatulence; Insulin Resistance; Postoperative Complications [*prevention & control]; Postoperative Nausea and Vomiting [prevention & control]; Preoperative Care [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Adult; Humans

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