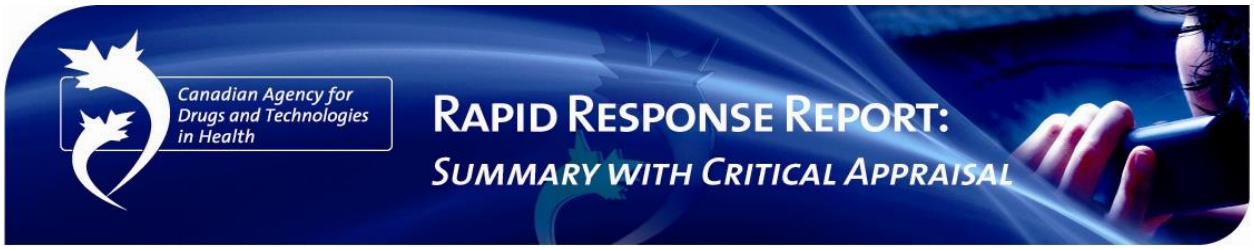

TITLE: Pre-Operative Carbohydrate Loading or Hydration: A Review of Clinical and Cost-Effectiveness, and Guidelines

DATE: 04 April 2016

CONTEXT AND POLICY ISSUES

Post-operative surgical complications result in considerable costs to the Canadian healthcare system.[1] Enhanced recovery after surgery (ERAS) clinical pathways aim to improve patient outcomes such as recovery time, length of stay, and surgical morbidity through a variety of evidence-based interventions administered before, during, and after surgery. Frequent features of ERAS protocols include patient education, analgesia, mechanical bowel preparation, antibiotic prophylaxis, thromboprophylaxis, avoidance of nasogastric tubes, peritoneal drains, laparoscopic surgery and various types of nutrition support. These pathways recognize differences in specific clinical populations and accordingly, tailored guidelines have been developed. For instance, orthopedic surgery patients may benefit from physiotherapy and pre-emptive analgesia prior to surgery,[2] while bariatric surgery patients may require special energy restricted diets.[3]

A common practice for surgery involving anesthetic is to require the patient to fast and consume no fluids or food (nil per os [NPO]) for a set period of time leading up to a procedure. This requirement aims to reduce the risk of aspiration of gastric contents.[4,5] However, evidence has been accumulating that this approach may not be optimal in all contexts, and that allowing reduced fasting time and providing pre-operative fluids and nutrition may improve patient outcomes.[4,6] One possible explanation is that prolonged fasting, which is common due to surgical delays and NPO orders, can lead to a metabolic shift towards starvation. The starvation state is characterized by depletion of liver glycogen, and a reduced ability to respond to injury. Patients who are hospitalized and healthy patients undergoing surgical procedures requiring extended recovery may already experience malnutrition, further impairing their pre-surgical nutrition status.[7] The metabolic changes that occur during starvation are exacerbated by surgical stress and immobilization, which leads to a hypermetabolic state of increased energy and protein requirements, pain, and inflammation.[8-11] These physical stresses can lead to an increased risk of infection, poor wound healing and pressure ulcers, bacterial colonization, and nutrient losses.[12-15]

Strategies for reduced fasting including pre-operative carbohydrate (CHO) loading and hydration are major nutritional components of ERAS protocols. These interventions aim to reduce the risk of

adverse effects of the catabolism induced by starvation and nutrition deficits caused by surgical stress. Standardized iso-osmolar CHO drinks have been proposed to reduce insulin resistance and glycogen loss, and may attenuate loss of muscle mass, hunger, thirst, anxiety, nausea, and vomiting as well as surgical complications and length of stay.[16,17] For patients who cannot consume oral CHOs due to dysphasia or aspiration risk, intravenous CHOs are also available. A systematic review (SR) published in 2003, reported that pre-operative provision of fluids did not result in a clinically significant difference in volume or pH of gastric contents, or other clinical outcomes associated with risk of aspiration.[4] Accordingly, clinical practice guidelines from the American Society of Anesthesiology and the Canadian Anesthesiologists Society support clear fluid intake (including CHO drinks) until within two hours of initiation of anesthesia for elective surgery.[18,19] The cost of oral CHO supplements ranges from low to moderate (£1.13 to £40.00 per patient per surgery based on a summary of European and Japanese products of varying formulations),[20] but the cost-effectiveness of their use is unclear. Evidence to support a clinical benefit of pre-surgical provision of CHOs and hydration is mixed, possibly owing to differences in the invasiveness and expected recovery time of the surgical procedure assessed, baseline clinical status of the patient population, and in pre and post-operative care pathways between studies.

This report will review the clinical and cost-effectiveness of pre-operative CHO loading and hydration (reduced fasting), as well as evidence-based guidelines regarding best practices for these interventions.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of pre-operative carbohydrate loading or hydration for patients undergoing surgery with a general anesthetic?

2. What is the cost-effectiveness of pre-operative carbohydrate loading or hydration for patients undergoing surgery with a general anesthetic?

3. What are the evidence-based guidelines associated with pre-operative carbohydrate loading or hydration for patients undergoing surgery with a general anesthetic?

KEY FINDINGS

Five systematic reviews and seven evidence-based guidelines were identified regarding the clinical effectiveness and guidelines for pre-operative carbohydrate loading or hydration in patients undergoing surgery with a general anesthetic. Overall, the majority of evidence indicated no benefit of treatment, with a minority of evidence suggesting modest benefits for length of stay, post-operative insulin resistance, return to gastrointestinal function, and patient wellbeing. Despite inconsistent evidence of patient benefits, the risk for post-operative complications, including aspiration, is not increased with the use of these interventions. Accordingly, evidence-based guidelines for various surgical populations recommend reducing fasting to two hours for liquids and six hours for solids, and providing pre-operative carbohydrates, unless contraindicated. These recommendations may be specific to, or extrapolated from specific clinical populations and should be interpreted with caution.

METHODS

Literature Search Methods

A limited literature search was conducted on key resources including PubMed, Medline, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments (HTAs), SRs, meta-analyses (MAs), randomized controlled trials (RCTs), economic studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and March 4, 2016.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adult or pediatric patients requiring surgery under a general anesthetic Subgroups of interest: patients with diabetes, patients with prior gastrointestinal surgeries, patients with reflux disease, in-patients undergoing emergency surgery who are on a standby list
Intervention	Pre-surgical carbohydrate loading (intravenous or oral) or hydration (intravenous or oral) alone or in combination
Comparator	Qs1 and 2: "Nil per os" (NPO) or nothing by mouth (i.e., food and drink) in the 12 hours prior to surgery; Placebo (e.g., flavored non-caloric fluids) Q3: No comparator required
Outcomes	Q1: Clinical effectiveness (e.g., clinical benefit, surgical outcome, post-operative recovery, symptom management [e.g., thirst, dehydration, hunger, anxiety, nausea, sodium overload], quality of life and satisfaction); Harms (e.g., post-operative complication rate, nausea and vomiting, aspiration) Q2: Cost-effectiveness outcomes Q3: Evidence-based guidelines regarding amount, timing, and indications for pre-surgical carbohydrate loading or hydration
Study Designs[a]	Health technology assessments, systematic reviews, meta-analyses, economic evaluations, evidence-based guidelines

[a]Due to the volume of literature available, final selection of articles was limited to the indicated study designs; relevant primary clinical studies are listed in Appendix 6

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2011. SRs and MAs that evaluated multiple or mixed interventions were not excluded if primary studies or subgroup analyses that met the inclusion criteria were presented. HTAs, SRs, MAs, and evidence-based guidelines were excluded if there was inadequate or unclear methodology or if they were superseded by an updated review or guideline. SRs were excluded if all primary studies were contained within another more recent or rigorous review. Due to the large volume of literature identified, a decision was made to restrict the final selection of articles to HTAs, SRs, MAs, and evidence-based guidelines; RCTs and non-randomized studies were not evaluated for this report and are listed in Appendix 6. Economic studies that reported costs only were also excluded.

Critical Appraisal of Individual Studies

The included SRs were critically appraised using A Measurement Tool to Assess Systematic Reviews (AMSTAR).[21] The methods used when conducting the literature search, study selection, quality assessment, data extraction, and for summarizing the data were assessed. Evidence-based guidelines were assessed with the AGREE II instrument.[22] The scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence of the guidelines were assessed. Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study or guideline is presented.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 493 citations were identified in the literature search. Following screening of titles and abstracts, 468 citations were excluded and 25 potentially relevant reports from the electronic search were retrieved for full-text review. After removal of duplicates and publications out of the specified date range, the grey literature search retrieved a further three potentially relevant publications. Of these 28 potentially relevant articles, 16 publications were excluded for various reasons. Twelve publications including five SRs,[20,23-26] and seven evidence-based guidelines,[27-33] met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Additional references of potential interest, including relevant RCTs, are provided in Appendix 6.

Summary of Study Characteristics

Detailed study characteristics are presented by study type in Appendix 2.

Systematic Reviews

Five SRs[20,23-26] were identified regarding the clinical effectiveness of pre-operative CHO loading or hydration for patients undergoing surgery with a general anesthetic.

There was some overlap among the primary studies included in the SRs (see Appendix 5). Every review had at least one common study with another review. Of the 43 primary studies reviewed within the SRs, 25 were common to at least two reviews, and 18 were unique to one review (eight

to Smith et al.,[25] two to Wallström et al.,[26] two to Awad et al.,[23] two to Li et al.,[24] and four to Bilku et al.[20]). Discrepancies in the included studies were due to different patient populations of interest, search time frames, comparators, and types of studies included.

Study Design

Four SRs included RCTs only,[20,23,24,26] and one included both RCTs and quasi-randomized trials.[25] Three SRs performed meta-analysis on relevant interventions and outcomes,[23-25] while two reported study results narratively.[20,26]

Country of Origin

The reviews were performed by study authors based in the United Kingdom,[20,23] New Zealand,[25] Sweden,[26] and China.[24]

Patient Population

All SRs focused on adult patients in hospitals undergoing general or elective surgery involving anesthesia, which included a range of procedures (see Table A1), though one SR only reported on abdominal surgery patients.[26] Two SRs reported that they excluded patients with diabetes[20,23] and one excluded patients with other metabolic disorders.[20]

Interventions and Comparators

All SRs investigated pre-operative CHO loading of various doses (i.e., 200 to 1000 mL) and timing of administration (i.e., 2 to 3 hours before anesthesia to the evening before surgery) as the intervention. One SR[26] evaluated other peri-operative interventions to reduce surgical complications, but only results related to CHO loading or hydration were reviewed. In some cases, the CHO intervention for a minority of primary studies included additional components, such as electrolytes, branched chain amino acids, or pre-operative advice.[20,26] The SRs compared the intervention to overnight fasting (or NPO) protocols, alternative doses or routes of administration (e.g., IV) of CHO, or placebo. Placebo was defined as non-caloric flavored water of the same volume as the intervention,[20,23,24] or clear liquids,[25] or less than 45 grams of CHO provided in liquid.[25]

Outcomes

Reported outcomes included length of hospital stay[23-26] postoperative complications including risk of aspiration,[23-25] insulin resistance or sensitivity,[20,23-25] gastrointestinal function (e.g., gastric residual volume, transit time, gastric pH),[20,24,26] nutritional status,[20] and patient well-being.[20,24,25]

Evidence-Based Guidelines

Seven evidence-based guidelines[27-33] were identified regarding the provision of pre-operative CHO loading or hydration for patients undergoing surgery with a general anesthetic. It should be noted that some of the SRs included in this report were considered as supporting evidence within some evidence-based guidelines.[27,29-32]

Clinical Society and Country of Origin

The guidelines were developed by the American Society for Parenteral and Enteral Nutrition,[31] the French Association of Anesthesia and Intensive Care,[27,30] The French Society of Digestive Surgery,[27] and the ERAS Society.[29,32,33] Two guidelines did not have a clear affiliation or were not endorsed by a clinical or governmental body.[28,30] The guidelines were developed by guideline development groups located multi-nationally,[29,32,33] in Australia,[31] France,[27] and the United Kingdom.[28,30]

Guideline Development and Methodology

Most guidelines utilized a SR process to collect evidence,[28-33] while the evidence retrieval and synthesis process of one guideline was unclear.[27] The types of studies included in the evidence-assessment process varied between guidelines. For example, one guideline included other evidence-based guidelines.[31] Most guidelines utilized the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to assessing quality of the evidence and formulating and weighting recommendations.[27,28,32,33] One guideline used subjective weighting of desirable and undesirable effects,[29] one used the AGREE domain to assess guideline quality and synthesized and reweighted recommendations based on this assessment,[31] and two guidelines[28,30] used Scottish Intercollegiate Guidelines Network (SIGN) criteria.[34] One guideline[27] reported a method of validation, which involved a Delphi consensus process and evaluation of the guideline by experts.

Targeted Users and Patient Population

The guidelines were targeted at health care practitioners providing care during, and patients undergoing procedures including general elective surgery,[31] gastrointestinal surgery,[29] gastrectomy,[32] elective colorectal surgery,[27] esophagectomy,[30] gynecologic and oncology surgery patients,[33] and breast cancer surgery.[28] One guideline specified that the recommendations applied to patients of all ages,[27] and the rest did not specify age-related criteria for the recommendations.

Interventions and Comparators

All guidelines assessed evidence and provided recommendations regarding either or both reduced fasting (i.e., provision of liquids or solids)[27-33] and CHO loading protocols.[27-30,32,33] The clinical outcomes of most of the evidence that was assessed included length of stay variables, safety and postoperative complications, and surrogate outcomes.

Economic Evaluations

No relevant evidence was identified regarding the cost-effectiveness of pre-operative CHO loading or hydration.

Summary of Critical Appraisal

A detailed summary of strengths and limitations of SRs and guidelines is provided in Appendix 3.

Systematic Reviews

The five SRs were of low-to-high quality.[20,23-26] Two SRs made reference to a protocol and a priori objectives,[25,26] and one SR[23] specified a priori subgroup analyses. Three SRs[23-25] conducted at least duplicate study selection, and two conducted duplicate data extraction.[24,25] Four SRs[23-26] conducted a comprehensive literature search using multiple databases and supplementary search strategies. No SRs restricted the search by publication status; three SRs[20,24,26] limited the search by language; and two limited the search by publication date.[23,26] All SRs included lists of included studies and study characteristics, and three did not provide a list of excluded studies.[20,23,24] Some relevant study characteristics, such as the full context of peri-operative care in which the intervention was delivered, were unclear.[20,23-26] All but one[20] SR formally assessed the quality of primary studies and considered study quality in the formulation of conclusions. The three SRs that used GRADE[23,25,35] considered study quality and confidence in findings prominently in the discussion of results. All SRs with meta-analysis[23-25] conducted statistical tests of heterogeneity, used random-effects models where appropriate, and considered clinical and methodological heterogeneity through subgroup and sensitivity analyses. Two SRs did not pool findings[20,26] and did not provide a reason for not combining results. Two SRs assessed the potential for publication bias using funnel plots or Egger's test.[23,25] The study authors of one SR declared funding by a manufacturer of oral CHO drinks.[23] It is unclear whether this affected the design of the review or interpretation of the results.

Evidence-Based Guidelines

Scope and Purpose

All guidelines[27-33] stated an overall objective, generally related to improving wellness of patients undergoing surgical procedures. The health questions were apparent in all guidelines, if not upfront then within recommendations; however, they were only explicitly stated by one.[27] In all cases, the target population was specifically described, but with varying degrees of specificity. In most cases, the health condition or procedure was specified, and other demographic characteristics of the target population such as age, gender, comorbidities, body mass index, and ethnicity were not mentioned.

Stakeholder Involvement

Two guidelines did not include individuals from all relevant professional groups in the guideline development team or failed to specify credentials of the guideline development group.[28,30] All other guidelines included individuals from different clinical disciplines relevant to the guideline topic. No guidelines sought the views and preferences of the target population. The target users of the guideline were clear in all cases.

Rigor of Development

Systematic methods were used to search for evidence in five cases.[28,30-33] One guideline conducted a comprehensive search, but disclosed that systematic methods were not used in study selection and that individual biases of the experts involved may have influenced the evidence that was reviewed.[29] In one case the literature search process was unclear, but study selection and review criteria were provided.[27] The strengths and limitations of the evidence were described by all guidelines, and explicit links between recommendations and supporting evidence were apparent. Methods for formulating recommendations were described by all guidelines. Health benefits, side effects, and risks were considered in formulating recommendations. In many cases,[28-33] with the

exception of one guideline[27] it was unclear whether external review of a draft by exports was conducted. No guidelines discussed a timeline for updating or associated procedures.

Applicability

In all cases, the applicability of the guideline was poorly discussed and supported. No guidelines described facilitators and barriers to its application, provided advice or tools on how recommendations could be put into practice, discussed potential resource implications, or presented monitoring or auditing criteria. These omissions may limit the usability and adaptability of the guideline.

Editorial Independence

Two guidelines included reviewers or authors who had affiliations with Nutricia[32,33] or other manufacturers of oral CHO beverages. Three guidelines declared no conflict of interest[28,30,31] and in two cases, potential conflicts of interest or funding issues were unclear.[27,29] Competing interests of guideline development group members were not discussed, outside of conflict of interest statements.

Summary of Findings

A detailed summary of study findings of SRs and MAs as well as guideline recommendations is presented in Appendix 4.

What is the clinical effectiveness of pre-operative carbohydrate loading or hydration for patients undergoing surgery with a general anesthetic?

Pre-Operative Carbohydrate versus Placebo (or Hydration Only)

Length of Hospital Stay

Based on pooled results from MAs, two SRs[24,25] reported that there was no evidence of reduced length of hospital stay overall with the provision of pre-operative CHO versus placebo. One SR[24] reported a significantly reduced length of hospital stay in the CHO group versus placebo in a subgroup analysis of colorectal surgery patients. Other subgroup analyses in patients undergoing major abdominal surgery,[25] minor abdominal surgery,[25] orthopedic surgery,[25] and cardiac surgery[24,25] were not significant.

Length of Intensive Care Unit Stay

Based on pooled results from MAs, one SR[24] reported no significant difference in the length of intensive care unit (ICU) stay between patients who received CHO and those who received placebo overall, or in the subgroup of cardiac surgery patients.

Return to Intestinal Function and Gastrointestinal Outcomes

One SR[25] reported no difference in time to first bowel motion between patients who received CHOs versus placebo, based on pooled results from a meta-analysis. One SR[24] reported no significant difference in postoperative gastric pH, or gastric residual volume between patients who received

CHO and those who received placebo, overall or in the subgroups of colorectal surgery or laparoscopic cholecystectomy patients, based on pooled results.

Patient Perceived Post-Operative Status or Well-Being

One SR[25] reported no difference in post-operative fatigue or well-being between patients who received CHO versus those who received placebo, based on pooled results from MAs.

Insulin Resistance or Sensitivity

Based on pooled results from MAs, one SR[25] suggest no difference in post-operative insulin resistance between CHO and placebo groups; however, a significant increase in insulin sensitivity was reported. One SR[24] reported no significant difference in insulin sensitivity index or insulin resistance index between patients who received CHO treatment and those received placebo, based on results from one study. In the subgroup of colorectal surgery patients, insulin sensitivity was significantly higher and insulin resistance was significantly lower in the CHO versus placebo group.[24] In the subgroup of laparoscopic cholecystectomy patients, no difference in insulin resistance index was observed between groups.[24]

Infection Rate

One SR[20] reported that based on the results of one study, there was no difference in the incidence of post-operative infection.

Nutritional Status

One SR[20] reported that the effect on nutrition status in patients who received CHO or placebo (hydration) versus those who fasted, as measured by anthropometric parameters or grip strength, was inconsistent, with most studies observing no difference in nutrition status, but one showing a significant reduction in grip strength in the control group..

Rate of Post-Operative Complications and Adverse Events

One SR[25] reported no difference in post-operative complication rate between CHO and placebo groups, based on pooled results from a MA. Further, this SR[25] reported no incidence of aspiration pneumonitis, and no difference in nausea up to 24 hours or the risk of vomiting. One SR[24] reported no difference in the risk of postoperative vomiting between patients who received CHO and those who received placebo overall, or in the subgroups of laparoscopic cholecystectomy patients or cardiac surgery patients, based on pooled results from MAs. No incidence of aspiration was reported by any primary study in either group.[24] Further, no difference in thirst, nausea, or dry mouth were observed.

Pre-Operative Carbohydrate versus Fasting

Length of Hospital Stay

Based on pooled results from MAs, one SR[25] reported a modest reduction in mean length of stay overall, and in the orthopedic surgery subgroup (based on the results of a single trial), but not major or minor abdominal or cardiac surgery subgroups. One SR[24] reported no difference overall or in

subgroups of colorectal surgery and cardiac surgery patients with regards to the pooled mean length of stay between patients who received CHO and those who fasted overnight.

Length of Intensive Care Unit Stay

One SR[24] reported no significant difference in the length of ICU stay between patients who received CHO and those who fasted overnight, overall, or in the subgroup of cardiac surgery patients, based on pooled results from a MA.

Return to Intestinal Function and Gastrointestinal Outcomes

One SR[25] reported that provision of CHO was associated with a significantly reduced time to first bowel movement and time to first flatus versus fasting, based on pooled results from MAs. One SR[24] reported no significant difference in postoperative gastric pH, or gastric residual volume, between patients who received CHO and those who fasted overnight, overall or in the subgroup of colorectal surgery or laparoscopic cholecystectomy patients, based on pooled results from MAs.

Patient Perceived Post-Operative Status or Well-Being

One SR[25] reported no difference in post-operative fatigue or well-being between patients who received CHO versus those who received a fasting protocol, based on pooled results from MAs.

Insulin Resistance or Sensitivity

One SR[25] reported no difference in post-operative insulin resistance, or insulin sensitivity between CHO and fasting groups, based on pooled results from MAs. One SR[24] reported no significant difference in pooled insulin sensitivity index overall between patients who received CHO treatment and those who fasted. In the subgroup of colorectal surgery patients, insulin sensitivity and insulin resistance were both significantly lower in the CHO versus overnight fasting group.[24]

Rate of Post-Operative Complications and Adverse Events

One SR[25] reported no difference in post-operative complication rate between CHO and fasting groups, based on pooled results from a MA. Further, this SR[25] reported no incidence of aspiration pneumonitis, and no difference in nausea up to 24 hours or the risk of vomiting. One SR[24] reported no difference in the pooled risk of postoperative vomiting between patients who received CHO and those who fasted overnight, overall, or in the subgroups of laparoscopic cholecystectomy patients or cardiac surgery patients. No incidence of aspiration was reported by any primary study in either group.[24] Significantly less thirst was observed in patients who received CHO versus overnight fasting, but no differences in nausea or dry mouth were reported.[24]

Pre-Operative Carbohydrate versus Placebo or Overnight Fasting

Length of Hospital Stay

Based on pooled results from MAs, one SR[25] reported a modest reduction in mean length of stay overall and in the major abdominal surgery subgroup, but not minor abdominal, cardiac or orthopedic surgery subgroups. Further, when subgroup analysis of unblinded and blinded studies was conducted, a significant reduction in length of stay was observed for the unblinded group. It should be noted that all subgroup analyses had substantial statistical heterogeneity, and the results

should be interpreted with caution. Based on pooled results, one SR[23] reported no reduction in mean length of stay overall or in the subgroup of operative procedures with expected length of stay less than or equal to two days, despite observing a significant reduction in the subgroup of major abdominal and orthopedic surgeries. One SR[26] reported results from three individual studies with conflicting results. One study reported no difference in length of hospital stay between patients who received pre-operative CHO and those who received standard care (water or NPO from midnight).[26] The other two studies reported a significantly reduced length of stay with the provision of CHO versus standard care.[26]

Return to Intestinal Function and Gastrointestinal Outcomes

One SR[25] reported no association between provision of CHO and reduced time to first bowel motion, or time to first flatus versus placebo or fasting, based on pooled results from MAs. One SR[20] reported that three individual studies observed comparable gastric pH between CHO and overnight fasting or placebo groups. One SR[26] reported results from a single study that showed no difference in time to first flatus between patients who received pre-operative CHO and those who received standard treatment. Another study summarized in said review reported significantly shorter time to restoration of bowel function in patients who received CHO versus those who received standard treatment.[26]

Patient Perceived Post-Operative Status or Well-Being

One SR[20], reported reductions in thirst, hunger, anxiety, malaise, un-fitness, and pain after provision of CHO versus overnight fasting or placebo according to the individual results of five relevant primary studies. One SR[25] reported no difference in post-operative fatigue or well-being between patients who received CHO versus those who received a fasting protocol or placebo, based on pooled results from MAs.

Post-Operative Insulin Resistance or Sensitivity

One SR[25] reported no difference in pooled post-operative insulin resistance or insulin sensitivity between patients who received CHO and those who received either placebo or fasting protocols. One SR[20] reported that insulin resistance was significantly reduced in six individual studies on patients undergoing hepatic resection, laparoscopic cholecystectomy, colorectal resection, simulation pre-operative preparation, and colorectal surgery; however the difference was not significant in one study on colorectal surgery patients. One SR[23] reported narratively on three individual studies, which demonstrated a significant reduction in postoperative insulin resistance based on assessment with the hyperinsulinaemic-euglycaemic clamp technique. Of three individual studies that used Homeostatic Model Assessment of Insulin Resistance calculations, two demonstrated reduced insulin resistance in the CHO group, whereas one did not. One study using the qualitative insulin sensitivity check index method also showed a reduction in insulin resistance.

Rate of Post-Operative Complications and Adverse Events

Two SRs[23,25] reported no difference in pooled post-operative or surgical complication rate between patients given CHOs versus those who received placebo or fasting protocols, based on pooled results from MAs. Further, one SR[25] reported no incidence of aspiration pneumonitis, and two SRs[23,25] reported no difference in pooled post-operative nausea or the risk of vomiting.

Pre-Operative Hydration versus Fasting

Patient Perceived Post-Operative Status or Well-Being

One SR[20] that summarized two individual studies, reported reductions in thirst, hunger, anxiety, nausea and vomiting, and pain after provision of water versus fasting.

What is the cost-effectiveness of pre-operative carbohydrate loading or hydration for patients undergoing surgery with a general anesthetic?

No evidence was identified regarding the cost-effectiveness of pre-operative CHO loading or hydration for patients undergoing surgery with a general anesthetic; therefore, no summary can be provided.

What are the evidence-based guidelines associated with pre-operative carbohydrate loading or hydration for patients undergoing surgery with a general anesthetic?

A description of the grading of recommendations used by each guideline is provided in Appendix 4, Table A6.

Pre-operative Carbohydrates

One guideline for patients undergoing gastrointestinal surgery[29] made strong recommendations that pre-operative CHOs can be administered safely in all patients except those with documented delayed gastric emptying or gastrointestinal motility disorders, or patients undergoing emergency surgery. The recommendation was also weak for diabetic and obese patients.

One guideline for patients undergoing gynecologic or oncology surgery[33] made a strong recommendation based on moderate quality evidence that CHO loading reduces postoperative insulin resistance and should be used routinely.

One guideline for patients undergoing gastrectomy[32] made a strong recommendation based on low quality evidence that, relying on data extrapolated from studies in major surgery, pre-operative oral CHOs should be given to all patients without diabetes.

One guideline for colorectal surgery patients,[27] is in strong agreement that pre-operative CHO rich isotonic fluids be recommended for patients with American Society of Anesthesiologists Physical Classification System Category 1 or 2 before elective colorectal surgery (Grade 1+), but not patients with diabetes or gastric emptying disorders (Grade 1-).

One guideline for patients undergoing esophagectomy[30] stated that while there was no direct evidence to inform the clinical effectiveness of CHO loading, pre-operative CHO drinks delivered orally if no dysphagia, or via enteral tube two to three hours before surgery may attenuate surgical stress and speed up discharge (Level 1+, grade B extrapolated).

One guideline for patients undergoing breast cancer surgery[28] states that pre-operative clear CHO fluid should be considered in all patients undergoing oncological breast surgery (Level of evidence 1, Grade B recommendation, extrapolated evidence).[28]

Pre-operative Fluids

One guideline for patients undergoing gastrointestinal surgery[29] made a strong recommendation that fluids be allowed up until two hours before initiation of anesthesia. This exact recommendation is stated by other guidelines for patients undergoing surgery requiring a pre-operative fasting protocol[31] (grade A recommendation), gynecologic or oncology surgery (moderate evidence, strong recommendation),[33] gastrectomy (high level of evidence, strong recommendation),[32] colorectal surgery (strong agreement),[27] esophagectomy with caution for patients with dysphagia (Level 1++, Grade A recommendation),[30] and patients undergoing breast cancer surgery (Level of evidence 1, Grade B recommendation, extrapolated evidence).[28]

One guideline[31] recommends that if an elective surgery is delayed, water should be provided to prevent excessive thirst or dehydration (grade E recommendation).

Pre-operative Solid Food

One guideline for patients undergoing gastrointestinal surgery[29] made a strong recommendation that solids be allowed up until six hours before initiation of anesthesia. This exact recommendation is stated by other guidelines for patients undergoing surgery requiring a pre-operative fasting protocol,[31] (grade C recommendation) gynecologic or oncology surgery (moderate evidence, strong recommendation),[33] gastrectomy (low level of evidence, strong recommendation),[32] colorectal surgery (strong agreement),[27] and esophagectomy with caution for patients with dysphagia (Level 1++, Grade A recommendation.[30]

One guideline[31] noted that milk in tea and coffee is considered solid as the amount is difficult to control and due to risk of curdling, and that the same fasting time should apply (grade C recommendation). Further, intake of fried or fatty foods may require a longer fasting period due to increased time needed for digestion (grade E recommendation).[31]

Pre-operative Reduced Fasting

One guideline for patients undergoing surgery requiring a pre-operative fasting protocol[31] recommended that pre-operative fasting be minimized and that NPO from midnight is unnecessary in most patients (grade A).

Limitations

Depending on the condition of the patient receiving CHO loading or fluids, baseline nutrition status and overall health status may differ substantially. Several studies failed to discuss or control for potential baseline imbalances in these determinants of peri-surgical health status, which may have influenced response to treatment.

Some of the primary studies reviewed by the SRs included in this review, as well as some SRs in their entirety focused on specific patient populations. This limits the generalizability of the findings, as patients with different health conditions, baseline status, comorbidities, and undergoing different procedures may respond differently to treatment. Further, their risk of surgical complications may differ. Similarly, most of the guidelines were aimed at specific surgical populations; however, some of the evidence used to inform them may have been extrapolated from different clinical populations, or broader patient populations. Conversely, guidelines aimed at general surgery patients may be informed by evidence from specific clinical populations. As such, generalizability of the recommendations in these guidelines to broader surgical populations or other specific clinical

populations is unclear. In addition, the appropriateness of using evidence not specific to the population of interest to inform guideline recommendations should be considered.

While this review attempted to limit scope to interventions containing CHOs and hydration agents, some SRs included a minority of studies with interventions that contained additional nutrients (e.g., protein, electrolytes). These discrepancies are highlighted where possible, but may further limit the generalizability of findings as some observed benefit or harm may be attributable to the other components of the intervention. Similarly, some reviews failed to consider different background treatments, such as other components of ERAS care. In these cases, observed benefits and harms cannot be completely attributable to CHO or hydration provision. Also, most studies monitored patients during the in-hospital period, so the effect of the intervention on complications or patient benefits beyond discharge is unclear.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Overall, the evidence did not suggest that providing pre-operative CHOs would result in a meaningful clinical benefit compared to placebo (or hydration). There was a stronger trend towards improvement in several clinical outcomes when pre-operative CHOs or hydration were compared to fasting, but the evidence was still mixed. Where a significant reduction in length of stay was observed, the reduction was modest amounting to less than one day. Whether this difference is meaningful may depend on the estimated length of stay for a procedure and patient and caregiver perspectives. Despite lacking evidence to demonstrate consistent benefits, there is no suggestion that post-operative complications are increased with treatment. As such, allowing the patient to reduce their fasting period, whether it results in meaningful clinical benefits or not, may improve tolerability of the pre-surgical period without introducing any risks. This may be due to improvements in patient important wellbeing parameters including thirst, hunger, or anxiety.

Recommendations made by multiple evidence-based guidelines[27,29-33] state that fasting should be minimized (two hours for liquids, six hours for solids) with care to reduce intake of solids, caloric liquids, and hard to digest foods, and that the common practice of NPO from midnight onwards is unnecessary. Intake of pre-operative CHOs was recommended for patients undergoing specific surgeries. Strong recommendations were made by many guidelines, despite weak or limited evidence. This was attributed to pros outweighing the cons of the intervention, as well as substantial evidence of no safety risks. These factors, as well as all the evidence summarized in the SRs not being available at the time of guideline publication, and the contribution of expert opinion and consensus, may explain the discordance between the strength of guideline recommendations and the clinical evidence that was summarized.

Generalizability of clinical findings should be considered in the interpretation of these results, acknowledging that diverse patient populations, interventions, and surgical procedures were assessed. Along these lines, heterogeneity in the evidence used to establish conclusions regarding clinical effectiveness and thus, guidelines, should be considered. Pooled results should be interpreted with caution and nuances observed in subgroup analyses should be reviewed. Further research is needed, particularly to inform the clinical effectiveness of provision of pre-operative CHOs and hydration for specific clinical populations that were not represented, and for which guideline recommendations rely on extrapolated evidence or are unavailable. Populations of interest may include patients with poor baseline nutrition status due to prolonged illness. No relevant evidence was identified regarding cost-effectiveness, so resource implications of the use of preoperative CHOs or hydration remains unclear.

In conclusion, while there is not compelling evidence to suggest improved surgical outcomes with the use of preoperative CHOs versus placebo or fasting, there is no evidence of potential for postoperative complications. Thus, if these interventions improve tolerability of the pre-surgical period, as guideline recommendations state, their use may be warranted.

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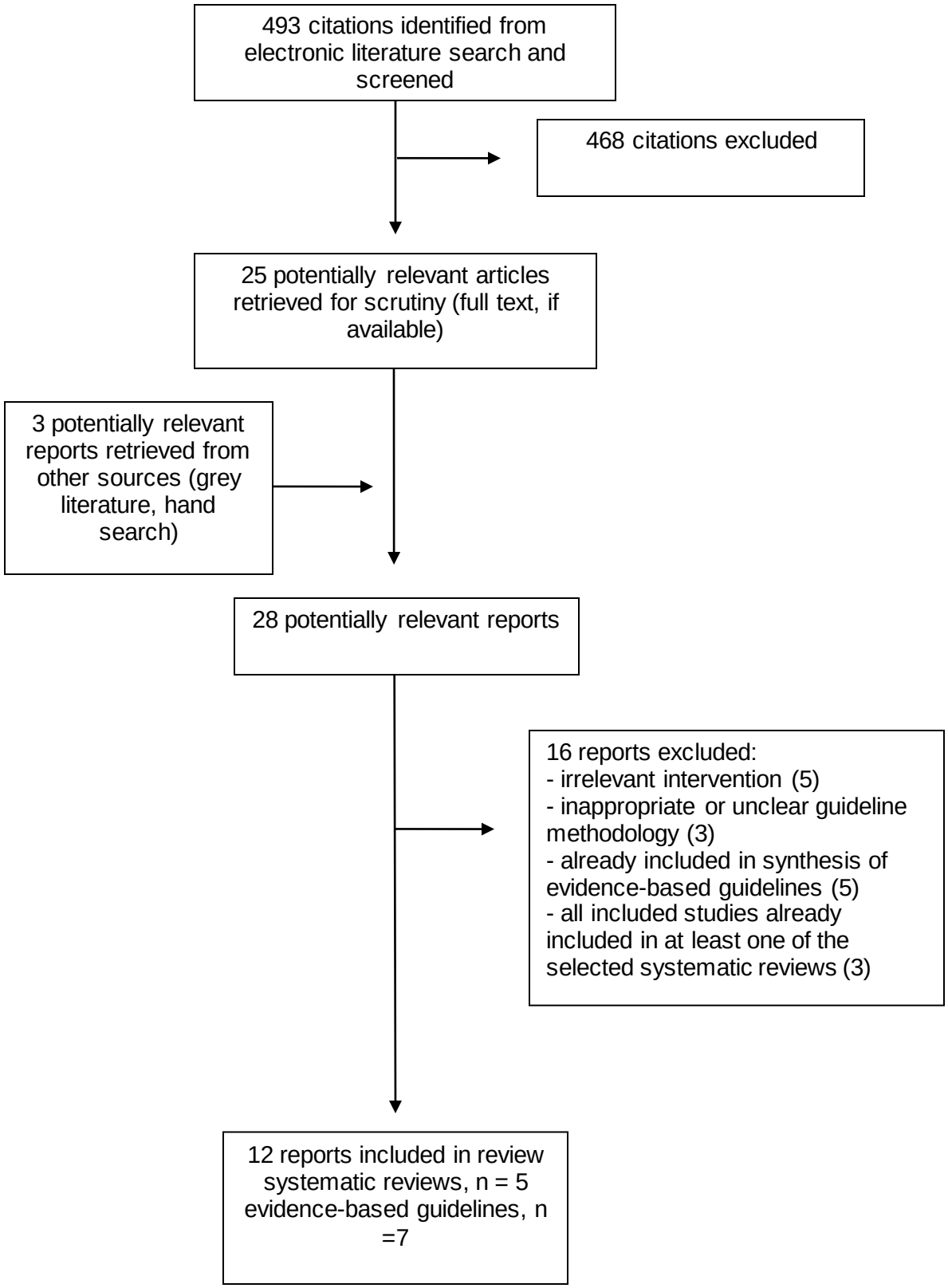
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Publications

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country; Search Dates and Databases	Types and numbers of primary studies included	Population Characteristics	Intervention	Comparator(s)	Clinical Outcomes, Length of Follow-Up
Bilku, 2014[20] United Kingdom PubMed only inception to September 2011	Randomized controlled trials, n = 17	Adult patients undergoing general surgical operations in hospital excluding those with metabolic disorders[a] n = 1445	Pre-operative CHO loading (oral [varying doses] or IV) with or without BCAAs, electrolytes	Overnight fasting, low CHO, placebo (flavored water)[b]	Results reported narratively for: insulin resistance (n = 7 studies), gastric emptying (n = 5 studies), gastric acidity (n = 3 studies), patient wellbeing (n = 8 studies), immunity and clinical outcome (n = 2 studies), nutritional status (n = 5 studies), Follow-up duration = unclear or up to 24 hours postoperatively
Smith, 2014[25] New Zealand CENTRAL, MEDLINE, EMBASE, CINAHL, and Web of Science from inception to March 2014	Randomized (n = 26) and quasi randomized (n = 1) controlled trials	Adults (> 18 years of age) undergoing any type of elective surgical procedure in hospital while under general, spinal or epidural anaesthesia,[c] n = 1976	Pre-operative CHO treatment (≥ 45 g), n = 935 Administered orally (n = 25), by IV (n = 1), and by either route (n = 1)	Placebo (< 45 g CHO or clear liquids only), n = 595 or pre-operative fasting, n = 446	Primary (quantitative synthesis): length of hospital stay (n = 18 studies), postoperative complication rate (n = 14 studies) Secondary (qualitative synthesis only): aspiration pneumonitis rate, insulin resistance or sensitivity, fatigue, general well-being, nausea or vomiting within 24 hours postoperatively; Follow-up duration = unclear or up to 24 hours postoperatively
Wallström, 2014[26] Sweden, January 2002 to January 2012, Medline, Scopus, CINAHL	Randomized controlled trials, n = 3[d]	Adult patients (> 19 years of age) undergoing colorectal neoplasm surgery, elective segmental colectomy for adenocarcinoma or adenoma (laparoscopic or open), and elective colorectal resections in hospital, n = 2243	Fast track protocols involving pre-operative CHO and hydration; Pre-operative carbohydrate or hydration alone[e]	Conventional care; Hydration only; Fasting	Results reported narratively for: Colonic transit time, gastric retention, time until first bowel movement or flatus, time until first tolerance of solid food, composite of time to tolerate solid food and bowel movement, length of hospital stay, time until ready for discharge;

Table A1: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country; Search Dates and Databases	Types and numbers of primary studies included	Population Characteristics	Intervention	Comparator(s)	Clinical Outcomes, Length of Follow-Up
					Follow-up duration = unclear or until return to bowel function (time unspecified)
Awad, 2013[23] United Kingdom January 1980 to April 2012, MEDLINE, EMBASE, Science Citation Index, Cochrane Library database	Randomized controlled trials, n = 21	Adult non-diabetic patients undergoing elective surgery[f] in hospital, n = 1685	Pre-operative CHO treatment (≥ 50 g), n = 733	Fasting or placebo (ingestion of an equivalent volume of non-caloric placebo drink), n = 952	Primary: length of hospital stay; Secondary: development of postoperative insulin resistance, complications, nausea and vomiting; Follow-up duration = unclear or until hospital discharge (for primary outcome)
Li, 2012[24] China PubMed, Cochrane Library, EMBASE, ISI Web of Knowledge, China Journal Full-text Database, Chinese Biomedical Database, Chinese Scientific Journals Full-text Database, CMA digital periodicals from inception to September 2010	Randomized controlled trials, n = 22	Adult surgical patients in hospital[g]	Pre-operative CHO (200 to 1000 mL at various intervals)	Overnight fasting, placebo (non-caloric flavored water), IV CHO	Changes in blood glucose and insulin levels, insulin resistance and sensitivity indexes, gastric pH or volume, length of hospital or ICU stay, pre-operative well-being (including anxiety, hunger, thirst, nausea, dry mouth), postoperative vomiting, aspiration during surgery; Follow-up duration = unclear or until hospital discharge

[a] Hepatic resection, colorectal resection, laparoscopic cholecystectomy, simulated pre-operative setting (no surgery), colorectal surgery, parathyroid surgery, thyroidectomy, bowel resection, abdominal surgery
[b] Also compared to no dietary supplement – unclear if fasting was part of this protocol;
[c] Including elective abdominal surgery, orthopedic surgery, cardiac surgery, spinal surgery, and thyroidectomy; excluding emergency surgery, urgent surgery
[d] Only studies related to pre-operative CHO or hydration are listed, total studies included in review, n = 27
[e] Review was on a variety of interventions to facilitate early bowel recovery, only some studies fit criteria
[f] Including major colorectal surgery, laparoscopic cholecystectomy, total hip replacement, major open abdominal surgery, orthopedic surgery, cardiac surgery, thyroid surgery, liver surgery, open cholecystectomy, unilateral inguinal hernia repair
[g] Including laparoscopic cholecystectomy, parathyroid surgery, colorectal surgery, total hip replacement, bowel resection, orthopedic surgery, elective abdominal surgery, colorectal resection, cardiac surgery, general surgery, gastrointestinal surgery, coronary artery bypass grafting surgery, thyroidectomy, hepatic resection
BCAA = branched chain amino acids; CHO = carbohydrate; ICU = intensive care unit; IV = intravenous

Table A2: Characteristics of Included Evidence-Based Guidelines

Objectives			Methodology			
Intended users/ Target population	**Intervention and Practice Considered**	**Major Outcomes Considered**	**Evidence collection, Selection and Synthesis**	**Evidence Quality and Strength**	**Recommendations Development and Evaluation**	**Guideline Validation**
Feldheiser, 2016,[29] Enhanced Recovery After Surgery (ERAS) Society						
Patients undergoing gastrointestinal surgery (age not specified) and healthcare providers	Enhanced Recovery after Surgery program including individual elements such as pre-operative fasting and CHO loading	Use of reduced fasting or CHO loading protocols	Systematic review	Subjective, weighting of desirable and undesirable effects	Consensus recommendations reached after critical appraisal of the literature and consideration of desirable effects of intervention weighted against undesirable effects	NR
Lambert, 2015[31] American Society for Parenteral and Enteral Nutrition						
Patients undergoing surgery requiring a pre-operative fasting protocol (age not specified) and healthcare providers	Pre-operative reduced fasting (fluids)	Use of reduced fasting protocols	Systematic review of evidence-based guidelines (n = 19, published between 2005 and 2012)	AGREE domain and overall quality scores	All recommendations retrieved and grading converted to American Society for Parenteral and Enteral Nutrition format based on original grading and analysis of the evidence-base informing recommendations. Recommendations originally graded high but informed by poor evidence were adjusted, whereas expert recommendations were not adjusted	Primary guidelines validated through assessment with AGREE II and confirmation of the evidence-base used to inform recommendations NR for evidence-synthesis
Nelson, 2015,[33] Enhanced Recovery After Surgery (ERAS) Society						
Gynecologic/oncology surgery patients (age not specified) and healthcare providers	Pre-operative fasting and CHO treatment[a]	Use of reduced fasting or CHO loading protocols	Systematic review	GRADE	Recommendations made according to GRADE, strong recommendations indicate panel confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, whereas weak recommendations indicate desirable effects probably	NR

Table A2: Characteristics of Included Evidence-Based Guidelines

Objectives			Methodology			
Intended users/ Target population	**Intervention and Practice Considered**	**Major Outcomes Considered**	**Evidence collection, Selection and Synthesis**	**Evidence Quality and Strength**	**Recommendations Development and Evaluation**	**Guideline Validation**
					outweigh the undesirable effects but that the panel has less confidence. Recommendations based on quality of evidence as well as the balance between desirable and undesirable effects, resource utilization not considered while making recommendations	
Mortensen, 2014,[32] Enhanced Recovery After Surgery (ERAS) Society						
Patients undergoing gastrectomy (age unspecified) and healthcare providers	Pre-operative fasting and pre-operative treatment with CHOs	Use of reduced fasting or CHO loading protocols	Systematic review	GRADE	Recommendations made according to GRADE assessment and based on the quality of evidence and the balance between wanted and unwanted effects and on values and preferences	NR
Alfonsi, 2013[27] French Association of Anesthesia and Intensive Care and the French Society of Digestive Surgery						
Patients (of any age) undergoing elective colorectal surgery (for cancer or otherwise) who were autonomous pre-operative and healthcare providers	Pre-operative fasting and isotonic CHO rich solutions	Duration of hospital stay and post operative complications as primary, surrogate outcomes secondary	Evidence collection and synthesis method unclear	GRADE	For parameters for which there was sufficient evidence, GRADE approach was applied	Vote made after validation using Delphi method
Findlay, 2014[30]						
Patients undergoing esophagectomy (age not specified) and healthcare providers	CHO Loading and Fasting	Use of reduced fasting or CHO loading protocols	Systematic review	Scottish Intercollegiate Guidelines Network criteria	Recommendations generated (with extrapolation when required) and graded in accordance with the Scottish Intercollegiate Guidelines Network	NR

Table A2: Characteristics of Included Evidence-Based Guidelines

Objectives			Methodology			
Intended users/ Target population	**Intervention and Practice Considered**	**Major Outcomes Considered**	**Evidence collection, Selection and Synthesis**	**Evidence Quality and Strength**	**Recommendations Development and Evaluation**	**Guideline Validation**
Arsalani-Zadeh, 2011[28]						
Breast cancer oncologists and surgeons, Patients undergoing breast cancer surgery (age not specified)	Perioperative fasting, hydration and provision of CHOs[a]	Safety, patient wellbeing, postoperative insulin resistance, patient satisfaction, electrolyte levels, urine output	Systematic review	Jadad and GRADE	Scottish Intercollegiate Guidelines Network approach to recommendation development	NR

[a]Guideline looked at ERAS protocols in general, but specifically addressed these components or interventions
CHO = carbohydrate; GRADE = Grading of Recommendations, Assessment, Development and Evaluation; NR = not reported

APPENDIX 3: Critical Appraisal of Included Publications

Table A3: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[21]

Strengths	Limitations
Bilku, 2014[20]	
• Reference lists of all included studies searched to identify additional articles • Search not restricted by publication status • List of included studies and study characteristics provided, organized by outcome	• No reference to protocol or a priori objectives • Unclear number of authors involved in study selection and data extraction • Only a single database (PubMed) searched • Only English language publications included • No formal search for unpublished studies undertaken • List of excluded studies not provided • Some characteristics of included studies including care context in which intervention was delivered unclear • No assessment of study quality performed • Study quality not considered in formulation of conclusions • No pooling of study results and no reason given for lack of pooling • No assessment of publication bias or formal search for unpublished trials • No disclosure of funding sources or potential conflict of interest
Smith, 2014[25]	
• Study protocol referenced and differences between protocol and review summarized (see page 103)[25] • Study selection and data extraction performed by two authors, consensus by a third author when required • Comprehensive literature search conducted on multiple databases • Search not restricted by language or publication status • List of included and excluded studies as well as study characteristics provided • Scientific quality of primary studies assessed using Cochrane's risk of bias tool and GRADE • Scientific quality of studies considered in formulation of conclusions • Heterogeneity assessed according to clinical and methodological diversity and by conducting subgroup analysis and statistical heterogeneity using the I^2 statistic • Publication bias assessed qualitatively using a funnel plot and statistically using Egger's test • Independent search for unpublished studies conducted by contacting authors in the field of study and by consulting clinical trial databases • Declaration of potential conflicts of interest and affiliations made	N/A
Wallström, 2014[20]	
• Reference to a priori objectives made by mention of original protocol • Comprehensive literature search performed on multiple databases • Quality assessed in duplicate using questions from Roe 2007[36]	• One reviewer involved in study selection and data extraction • Search restricted by publication date, to English language publications, and to human studies • Meta-analysis not performed for intervention of interest, no reason provided

Table A3: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[21]

Strengths	Limitations
• List of included studies and study characteristics provided • List of excluded studies provided along with reason for exclusion • Quality considered in the formulation of conclusions	• Clinical experts consulted to probe for potential unpublished studies • Publication bias not assessed as no meta-analysis performed • Authors declared no conflict of interest
Awad, 2013[23]	
• Duplicate study selection • Comprehensive literature search performed on multiple databases • No restrictions by language or publication type • List of included studies and study characteristics provided • Quality of studies assessed using GRADE, which incorporates the Cochrane Risk of Bias tool • Quality considered prominently in the formulation of conclusions • Heterogeneity calculated using the I^2 statistic and both random and fixed effects models calculated for all outcomes • Funnel plots used to evaluate publication bias	• No reference to protocol or a priori objectives; however a priori subgroup analyses were presented • Unclear number of authors involved in data extraction • Search restricted to publications from 1980 onward • Manufacturers were contacted directly for unpublished research • List of excluded studies not provided • Several authors have affiliations with Nutricia Clinical Care who manufacture carbohydrate drinks
Li, 2012[24]	
• Triplicate study selection and data extraction conducted • Comprehensive literature search performed on multiple databases • Publications not excluded based on publication status • List of included studies and study characteristics provided • Quality assessed in triplicate according to the Cochrane handbook 5.0 recommended standards, and GRADE criteria • Quality considered prominently in the formulation of conclusions • Heterogeneity assessed using I^2 statistic, and random effects models used where significant statistical heterogeneity detected • Authors declared that they had no conflict of interest	• No reference to protocol or a priori objectives • Publications excluded if not in English or Chinese • List of excluded studies not provided • Trials included in the meta-analysis determined to have significant heterogeneity, even within subgroup analyses • Publication bias not assessed, but authors searched for unpublished studies on clinicaltrials.gov and inquired with authors for unpublished data • Results presented in narrative summaries, no forest plots provided, despite the use of meta-analysis

GRADE = Grading of Recommendations, Assessment, Development and Evaluation; N/A = not applicable

Table A4: Strengths and Limitations of Guidelines using AGREE II[22]

Item	Author						
	Feldheiser, 2016[29]	Lambert, 2015[31]	Nelson, 2015[33]	Mortensen, 2014[32]	Alfonsi, 2013[27]	Findlay, 2014[30]	Arsalani-Zadeh, 2011[28]
Domain 1: Scope and Purpose							
1. The overall objective(s) of the guideline is (are) specifically described.	•	•	•	•	•	•	•
2. The health question(s) covered by the guideline is (are) specifically described.	•	•	•	•	•	•	•
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	•	•	•	•	•	•	•
Domain 2: Stakeholder Involvement							
4. The guideline development group includes individuals from all relevant professional groups.	•	•	•	•	•	X	X
5. The views and preferences of the target population (patients, public, etc.) have been sought.	X	X	X	X	X	X	X
6. The target users of the guideline are clearly defined.	•	•	•	•	•	•	•
Domain 3: Rigour of Development							
7. Systematic methods were used to search for evidence.	X	•	•	•	X	•	•
8. The criteria for selecting the evidence are clearly described.	•	•	•	•	X	•	•
9. The strengths and limitations of the body of evidence are clearly described.	•	•	•	•	•	•	•
10. The methods for formulating the recommendations are clearly described.	•	•	•	•	•	•	•
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	•	•	•	•	•	•	•
12. There is an explicit link between the recommendations and the supporting evidence.	•	•	•	•	•	•	•
13. The guideline has been externally reviewed by experts prior to its publication.	X	X	X	X	•	X	X

Table A4: Strengths and Limitations of Guidelines using AGREE II[22]

Item	Author						
	Feldheiser, 2016[29]	Lambert, 2015[31]	Nelson, 2015[33]	Mortensen, 2014[32]	Alfonsi, 2013[27]	Findlay, 2014[30]	Arsalani-Zadeh, 2011[28]
14. A procedure for updating the guideline is provided.	X	X	X	X	X	X	X
Domain 4: Clarity of Presentation							
15. The recommendations are specific and unambiguous	•	•	•	•	•	•	•
16. The different options for management of the condition or health issue are clearly presented.	•	•	•	•	•	•	X
17. Key recommendations are easily identifiable.	•	•	•	•	•	•	•
Domain 5: Applicability							
18. The guideline describes facilitators and barriers to its application.	X	X	X	X	X	X	X
19. The guideline provides advice and/or tools on the recommendations can be put into practice.	X	X	X	X	X	X	X
20. The potential resource implications of applying the recommendations have been considered.	X	X	X	X	X	X	X
21. The guideline presents monitoring and/or auditing criteria.	X	X	X	X	X	X	X
Domain 6: Editorial Independence							
22. The views of the funding body have not influenced the content of the guideline.	X	•	X	X	X	•	•
23. Competing interests of guideline development group members have been recorded and addressed	X	X	X	X	X	X	X

X = no or unclear, • = yes

APPENDIX 4: Main Study Findings and Author's Conclusions

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
Bilku, 2014[20]				
			p-value	
Insulin Resistance, n = 7 studies	• Oral CHO (i.e., Amintoleban [50 g CHO and BCAAs] twice daily, various formulations [200 to 800 mL, single or multiple doses per day]) • IV CHO (10% glucose 500 mL infusion, or 5 mg/kg/min)	• Overnight fasting • Placebo	p = <0.01 to 0.05	Insulin resistance as measured by artificial pancreas with closed loop system, quantitative insulin sensitivity index check, Homeostatic Model Assessment of Insulin Resistance, or hyperinsulinemic clamp was significantly reduced (p = <0.01 to 0.049) in six studies[37-42] on patients undergoing hepatic resection, Laparoscopic cholecystectomy, colorectal resection, simulation pre-operative setting (no surgery), and colorectal surgery; however, in one study on colorectal resection patients the difference was not significant (p = 0.05)[43]
Gastric Emptying, n = 5 studies	• Oral CHO (i.e., various formulations [400 to 800 mL, single or multiple doses per day]) • IV CHO (10% glucose 500 mL infusion + electrolytes)	• Overnight fasting • Water (400 mL, or ad libitum until 3 hours before induction) • Placebo	p = NR to 0.61	Gastric emptying (as assessed by gastric fluid volume determined by nasogastric tube, gamma camera with radiotracer, or dye dilution technique was reported to be not significantly different (p = NR to 0.61) by all five studies assessing this outcome[17,43-46] in colorectal resection, laparoscopic cholecystectomy, parathyroid surgery, thyroidectomy, or bowel resection patients One study in diabetic patients reported no delay in gastric emptying with the provision of CHO versus controls[47]
Gastric Acidity, n = 3 studies	• Oral CHOs (i.e., various formulations [400 to 800 mL, single or multiple doses per day]) • IV CHO (10% glucose 500 mL infusion + electrolytes)	• Overnight fasting • Placebo	NR	Gastric pH as measured by biochemical indicator paper, urine pH meter, or automatic back titration with sodium hydroxide to pH 7 was comparable between groups in all three studies[43,44,46]
Patient Wellbeing	• Oral CHOs (i.e., various	• Overnight fasting	NR	As measured by modified Beck questionnaire, VAS, or objective

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
	formulations [400 to 800 mL, single or multiple doses per day]) • IV CHOs (10% glucose 500 mL infusion, 5% dextrose 1000 mL infusion)	• Placebo • Water 400 mL or ad libitum until 3 to 4 hours before anesthesia induction		assessment by nursing staff, reductions in thirst,[17,43,48] hunger,[43,46,48] anxiety,[43,46] malaise,[46] unfitness,[46] and pain[43] after CHOs was observed; Reductions in thirst,[17] hunger,[17] anxiety,[17] nausea and vomiting,[49] and pain after water was observed by some studies. Other studies observed no differences between groups[45,50,51] for benefits or harms related to patient wellbeing.
Immunity and clinical outcomes (n = 2 studies)	Pre-operative CHO drink	• Water • Placebo	NR	One study reported no difference in the incidence of postoperative infections in CHO versus placebo group, or benefit with regards to length of stay or time to intake of oral diet, whereas another study reported reduced length of stay in Cho versus placebo or water and an earlier return of gut function[50,52]
Nutritional status (n = 5 studies)	Oral CHO (dose unspecified)	• Water • Placebo	p <0.05 where results reported as significant in next column	Based on status assessments using anthropometric measurements, grip strength, skinfold thickness, and mid-arm circumference, some studies observed no difference between groups,[45] one study reported a significant reduction in grip strength in fasted patients but not CHO and placebo groups.[52] Another study observed a similar trend but it was not statistically significant.[43] One study observed no difference in BMI or a difference in loss of fat mass, despite a significantly improved preservation of muscle mass.[53] Another study did not observe a greater preservation of muscle mass or attenuation of postoperative nitrogen loss.[50]
Smith, 2014[25]				
	CHOs (≥ 45 g)	**Placebo, Fasting, or Placebo or Fasting**		
Length of Hospital Stay (days), n = 15 studies			**Mean difference (95% CI), I^2**	
CHO	CHO	Placebo	-0.13 (-0.38 to 0.12), 17%	Overall, there was no evidence of reduced length of hospital stay with

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
				the use of pre-operative CHO versus placebo
Subgroup Analyses				
Major abdominal surgery (n = 7 studies)	CHO	Placebo	-1.23 (-2.79 to 0.33), 69%	No evidence of reduced length of hospital stay in any of the four subgroups
Minor abdominal surgery (n = 3 studies)	CHO	Placebo	-0.05 (-0.12 to 0.02), 0%	
Orthopedic surgery (n = 4 studies)	CHO	Placebo	-0.26 (-1.11 to 0.58), 68%	
Cardiac surgery (n = 1 study)	CHO	Placebo	1.00 (-0.90 to 2.90, N/A	
Overall, n = 11 studies	CHO	Fasting	-0.42 (-0.79 to -0.06)	**Provision of pre-operative CHO treatment versus fasting was associated with a moderate reduced mean length of stay**
Subgroup Analyses				
Major abdominal surgery, n = 5 studies	CHO	Fasting	-2.02 (-4.13 to 0.08), 87%	Reduced mean length of stay only observed for the orthopedic surgery subgroup, though this evidence is from a single trial.
Minor abdominal surgery, n = 3 studies	CHO	Fasting	-0.07 (-0.18 to 0.03), 0.0%	
Orthopedic surgery, n = 1 study	CHO	Fasting	-1.00 (-1.73 to -0.27), N/A	
Cardiac surgery, n = 3 studies	CHO	Fasting	-0.47 (-3.41 to 2.47), 80%	
Overall, n = 18 studies	CHO	Placebo or Fasting	-0.30 (-0.56 to - 0.04), 74%	Administration of pre-operative CHO associated with a modest reduction in hospital stay compared with placebo or fasting
Subgroup Analyses				
Major abdominal surgery, n = 10 studies	CHO	Placebo or Fasting	-1.66 (-2.97 to -0.34), 78%	A significant reduction in length of stay was observed for the major abdominal surgery group; however substantial heterogeneity and variation in study quality should be considered in interpretation of these results
Minor abdominal surgery, n = 4 studies	CHO	Placebo or Fasting	-0.07 (-0.14 to 0.00), 0%	Length of hospital stay was not significantly different between CHO and placebo or fasting groups in minor abdominal surgery, orthopedic surgery, or cardiac surgery subgroups When studies were divided by
Orthopedic surgery, n = 4 studies	CHO	Placebo or Fasting	-0.29 (-1.18 to 0.60), 78%	
Cardiac Surgery, n = 2 studies	CHO	Placebo or Fasting	-0.44 (-3.37 to 2.50), 82%	

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
Adequate blinding, n = 4 studies	CHO	Placebo or Fasting	-0.59 (-1.73 to 0.55), 10%	blinded studies and unblinded (or unclear) studies, only the studies that were unblinded (or unclear) showed a significant modest reduction in length of stay; however, substantial heterogeneity should be considered in interpretation of these results
Unclear or inadequate blinding, n = 16 studies	CHO	Placebo or Fasting	-0.29 (-0.55 to -0.02), 77%	
Post-Operative Complication Rate (n)			**Risk Ratio (95% CI), I^2**	
Overall, n = 10 studies	CHO 73/292	Placebo 84/302	0.92 (0.73 to 1.16, 0.0%	No evidence of a benefit of pre-operative CHO on post-operative complicate rate versus placebo
Overall, n = 6 studies	CHO	Fasting	1.00 (0.87 to 1.16), 0.0%	Pre-operative CHO provision was not associated with a reduced post-operative complication rate versus fasting
Overall, n = 14 studies	CHO 107/415	Placebo or Fasting 121/498	0.98 (0.86 to 1.11), 0.0%	Pre-operative CHO treatment was not associated with a reduced post-operative complication rate versus placebo or fasting
Post-Operative Insulin Resistance (HOMA-IR)			**Mean Difference (95% CI), I^2**	
Overall, n = 4 studies	CHO	Placebo	-4.00 (-8.19 to 0.18), 90%	No evidence of a benefit of pre-operative CHO on post-operative insulin resistance versus placebo
Overall, n = 4 studies	CHO	Fasting	-1.33 (-4.12 to 1.47), 87%	No evidence of a benefit of pre-operative CHO on post-operative insulin resistance versus fasting
Overall, n = 7 studies	CHO	Placebo or Fasting	-1.59 (-3.35 to 0.17)	No significant reduction in postoperative insulin resistance was observed with provision of CHO versus placebo or fasting
Post-Operative Insulin Sensitivity (Clamp)			**Mean Difference (95% CI), I^2**	
Overall, n = 2 studies	CHOs (≥ 45 g)	Placebo	0.70 (0.14 to 1.26), 0.0%	Increased inulin sensitivity was reported in the pre-operative CHO group versus placebo
Overall, n = 1 study	CHOs (≥ 45 g)	Fasting	NR	No evidence of an effect of pre-operative CHO on insulin sensitivity in the single study
Overall, n = 3 studies	CHO	Placebo or Fasting	0.76 (0.24 to 1.29), 0.0%	No significant improvement in postoperative insulin sensitivity was observed with provision of Cho versus placebo or fasting

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
Post-Operative Fatigue			**Mean Difference (95% CI), I^2**	
Overall, n = 4 studies	CHOs (≥ 45 g)	Placebo	0.13 (-0.27 to 0.54)	No difference in the extent of post-operative fatigue was reported between groups
Overall, n = 2 studies	CHOs (≥ 45 g)	Fasting	-0.08 (-0.47 to 0.31), 0.0%	No difference in the extent of post-operative fatigue reported between groups
Overall, n = 6 studies	CHOs (≥ 45 g)	Placebo or Fasting	0.06 (-0.23 to 0.35), 64%	No difference in the extent of post-operative fatigue reported between groups
Post-Operative Well-Being			**Mean Difference (95% CI), I^2**	
Overall, n = 3 studies	CHOs (≥ 45 g)	Placebo	0.00 (-0.25 to 0.25)	No difference in overall well-being was reported between groups
Overall, n = 2 studies	CHOs (≥ 45 g)	Fasting	0.04 (-0.40 to 0.47), 0.0%	No difference in overall well-being reported between groups
Overall, n = 4 studies	CHOs (≥ 45 g)	Placebo or Fasting	0.00 (-0.22 to 0.23), 0.0%	No difference in overall well-being reported between groups
Postoperative Adverse Events			**Mean Difference (95% CI)** unless otherwise specified, **I^2**	
Aspiration pneumonitis, n = 10 studies	CHOs (≥ 45 g)	Placebo	N/A	No incidence of aspiration pneumonitis was reported in any of the ten studies
Aspiration pneumonitis, n = 5 studies	CHOs (≥ 45 g)	Fasting	N/A	No incidence of aspiration pneumonitis was reported in any of the five studies
Aspiration pneumonitis, n = 13 studies	CHOs (≥ 45 g)	Placebo or Fasting	N/A	No incidence of aspiration pneumonitis was reported in any of the 13 studies
Nausea at 24 hours, n = 2 studies	CHOs (≥ 45 g)	Placebo	-1.71 (-4.06 to 0.64), 0.0%	No difference in nausea up to 24 hours between groups
Nausea at 24 hours, n = 1 studies	CHOs (≥ 45 g)	Fasting	-2.00 (-5.52 to 1.52)	No difference in nausea up to 24 hours between groups in the single study
Nausea at 24 hours, n = 2 studies	CHOs (≥ 45 g)	Placebo or Fasting	-1.69 (-4.12 to 0.74), 0.0%	No difference in nausea up to 24 hours between groups
Vomiting, n = 3 studies	CHOs (≥ 45 g)	Placebo	RR = 1.18 (0.65 to 2.12), 0/0%	No difference in the risk of vomiting observed between groups
Vomiting, n = 3 studies	CHOs (≥ 45 g)	Fasting	RR = 1.24 (0.58 to 2.63), 0.0%	No difference in the risk of vomiting observed between groups

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
Vomiting, n = 4 studies	CHOs (≥ 45 g)	Placebo or Fasting	RR = 1.25 (0.77 to 2.04), 0.0%	No difference in the risk of vomiting observed between groups
Postoperative Time to First Bowel Motion/Movement			**Mean Difference (95% CI), I^2**	
Overall, n = 3 studies	CHOs (≥ 45 g)	Placebo	-0.34 (-0.74 to 0.05), 69%	Pre-operative CHO provision was not associated with a reduced time to first bowel motion versus placebo
Overall, n = 2 studies	CHOs (≥ 45 g)	Fasting	-0.18 (-0.29 to -0.07), 0.0%	**Overall, time to first bowel movement was significantly reduced in the pre-operative CHO group; however, in sensitivity analysis, the effect in patients receiving major abdominal surgery (versus minor abdominal surgery) was not statistically significant**
Overall, n = 3 studies	CHOs (≥ 45 g)	Placebo or Fasting	-0.28 (-0.62 to 0.05), 63%	Pre-operative CHO provision was not associated with a reduced time to first bowel motion versus placebo or fasting
Postoperative Time to Passage of First Flatus			**Mean Difference (95% CI), I^2**	
Overall, n = 2 studies	CHOs (≥ 45 g)	Fasting	-0.39 (-0.70 to -0.07), 0.0%	**Pre-operative CHO provision was associated with a faster time to passage of flatus; however, results were highly influenced by a single study**
Overall, n = 2 studies	CHOs (≥ 45 g)	Placebo or Fasting	-0.39 (-0.70 to -0.07), 0.0%	Pre-operative CHO provision was associated with a reduction in the mean time to passage of flatus; however, results were highly influenced by a single study
Wallström, 2013[26]				
Time to first passage of flatus	Pre-operative CHO, alone or plus information, postoperative prokinetics and laxatives	Standard treatment or conventional care	NR	Despite a trend towards benefit, time to first passage of flatus was not significantly different between groups in one study[52] comparing pre-operative CHO to standard treatment One study[54] comparing multimodal treatment involving pre-operative CHO to standard treatment observed a significantly shorter time to restoration of bowel function
Length of hospital stay	Pre-operative CHO alone or plus information,	Standard treatment or conventional	NR	Despite a trend towards benefit, length of hospital stay was not significantly different between

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
	postoperative prokinetics, and laxatives	care		groups in one study[52] comparing pre-operative CHO to standard treatment Two studies[54,55] comparing multimodal treatment involving pre-operative CHO to standard treatment observed a significantly reduced length of stay
Awad, 2013[23]				
Length of hospital stay (defined as either actual length of stay or fitness to discharge, or unspecified)			**Mean Difference (95 % CI), I^2**	
Overall, n = 12 studies	CHO	Fasting or placebo	-0.19 (-0.46 to 0.08), 83%	Overall, provision of CHO did not result in a reduced length of stay; however, in major abdominal surgery and orthopedic surgery subgroups length of stay was significantly reduced, but not in studies that included operative procedures with expected length of stay less than or equal to 2 days
Subgroup Analyses				
Major abdominal surgery, n = 7 studies	CHO	Fasting or placebo	-1.08 (-1.87 to -0.29), 60%	
Operative procedures with expected length of stay less than or equal to 2 days, n = 3 studies	CHO	Fasting or placebo	-0.00 (-0.03 to 0.03), 0%	
Orthopedic surgery, n = 2 studies	CHO	Fasting or placebo	-0.48 (-0.23 to -0.73), 0%	
Surgical Complications (In-Hospital, Pulmonary and Surgical)			RR, 95% CI, I^2	
Overall	CHO	Fasting or placebo	0.88 (0.50 to 1.53), 41%	No significant difference in the rate of surgical complications observed in patients who received CHO versus those who fasted or received placebo
Post-operative nausea and vomiting	CHO	Fasting or placebo	NR	Three studies reported no difference in the occurrence of nausea and vomiting between groups, one study reported fewer instances and one study reported more instances in the CHO group; may have been confounded by the use of anti-emetics
Insulin resistance	CHO	Fasting or placebo	NR	Three studies assessing insulin resistance using the hyperinsulinaemic-euglycaemic clamp technique demonstrated significant reduction in postoperative insulin resistance, whereas three studies that used the

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
				Homeostatic Model Assessment of Insulin Resistance calculations demonstrated a reduction in two studies, but not one, and one study using the quantitative insulin sensivitiy check index also showed a reduction
Li, 2012[24a]				
			SMD (95% CI) (unless otherwise specified), **I^2**	
Insulin Sensitivity Index	CHO	Placebo, n = 1 study	1.06 (0.32 to 1.81), N/A	Overall, no significant difference was observed in insulin sensitivity index between patients who received CHO and patients who received placebo, or patients who received CHO and those who fasted overnight. In subgroup analysis of colorectal surgery patients, insulin sensitivity index was significantly lower in the CHO versus overnight fasting group and significantly higher in the CHO versus placebo group
	CHO	Overnight fasting, n = 4 studies	0.34 (-0.73 to 1.40), 93%	
Insulin Resistance Index	CHO	Placebo n = 2 studies	-0.61 (-1.96 to 0.75), 90%	Overall, no significant difference in insulin resistance index was observed between patients who received CHO and those who received either placebo, or fasted overnight. In subgroup analysis of colorectal surgery patients, insulin resistance index was significantly lower in the CHO versus overnight fasting and placebo groups In the subgroup of laparoscopic cholecystectomy patients, there was no significant difference between groups
	CHO	Overnight fasting, n = 2 studies	-1.02 (-2.60 to 0.56), 86%	
Length of Hospital Stay	CHO	Placebo, n = 5 studies	-0.32 (-0.81 to 0.17), 77%	Overall, no significant difference in the length of hospital stay was observed between patients who received CHO and those who received either placebo or fasted overnight. In subgroup analysis of colorectal surgery patients, the length of
	CHO	Overnight fasting, n = 3 studies	-0.06 (-0.49 to 0.37), 65%	

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
				hospital stay was significantly lower in the CHO versus placebo group, but not overnight fasting group In the subgroup of cardiac surgery patients there was no significant difference between groups
Length of ICU Stay	CHO	Placebo, n = 1 study	0.22 (-0.14 to 0.59), N/A	Overall, no significant difference in the length of ICU stay was observed between patients who received CHO and those who received either placebo or fasted overnight. In the subgroup of cardiac surgery patients there was no significant difference between groups
	CHO	Overnight fasting, n = 2 studies	-0.15 (-0.44 to 0.14), 7%	
Postoperative gastric pH	CHO	Placebo, n = 2 studies	-0.08 (-0.37 to 0.20), 12%	Overall, no significant difference was observed in postoperative gastric pH between patients who received CHO versus those who received either placebo or fasted overnight. In subgroup analysis of colorectal surgery patients, the postoperative gastric pH was not significantly different between groups In the subgroup of laparoscopic cholecystectomy patients there was no significant difference between groups
	CHO	Overnight fasting, n = 3 studies	0.01 (-0.35 to 0.36), 56%	
Gastric residual volume	CHO	Placebo, n = 2 studies	-0.03 (-0.30 to 0.24), 4%	Overall, no significant difference was observed in gastric residual volume between patients who received CHO and those who received either placebo or fasted overnight. In subgroup analysis of colorectal surgery patients, the gastric residual volume was not significantly different between groups In the subgroup of laparoscopic cholecystectomy patients there was no significant difference between groups
	CHO	Overnight fasting, n = 3 studies	-0.11 (-0.36 to 0.15), 19%	
Postoperative vomiting	CHO	Placebo, n = 2 studies	RR = 1.31 (0.23 to 7.45)	Overall, there was no difference in the risk of postoperative vomiting between patients who received CHO and those who received either
	CHO	Overnight fasting, n = 3	RR = 0.90 (0.47 to 1.72),	

Table A5: Summary of Findings of Included Systematic Reviews and Meta-Analyses

Outcome	Intervention Group	Placebo or Comparator Group	Pooled Estimates of Effect or Narrative Findings of Primary Studies	Author's Conclusions or Interpretation
		studies	NR	placebo or fasted overnight. In the subgroup of laparoscopic cholecystectomy patients the rate of vomiting was not significantly different between groups In the subgroup of cardiac surgery patients there was no significant difference in the risk of vomiting between groups
Aspiration during surgery	CHO	Placebo, NR	NR	Six trials mentioned aspiration as an outcome and none reported any incidence in CHO, placebo or overnight fasting groups
	CHO	Overnight fasting, NR	NR	
Pre-operative Wellbeing	CHO	Placebo	NR	No significant differences in thirst, nausea, or dry mouth
	CHO	Overnight fasting	NR	Less thirst observed in CHO group, no significant differences in nausea or dry mouth

[a]Number of studies contributing to pooled results unclear
CHO = carbohydrate; CI = confidence interval; IV = intravenous; N/A = not applicable; NR = not reported; RR = relative risk; SMD = standardized mean difference; VAS = visual analogue scale

Table A6: Summary of Findings of Included Evidence-Based Guidelines	
Recommendation	**Grade/Strength of Recommendation or Interpretation**
Feldheiser, 2016[29,a]	
"Fluids should be allowed until 2 h before induction of anesthesia. Solids should be allowed until 6 h." *See: pages 295 to 296*	Strong recommendation
"Pre-operative treatment with oral CHOs can be administered safety expect in patients with documented delayed gastric emptying or gastrointestinal motility disorders and as well in patients undergoing emergency surgery." *See: pages 295 to 296*	Strong recommendation overall; weak recommendation for diabetic and obese patients
Lambert, 2015[31,b]	
"Pre-operative fasting should be minimized and fasting from midnight is unnecessary in most patients."[56] *See: page 5*	A
"Patients can drink clear fluids and an unlimited amount of water up to 2 hours before anesthesia administration."[18,56-59] *See: page 5*	A
"Patients can consume solids up to 6 hours prior to anesthesia administration."[18,56-59] *See: page 5*	C
"Milk in tea and coffee is considered a solid since amount and possibility of curdling are difficult to control. It should therefore have the same fasting time as solids." *See: page 5*	C
"Intake of fried or fatty food or meat may require a longer fasting time (i.e., 8 hours or more)."[18] *See: page 5*	E
"If an elective operation is delayed there should be consideration to provide the patient with a drink of water to prevent excessive thirst or dehydration." *See: page 5*	E
Nelson, 2015[33]	
"Clear fluids should be allowed up to 2 hours and solids up to 6 hours prior to induction of anesthesia." *See: page 314*	Evidence level: Moderate Recommendation grade: Strong
"Carbohydrate loading reduces postoperative insulin resistance and should be used routinely." *See: page 314*	Evidence level: Moderate Recommendation grade: Strong
Mortensen, 2014[32]	
"Pre-operative fasting should be limited to 2 hours for clear fluids and 6 hours for solids. Data extrapolation from studies in major surgery suggests that pre-operative oral carbohydrate treatment should be given to patients without diabetes." *See: page 1215*	Evidence level: Fluid intake, high Solid intake, low Carbohydrate loading, low Recommendation grade: Fasting, strong Carbohydrate loading, strong
Alfonsi, 2013[27,c]	
"The recommendations of learned societies (2 hours of fasting for liquids and 4 to 6 hours for solids) are valid." *See: page 69*	Strong agreement
"Pre-operative oral administration of carbohydrate-rich isotonic fluids is recommended for ASA 1 or 2 patients before elective colorectal surgery (Grade 1+)." *See: page 70*	Strong agreement
"Pre-operative oral administration of carbohydrate-rich isotonic fluids is NOT RECOMMENDED for patients with	Strong agreement

Table A6: Summary of Findings of Included Evidence-Based Guidelines	
Recommendation	**Grade/Strength of Recommendation or Interpretation**
diabetes or gastric emptying disorders (Grade 1-)." *See: page 70*	
Findlay, 2014[30,d]	
"No studies have assessed carbohydrate loading or fasting in esophagectomy. However, minimizing pre-operative fasting to 6 hours for solids and 2 hours for fluids is recommended with caution among those with dysphagia." *See: pages 415 and 416*	Level 1++; Grade A
"Pre-operative carbohydrate drinks (delivered orally if permitted by dysphagia or via enteral tube) 2 to 3 hours before surgery attenuate the surgical stress response and expedite discharge." *See: pages 415 and 416*	Level 1+; Grade B extrapolated
Arsalani-Zadeh, 2011[28,d]	
"Patients (breast cancer surgery) should be allowed to drink clear fluid for up to two hours before surgery. Pre-operative clear carbohydrate fluid should be considered in all patients undergoing oncological breast surgery." *See: page 183*	Level of evidence, 1; grade of recommendation, B – extrapolated evidence

[a]Based on GRADE criteria "Strong recommendations indicate that the panel was confident that the desirable effects of adherence to a recommendation out-weighed the undesirable effects. Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweighed the undesirable effects, but the panel was less confident. Recommendations were based on the balance between desirable and undesirable effects, and on values and preferences." (see page 291,[29] page 314,[33] page 1210[32])

[b]Guidelines excluded from this report due to inclusion in Lambert et al.,[31] are cited where possible; for grading of recommendations letters closer to the beginning of the alphabet indicate a stronger recommendation (see pages 4 and 5 for explanation)[31]

[c]"The final formulation of recommendation is always binary, either positive or negative and can be either strong or weak (strong: definitely "do it", or "do not do it" [GRADE 1+ or 1-], weak: probably "do it" or probably "do not do it" [GRADE 2+ or 2-])[27] page 67

[d]Lower numerical score indicates higher quality of evidence, letters closer to the beginning of the alphabet indicate greater confidence in the recommendation[34]

ASA = American Society of Anesthesiologists Anesthesia Physical Classification System; NR = not reported

APPENDIX 5: Overlap Amongst Systematic Reviews

Table 2. Overlap Among Primary Studies Included in Systematic Reviews[a]

Primary Study First Author, Publication Year	Systematic Review First Author, Publication Year				
	Smith 2014[25]	Wallström, 2013[26]	Awad 2013[23]	Li 2012[24]	Bilku 2014[20]
An 2008	•			•	
Aronsson				•	
Awad 2010			•		
Bisgaard 2004	•		•	•	•
Braga 2012	•				
Breuer 2006	•			•	
Dock-Nascimento 2012			•		
Faria 2009				•	•
Harsten 2012	•				
Hausel 2001			•	•	•
Hausel 2005	•		•	•	•
Helminen 2009				•	•
Henriksen 2003	•		•		•
Ionescu 2009		•			
Jarvela 2008	•		•	•	
Kaska 2010	•		•	•	•
Lauwick 2009	•		•		
Lidder 2013	•		•		
Ljunggren 2012	•				
Ljungqvist 1994	•				•
Mathur 2010	•		•	•	•
Melis 2006			•	•	
Noblett 2006	•	•	•	•	•
Nygren 1995				•	•
Nygren 1999			•		•
Okabayashi 2010					•
Ozdemir 2011	•				
Perrone 2011	•		•		
Pexe-Machado, 2013	•				
Pu 2005				•	
Rapp-Kesek 2007	•		•		
Soop 2001	•		•	•	
Soop 2004	•		•		
Svanfeldt 2005					•
Svanfeldt 2007					•
Tran 2013	•				
van Bree 2011		•			
Wang 2010	•		•	•	
Yagci 2008			•	•	•
Yang 2012	•			•	
Yildiz 2013	•				
Yuill 2005	•		•	•	•
Zelic 2012	•				

[a]Not all listed studies meet the inclusion criteria of this report as some systematic reviews had broader inclusion criteria; however, all studies listed focused on CHO loading or hydration (reduced fasting) protocols

APPENDIX 6: Additional References of Potential Interest

Evidence-Based Guidelines – Included in Lambert et al.[31]

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