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Nutritional support for liver disease (Review)

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[Intervention Review]

Nutritional support for liver disease

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ABSTRACT

Background

Weight loss and muscle wasting are commonly found in patients with end-stage liver disease. Since there is an association between malnutrition and poor clinical outcome, such patients (or those at risk of becoming malnourished) are often given parenteral nutrition, enteral nutrition, or oral nutritional supplements. These interventions have costs and adverse effects, so it is important to prove that their use results in improved morbidity or mortality, or both.

Objectives

To assess the beneficial and harmful effects of parenteral nutrition, enteral nutrition, and oral nutritional supplements on the mortality and morbidity of patients with underlying liver disease.

Search methods

The following computerised databases were searched: the Cochrane Hepato-Biliary Group Controlled Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*), MEDLINE, EMBASE, and Science Citation Index Expanded (January 2012). In addition, reference lists of identified trials and review articles and Clinicaltrials.gov were searched. Trials identified in a previous systematic handsearch of Index Medicus were also considered. Handsearches of a number of medical journals, including abstracts from annual meetings, were done. Experts in the field and manufacturers of nutrient formulations were contacted for potential references.

Selection criteria

Randomised clinical trials (parallel or cross-over design) comparing groups of patients with any underlying liver disease who received, or did not receive, enteral or parenteral nutrition or oral nutritional supplements were identified without restriction on date, language, or publication status. Six categories of trials were separately considered: medical or surgical patients receiving parenteral nutrition, enteral nutrition, or supplements.

Data collection and analysis

The following data were sought in each report: date of publication; geographical location; inclusion and exclusion criteria; the type of nutritional support and constitution of the nutrient formulation; duration of treatment; any nutrition provided to the controls; other interventions provided to the patients; number, sex, age of the study participants; hospital or outpatient status; underlying liver disease; risks of bias (sequence generation, allocation concealment, blinding, incomplete outcome reporting, intention-to-treat analysis, selective outcome reporting, others (vested interests, baseline imbalance, early stopping)); mortality; hepatic morbidity (development or resolution of ascites or hepatic encephalopathy, occurrence of gastrointestinal bleeding); quality of life scores; adverse events; infections; lengths of stay in the hospital or intensive care unit; costs; serum bilirubin; postoperative complications (surgical trials only); and nutritional outcomes (nitrogen balance, anthropometric measurements, body weight). The primary outcomes of this review were mortality, hepatic morbidity, quality of life, and adverse events. Data were extracted in duplicate; differences were resolved by consensus.

Data for each outcome were combined in a meta-analysis (RevMan 5.1). Estimates were reported using risk ratios or mean differences, along with the 95% confidence intervals (CI). Both fixed-effect and random-effects models were employed; fixed-effect models were reported unless one model, but not the other, found a significant difference (in which case both were reported). Heterogeneity was assessed by the Chi^2 test and I^2 statistic. Subgroup analyses were planned to assess specific liver diseases (alcoholic hepatitis, cirrhosis, hepatocellular carcinoma), acute or chronic liver diseases, and trials employing standard or branched-chain amino acid formulations (for the hepatic encephalopathy outcomes). Sensitivity analyses were planned to compare trials at low and high risk of bias and trials reported as full papers. The following exploratory analyses were undertaken: 1) medical and surgical trials were combined for each nutritional intervention; 2) intention-to-treat analyses in which missing dichotomous data were imputed as best- and worst-case scenarios; 3) all trials were combined to assess mortality; 4) effects were estimated by absolute risk reductions.

Main results

Thirty-seven trials were identified; only one was at low risk of bias. Most of the analyses failed to find any significant differences. The significant findings that were found were the following: 1) icteric medical patients receiving parenteral nutrition had a reduced serum bilirubin (mean difference (MD) -2.86 mg%, 95% CI -3.82 mg% to -1.89 mg%, 3 trials) and better nitrogen balance (MD 3.60 g/day, 95% CI 0.86 g/day to 6.34 g/day, 1 trial); 2) surgical patients receiving parenteral nutrition had a reduced incidence of postoperative ascites only in the fixed-effect model (RR 0.65, 95% CI 0.48 to 0.87, 2 trials, I^2 = 70%) and one trial demonstrated a reduction in postoperative complications, especially infections (pneumonia in particular); 3) enteral nutrition may have improved nitrogen balance in medical patients (although a combination of the three trials was not possible); 4) one surgical trial of enteral nutrition found a reduction in postoperative complications; and 5) oral nutritional supplements had several effects in medical patients (reduced occurrence of ascites (RR 0.57, 95% CI 0.37 to 0.88, 3 trials), possibly (significant differences only seen in the fixed-effect model) reduced rates of infection (RR 0.49, 95% CI 0.24 to 0.99, 3 trials, I^2 = 14%), and improved resolution of hepatic encephalopathy (RR 3.75, 95% CI 1.15 to 12.18, 2 trials, I^2 = 79%). While there was no overall effect of the supplements on mortality in medical patients, the one low risk of bias trial found an increased risk of death in the recipients of the supplements. Three trials of supplements in surgical patients failed to show any significant differences. No new information was derived from the various subgroup or sensitivity analyses. The exploratory analyses were also unrevealing except for a logical conundrum. There was no difference in mortality when all of the trials were combined, but the trials of parenteral nutrition found that those recipients had better survival (RR 0.53, 95% CI 0.29 to 0.98, 10 trials). Either the former observation represents a type II error or the latter one a type I error.

Authors' conclusions

The data do not compellingly justify the routine use of parenteral nutrition, enteral nutrition, or oral nutritional supplements in patients with liver disease. The fact that all but one of these trials were at high risks of bias even casts doubt on the few benefits that were demonstrated. Data from well-designed and executed randomised trials that include an untreated control group are needed before any such recommendation can be made. Future trials have to be powered adequately to see small, but clinically important, differences.

PLAIN LANGUAGE SUMMARY

Nutritional support for patients with liver disease

Patients with liver diseases, especially decompensated cirrhosis, commonly have weight loss and muscle wasting. It is known that such patients have poorer clinical outcomes than patients with similar diagnoses but without such weight loss or muscle wasting. If the problem is just deprivation of nutrients, it would be expected that the provision of some type of nutrition should result in better outcomes. Nutrients in addition to food, or in place of food when food is not taken in sufficient amounts, can be provided in a manner whereby the patient voluntarily consumes them by drinking various nutrient formulations. Nutrients can also be provided in an involuntary manner; tubes can be placed in the vein (parenteral nutrition) or intestinal tract (enteral nutrition) and nutrient solutions infused through them. All of these nutritional interventions have associated economic costs and also can produce a variety of complications (including vomiting, diarrhoea, and altered metabolic functions (for example, high blood sugar)). Thus, it is important to determine if such nutritional interventions (that is, the provision of nutrients in some manner other than just as food) do result in improvements in clinical outcomes. Since the best way to make such a determination is to undertake randomised trials, in which patients are assigned by chance to receive, or not receive, one or another of these treatments, this systematic review was undertaken to identify and summarise this information. Randomised trials comparing patients with liver diseases who were assigned to receive parenteral nutrition, enteral nutrition, or oral nutritional supplements to similar patients assigned not to receive any nutritional intervention were collected. The three nutritional interventions were considered separately. In addition, within each category of nutritional intervention, patients with medical conditions were compared separately from patients with surgical conditions. Thus there were six primary analyses, medical patients receiving or not receiving parenteral nutrition, surgical patients receiving or not receiving parenteral nutrition, medical patients receiving or not receiving enteral nutrition, surgical patients receiving or not receiving enteral nutrition, medical patients receiving or not receiving supplements by mouth, and surgical patients receiving or not receiving supplements by mouth. The outcomes of interest were mortality, hepatic morbidity (ascites, gastrointestinal bleeding, encephalopathy), quality of life, adverse events, infections, cost, duration of hospitalisation, jaundice, postoperative complications (only for the surgical trials), and nutritional outcomes (for example, body weight). A total of 37 randomised trials were identified. All but one had a high risk of systematic error (bias, that is overestimation of benefits and underestimation of harms). When the data were combined, most of the analyses failed to demonstrate a difference. There were some significant differences observed. These were that 1) parenteral nutrition reduced serum bilirubin more rapidly and improved one type of nutritional outcome (nitrogen balance) in med-

ical patients with jaundice, and may have reduced some postoperative complications; 2) enteral nutrition may have improved nitrogen balance in medical patients, and reduced postoperative complications in surgical patients; and 3) supplements reduced the occurrence of ascites and also may have decreased the number of infections. Furthermore, the receipt of supplements (especially ones containing branched-chain amino acids) may have been helpful in the treatment of patients with hepatic encephalopathy. No significant effects were seen from the use of supplements in surgical patients. None of these observed benefits can be said to be definitively present because of the presence of methodologic flaws in the trials, which may have produced an overestimation of the observed effect. Moreover, due to too few patients included in the trials with two few outcome measures, both spurious significant findings and spurious insignificant findings cannot be excluded. The data are not strong enough to justify a recommendation to use these nutritional interventions routinely. We need well-designed and well-conducted randomised trials to prove that such therapy is indeed efficacious.

BACKGROUND

In 1936, Studley observed that patients undergoing surgery for peptic ulcer disease who had lost more than 20% of their body weight had a significantly higher postoperative mortality than patients with less profound weight loss (Studley 1936). Since then, a number of other observational studies have demonstrated an association between malnutrition and a poor outcome in a variety of disease states (Buzby 1980; Reinhardt 1980; Baker 1982) including liver disease (Nielsen 1993; Italian Multicentre Cooperative Project 1994; Alvares-da-Silva 2005; Norman 2006; Sanchez 2006). Furthermore, any person who is deprived of nutrients for a long enough period of time (usually weeks) will develop morbidity, and ultimately die, from malnutrition (Keys 1962). Based on this latter observation, as well as an assumption that the association between malnutrition and outcome was causative, recommendations to provide protein and calories to malnourished patients with liver disease, particularly cirrhosis, have been promulgated (Kondrup 1997; Alberino 2001; Tajika 2001).

The development of parenteral nutrition in the 1960s allowed clinicians to infuse high density nutrient formulations intravenously to patients who, for various reasons, were not eating sufficient amounts of nutrients to maintain body weight (Rhoads 1981). The advent of this technology led to the wide-spread implementation of parenteral nutrition. In 1971, a narrative review of this intervention claimed that the adverse course of a wide variety of disease states would be influenced favourably by the provision of these additional nutrients (Dudrick 1971). This enthusiasm was transferred to enteral nutrition when it became clear that patients with intact gastrointestinal function could have calorie-dense nutrient formulations infused through tubes located in the stomach or small intestine.

Neither parenteral nutrition nor enteral nutrition should be confused with eating. These nutritional interventions require the placement of tubes (in the venous system or gastrointestinal tract) through which the liquid formulations of nutrients can be infused. The formulations are prepared in areas that look more like laboratories or pharmacies than kitchens. Furthermore, the nutrient provision does not require any active effort by the recipient. To make a distinction with regard to this latter point, other liquid (or powders to which water is added) formulations containing calories and source(s) of nitrogen have been tested and marketed as nutrient supplements that are consumed orally; these require the volitional actions of the patient (that is, the patient has to swallow them) in order for the contents to be assimilated in the body.

Since association should not be confused with causation, and since it is well established that individuals can tolerate a few weeks of nutrient deprivation without adverse consequences (Keys 1962), one cannot assume that these various techniques (parenteral nutrition, enteral nutrition, or oral supplements) are effective therapeutic interventions. Since they all have associated potential harms (including cost), efficacy needs to be demonstrated in randomised clinical trials comparing the use of the intervention to a control group that is not receiving any nutritional intervention.

Furthermore, the perspective regarding what causes 'malnutrition' has been broadened (Jensen 2010) to consider the role of the underlying disease. It is now being recognised that weight loss is not just a matter of poor nutrient intake. Rather, underlying inflammatory processes may produce various chemical substances (for example, cytokines) that impair protein synthesis and increase protein degradation. In such situations, it would not necessarily be expected that simply providing exogenous nutrients would improve clinical outcomes. In fact, it might even be possible that such nutrient provision simply further stokes the catabolic fires. This more recent perspective further emphasises the need for establishing proof of efficacy with randomised trials.

A systematic review published in 2001 (Koretz 2001) assessed the utility of parenteral nutrition versus no nutritional therapy in a wide variety of disease states. The available evidence at that time indicated that parenteral nutrition was not, in general, beneficial. In fact, when all of the trials were considered together, the use of parenteral nutrition resulted in more infectious complications. Eight of the randomised clinical trials addressed patients with liver disease; parenteral nutrition was not found to have any significant effect on morbidity or mortality when those trials were considered together (Koretz 2001).

A subsequent systematic review assessed the utility of enteral nutrition and oral supplements (Koretz 2007). When various subgroup combinations of all of these trials were considered, some benefits were teased out. With regard to liver disease, five trials of oral supplements did not find that this intervention significantly improved morbidity or mortality in general (Koretz 2007). Five other trials failed to show that enteral nutrition had any impact on morbidity (Koretz 2007). However, when the three enteral nutrition trials that reported mortality were combined in a meta-analysis, a significant benefit was observed (Koretz 2007). Unfortunately, all of the observed effects were confounded by the fact that they were only seen in trials with high risks of bias (Koretz 2007).

It has been claimed that the parenteral infusion or enteral delivery of special nutrient formulations that are rich in branched-chain amino acids (BCAA) are helpful in patients with liver disease, especially in the treatment of hepatic encephalopathy. The postulated mechanism has been that the encephalopathy is due to an excess of aromatic amino acids in the central nervous system and that BCAA can compete for uptake in the brain thereby restoring a more normal balance (Fischer 1971; Morgan 1990). A previous Cochrane review (Als-Nielsen 2003) described an improvement in hepatic encephalopathy associated with the use of BCAA, but the effect was only seen in trials with high risks of bias.

Other than these two somewhat dated systematic reviews (Koretz 2001; Koretz 2007) and a Cochrane protocol designed to assess nutritional interventions in patients with liver transplantation (Langer 2009), no systematic reviews of the nutritional interventions of parenteral nutrition, enteral nutrition, or oral supplements in liver disease are available. It is the purpose of this systematic review to address the question of whether or not any of these nutritional interventions favourably impact on the morbidity or mortality of patients with liver disease other than those who have undergone liver transplantation.

OBJECTIVES

We assessed the beneficial and harmful effects of parenteral nutrition, enteral nutrition, and oral nutritional supplements (liquid formulations containing at least a source of nitrogen and non-nitrogen calories) on the mortality and morbidity of patients with underlying liver disease.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised clinical trials of parallel or cross-over design evaluating the effect of enteral or parenteral nutrition or multicomponent oral supplements for patients with liver disease. For cross-over trials we only planned to use the data from the first period (although no such trials were identified). For trials with multifactorial designs, we planned on only using the groups receiving the nutritional intervention and the group receiving no intervention, if possible. If not, we compared all patients receiving the nutritional intervention to all patients not receiving this intervention. We did not apply any restrictions on date of publication, language of publication, or publication status (published or unpublished work). For trials published in a language other than English, we planned to obtain a translation done by a person who was fluent in both English and the language of the paper. If a full translation was not available but there was an English abstract, the trial was treated as one that was available only in abstract form.

Types of participants

Patients of any age, sex, and ethnic group with any underlying acute or chronic liver disease and who were treated as inpatients or outpatients were considered.

There were two general categories of patients, medical and surgical. Since there is a planned systematic review of nutritional interventions in liver transplantation (Langer 2009), in general trials in transplanted patients were not included in this review. The exceptions to this rule were trials that provided perioperative nutritional support in patients undergoing liver transplantation, since this is analogous to perioperative trials for other types of surgery in patients with liver disease. In such trials, only clinical events in the immediate post-transplant course (the hospitalisation for the transplant or the first 30 postoperative days, or both) were considered as outcomes. (If the trial enrolled patients on a transplant list but did not follow them through the transplant surgery, that trial was considered to be a medical trial in patients with cirrhosis.) The surgical and medical trials were assessed separately. Thus, there were six planned primary analyses, namely each of the three nutritional interventions in medical patients, and each of the three in surgical patients.

Alcoholic hepatitis was defined in whatever manner the original investigators chose, but a necessary component of that definition was that there was a history of recent alcohol use (within the preceding two weeks).

Types of interventions

We included trials that compared parenteral or enteral nutrition or oral nutritional supplements (as defined in the following paragraphs) to placebo or no treatment. The intervention had to be provided for at least five days; we assumed that nutritional support would not have an effect if it was given for a shorter period of time. Trials that compared different types of nutritional interventions but did not include a group receiving placebo or no intervention were excluded.

Parenteral nutrition was defined as the receipt of intravenous fluids containing a source of nitrogen (as amino acids or protein hydrolysate) and some quantity of non-protein calories (as fat or carbohydrate), which were greater than the intravenous calories given to the control group. The intravenous infusion of only a source of nitrogen (without additional calories) was not considered to be parenteral nutrition. In a previous systematic review of parenteral nutrition, a distinction was made between full parenteral nutrition and 'protein-sparing therapy' or hypocaloric parenteral nutrition (Koretz 2001). These two forms of parenteral nutrition differed with regard to the amount of calories that were provided. In this review, this distinction was disregarded.

Enteral nutrition was defined as the intestinal infusion (through a tube) of a liquid formulation containing at least a source of nitrogen (as amino acids, protein hydrolysates, or intact protein) and some quantity of non-protein calories (as fat or carbohydrate) such that the planned total (intravenous fluids and enteral nutrition) caloric intake was greater than the intravenous calories given to the control group. The site of infusion could be the stomach or small intestine.

Oral nutritional supplements were defined as liquid formulations containing a source of nitrogen (as amino acids, protein hydrolysates, or intact protein) and a non-protein source of calories (as fat or carbohydrate). These formulations could be commercially available or specifically manufactured or developed by the investigators. Powdered formulations that were mixed with water prior to ingestion were acceptable. Trials of supplements that consisted only of additional food or of vitamins or minerals, or both, were excluded.

Control patients received no nutrient intake beyond that contained in ad libitum feedings or 5% (or in the case of neonatal trials, 10%) dextrose intravenously, or both, as maintenance fluid. If cross-over to a nutritional intervention was designed to occur in a parallel group trial, and in fact was done in at least one patient before at least five days, the trial was excluded. (Since the question is the use or non-use of nutritional support, we assumed that a period of at least five days of no support would provide a minimum time for the effects of the nutrient deprivation to become manifest.)

Trials that included more than one nutritional intervention were included provided that there was also a group that received placebo or no intervention; each intervention was compared to the no-treatment group. However, trials that compared different types of nutritional interventions but did not include a group receiving placebo or no intervention were excluded.

If the treatment group received more than one nutritional intervention (for example, some patients received enteral nutrition and others received oral supplements), we classified the trial according to the intervention that the majority of patients in the treatment group received. (No such trials were identified.)

Cointerventions were acceptable as long as they were provided in the same manner to both arms of the trial.

Types of outcome measures

Primary outcomes

1. Mortality.
2. Hepatic morbidity (appearance or failure of resolution of ascites, appearance of gastrointestinal bleeding, appearance or failure of resolution of hepatic encephalopathy).

3. Health-related quality of life as assessed by the original investigators.
4. Adverse events.

Depending on the availability of data, we attempted to classify adverse events as serious or non-serious. Serious adverse events were defined as any untoward medical occurrence that was life threatening; resulted in death, or persistent or significant disability; or any medical event which may have jeopardised the patient or required intervention to prevent it (ICH-GCP 1997). All other adverse events (that is, any medical occurrence not necessarily having a causal relationship with the treatment but did, however, cause a dose reduction or discontinuation of the treatment were considered as non-serious.

Secondary outcomes

1. Serum bilirubin as a manifestation of jaundice; only trials in which the average baseline bilirubin level in the participants was at least 3 mg% (51.3 µmol/l) were employed.
2. Infection.
3. Postoperative surgical complications (for the surgical trials only) (if the surgical trial involved patients without cirrhosis, the outcomes of liver failure (ascites, variceal bleeding, and encephalopathy) would not be expected to be reported):
   - total;
   - intra-abdominal;
   - pneumonia;
   - wound problems.
4. Duration of hospitalisation (including duration of stay in an intensive care unit for critically ill patients).
5. Costs or other economic outcomes, or both, as assessed by the original investigators.
6. Nutritional variables (body weight, anthropometrics (triceps skinfold thickness, midarm muscle circumference, midarm circumference), nitrogen balance).

Search methods for identification of studies

We searched the Cochrane Hepato-Biliary Group Controlled Trials Register (Gluud 2011), Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*, MEDLINE, EMBASE, and Science Citation Index Expanded (Royle 2003). The search strategies (designed at the protocol stage) are available in Appendix 1 with the time span for the searches. As it was expected that thousands of potential titles would be identified, RK did the preliminary review of all of the titles. One of the other authors (AA) was given a sample of 500 titles to also check. If it was discovered that RK had missed any pertinent references, the remaining citations were then to be searched in duplicate; however, no new trials were identified in this second review. We also searched the reference lists of identified trials and review articles for additional publications of interest.

In addition, RK has already conducted a handsearch of a number of medical subject headings (alimentation; branched chain amino acids; dietary disorders; enteral nutrition; enterostomy; fat emulsion; food, formulated; gastrostomy; hyperalimentation; hypocaloric alimentation; hypocaloric nutrition; intragastric feeding; intragastric feeds; intragastric nutrition; nutrition; nutrition diseases; nutrition disorders; nutrition supplement; parenteral nutrition; percutaneous endoscopic gastrostomy; peripheral parenteral nutrition; permissive underfeeding; post-pyloric feeding; post-pyloric nutrition; protein hydrolysate; supplemental feeding; supplemental feeds; total parenteral nutrition) in Index Medicus from 1960 until it ceased publication in 2000.

RK conducted hand searches of several medical journals (including published abstracts of meetings of the American Society of Parenteral and Enteral Nutrition, the European Society of Parenteral and Enteral Nutrition, the American Gastroenterological Association, and the American Association for the Study of Liver Diseases) from 1965 to the present (January 2012). These journals included Annals of Internal Medicine, Clinical Nutrition, Gastroenterology, Hepatology, Journal of Parenteral and Enteral Nutrition, Lancet, and The New England Journal of Medicine.

We contacted experts in the field, including scientific societies for nutritional support, and asked whether they have been involved in, or were aware of, any further trials (recent or ongoing) on the effects of parenteral nutrition, enteral nutrition, or supplements for patients with liver disease. We have also tried to identify unpublished studies by contacting manufacturers of nutritional support formulations that have been sold for use in liver disease. (The registered products identified were Hepatic-Aid II™ (Hormel Healthlabs), NutriHep™ (Nestle USA), HepatAmine™ (B. Braun Medical), and Aminoleban™ (Otsuka); three companies were contacted via email through the contact mechanism available on the company website (Nestle, B. Braum, Otsuka), and the fourth was contacted via an email address available on that website (Hormel Healthlabs).)

Finally, we searched Clinicaltrials.gov in an effort to identify unpublished trials (Appendix 1).

We had planned to modify the search strategies if required as the review progressed, but this was not necessary.

Data collection and analysis

Selection of studies

RK assessed the retrieved references for eligibility in the manner described above. The excluded studies and the reasons for their exclusion are listed in the Characteristics of excluded studies table. Trials deemed to be eligible for inclusion were reviewed by a second individual (either AA or TL).

Data extraction and management

We extracted data on source (the geographical region where the trial was conducted, the year of publication); type of nutritional intervention (parenteral nutrition, enteral nutrition, oral nutritional supplement); inclusion and exclusion criteria; description of participants (number, sex distribution, age distribution, surgical or medical, underlying liver disease: acute (hepatitis (viral, alcoholic in absence of cirrhosis, drug-induced, other), obstructive jaundice, other), chronic (cirrhosis with etiology (viral, alcoholic, autoimmune, drug-induced, metabolic, other), hepatitis (alcoholic with cirrhosis, viral, other)), or acute-on-chronic); presence or absence of hepatic decompensation (ascites, encephalopathy, variceal bleeding); and setting (inpatient or outpatient); interventions and co-interventions; outcomes; factors assessing risk of bias (see next section); and sample size calculation using a data extraction sheet.

For each of the groups of trials, we reported total number of patients randomised and the demographic features of sex and age; for these latter two estimations, we used whatever data were avail-

able. We assumed that when these features were not reported for the dropouts in a particular trial they were comparable to the features of those reported. We also assumed that when the sex distribution or age was not reported for a particular trial the averages reported for the remaining trials were representative of the missing data. Medians were used as means if the means were not reported and the averages were calculated on a weighted basis rather than calculating a simple average from the average age or percentage male in each trial.

Assessment of risk of bias in included studies

Two investigators (RK and either AA or TL) independently assessed the methodological quality of the trials without masking the trial names. These assessments followed the instructions given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and the Cochrane Hepato-Biliary Group Module (Gluud 2011). Due to the risk of biased overestimation of intervention effects in randomised trials with inadequate methodological quality (Schulz 1995; Moher 1998; Kjaergard 2001; Wood 2008), we looked at the influence of methodological quality of the trials on the results by evaluating the reported randomisation and follow-up procedures in each trial. If information was not available in the published trial, we attempted to contact authors of the publications in order to assess the trials correctly; the details of these contact attempts are summarised in the descriptions of each included trial. We assessed generation of the allocation sequence, allocation concealment, blinding, incomplete outcome data, intention-to-treat analysis, selective outcome reporting, and other biases (baseline imbalance, early stopping, and vested interest bias) using the following criteria.

Generation of the allocation sequence

- Low risk, sequence generation was achieved using computer random number generation or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice are adequate if performed by an independent adjudicator.
- Unclear risk, the trial was described as randomised but the method of sequence generation was not specified.
- High risk, the sequence generation method is not, or may not be, random. Quasi-randomised studies, those using dates, names, or admittance numbers in order to allocate patients, are inadequate and were excluded for the assessment of benefits but not for the assessment of harms.

Allocation concealment

- Low risk, allocation was controlled by a central and independent randomisation unit; sequentially numbered, opaque and sealed envelopes, or similar; so that intervention allocations could not have been foreseen in advance of, or during, enrolment.
- Unclear risk, the trial was described as randomised but the method used to conceal the allocation was not described, so that intervention allocations may have been foreseen in advance of or during enrolment.
- High risk, if the allocation sequence was known to the investigators who assigned participants or if the study was quasi-randomised. Quasi-randomised studies were excluded for the assessment of benefits but not for the assessment of harms.

Blinding

- Low risk, the trial was described as double blind and the method of blinding was described, so that knowledge of allocation was adequately prevented during the trial.
- Unclear risk, the trial was described as double blind but the method of blinding was not described, so that knowledge of allocation was possible during the trial.
- High risk, the trial was not double blind, so that the allocation was known during the trial.

Incomplete outcome data

- Low risk, the numbers and reasons for dropouts and withdrawals in all intervention groups were described, or if it was specified that there were no dropouts or withdrawals.
- Unclear risk, the report gave the impression that there had been no dropouts or withdrawals but this was not specifically stated.
- High risk, the number or reasons for dropouts and withdrawals were not described.

Intention-to-treat analysis

- Low risk, all patients randomised into the trial were accounted for in the analyses or, if not, it was possible from the available data to perform such analyses.
- Unclear risk, the report gave the impression that all of the patients were included in the analyses but the actual numbers were not available.
- High risk, not all of the patients were accounted for in the analyses and it was not possible to redo the analyses from the data provided.

Selective outcome reporting

- Low risk, predefined, or clinically relevant and reasonably expected outcomes were reported on. For these trials, there should be data regarding mortality and at least one element of hepatic (or, for the surgical trials in patients without cirrhosis, postoperative) morbidity.
- Unclear risk, not all predefined or clinically relevant and reasonably expected outcomes (mortality and at least one element of hepatic or postoperative morbidity) were reported on or were not reported fully, or it was unclear whether data on these outcomes were recorded or not.
- High risk, one or more of the clinically relevant and reasonably expected outcomes (mortality and at least one element of hepatic morbidity) were not reported on; data on these outcomes should have been likely to have been recorded.

Potential vested interest biases (of investigators or sponsors, or both)

- Low risk, the trial was not sponsored (in part or in whole) by funders who would have an apparent interest in the outcome and the trial was conducted by investigators without previous work in the same area that might have produced a vested interest in them.
- Unclear risk, identity of sponsors or prior work of investigators was not available.
- High risk, trial sponsored by funders with potential vested interest or the trial conducted by investigators with previous publications that would suggest vested interest, or both.

Definition of low and high risk of bias

It was expected that few, if any, of the identified trials would be blinded. If blinding was not assessed as being adequate, trials with lower risk of bias were to be defined as those with the following features.

1. Low risk assessment of generation of allocation sequence.
2. Low risk assessment of allocation concealment.
3. Low risk assessment of handling of incomplete outcome data.
4. Low risk assessment of intention-to-treat analysis.
5. Low risk assessment of selective outcome reporting.
6. Low risk assessment of vested interest bias.

If a trial was adequately blinded, it was to be considered to be at lower risk of bias if the following features were present.

1. Low risk assessment of generation of allocation sequence.
2. Low risk assessment of allocation concealment.
3. Low risk assessment of handling of incomplete outcome data.
4. Low risk assessment of intention-to-treat analysis.
5. Low risk assessment of selective outcome reporting.

All other trials were considered to be at high risk of bias.

Measures of treatment effect

Most of the primary outcomes (mortality, appearance or failure of resolution of ascites, appearance of gastrointestinal bleeding, appearance or failure of resolution of hepatic encephalopathy, adverse events) are dichotomous and were assessed as present or absent. Two of the secondary outcomes (infections, postoperative complications) were also similarly assessed. The continuous data (duration of hospitalisation or duration of stay in an intensive care unit for critically ill patients, nutritional outcomes (body weight, anthropometrics, nitrogen balance), and economic parameters) were treated as continuous variables and were assessed as means and standard deviations. Health-related quality of life (defined by the investigators of the individual trials) was also expected to be presented as scales representing continuous variables. The end-of-study serum bilirubin was used with the assumption that the value at the beginning of the trial was the same in both groups.

If the report did not describe the number of patients with a particular outcome, but only the total number of outcomes, it was assumed that each outcome occurred in an individual patient.

If the report did not specify the number of patients who newly developed one of the prespecified outcomes (that is, ascites, encephalopathy, infections, or the postoperative complications) or which of the patients had one of these conditions at the beginning of the trial and failed to resolve it but only noted the numbers of patients with these outcomes at the beginning and the end of the study, it was assumed that the difference between the numbers represented the number who failed to resolve it (if there were more outcomes at the beginning than at the end) or developed it (if the number at the end was greater than the number at the beginning). (For example, if the report only stated that there were five patients with ascites at the beginning and one at the end, it was assumed that four of the five had the ascites resolve and one did not.)

Unit of analysis issues

Health-related quality of life measurements were expected to vary from trial to trial and it was planned to perform the analysis after standardisation. However, the data that were presented employed a large number of scales, often without any explanation regarding what a normal value was nor whether a high number was favourable or unfavourable, so these data were presented only qualitatively.

Dealing with missing data

See section on exploratory analyses (Sensitivity analysis)

Assessment of heterogeneity

Heterogeneity was explored by the Chi^2 test, with significance set at $P \leq 0.10$, and with the I^2 statistic. The value of I^2 is considered to represent the amount of heterogeneity that is present in a meta-analysis (Higgins 2002); values $\leq 30\%$ were defined as representing limited heterogeneity.

Assessment of reporting biases

We planned to use a funnel plot to explore bias (Egger 1997; Macaskill 2001) and the linear regression approach described by Egger et al to determine the funnel plot asymmetry (Egger 1997). However, with the exception of the medical trials of supplements, no category had a sufficient number of trials (at least 10) to make such an analysis worthwhile.

Data synthesis

We conducted primary analyses in the following six categories of comparisons.

Parenteral nutrition versus placebo or no intervention

- Medical patients
- Surgical patients

Enteral nutrition versus placebo or no intervention

- Medical patients
- Surgical patients

Oral supplements versus placebo or no intervention

- Medical patients
- Surgical patients

We performed meta-analyses of these categories according to the recommendations of The Cochrane Collaboration (Higgins 2011) and the Cochrane Hepato-Biliary Group Module (Gluud 2011). We used the software package Review Manager 5 (RevMan 2011). For dichotomous variables, we calculated the risk ratio (RR) (previously known as the 'relative risk') with 95% confidence interval (CI). For continuous variables, we calculated the mean difference (MD) with 95% CI. We used both a random-effects model (DerSimonian 1986) and a fixed-effect model (DeMets 1987). In the case of discrepancy between the two models we reported both results; otherwise we only reported the results from the fixed-effect model.

Subgroup analysis and investigation of heterogeneity

We planned to perform the following subgroup analyses.

- Low risk of bias trials and high risk of bias trials as separate analyses.
- Trials of acute and trials of chronic liver disease as separate analyses (for the purposes of these analyses, alcoholic hepatitis and hepatocellular carcinoma were considered to be chronic liver disease).
- Patients with cirrhosis of any aetiology.
- Trials of alcoholic hepatitis.
- Trials in patients with hepatocellular carcinoma.
- Publication status (only trials reported as full papers).
- Trials of branched-chain amino acids and trials of standard amino acids in patients with hepatic encephalopathy as separate analyses.
- Surgical trials excluding the liver transplant ones.

Sensitivity analysis

We planned to perform the following exploratory analyses.

- Combining the surgical and medical trials for each intervention.
- Intention-to-treat analysis employing worst-best case (assuming the worst outcome for all patients with missing data in the treatment group and best outcome for all patients with missing data in the control group) and best-worst case (assuming best outcome for all patients with missing data in the treatment group and worst outcome for all patients with missing data in the control group) scenarios. (These analyses provide the maximum extremes in effect estimates.)
- Using the absolute risk difference (ARD) as a measure of treatment effect.
- Combining all of the trials for an assessment of mortality.
- Because of the finding of a beneficial effect of enteral nutrition on mortality without any demonstrable effect on morbidity in a previous systematic review of enteral nutrition (Koretz 2007), we employed trial sequential analysis to evaluate if significant differences in the primary outcomes could be due to random error (Brok 2008; Wetterslev 2008; Brok 2009; Thorlund 2009).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

Initially, we identified 15,033 references from the computer searches performed through January 2012. Most of these were duplicates or clearly irrelevant. We reviewed 322 citations in more detail; these were reports from 224 separate randomised trials and non-randomised or observational studies, review articles, and editorials. A total of 181 of these 224 studies and other publications did not meet the inclusion criteria and the 254 associated references were excluded; these are all listed in the table entitled Characteristics of excluded studies. Nine other studies (10 publications) were published in journals that were not readily available, in languages that required translation, failed to completely explain how the control groups were treated, or did not provide quantitative data (Fink 1978; Leweling 1980; Caballera Rovira 1987; Hartung 1989; Zhuming 2001; Khlynov 2009; Macias-Rosales 2010; Chen 2011; Korenaga 2011); these are listed in the Characteristics of studies awaiting classification. The remaining 34 trials, reported in 58 publications, were eligible for this review. Finally, a search of the records of RK identified an additional three eligible trials (Guy 1995; Sievert 1999; Schuetz 2006) that were reported in abstract format only. The details of the 37 eligible trials are presented in the table entitled Characteristics of included studies and Table 1.

A search of clinicaltrials.gov identified 224 titles but most of them were not relevant to this topic. Seven potential (registered but unpublished) trials (Córdoba; Mao; Pirlich; Seguin; Soriano; Tayek; Van Erpecum) were identified; three of these were clearly not going to be eligible and are also listed in the Characteristics of excluded studies (Córdoba; Soriano; Tayek) and the others (Mao; Pirlich; Seguin; Van Erpecum) are listed in Characteristics of ongoing studies.

Five of the 37 eligible trials (Calvey 1985; Reilly 1990; Hasse 1997; Sievert 1999; Qiu 2009) included more than one treatment group. In four of them, one treatment group was given standard amino acid formulations and the second treatment group was given branched-chain amino acid formulations (Calvey 1985; Reilly 1990; Hasse 1997; Sievert 1999). In the fifth, one treatment group was given a standard amino acid formulation and a second treatment group was given a formulation enriched with glutamine (Qiu 2009). For most of the analyses, the two treatment groups were combined; in the subgroup analyses that assessed the different amino acid formulations, only the appropriate treatment group was included and compared with the common control group. One of these trials (Reilly 1990) provided continuous data for each group separately; in order to accommodate this in the RevMan software, the mean value was calculated for both groups and the smaller standard deviation was used (Reilly 1990).

Two trials were designed to include two separate interventions and the patients were separately randomised to each one (Bonkovsky 1991; Hendry 2010). In the former (Bonkovsky 1991), patients were also randomised to receiving or not receiving oxandrolone; data were provided for all four groups and only the data from those receiving the parenteral nutrition and those not receiving either intervention were used. The latter report (Hendry 2010) also randomised the patients to the receipt or non-receipt of postoperative laxatives; the data were only reported for the combined groups, so all of the patients who received the supplements were compared with all of the patients not receiving the supplements (regardless of whether or not laxatives were also received).

Included studies

See 'References to studies' (Included studies).

Excluded studies

See 'References to studies' (Excluded studies).

Risk of bias in included studies

One unblinded trial of supplements in medical patients did meet the other six criteria and was judged to be at lower risk of bias after we received more information from the investigator (Kobashi 2006). All of the remaining trials were assessed as being at high risk of bias and were judged to be inadequate or unclear in at least two of the six domains. These risks are summarised in Figure 1 and Figure 2.

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

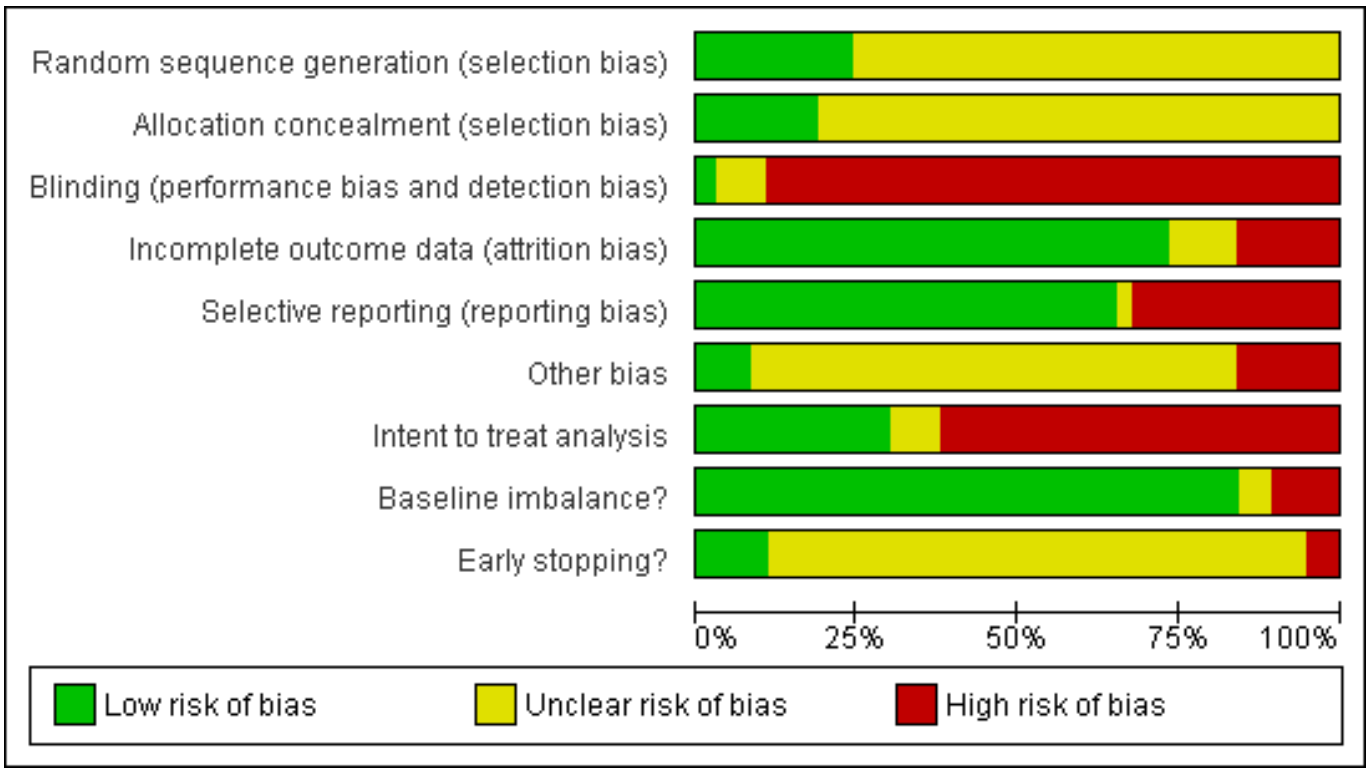


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

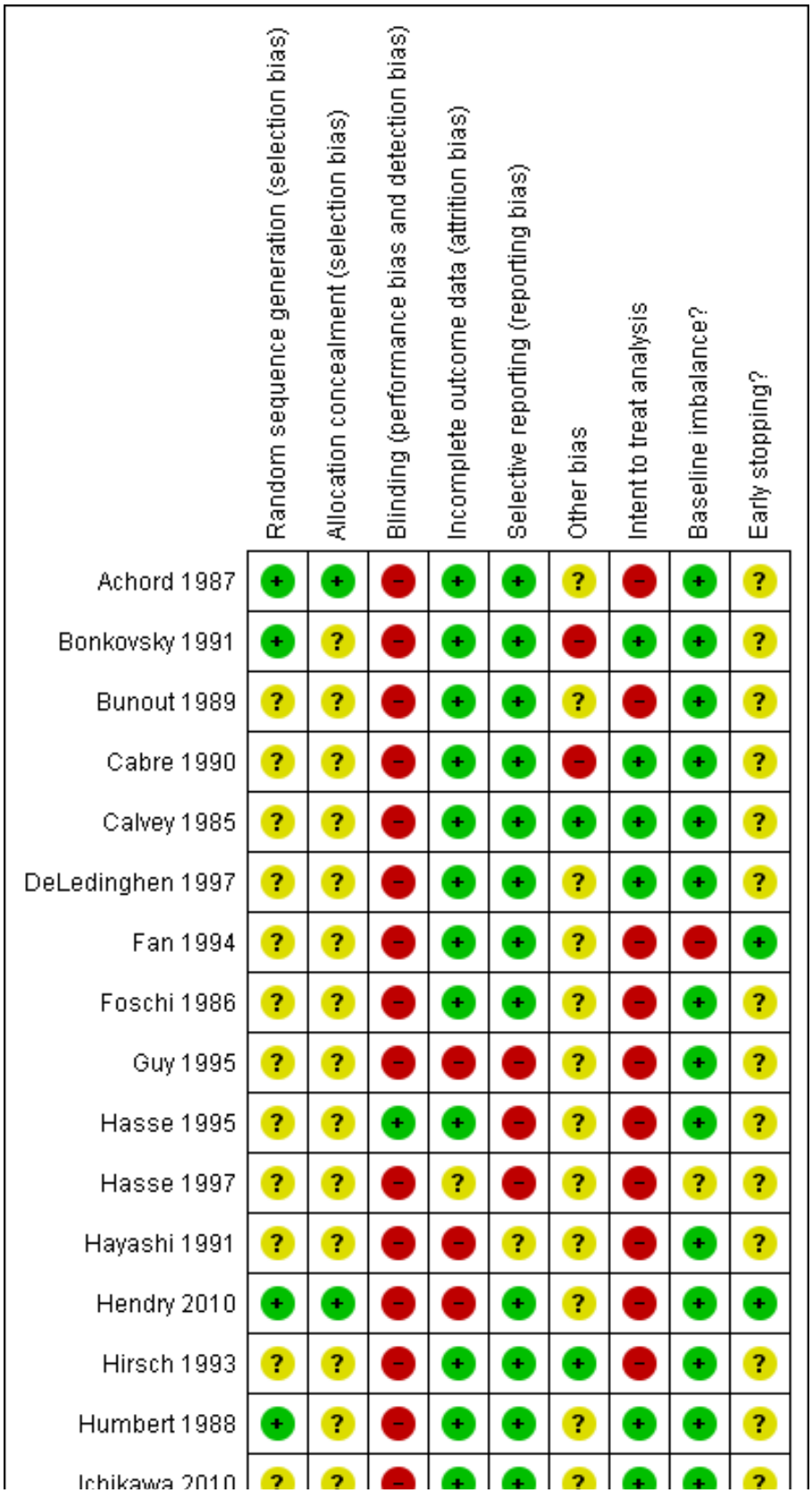


Figure 2. (Continued)

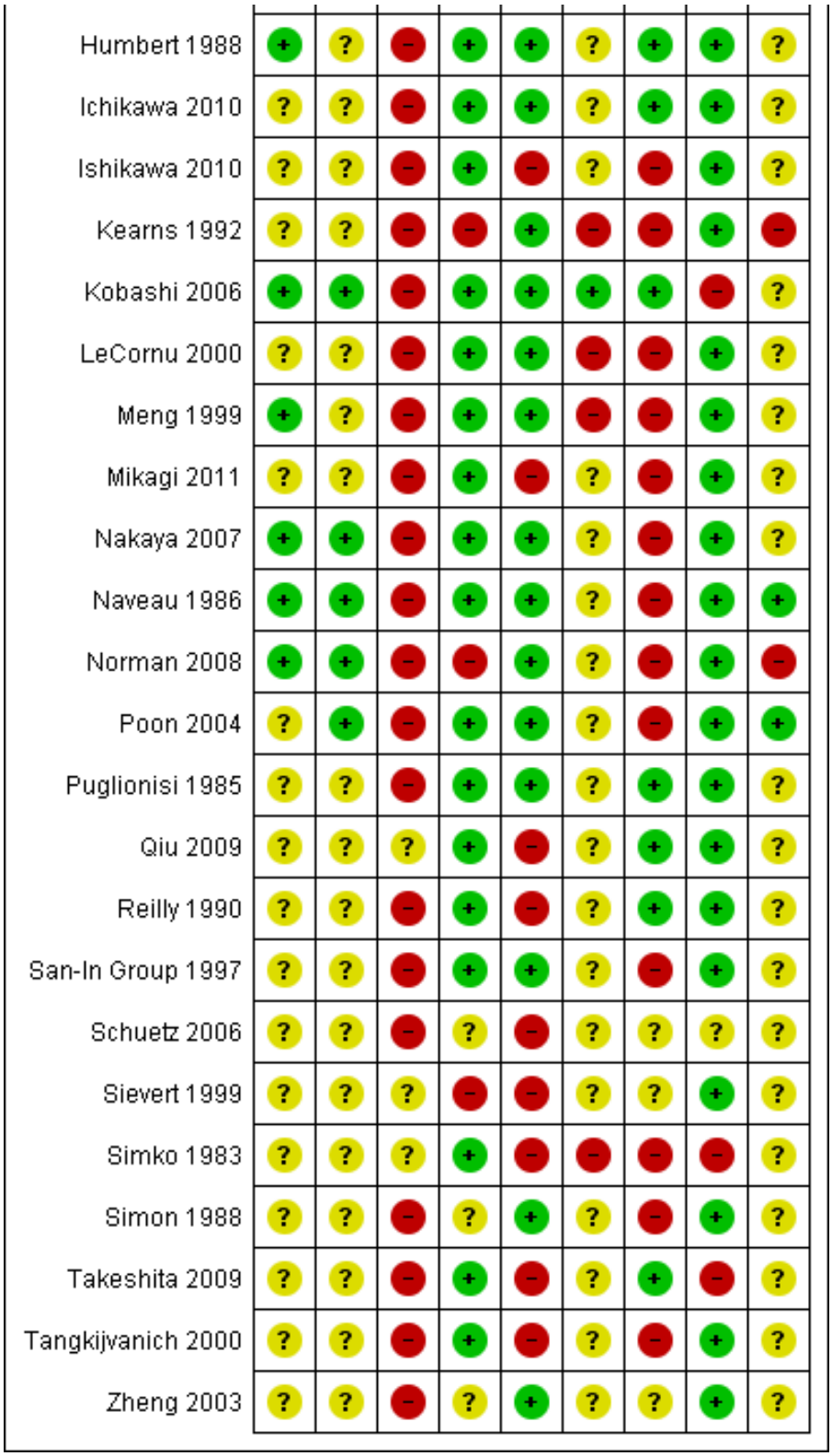
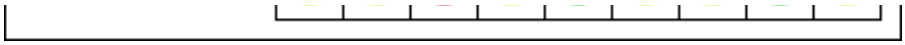


Figure 2. (Continued)



Allocation

Only nine trials (Naveau 1986; Achord 1987; Humbert 1988; Bonkovsky 1991; Meng 1999; Kobashi 2006; Nakaya 2007; Norman 2008; Hendry 2010) described an adequate method for generating the randomisation sequence. The employed methods included random number tables, blind drawing of cards, and computer generation. Only seven trials provided information to suggest that the allocation sequence was adequately concealed (Naveau 1986; Achord 1987; Poon 2004; Kobashi 2006; Nakaya 2007; Norman 2008; Hendry 2010); the techniques included serially numbered, sealed, opaque envelopes; central registration; and blind drawing of a card at the time of randomisation.

Blinding

Only two of the trials (Simko 1983; Sievert 1999) even mentioned potential blinding in the details of the methodology. In these two trials of supplements (Simko 1983; Sievert 1999) the 'placebo' was not described.

Incomplete outcome data

All but 10 of the trials (Simon 1988; Hayashi 1991; Kearns 1992; Guy 1995; Hasse 1997; Sievert 1999; Zheng 2003; Schuetz 2006; Norman 2008; Hendry 2010) accounted for dropouts. In 10 of the remaining 27 trials, there were no dropouts (Calvey 1985; Puglionisi 1985; Cabre 1990; Reilly 1990; Bonkovsky 1991; DeLedinghen 1997; Kobashi 2006; Qiu 2009; Takeshita 2009; Ichikawa 2010). Thus, in spite of adequate reporting of dropouts, intention-to-treat analysis could only be done in the 10 trials in which there were no dropouts (Calvey 1985; Puglionisi 1985; Cabre 1990; Reilly 1990; Bonkovsky 1991; DeLedinghen 1997; Kobashi 2006; Qiu 2009; Takeshita 2009; Ichikawa 2010) or in one trial where, in spite of dropouts being described, an intention-to-treat analysis was reported (Humbert 1988).

Selective reporting

Most of the trials reported mortality and one or more variables of morbidity. Eight trials (Simko 1983; Hayashi 1991; Guy 1995; Hasse 1995; Hasse 1997; Sievert 1999; Tangkijvanich 2000; Mikagi 2011) did not report mortality and three (Reilly 1990; Qiu 2009; Takeshita 2009) provided mortality but not morbidity data. While one trial did not explicitly report mortality, quality of life data were presented for all of the patients at the end of the eight-week follow-up, inferring that there were no deaths (Ichikawa 2010). Finally, two trials were assessed as inadequate in this category because the methods sections explicitly described outcomes to be assessed and for which no quantitative or qualitative data were reported (Takeshita 2009; Ishikawa 2010).

Other potential sources of bias

Baseline imbalance was absent in most of the trials. Baseline differences between the treated and control groups were present in four trials (Simko 1983; Fan 1994; Kobashi 2006; Takeshita 2009). Baseline characteristics were not reported in two trials (Hasse 1997; Schuetz 2006); both of these trials were reported only as abstracts.

Most of the investigators did not provide information to suggest that a sample size was predetermined, so it was not possible to be sure whether or not that trial was stopped prematurely. One trial was stopped early because the investigator left the institution (Norman 2008). Five trials did describe predetermined sample sizes (Naveau 1986; Kearns 1992; Fan 1994; Poon 2004; Hendry 2010); one of these was stopped after an unplanned interval analysis (Kearns 1992).

Most of the reports did not indicate how the trial was funded. Industry provided at least partial funding for six (Simko 1983; Cabre 1990; Bonkovsky 1991; Kearns 1992; Hasse 1995; Meng 1999) and three of the trials were funded by governmental or educational agencies (Calvey 1985; Bunout 1989; Hirsch 1993). One other trial was performed by investigators who had previously published a paper showing an association between malnutrition and a poor clinical outcome (LeCornu 2000).

Effects of interventions

Parenteral nutrition

Medical disorders

Four trials compared parenteral nutrition with no parenteral nutrition (Naveau 1986; Achord 1987; Simon 1988; Bonkovsky 1991) (170 patients, 59% male, average age 46 years). All of these trials were conducted in patients hospitalised with various forms of alcoholic liver disease.

All four trials reported mortality data (Naveau 1986; Achord 1987; Simon 1988; Bonkovsky 1991). When the data were combined, parenteral nutrition had no demonstrable effect. No effect was observed with regard to the appearance (Achord 1987; Simon 1988) or resolution (Naveau 1986; Achord 1987; Simon 1988) of ascites. No effect was demonstrated on the appearance (Naveau 1986; Achord 1987; Simon 1988) or resolution (Achord 1987; Simon 1988) of hepatic encephalopathy; all of these trials employed standard amino acid formulations. None of the trials reported data for gastrointestinal bleeding.

Adverse events, thrombophlebitis with or without sepsis in particular, were noted in occasional patients in the parenteral nutrition arms but no comparable data were available concerning the occurrence of similar complications in the control groups (Naveau 1986; Achord 1987; Simon 1988; Bonkovsky 1991). No quality of life data were available.

Only one trial (Naveau 1986) provided information regarding infections. There were four such events in the recipients of the parenteral nutrition versus none in the control group, a difference that was not statistically significant. Parenteral nutrition was associated with a larger reduction in the serum bilirubin (MD -2.86 mg%, 95% CI -3.82 mg% to -1.89 mg%, 3 trials) (Naveau 1986; Achord 1987; Simon 1988). No data were available regarding duration of hospitalisation or cost.

One trial (Bonkovsky 1991) did provide data regarding nitrogen balance; it was significantly better in the recipients of the parenteral nutrition (MD 3.60 g/day, 95% CI 0.86 grams/day to 6.34 g/day). Other nutritional outcomes that were assessed were reported in different ways and could not be combined in a meta-analysis; no differences were seen with regard to body weight (Bonkovsky 1991) or anthropometric measurements (Naveau 1986; Bonkovsky 1991).

Surgical disorders

Five trials assessed the use of parenteral nutrition in patients with liver disease undergoing surgery (Puglionisi 1985; Reilly 1990; Fan 1994; Zheng 2003; Qiu 2009) (333 patients, 68% male, average age

52 years). The surgical procedures were resection of hepatocellular carcinoma (Fan 1994), portocaval shunt (Puglionisi 1985), liver transplantation (Reilly 1990; Qiu 2009), and various hepatobiliary procedures in patients with cirrhosis (Zheng 2003).

Parenteral nutrition did not have a significant effect on mortality (Puglionisi 1985; Reilly 1990; Fan 1994; Zheng 2003; Qiu 2009). The fixed-effect model analysis of two trials (Fan 1994; Zheng 2003) suggested that ascites was less likely to occur postoperatively in the recipients of the parenteral nutrition (RR 0.65, 95% CI 0.48 to 0.87) but there was statistical heterogeneity in these trials (I^2 = 70%) and the significant difference was not seen in the random-effects model (RR 0.67, 95% CI 0.39 to 1.15). There was no significant difference in the incidence of postoperative encephalopathy in two trials, both employing branched-chain amino acid formulations (Puglionisi 1985; Fan 1994). Patients with pre-existent ascites or encephalopathy were not enrolled into the surgical trials. Only one trial reported data regarding gastrointestinal bleeding (Fan 1994) or jaundice (Qiu 2009); parenteral nutrition was not shown to affect either outcome.

No data were available concerning adverse events or quality of life.

One trial reported data regarding infections (Fan 1994); there were fewer in the group receiving the parenteral nutrition (RR 0.47, 95% CI 0.25 to 0.88). Parenteral nutrition had no effect on the serum bilirubin (Reilly 1990; Zheng 2003). Postoperative complications were only reported in one trial (Fan 1994); parenteral nutrition was associated with an improvement in total complications and pneumonia but not in intra-abdominal complications or wound infections. Duration of hospitalisation (including days in the intensive care unit) and cost were reported in one trial (Reilly 1990); no differences were seen.

Nutritional variables were reported in two trials (Fan 1994; Zheng 2003). Body weight loss or gain was improved by parenteral nutrition (Fan 1994; Zheng 2003) as was nitrogen balance (reported as 'accumulated nitrogen equilibrium' and thus not entered into the meta-analysis) (Zheng 2003). Anthropometric variables were improved in one (Zheng 2003) but not the other (Fan 1994) trial.

Enteral nutrition

Medical disorders

Seven trials assessed the role of enteral nutrition in various medical conditions (Calvey 1985; Cabre 1990; Kearns 1992; Guy 1995; DeLedinghen 1997; Schuetz 2006; Norman 2008) (279 patients, 59% male, average age 51 years). The underlying medical conditions included malnourished cirrhosis (Cabre 1990), alcoholic liver disease (Calvey 1985; Kearns 1992), stabilised variceal bleeding (DeLedinghen 1997); patients awaiting liver transplantation (Guy 1995); and decompensated cirrhosis with (Schuetz 2006) or without (Norman 2008) associated hepatic encephalopathy. All seven trials were conducted in hospitalised patients.

Enteral nutrition did not have any significant impact on mortality (Calvey 1985; Cabre 1990; Kearns 1992; DeLedinghen 1997; Norman 2008). Only one trial reported any data regarding ascites (Cabre 1990); there was no difference in the incidence of ascites resolution. Four trials (Calvey 1985; Kearns 1992; Guy 1995; Schuetz 2006) reported data on the appearance and two trials (Calvey 1985; Kearns 1992) reported data on the resolution of hepatic encephalopathy; no significant differences were observed regardless of whether standard (Calvey 1985; Kearns 1992; Guy 1995; Schuetz 2006) or branched-chain amino acid (Calvey 1985) formulations were employed. (The hepatic encephalopathy that was present as an inclusion criterion in one of these trials (Schuetz 2006) was subclinical; no frank episodes of encephalopathy developed in any patients during the trial.) Four trials failed to find any effect of the enteral nutrition on the subsequent development of gastrointestinal bleeding (Calvey 1985; Cabre 1990; DeLedinghen 1997; Norman 2008). Likewise, two trials (Kearns 1992; Norman 2008) failed to show that enteral nutrition had any effect on the serum bilirubin levels in icteric patients.

Only one trial reported adverse events (Kearns 1992). No significant differences were seen in the occurrence of renal insufficiency or diarrhoea. On average, the nasoduodenal tube had to be replaced three times in the recipients of the enteral nutrition over the course of the 28-day trial.

No data were available regarding quality of life.

No significant effect was observed on the rate of infection (Calvey 1985; Cabre 1990; DeLedinghen 1997; Norman 2008) or duration of hospitalisation (Cabre 1990; Kearns 1992; DeLedinghen 1997); one of these trials was not included in the meta-analysis (Kearns 1992) because the standard deviation or standard error was not provided. No cost data were available.

Nitrogen balance was reported differently in three trials (Calvey 1985; Kearns 1992; DeLedinghen 1997). It was significantly better in the recipients of enteral nutrition in one trial (Kearns 1992) but there was no difference between the groups in another (DeLedinghen 1997); the third trial (Calvey 1985) did not report any statistical analysis but the median balance was higher in the recipients of the branched-chain amino acid formulation (+2.3 g/day) than in those who received a standard amino acid formulation (+0.4 g/day) or in the controls (+0.3 g/day). There was a significantly higher weight loss in the control group in one trial (Kearns 1992) but no difference in the body mass index in another (DeLedinghen 1997). There was no apparent effect of the enteral nutrition on anthropometric measurements (Calvey 1985; Cabre 1990; Kearns 1992; DeLedinghen 1997).

Surgical disorders

Only two trials assessed the use of enteral nutrition in liver disease, one in patients with obstructive jaundice (Foschi 1986) and the other in patients in the immediate postoperative period after liver transplantation (Hasse 1995) (110 patients, 62% male, average age 60 years).

The enteral nutrition did not have any significant impact on mortality (Foschi 1986). No data were available to assess the outcomes of the appearance or resolution of ascites or hepatic encephalopathy, gastrointestinal bleeding, quality of life, or serum bilirubin (although the intraoperative biliary drainage that was performed in all patients in one trial (Foschi 1986) would have confounded such an analysis).

With regard to adverse events, only one trial (Hasse 1995) stated that there were no significant differences between the two groups with regard to organ rejection or rehospitalisation.

There was no significant effect of the enteral nutrition on the rate of infection (Foschi 1986; Hasse 1995), the duration of hospitalisation (including length of stay in the intensive care unit) (Hasse 1995), or

cost (Hasse 1995). There was a significant reduction in total postoperative complications in the one trial that provided such data (Foschi 1986) (RR 0.38, 95% CI 0.16 to 0.91) but not in any of the specific ones (intra-abdominal complications, pneumonia, or wound infections) (Foschi 1986). Furthermore, these data were limited by the fact that four patients dropped out of the treatment group of the trial for reasons related to factors of illness (including two who had complications of biliary drainage).

With regard to nutritional outcomes, no significant differences were seen for weight (Foschi 1986), triceps skinfold thickness (Foschi 1986), or nitrogen balance (Hasse 1995).

It must be appreciated that the available data were limited.

Oral nutritional supplements

Medical disorders

Fourteen trials compared the use of oral nutritional supplements versus no supplements in patients with liver disease (Simko 1983; Humbert 1988; Bunout 1989; Hayashi 1991; Hirsch 1993; Hasse 1997; San-In Group 1997; Sievert 1999; Tangkijvanich 2000; Poon 2004; Kobashi 2006; Nakaya 2007; Takeshita 2009; Ichikawa 2010) (987 patients, 74% male, average age 66 years). The underlying disease states included alcoholic liver disease (Hirsch 1993), compensated cirrhosis (Ichikawa 2010), malnourished patients with cirrhosis (Bunout 1989; Hasse 1997; Sievert 1999), patients with cirrhosis and hepatic encephalopathy (Simko 1983; Hayashi 1991), decompensated cirrhosis (Humbert 1988; Tangkijvanich 2000; Nakaya 2007), and patients with hepatocellular carcinoma and cirrhosis without any other criteria (Kobashi 2006) or who had recently undergone an attempted curative resection (San-In Group 1997) or who were receiving transarterial chemoembolisation for unresectable disease (Poon 2004; Takeshita 2009). All but three of these trials (Bunout 1989; Hayashi 1991; Takeshita 2009) were conducted in outpatients.

Nine trials (including the one trial in which no mortality was inferred (Ichikawa 2010)) reported data regarding mortality (Humbert 1988; Bunout 1989; Hirsch 1993; San-In Group 1997; Poon 2004; Kobashi 2006; Nakaya 2007; Takeshita 2009; Ichikawa 2010); no significant difference was seen when all of the trials were considered (RR 1.08, 95% CI 0.87 to 1.33, $I^2 = 35\%$) but mortality was significantly higher in the recipients of the oral supplements in the one low risk of bias trial (RR 1.37, 95% CI 1.03 to 1.72) (Kobashi 2006).

Twelve trials provided data regarding the appearance of hepatic encephalopathy (Simko 1983; Humbert 1988; Bunout 1989; Hayashi 1991; Hirsch 1993; Hasse 1997; Sievert 1999; Tangkijvanich 2000; Poon 2004; Kobashi 2006; Nakaya 2007; Ichikawa 2010). No significant differences were present when all of the trials were combined or when the trials that employed standard or branched-chain amino acids were considered separately. (Two of these trials (Hasse 1997; Sievert 1999) included three study groups, with two of them receiving one or the other solution.) Only two trials assessed the utility of supplements in resolving hepatic encephalopathy; one trial employed a standard amino acid-based formulation (Bunout 1989) and the other a branched-chain amino acid formulation (Hayashi 1991). Again, remembering that an RR > 1.0 favours the intervention group, there was an improved resolution when both trials were combined with the fixed-effect model (RR 3.75, 95% CI 1.15 to 12.18) but not with the random-effects model (RR 2.04, 95% CI 0.06 to 75.19). The I^2 was 79% and the P value for the Chi^2 test was 0.03 when these trials were combined. This effect was not seen in the trial of standard amino acids (RR 0.29, 95% CI 0.02 to 4.29) but was present in the trial of the branched-chain amino acid formulation (RR 11.30, 95% CI 1.62 to 78.95).

While two trials did not find any significant effect of the supplements on the resolution of ascites (Hayashi 1991; Nakaya 2007), four trials indicated that there was a reduced incidence regarding the appearance of ascites (RR 0.58, 95% CI 0.38 to 0.87) (Hirsch 1993; Poon 2004; Kobashi 2006; Nakaya 2007). There was no heterogeneity in this analysis and the estimated effect was comparable with the fixed-effect and random-effects models. An external peer reviewer asked us to assess the effect of supplements on serum albumin levels in these medical trials. A meta-analysis of nine trials that provided end-of-trial serum albumin levels (Humbert 1988; Bunout 1989; Hayashi 1991; Hirsch 1993; San-In Group 1997; Tangkijvanich 2000; Nakaya 2007; Takeshita 2009; Ichikawa 2010) indicated that, if anything, it was slightly better in the control group (MD -0.09 g%, 95% CI -0.18 to 0.00). When only the four trials that provided the ascites data were considered with regard to the effect of the supplements on serum albumin, two failed to see any differences (Hirsch 1993; Nakaya 2007), one did not provide any data (Kobashi 2006), and one that could not be included in the meta-analysis because the standard deviation or standard error was not reported found significant improvements at three, six, and nine months but not at the end of the trial (12 months) (Poon 2004).

Five trials reported data regarding the subsequent development of gastrointestinal bleeding (Hirsch 1993; Tangkijvanich 2000; Poon 2004; Kobashi 2006; Nakaya 2007); no significant differences were seen. The serum bilirubin was not affected by the supplements in two trials (Bunout 1989; Hirsch 1993).

Three trials reported no significant difference in various quality of life scores (Functional Assessment of Cancer Therapy (Poon 2004); Karnofsky score (Hayashi 1991); SF-36 questionnaire (Nakaya 2007)). A fourth trial (Kobashi 2006) stated that there was a better improvement in three domains of the SF-36 questionnaire in the recipients of the supplement, a branched-chain amino acid formulation. A fifth trial (San-In Group 1997) found that more controls had a deterioration of the performance status score over the course of the trial. Finally, one trial found that the Epworth Sleepiness Score improved as a consequence of the ingestion of a branched-chain amino acid supplement at night (Ichikawa 2010).

Adverse events were reported in a variety of different ways in six trials (Hayashi 1991; San-In Group 1997; Sievert 1999; Tangkijvanich 2000; Poon 2004; Nakaya 2007). Hayashi et al observed no differences in serious events, defined as the need for an additional intervention or the cessation of the experimental therapy (Hayashi 1991). On the other hand, 5/41 patients receiving supplements and 14/43 controls were readmitted for complications of chemoembolisation in the trial by Poon et al (Poon 2004); this difference was significant. Nakaya et al noted five serious adverse events, four in the 19 recipients of the supplements (one fatal cerebral bleed, one bone fracture, and two increased ascites) and one in the 19 controls (worsening encephalopathy) (Nakaya 2007). Minor gastrointestinal adverse events (diarrhoea, vomiting, abdominal pain or distension, loss of appetite) were reported as consequences of the supplements (without any comparable data for the control groups) in two trials (San-In Group 1997; Tangkijvanich 2000). The incidence of diarrhoea, vomiting, or abdominal pain was not significantly dif-

ferent from what was observed in the control group in two trials (Sievert 1999; Nakaya 2007).

The incidence of subsequent infection was lower in the patients treated with supplements (RR 0.49, 95% CI 0.24 to 0.99, 4 trials) (Hirsch 1993; Sievert 1999; Poon 2004; Nakaya 2007) when the fixed-effect model was used (I^2 = 14%, P = 0.28) but not when the random-effects model was employed (RR 0.49, 95% CI 0.20 to 1.23). In addition, one trial only reported the number of episodes of spontaneous bacterial peritonitis (Tangkijvanich 2000); none was seen in either group. No difference was seen with regard to the length of hospitalisation in the single trial that reported such data (Bunout 1989). In two trials conducted in outpatients (Poon 2004; Ichikawa 2010), no differences were seen with regard to the length of time they spent in the hospital receiving transarterial chemoembolisation in one (Poon 2004) and no patients required hospitalisation in the other (Ichikawa 2010). One trial did not provide any numerical data (Takeshita 2009) but the investigators stated that no difference was observed with regard to the duration of hospitalisation. No cost data were available.

One trial provided data regarding nitrogen balance (Nakaya 2007); it was more positive in the experimental group but the difference did not quite achieve significance (weighted mean difference (WMD) 1.54 g/day, 95% CI -0.01 g/day to 3.09 g/day). Body weight was again reported in a variety of ways; most of the trials did not find any significant differences (Simko 1983; Bunout 1989; Hayashi 1991; Hirsch 1993; San-In Group 1997; Sievert 1999; Tangkijvanich 2000; Poon 2004; Takeshita 2009; Ichikawa 2010). One trial noted that the patients in the treated, but not those in the control, group gained weight (Nakaya 2007). Only one trial reported a significant improvement in any anthropometric measurement (triceps skinfold thickness (Simko 1983)); other trials failed to find any effect of the supplements on triceps skinfold thickness (Humbert 1988; Bunout 1989; Hirsch 1993; Poon 2004), midarm muscle circumference (Simko 1983; Humbert 1988; Tangkijvanich 2000), midarm circumference (Bunout 1989; Hirsch 1993; Poon 2004), or anthropometrics generically (Hasse 1997).

Surgical disorders

Five trials compared the use of oral nutritional supplements with no supplements in surgical patients (Meng 1999; LeCornu 2000; Hendry 2010; Ishikawa 2010; Mikagi 2011) (271 patients, 68% male, average age 57 years). One assessed malnourished patients with cirrhosis who were undergoing liver transplantation (LeCornu 2000) and the other four included patients who were scheduled to have resections of hepatocellular carcinomas (Meng 1999) or a variety of benign and malignant lesions (Hendry 2010; Ishikawa 2010; Mikagi 2011).

No significant differences in mortality were seen when four trials were combined (Meng 1999; LeCornu 2000; Hendry 2010; Ishikawa 2010). Two trials failed to see any hepatic encephalopathy appear in either group (Meng 1999; Ishikawa 2010). No data were available regarding the appearance of ascites or the resolution of ascites or encephalopathy. One trial reported no difference in gastrointestinal bleeding (Meng 1999). It should be remembered, however, that three of these trials assessed patients who did not necessarily have underlying cirrhosis (Hendry 2010; Ishikawa 2010; Mikagi 2011).

No significant difference in the occurrence of infection was seen in three trials (Meng 1999; Ishikawa 2010; Mikagi 2011). No significant differences were found with regard to any of the postoperative complications in four trials (Meng 1999; Hendry 2010; Ishikawa 2010; Mikagi 2011). The fifth trial did not present any numerical data but stated that there were no differences in postoperative complications (LeCornu 2000). Serum bilirubin was not different between the two groups in one trial (LeCornu 2000) (given the confounding factor of a new liver) but was improved more in the recipients of the supplements in another (Meng 1999). One trial reported a shorter duration of stay in the hospital in the treated group (Meng 1999) but there was no such difference in three others (LeCornu 2000; Hendry 2010; Mikagi 2011). The data were not reported in a manner that permitted meta-analysis. One trial did not find any differences in the lengths of stay in the intensive care unit (LeCornu 2000). No cost or quality of life data were identified.

There was limited information regarding adverse events. No differences between the groups were seen with respect to rejection episodes (LeCornu 2000). A second report simply stated that no significant adverse events regarding the supplement were seen (Meng 1999). Finally, three out of 25 patients initially randomised to supplements, but none to a control group, were subsequently excluded for "side effects" (Mikagi 2011). No data regarding quality of life were available.

No significant differences were seen with regard to some nutritional outcomes. These included weight (Meng 1999; Hendry 2010), triceps skinfold thickness (Meng 1999; LeCornu 2000), midarm muscle circumference, or midarm circumference (Meng 1999; LeCornu 2000). No data were provided regarding nitrogen balance.

Again, it should be appreciated that these data were limited by both the low numbers of trials and the methodologic problems (high risks of bias) in the trials.

Summary of significant findings in these primary analyses

Parenteral nutrition resulted in reduction in the serum bilirubin levels and better nitrogen balance in medical patients. In surgical patients, the fixed-effect model (but not the random-effects model) estimated that it reduced the appearance of ascites after surgery. In one trial, this nutritional intervention reduced postoperative complications, especially infections (pneumonia in particular).

Enteral nutrition may have resulted in better nitrogen balance in medical patients. In one trial of surgical patients, there were fewer postoperative complications in the recipients of the enteral nutrition.

Oral nutritional supplements reduced the occurrence of ascites in medical patients. Analyses employing the fixed-effect model suggested that the treated medical patients had fewer infections and better improvement of pre-existent hepatic encephalopathy (especially when a branched-chain amino formulation was employed) but these benefits were not seen in the random-effects model. In five trials of supplements in surgical patients, no benefits were observed.

Subgroup and sensitivity analyses

Effect of risk of bias assessments

Since only one of the trials Kobashi 2006 was at low risk of bias, these analyses could not be performed. However, as noted, the mortality was higher in the recipients of the oral nutritional supplement in that trial. On the other hand, three quality of life measures

were improved in the treated arm and there was a trend (RR 0.60, 95% CI 0.35 to 1.05) for there to be less appearance of ascites in that trial.

Acute compared to chronic liver disease

The patients in each of the trials had some type of underlying liver disease. Even though a surgical intervention could be viewed as an acute event, the underlying liver disease was still a chronic one. As such, these analyses were not performed.

Alcoholic hepatitis

Three trials of parenteral nutrition (Achord 1987; Simon 1988; Bonkovsky 1991), two of enteral nutrition (Calvey 1985; Kearns 1992), and two of oral nutritional supplements (Bunout 1989; Hirsch 1993) were conducted in patients with alcoholic hepatitis. In all of these trials, there were only a few significant differences.

In two trials of parenteral nutrition (Achord 1987; Simon 1988), the intervention resulted in a lower serum bilirubin level (MD -6.41 mg %, 95% CI -9.41 mg% to -3.40 mg%). Nitrogen balance was also significantly better in patients with alcoholic hepatitis (Bonkovsky 1991) who received parenteral nutrition (MD +3.60 g/day, 95% CI 0.86 g/day to 6.34 g/day).

Enteral nutrition did not have any demonstrable effect on mortality, the occurrence of gastrointestinal bleeding, the appearance or resolution of hepatic encephalopathy, infection rates, or serum bilirubin. However, only one or two trials contributed data for each of these analyses.

Likewise, there were only a limited number of trials of supplements. No effect was demonstrated from this intervention with regard to mortality, appearance of ascites, occurrence of gastrointestinal bleeding, the appearance or resolution of hepatic encephalopathy, serum bilirubin, or length of stay in the hospital. One trial reported infection rates (Hirsch 1993); this outcome was significantly reduced in the recipients of the supplement.

Cirrhosis

Two trials of parenteral nutrition (Puglionisi 1985; Naveau 1986), five of enteral nutrition (Cabre 1990; Guy 1995; DeLedinghen 1997; Schuetz 2006; Norman 2008), and nine of oral nutritional supplements (Simko 1983; Humbert 1988; Hayashi 1991; Hirsch 1993; Hasse 1997; Sievert 1999; Tangkijvanich 2000; Nakaya 2007; Ichikawa 2010) assessed patients with cirrhosis, including two trials that addressed the use of enteral nutrition (Guy 1995) or supplements (Hasse 1997) in patients undergoing liver transplantations.

Parenteral nutrition did not appear to affect mortality in the two trials (Puglionisi 1985; Naveau 1986). Only one trial provided any further information (Naveau 1986). No significant differences were seen with regard to the appearance of hepatic encephalopathy or infections. However, there was a significant reduction in the serum bilirubin level (-1.6 mg%, 95% CI -2.74 mg% to -0.46 mg%). On the other hand, the recipients of the parenteral nutrition were less likely to resolve their pre-existent ascites (RR 0.57, 95% CI 0.37 to 0.88). (In this analysis a RR < 1.0 favoured the control group.)

Enteral nutrition was not shown to have any significant effect on mortality, the resolution of ascites, the occurrence of gastrointestinal bleeding, the appearance of encephalopathy, subsequent infections, serum bilirubin, duration of hospitalisation, or nitrogen balance. Supplements also did not appear to have any impact on mortality, the appearance or resolution of ascites, occurrence of gastrointestinal bleeding, appearance of encephalopathy, infections, or bilirubin levels. One trial of a branched-chain amino acid supplement (Hayashi 1991) did find a significant improvement in the resolution of encephalopathy (RR 11.30, 95% CI 1.62 to 78.95).

Supplements may have improved nitrogen balance in one trial (Nakaya 2007) although the 95% CI just crossed the line of equivalence (+1.54 g/day, 95% CI -0.01 g/day to + 3.09 g/day). When this trial was combined with the single trial of enteral nutrition that also reported this outcome (DeLedinghen 1997) the nutritional interventions had an effect (+1.53 g/day, 95% CI +0.06 g/day to +2.99 g/day).

Hepatocellular carcinoma

One trial of parenteral nutrition (Fan 1994) and five of supplements (San-In Group 1997; Meng 1999; Poon 2004; Kobashi 2006; Takeshita 2009) included patients with hepatocellular carcinoma. Two of the trials assessed the effect of immediate postoperative parenteral nutrition (Fan 1994) or an enteral supplement (Meng 1999) after undergoing attempted curative resection. Another trial compared the use of an oral nutritional supplement to no specific nutritional therapy in patients who had undergone such surgery two weeks earlier (San-In Group 1997). The other three trials evaluated patients who still had known cancer (Poon 2004; Kobashi 2006; Takeshita 2009); in two of these trials, the patients were receiving transarterial chemoembolisation (Poon 2004; Takeshita 2009).

Whether all of the trials were considered together or as one trial of parenteral nutrition and five of supplements, there was no significant beneficial effect of the intervention(s) on mortality. In fact, the only low risk of bias trial (Kobashi 2006) reported increased mortality in those receiving supplements. For the remainder of the outcomes, data were only available for one or two trials. With this limitation, no significant differences were seen with regard to the occurrence of encephalopathy or gastrointestinal bleeding. Ascites was significantly less likely to occur with the use of supplements (Poon 2004; Kobashi 2006) (RR 0.53, 95% CI 0.32 to 0.87). Infections were less common in the parenteral nutrition trial (Fan 1994) (RR 0.47, 95% CI 0.25 to 0.86) but not in one of the supplement trials (Poon 2004). As noted earlier, there were also fewer total postoperative complications as well as less pneumonia in the recipients of parenteral nutrition in that trial (Fan 1994). The use of supplements resulted in significantly fewer total postoperative complications in the other surgical trial (Meng 1999) (RR 0.71, 95% CI 0.62 to 0.97).

Publication status

When only the trials published as full papers were considered, no significant differences were seen in most of the outcomes. As reported above, two trials of parenteral nutrition (Fan 1994; Zheng 2003) and two trials of supplements (Hirsch 1993; Poon 2004) found a significant reduction in the appearance of ascites when the fixed-effect (but not when the random-effects) model was employed. As also noted earlier, resolution of hepatic encephalopathy was more common when two trials of supplements in medical patients (Bunout 1989; Hayashi 1991) were combined with a fixed-effect model.

Branched-chain versus standard amino acid formulations for hepatic encephalopathy

These results have been discussed previously. None of the trials, separately or in various combinations, found any significant differences with either standard or branched-chain amino acid formulations in preventing encephalopathy; and only one trial using a branched-chain amino acid supplement (Hayashi 1991) showed that any of these nutritional interventions were better than no therapy in resolving pre-existent hepatic encephalopathy.

Surgical trials excluding liver transplantation

Because of the ongoing systematic review of nutritional interventions in liver transplantation (Langer 2009), an analysis was undertaken to assess only the trials that did not include patients during the perioperative phase of liver transplantation. Largely driven by the findings of one trial (Fan 1994), parenteral nutrition was associated with less postoperative ascites and fewer postoperative complications, especially infections (pneumonia in particular). One of the remaining surgical trials (assessing enteral nutrition) also identified fewer total postoperative complications in the recipients of enteral nutrition (Foschi 1986).

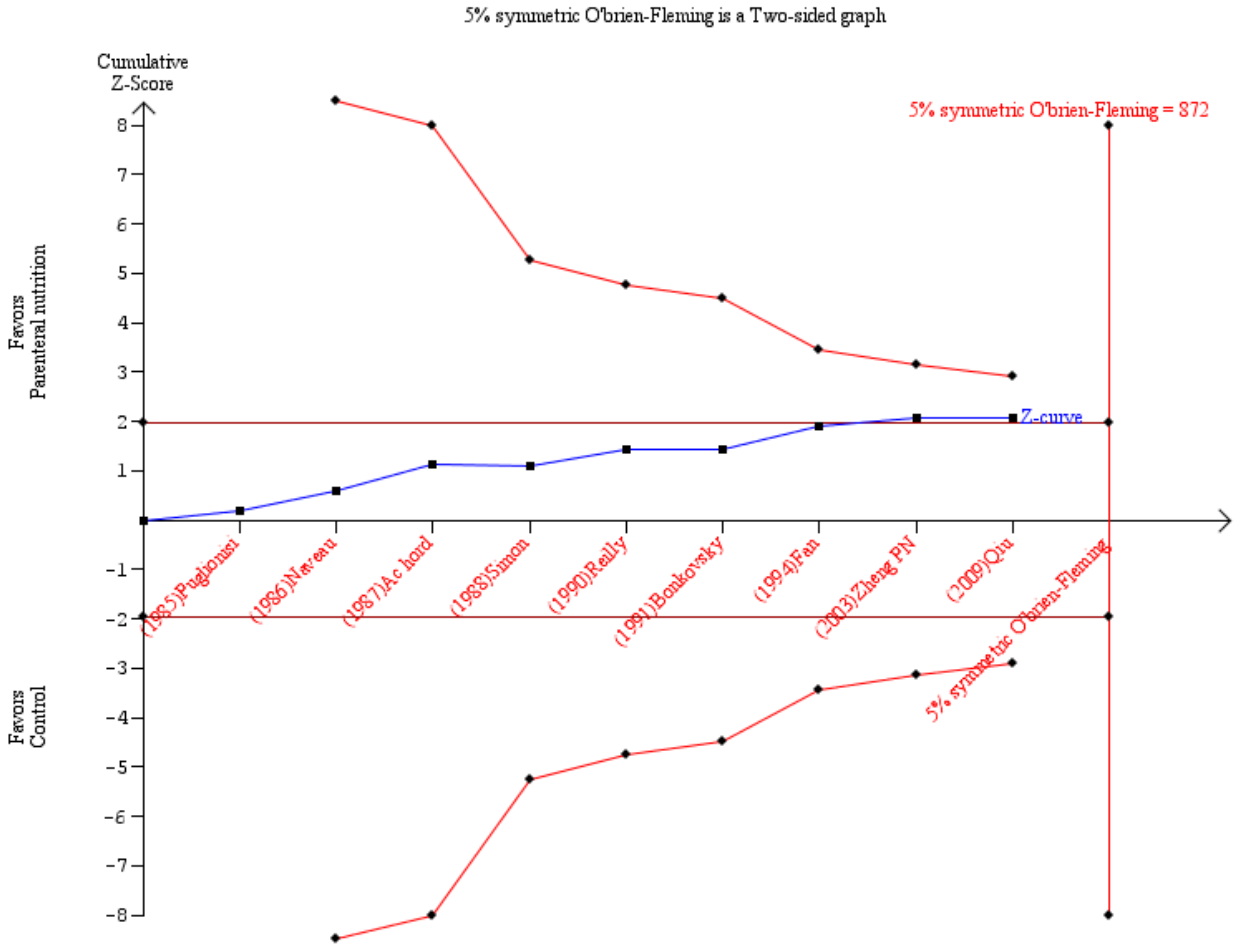
Exploratory analyses

Combining medical and surgical trials for each intervention

Most of these analyses did not find any significant differences. Not surprisingly, given the previous observations, parenteral nutrition was associated with a significant reduction in the serum bilirubin levels (-2.52 mg%, 95% CI -3.45 mg% to -1.60 mg%). Also as previously noted, the fixed-effect model indicated that both parenteral nutrition and supplements resulted in a lower incidence of ascites but the significant difference was lost when the random-effects model was used in the parenteral nutrition analysis. (There were no surgical trials in the analysis of the supplement trials.)

Parenteral nutrition was associated with a significant reduction in mortality in the fixed-effect model (RR 0.53, 95% CI 0.29 to 0.98) but not in the random-effects model (RR 0.55, 95% CI 0.29 to 1.01). The tests for heterogeneity did not suggest that there was an issue with heterogeneity (P = 0.96, I^2 = 0%) although there clearly were substantial differences in the various trials. Nine trials provided data for this analysis (Puglionisi 1985; Naveau 1986; Achord 1987; Simon 1988; Reilly 1990; Bonkovsky 1991; Fan 1994; Zheng 2003; Qiu 2009) but over one-third of the weight in both analyses was from the single surgical trial that reported the most impressive postoperative morbidity outcomes. Two of the trials did not contain any deaths; when the estimate was calculated using the absolute risk difference (ARD), the 95% CI in the fixed-effect model touched the line of equivalence (ARD -0.05, 95% CI -0.11 to 0.00). We undertook a trial sequential analysis, assuming that the mortality was 10% in the controls; even using the optimistic assumption that parenteral nutrition could reduce that incidence by half the Z-curve did not cross the boundary limits (Figure 3).

Figure 3. Trial sequential analysis for parenteral nutrition trials that reported mortality; assumed mortality rate in controls = 10% and RR - 0.50.



Best-worst and worst-best case scenario intention-to-treat analyses

One way to test the robustness of a significant finding with regard to dropouts in the trials is to see if the finding persists under extreme conditions. In this case, intention-to-treat analyses were conducted so that all of the missing patients were included. In the truly best-worst case scenario (for the intervention) all of the dropouts in the treated arm were considered to have a successful outcome and all of the controls were given an adverse one. A truly worst-best case scenario was the opposite, namely the missing treatment arm patients were assigned a bad outcome and the missing controls a good one. The dichotomous data (mortality, hepatic morbidity, rates of infection) were reanalysed under these two hypotheses.

Although 21 trials described dropouts, not all of them could be used in these analyses. Five trials (Naveau 1986; Bunout 1989; Hayashi 1991; Hendry 2010; Ishikawa 2010) stated that dropouts did occur but did not specify how many were lost in each experimental group. In four trials (Achord 1987; Simon 1988; LeCornu 2000; Nakaya 2007) the dichotomous data for hepatic morbidities were not provided in a manner that was suitable for use in these analyses (for example, data only reported for subgroups). One other trial (Kearns 1992) did have dropouts from the trial but it was not clear if those dropouts did or did not have some clinical data provided before exiting from the trial. Fourteen trials (Simko 1983; Foschi 1986; Achord 1987 (mortality data only); Hirsch 1993; Fan 1994; Guy 1995; Hasse 1995; Hasse 1997; San-In Group 1997; Meng 1999; Tangkijvanich 2000; Poon 2004; Norman 2008; Mikagi 2011) provided sufficient information to be included in some or all of these analyses.

In the analyses, all of the significant differences in the dichotomous variables were either observations from a single trial or were only seen in the fixed-effect model. None of them persisted in both extremes of the intention-to-treat analyses.

Outcomes expressed as absolute risk differences

One of the limitations of the risk ratio (RR) calculation is that trials with no events cannot be included in the analyses. This is not the case for ARD calculations. For this reason, all of the analyses were redone using the ARD as the measure of the effect.

With regard to parenteral nutrition, mortality was possibly improved in five surgical trials; a borderline effect (confidence interval included but did not overlap the line of equivalence) was seen with the fixed-effect model (ARD -0.06, 95% CI -0.12 to 0.00) but not with the random-effects model (ARD -0.03, 95% CI -0.08 to +0.02).

(The tests for statistical heterogeneity indicated a P value of 0.47 and an $I^2 = 0\%$.) As was the case when the mortality rates in all of the parenteral nutrition trials were considered, the Fan trial (Fan 1994) accounted for about 40% of the weight in the fixed-effect model. The finding of a reduced postoperative incidence of ascites in the surgical trials persisted. In the only trial of parenteral nutrition in medical patients that provided data (Naveau 1986) there was an increased rate of infection in the recipients of the therapy (ARD +0.20, 95% CI +0.01 to +0.39).

The only new finding in the trials of enteral nutrition related to the rates of postoperative infections. These were significantly better in the recipients of the treatment (ARD -0.18, 95% CI -0.35 to -0.01).

The observations regarding the reduced incidences of ascites and infections in the trials of supplements in the medical patients were seen again. In two small trials assessing oral nutritional supplements in medical patients (Hayashi 1991; Nakaya 2007), the recipients of the supplements were less likely to resolve pre-existent ascites (ARD 0.40, 95% CI 0.08 to 0.71).

Mortality when all trials were combined

Mortality data were available in 27 of the 35 trials. When these were all combined, no significant difference was observed (RR 0.91, 95% CI 0.76 to 1.09).

Funnel plot analyses

Funnel plot analyses were only conducted if there were at least 10 trials; it was only possible to assess the effect of supplements on mortality and the appearance of hepatic encephalopathy in the medical patients. No asymmetry was apparent.

DISCUSSION

'Malnutrition' is commonly encountered in patients with liver disease, especially those with end-stage processes. As a consequence, efforts have been expended to supply nutrients with the intent of improving the nutritional status. This problem has been blamed on a variety of underlying processes, including poor caloric and other nutrient intake, problems with the assimilation and absorption of ingested nutrients, and abnormalities in metabolism. While the first two processes might be fixed with the provision of nutrients, the third is more a result of the disease itself. If the issue is abnormal metabolism, there would be no reason to believe that the simple addition of more fuel or other nutrients will alter anything. In fact, if the abnormal metabolism is bad for the patient, providing more nutrients might make the problem worse.

The best way to prove that any intervention is useful is to compare its use to non-use in patients who have been randomised to one or the other group. It was the intent of this review to summarise the trials that have addressed this question. The data to date have certainly not unequivocally shown that the interventions are useful.

Summary of main results

A total of 37 randomised trials of parenteral nutrition, enteral nutrition, or oral nutritional supplements compared with no nutritional intervention was identified. Because of the high risks of bias of almost all of the trials, significant findings of benefit have to be considered as being potentially overestimated. Even with this limitation, there were only a few areas where the treatments were found to have benefit. The benefits were typically limited to the findings from a single trial or the result of combining data with the fixed-effect model. The benefits that were identified were the following.

Parenteral nutrition produced a more rapid reduction in serum bilirubin and also improved nitrogen balance in icteric patients with medical liver diseases. (In a previously published analysis of all of the trials of artificial (parenteral or enteral) nutrition, the improvement of some nutritional parameters, body weight, and nitrogen balance in particular was commonly accomplished, but these effects did not translate into improvements in clinical outcomes (Koretz 2005). In postoperative liver patients, parenteral nutrition may have reduced postoperative untoward events (ascites and infection, particularly pneumonia). The significant reduction in postoperative ascites was only seen in the fixed-effect model and there was substantial heterogeneity ($I^2 = 70\%$) in the two trials identified. The reduction in other postoperative complications was only seen in one trial.

Enteral nutrition may have improved nitrogen balance and body weight in medical patients although these findings were not consistently found. While one surgical trial suggested that enteral nutrition had a favourable impact on postoperative complications (Foschi 1986), dropouts appeared to be a confounding factor. A previous systematic review of enteral nutrition in surgical trials also found such an effect, but it was only demonstrated in trials with high risks of bias (Koretz 2007).

Over half of the trials (19/37) assessed the use of oral nutritional supplements. The use of these agents appeared to reduce the incidence of ascites. Four (Hirsch 1993; Sievert 1999; Poon 2004; Nakaya 2007) and two (Bunout 1989; Hayashi 1991) trials found a reduction in infections and improvement in pre-existent encephalopathy, respectively, but the significant differences were only found in the fixed-effect model ($I^2 = 21\%$ in the former, and 79% in the latter analysis). The improvement in hepatic encephalopathy was associated with the usage of branched-chain amino acids. Some (but not all) of the trials in medical patients suggested that there may have been an improvement in quality of life scores (although the lack of blinding will always compromise endeavours to study such an outcome). On the other hand, the single trial with a lower risk of bias indicated that mortality was increased with the use of a supplement.

The subgroup and sensitivity analyses did not provide any additional insight. The effect of the nutritional interventions in the three predefined liver diseases (alcoholic hepatitis, cirrhosis, hepatocellular carcinoma) largely paralleled the findings of these nutritional interventions in all liver diseases. Employing only full papers did not provide any further insights. A comparison of the trials at high versus lower risks of bias could not be done.

The exploratory analyses did make one additional observation, namely that parenteral nutrition resulted in improved mortality. When all of the trials were combined, no significant differences were seen. These two observations create a logical paradox; either the analysis of the parenteral nutrition represents a type I error or the analysis of all of the trials contain a type II error.

Overall completeness and applicability of evidence

Since trials assessing nutritional interventions in general have been systematically collected by one of the authors (RK) for over three decades, it is unlikely that a substantial number of relevant publi-

cations have not been identified. Thus, at this time, the findings of this systematic review challenge the practice of widely employing these nutritional interventions. This inability to identify clear benefits from nutritional interventions is consistent with the proposal that the malnutrition observed in many patients with liver disease is actually due to fundamental problems with metabolism, not to simple nutrient deprivation. This concept of viewing malnutrition as being more than simple nutrient deficiency is now being adopted by nutrition support societies (Jensen 2010).

Quality of the evidence

All but one of the trials were at high risk of bias. Since such trials tend to overestimate therapeutic efficacy, the actual effect may be even less advantageous to patients than what was observed.

Potential biases in the review process

As noted, for many of the outcomes the data were derived from a relatively small number of trials, and type I and type II errors (either for benefit or harm) may be present. The high risk of bias in almost all of the individual trials does challenge the reliability of the estimates, especially of the few benefits that were observed.

Agreements and disagreements with other studies or reviews

While no other formal systematic review of the effect of these interventions in liver disease in general was identified, the results are consistent with what has been observed about these interventions in other disease states (Koretz 2001; Koretz 2007).

AUTHORS' CONCLUSIONS

Implications for practice

There are no compelling data to justify the use of artificial nutrition (parenteral or enteral nutrition) or oral nutritional supplements as a component of a treatment program for patients with liver disease. Since these interventions do have defined economic costs (and less well-defined but real adverse effects), the available evidence does not support the routine use of either form of artificial nutrition, or marketed oral nutritional supplements, in patients with liver disease.

Implications for research

There is, at this time, no compelling evidence to support the use of these interventions. Thus, parenteral or enteral nutrition, or commercial nutritional supplements, should only be employed within the context of well-designed and executed randomised clinical trials. Given the absence of strong supportive data to date, these trials need to include a control group that does not receive the therapy. Furthermore, it is apparent that any potential benefit from such treatment is not going to be dramatic, so trials need to be powered adequately to see important but less dramatic differences. Given the dissociation between the effect of nutritional interventions on so-called 'nutritional outcomes' (for example, nitrogen balance), future clinical trials have to use true clinical outcomes (mortality, hepatic morbidity, quality of life, or costs) rather than unvalidated nutritional surrogates.

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Protocol

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Contact Editor: Christian Gluud, Denmark.

Review

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Contact Editor: Christian Gluud, Denmark.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Achord 1987

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in hospitalized patients with alcoholic hepatitis. Geographical location: Jackson, Mississippi, USA. Paper published 1987.
Participants	Inclusion criteria: alcoholic hepatitis. Exclusion criteria: none cited. 40 hospitalized patients randomised, but demographics only available for the 28 who completed trial (23 male/5 female, mean age 46/51 in treatment/control groups).
Interventions	Intervention group received parenteral nutrition (21.25 g amino acids, 430 kcal/liter, 2 liters/day) + conventional diet; Controls received conventional diet (2675 kcal, 100 gm protein, 119 gm fat, 295 gm carbohydrates with salt restriction as needed). Duration therapy at least 21 days.
Outcomes	Mortality, appearance/resolution ascites, appearance/resolution hepatic encephalopathy, serum bilirubin (estimated from Figure 1A). One patient in parenteral nutrition group noted to have thrombophlebitis, but data regarding adverse events did not appear to have been systematically obtained.
Category of study	Parenteral nutrition/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Patients in parenteral nutrition group also given 10 mg cortisol/1000 IU heparin/d for thrombophlebitis prophylaxis; it was decided that these agents were not likely to impact on the clinical course. Request for further information sent to Dr Achord via US mail on September 12, 2011. (Address = James L Achord, MD, Emeritus Professor at University of Mississippi, University of Mississippi, P.O. Box 1848, University, MS 38677), but the letter returned as undeliverable.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Blind drawing of coded cards at time of assignment.
Allocation concealment (selection bias)	Low risk	Blind drawing of coded cards at time of assignment.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 dropouts in treatment group and 5 dropouts in control group all accounted for.

Achord 1987 *(Continued)*

Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funder of trial not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No imbalance identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Bonkovsky 1991

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in hospitalized patients with alcoholic hepatitis. Geographical location Atlanta, Georgia, USA. Paper published 1991.
Participants	Inclusion criteria: 1) Prolonged alcohol intake (100 g/d for at least 5 days/week for at least 1 year); 2) AST < 500, AST/ALT >1.5, albumin < 3.0 gm%, bilirubin > 5 mg%, PT > 6 sec over control; 3) Alcohol cessation within last 5-14 days). Exclusion criteria: Recent bleeding (within 2 days), severe ascites, severe hepatic encephalopathy, creatinine > 2 mg%, sepsis, acute pancreatitis, hemodynamic instability (systolic blood pressure < 80 mm Hg or fluctuating > 20 mm Hg), advanced pulmonary disease (pO2 < 50/pCO2 > 50 mm Hg), diabetes mellitus, active cancer. 21 patients (11 male/10 female, mean age 43).
Interventions	Intervention group received intravenous formulation (35 gm amino acids (Aminosyn II, Abbott), 5% dextrose, minerals, 500 units heparin, 5 mg hydrocortisone/liter), 2 liters/day + daily diet; Controls received daily diet (30 kcal/kg/d, 1 g protein/kg/d). Duration therapy 21 days.
Outcomes	Mortality, serum bilirubin body weight and nitrogen balance (estimated from figures); triceps skinfold thickness and midarm circumference assessed but not reported numerically. One case each of thrombophlebitis and hyponatraemia reported in parenteral nutrition group, but data regarding adverse events did not appear to have been systematically obtained.
Category of study	Parenteral nutrition/Medical.
Sample size calculation	None reported if done.
Full paper or abstract only	Full paper.
Notes	Treatment group got 1000 units heparin and 10 mg hydrocortisone per day for thrombophlebitis prophylaxis; it was decided that these agents were not likely to impact on any outcomes. There were two other trial groups that received oxandrolone with or without parenteral nutrition, but, because of the use of this agent, these groups not considered in the analysis. Request for further information made by e-mail on September 11, 2011 that failed (address = bonkovsh@ummhc.org) and then by US mail on September 12, 2011 (Address = Herbert L Bonkovsky, MD, Division of Digestive Disease & Nutrition, The Liver-Biliary-Pancreatic Center, University of Massachusetts Medical School, 55 Lake Ave., North Worcester, MA 01655). The letter was returned with a note on envelope that Dr Bonkovsky was no longer there.

Risk of bias

Bias	Authors' judgement	Support for judgement

Bonkovsky 1991 *(Continued)*

Random sequence generation (selection bias)	Low risk	Random number table, no blocks.
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	Low risk	Bilirubin reported and this accepted as hepatic morbidity.
Other bias	High risk	Partial funding by Miles Laboratory.
Intent to treat analysis	Low risk	Performed.
Baseline imbalance?	Low risk	No imbalance identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Bunout 1989

Methods	Randomised trial comparing supplements to no supplements in hospitalized patients with alcoholic liver disease. Geographical location Santiago, Chile. Paper published 1989.
Participants	Inclusion criteria: Excessive alcohol ingestion for at least 2 years, 2 or more signs of liver failure (jaundice, hepatic encephalopathy, ascites, hepatomegaly, collateral circulation, edema) who had not been in hospital > 3 days. Exclusion criteria: Contraindication for oral or enteral feeding, current upper gastrointestinal bleeding, grade IV hepatic encephalopathy, extrahepatic major organ (cardiac, pulmonary, renal) failure. 40 patients (no details regarding sex, mean age 49).
Interventions	Intervention group received nutritional supplement (casein, maltodextrin, MCT, sunflower oil) to increase intake to 50 kcal/kg and 1.5 gms protein/kg per day; Controls received standard diet containing 35 kcal/kg and 0.8 gm protein/kg per day. All patients received bed rest, sodium restriction prn, vitamins. Duration therapy 3 to 4 weeks.
Outcomes	Mortality, appearance/resolution hepatic encephalopathy, duration hospitalization, bilirubin.
Category of study	Supplement/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for further information sent via e-mail on September 18, 2011 (dbunout@inta.cl). No response has been received as of March 20, 2012.
Risk of bias	

Bunout 1989 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Four dropouts accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funder of trial not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No imbalance identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Cabre 1990

Methods	Randomised trial comparing enteral nutrition to no enteral nutrition in hospitalized malnourished patients with cirrhosis. Geographical location: Barcelona and Girona, Spain. Paper published 1990.
Participants	Inclusion criteria: Patients with cirrhosis who were malnourished (at least 1 of 3 [triceps skinfold thickness, mid-arm muscle circumference, albumin] below 5th percentile of healthy persons). Exclusion criteria: Hepatocellular carcinoma, current upper gastrointestinal bleeding. 35 hospitalized patients (23 male/5 female, mean age 51).
Interventions	Intervention group received enteral nutrition through nasogastric tube (2115 kcal [38 gm fat {including MCTs}, carbohydrate [367 gm as maltodextrin], 71 gm protein/day [UNIASA, Granada, Spain] with no change in protein intake for hepatic encephalopathy); Control group given oral diet (18-2400 kcal, 70-100 gm protein daily [decreased to 40-60 gm for hepatic encephalopathy]) + intravenous dextrose (5-20%) as needed. Duration therapy planned to be 3 weeks.
Outcomes	Mortality, resolution ascites, gastrointestinal bleeding, infections, duration hospitalization, triceps skinfold thickness, midarm muscle circumference.
Category of study	Enteral nutrition/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Child's Pugh score also reported, but this was not one of the planned outcomes to assess. E-mail request for further information sent to Drs Cabre and Gassul on September 15, 2011 (ecabre.germans-

Cabre 1990 *(Continued)*

trias@gencat.cat and ecabre.germanstrias@gencat.net). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomised".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	High risk	Funded by industry.
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No imbalance identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Calvey 1985

Methods	Randomised trial comparing artificial (majority receiving enteral) nutrition (branched chain or standard amino acid formulation) to no enteral nutrition in patients hospitalized with alcoholic hepatitis. Geographical location: London, England. Paper published 1985.
Participants	Inclusion criteria: Patients with alcoholic hepatitis (clinical and biochemical evidence of hepatocellular damage, alcohol intake > 80 gm for several years and up to present, poor uptake tracer on liver scan, no evidence active hepatitis A or B serologically. Exclusion criteria: Hepatocellular carcinoma, hypotensive (usually from current upper gastrointestinal bleeding). 64 hospitalized patients (31 male/33 female, mean age 49).
Interventions	Intervention group received enteral nutrition through nasogastric tube (either branched chain amino acid formulation [described in Calvey 1985 - BCAA] or standard amino acid formulation [described in Calvey 1985 - SAA] + oral diet given to controls); Control group given oral diet (18-2400 kcal, 70-100 gm protein daily [decreased to 40-60 gm for hepatic encephalopathy]) + intravenous dextrose (5-20%) as needed. Duration therapy planned to be 3 weeks.
Outcomes	Mortality, gastrointestinal bleeding, appearance/resolution of hepatic encephalopathy, infections, nitrogen balance (in subgroup without renal insufficiency. Triceps skinfold thickness and midarm muscle circumference reported only as showing "no difference".
Category of study	Enteral nutrition/Medical.

Calvey 1985 *(Continued)*

Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Enteral nutrition (or supplements) changed to parenteral nutrition if gastrointestinal bleeding or other gastrointestinal problems prevented enteral delivery of nutrients. Days of observation reported, but not clear if this equivalent to duration of hospitalization. E-mail request for more information sent to Dr Williams (since we were not able to identify address for Dr Calvey) on September 15, 2011 (r.williams@researchinliver.org.uk). Response from Dr Williams received on September 19, 2011; Dr Calvey died several years ago and no data available except what is in paper.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly allocated".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Assumption made that only the reported patients were randomised.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Low risk	Funded by Joint Research Committee of King's College Hospital and Medical School.
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No imbalance identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

DeLedinghen 1997

Methods	Randomised trial comparing enteral nutrition to no enteral nutrition in patients hospitalized with variceal bleeding associated with cirrhosis. Geographical location: Poitiers, France. Paper published 1997.
Participants	Inclusion criteria: Patients admitted for active variceal bleeding which had been stabilized associated with cirrhosis. Exclusion criteria: Hepatocellular carcinoma, hepatorenal syndrome, severe hepatic encephalopathy, age > 80 years. 22 hospitalized patients (17 male/5 female, mean age 56).
Interventions	Intervention group received enteral nutrition through nasogastric tube (commercial formulation [Dripac Sondalis, Sopharga, France] with 1665 kcal and 71 gm protein/day until second sclerotherapy) + standard feeding;

DeLedinghen 1997 *(Continued)*

	Control group given oral diet (nothing by mouth X 3 days, low-Na milk on day 4, mixed warm low-Na diet on day 5, 1800 kcal low Na diet from day 6 on). Mean duration of therapy 8.5 days.
Outcomes	Mortality, gastrointestinal bleeding, infections, duration of hospitalization, bilirubin, body weight, triceps skinfold thickness, midarm muscle circumference, nitrogen balance.
Category of study	Enteral nutrition/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for information sent via e-mail on September 16, 2011 (victor.deledinghen@chu-bordeaux.fr). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly assigned patients".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Fund source not reported.
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No imbalance identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Fan 1994

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in patients hospitalized for resection of hepatocellular carcinoma. Geographical location Hong Kong. Study published 1994.
Participants	Inclusion criteria: Potentially resectable hepatocellular carcinoma. Exclusion criteria: None cited. 150 patients initially randomised, but 26 dropped out because metastatic disease found at time of surgery, leaving 124 patients (109 men/15 women, median age 54).
Interventions	Intervention group received parenteral nutrition (35% branched-chain amino acids [1.5 gm/kg], intravenous dextrose and lipid [30 kcal/kg], vitamins, minerals/day) provided for 12 hours at night for 7 days

Fan 1994 *(Continued)*

	preoperatively and for 7 days postoperatively as continuous infusion with 1.75 liter/d fluid restriction; Controls received usual diet preoperatively, 5% dextrose in normal saline postoperatively. Both groups received cefotaxime at time of anesthesia, normal diet preoperatively, and 25 gm intravenous albumin X 5d postop Duration 14 days.
Outcomes	Mortality, appearance ascites/gastrointestinal bleeding/encephalopathy, infections, median duration hospitalization, postoperative complications (total/intra-abdominal/pneumonia/wound), median body weights, median triceps skinfold thickness, median midarm circumference. Adverse event recorded for parenteral nutrition group, but no evidence that similar complications were sought in control arm. Bilirubin only reported as "no difference".
Category of study	Parenteral nutrition/surgical (hepatocellular carcinoma resection).
Sample size calculation	Planned to reduce mortality by 50% and needed 60 patients per group.
Full paper or abstract only	Full paper.
Notes	E-mail sent to Dr Fan on September 13, 2011 (stfan@hku.hk). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	11 dropouts in parenteral nutrition group and 15 in control group for metastatic disease (all accounted for).
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	More patients in parenteral nutrition group retained > 10% indocyanine green at 15 minutes (difference in baseline characteristics); funding source not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	High risk	Parenteral nutrition patients may have been less ill.
Early stopping?	Low risk	Achieved planned number.

Foschi 1986

Methods	Randomised trial comparing artificial nutrition (most receiving enteral nutrition) to no artificial nutrition in patients hospitalized for surgery for obstructive jaundice. Geographical location Milan, Italy. Study published 1986.

Foschi 1986 *(Continued)*

Participants	Inclusion criteria: Patients with obstructive jaundice with bilirubin > 200 micromol/l who were eligible for surgery with preoperative transhepatic biliary drainage. Exclusion criteria: None cited. 60 patients (39 men/21 women, mean age 64) described, but there were 4 other dropouts.
Interventions	Intervention group received preoperative enteral nutrition through nasogastric tube (commercial formulation [Precision BR] with 10% peptides, 0.8% lipid, 81.9% carbohydrate); some patients received parenteral nutrition (50% dextrose and 8.5% AA [Freamine III]); a "few" enteral nutrition recipients received amino acids through nasogastric tube volume was 2-3 liters/day. Controls received standard diet. Duration at least 12 days (mean 20 days). All patients received biliary decompression preoperatively.
Outcomes	Mortality, infections, postoperative total/intra-abdominal/pneumonia/wound complications. Body weight and triceps skinfold thickness noted not to be different, but no numerical data.
Category of study	Enteral nutrition/surgery.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	E-mail request for more information sent to Dr Foschi on September 17, 2011 (Diego.Foschi@unimi.it). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly divided".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Four dropouts accounted for.
Selective reporting (reporting bias)	Low risk	Molrtality and morbidity outcomes reported.
Other bias	Unclear risk	Funding source not identified.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No difference in per protocol group of 60 patients.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Guy 1995

Methods	Randomised trial comparing enteral nutrition to no enteral nutrition in patients hospitalized awaiting liver transplant. Geographical location: New York, New York, USA. Abstract published 1995.
Participants	Inclusion criteria: Hospitalized patients awaiting liver transplantation > 18 years. Exclusion criteria: Hospitalized in ICU, grade 4 hepatic encephalopathy, infections precluding transplantation. 42 hospitalized patients (no data regarding sex or age; 10 dropped out).
Interventions	Intervention group received enteral nutrition through nasogastric tube (Commercial formulation [Impact®]) + unrestricted oral diet prior to transplant; Control group given unrestricted oral diet. Mean duration of therapy at least 5 days (excluded if fewer days).
Outcomes	Hepatic encephalopathy.
Category of study	Enteral nutrition/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Abstract.
Notes	Randomised patients who received transplant within 5 days were excluded from analysis. Data obtained from author at poster. Request for further information sent via US mail on September 16, 2011 to senior author, Dr Miller, as Dr Guy could not be located. (Charles Miller, MD, Transplantation Center, Director, Cleveland Clinic Main Campus, Mail Code A80, 9500 Euclid Avenue, Cleveland, OH 44195). Dr Miller responded on September 24, 2011; he had no information but suggested that we try to contact Dr Steve Guy at Hahneman. A search for a Dr Stephen Guy turned up the following address: Stephen Guy, MD, Drexel Transplant Associates, 216 N. Broad Street, Feinstein Building, 5th Floor, Philadelphia, PA 19102 and letter sent to him on September 26, 2011. No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "prospective randomised trial".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	10 dropouts (unknown how many from each group nor reasons for all of them, although at least some probably had transplant within 5 days of randomisation).
Selective reporting (reporting bias)	High risk	No mortality data provided.
Other bias	Unclear risk	Funding source not identified.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	Although no numbers were presented, poster stated that there were no differences.

Guy 1995 *(Continued)*

Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Hasse 1995

Methods	Randomised trial comparing postoperative enteral nutrition to no enteral nutrition in patients undergoing liver transplant. Geographical location Dallas, Texas, USA. Study published 1995.
Participants	Inclusion criteria: Liver transplant individuals who had required continuous medical care (not necessarily in hospital) and were status 2 who then underwent transplant (randomised after transplant). Exclusion criteria: Requirement for hemodialysis, performance of choledochojejunostomy. 31 patients (17 men/14 women, mean age 51); an additional 19 dropouts also randomised.
Interventions	Intervention group received preoperative enteral nutrition through nasojejunal tube (commercial formulation [Reabilin HN)] beginning at 20 cc/hr and advancing to 40 cc/hr); Control group received standard progression of diet from clears to solids; those who were begun on artificial nutrition were to be dropped from trial. Planned duration 12 days.
Outcomes	Infections, duration hospitalization/intensive care unit, cost, nitrogen balance. No numerical data, but stated no differences in rejections or rehospitalizations.
Category of study	Enteral nutrition/surgery (liver transplant).
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	E-mail request for more information sent to Dr Hasse on September 17, 2011 (jm.hasse@baylorhealth.edu). Dr Hasse did acknowledge receipt of the request, but has not yet (March 20, 2012) provided further data.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Only states "patients randomised at time of transplant".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	Low risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 19 dropouts (38% of those randomised) accounted for.
Selective reporting (reporting bias)	High risk	No mortality data provided.
Other bias	Unclear risk	Partial funding by industry.
Intent to treat analysis	High risk	Could not be done.

Hasse 1995 *(Continued)*

Baseline imbalance?	Low risk	No differences in per protocol groups.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Hasse 1997

Methods	Randomised trial comparing supplements (standard or branched chain amino acids) to no supplements in outpatients awaiting liver transplant. Geographical location Dallas, Texas, USA. Paper published 1997.
Participants	Inclusion criteria: Malnourished outpatient cirrhotic patients with history of encephalopathy awaiting liver transplantation. Exclusion criteria: None cited. 36 patients (no details regarding sex, age).
Interventions	Intervention group received commercial nutritional supplement (Ensure® or Hepatic-Aid® [0.5 gm/kg/d protein and non-protein calories]); Controls received standard diet. Duration therapy 64-143 days.
Outcomes	Appearance hepatic encephalopathy. Text indicates no difference in triceps skinfold thickness, midarm circumference, midarm muscle circumference, but no numerical data.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Abstract.
Notes	Information regarding dropouts and hepatic encephalopathy admissions obtained from author at poster. E-mail request for more information sent to Dr Hasse on September 17, 2011 (jm.hasse@baylorhealth.edu). See above note regarding response.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomised 2:2:1".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Large number dropouts for variety of reasons.
Selective reporting (reporting bias)	High risk	No mortality data.
Other bias	Unclear risk	Funder of trial not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Unclear risk	No data in abstract.

Hasse 1997 *(Continued)*

Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Hayashi 1991

Methods	Randomised trial comparing supplements (standard or branched chain amino acids) to no supplements in patients hospitalized with cirrhosis and hepatic encephalopathy. Geographical location Tokyo, Japan. Paper published 1991.
Participants	Inclusion criteria: Hospitalized patient with cirrhosis (documented clinically and histologically) and Grade I or II encephalopathy or abnormal psychometric testing or abnormal sleeping pattern. Exclusion criteria: <15 years of age, gastrointestinalI bleeding, hepato-renal syndrome, recent/current cancer treatment, recent/current sclerotherapy for varices, women who were pregnant or thought to be. 67 patients (44 men/21 women [2 other dropouts], age in both groups < 39 to >70).
Interventions	Intervention group received nutritional supplement (elemental diet [300 kcal, 11.2 gm amino acid {5.45 grams BCAA]/80} gm pack]), 2 packs/day orally or via tube + oral diet (1400 kcal/40 gm protein per day); Controls received oral diet (2000 kcal, 60 gm protein). Aminoleban EN®, and intravenous amino acids prohibited in general, but Aminoleban® PO/intravenous albumin prn; lactulose, antibiotics, other concomitant drugs used in fixed doses. Duration therapy 21 days.
Outcomes	Resolution ascites, appearance/resolution hepatic encephalopathy, Karnofsky score, serious/non-serious adverse events, bilirubin, body weight (only in patients without ascites).
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full report (manuscript of PhD thesis or submitted paper).
Notes	Information from trial came from a thesis that RLK received years ago as well as abstract; no address found for Dr Hayashi, so no information request could be sent.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Only states "envelope method".
Allocation concealment (selection bias)	Unclear risk	"envelop method" (no other details).
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	2 patients dropped out for being "in appropriate" but unknown from which group.
Selective reporting (reporting bias)	Unclear risk	No mortality data.
Other bias	Unclear risk	Funder of trial not reported.

Hayashi 1991 *(Continued)*

Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Hendry 2010

Methods	Randomised trial comparing carbohydrate drink the evening before surgery and 30 days postoperative oral supplements to regular eating in patients undergoing hepatic resections for liver tumors. Geographical location Scotland and the Netherlands. Paper published 2010.
Participants	Inclusion criteria: Resectable benign or malignant liver tumor, age 18-80, BMI 18-30 scheduled for surgery between July 2006 and June 2008. Exclusion criteria: Pre-existing conditions limiting mobility, underlying cirrhosis, history of liver resection, need for bile duct excision, need for central or extended hepatectomy.
Interventions	Intervention group received 400 ml commercial loading drink (Nutricia Preop®) 10 PM/4AM preop; 400 ml commerical supplement (Nutricia Fortisip®) bid postop (for one month). Control group received regular diet.
Outcomes	Primary outcome was time to passage of stool; secondary outcomes included mortality, postoperative complications. duration of hospitalization, rehospitalizations, and reoperations
Category of study	Supplements/Surgical.
Sample size calculation	Yes, but powered to see difference in time of appearance of stool.
Full paper or abstract only	Full paper.
Notes	Trial had factorial design in which patients also randomised to receiving or not receiving laxative (magnesium oxide) during hospitalization; data in paper presented only for combination groups (supplements versus no supplements and laxative versus no laxative). E-mail request for further information sent to Dr Hendry on 2/17/12 at paul.hendry@ed.ac.uk., but no further information has been received as of March 20, 2012.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation with random number table.
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes (not noted if serially numbered, but accepted as adequate concealment of allocation).
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	6/74 patients dropped out of trial by investigators because the planned resection could not be accomplished and palliative surgery done instead; no indication how many from each group. However, given the block design and the fact

Hendry 2010 *(Continued)*

		that 30 treated versus 38 control patients were compared, it is likely that most, or even all, came from treatment arm (which may have resulted in the removal of higher risk patients).
Selective reporting (reporting bias)	Low risk	Mortality and morbidity reported, but data presented for individuals who also did, or did not, receive laxatives postoperatively.
Other bias	Unclear risk	Unclear funder although commercial company provided the nutrient solutions.
Intent to treat analysis	High risk	Unknown from which arm each dropout came, so intent to treat analysis could not be done.
Baseline imbalance?	Low risk	No differences in baseline characteristics of the per protocol arms.
Early stopping?	Low risk	Sample size calculation indicated need for 14 patients for each of the four arms, and more than that reported.

Hirsch 1993

Methods	Randomised trial comparing supplements (standard or branched-chain amino acids) to no supplements in outpatients with alcoholic liver disease. Geographical location Santiago, Chile. Paper published 1993.
Participants	Inclusion criteria: At least 5 years alcohol consumption (> 150 gm/day), clinical evidence of alcoholic liver disease (2 or more of: jaundice, hepatic encephalopathy, ascites, edema, spiders, collateral circulation, bleeding disorder, varices), residence in Santiago. Exclusion criteria: HBsAg+, significant renal/pulmonary/cardiac disease, diabetes mellitus, malignancy. 65 patients (42 men/9 women (14 other dropouts), mean age 48).
Interventions	Intervention group received nutritional supplement (commercial casein-based supplement (1 liter/day) - 34 gm protein, 1000 kcal/day [ADN®, Laboratorios Davis, Santiago, Chile]) + diet; Controls received 1 placebo tablet + diet. Duration therapy 12 months.
Outcomes	Mortality, appearance ascites/hepatic encephalopathy/gastrointestinal bleeding, infections, bilirubin, body weight, triceps skinfold thickness, midarm circumference.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for more information sent via e-mail on September 18, 2011 (shirsch@inta.cl). No response has been received as of March 20, 2012.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Only states "patients were assigned randomly".
Allocation concealment (selection bias)	Unclear risk	No details.

Hirsch 1993 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Six dropouts in treatment group and eight in control group accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Low risk	Funded by Chilean government.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences in per protocol group.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Humbert 1988

Methods	Randomised trial comparing supplements (branched-chain amino acids) to no supplements in outpatients with cirrhosis. Geographical location Barcelona, Spain. Paper published 1988.
Participants	Inclusion criteria: Cirrhosis (almost all of the patients were Childs B or C). Exclusion criteria: None cited. 49 patients (31 men/18 women , mean age 54).
Interventions	Intervention group received nutritional supplement (branched-chain amino acid-enriched amino acid supplement [65 gm/d in 300 cc water {2224 kcal, 19.6 gm amino acids with 40% as branched chain-amino acids}]; Controls did not receive supplement. All participants received 80-90-gm protein diet, standard treatment for complications. Duration therapy six months.
Outcomes	Mortality, appearance hepatic encephalopathy, bilirubin, triceps skinfold thickness, midarm muscle circumference.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full report.
Notes	Number of episodes of hepatic encephalopathy were total; for purposes of meta-analysis, assumed one per patient. Article in Spanish. Unable to find any contact address or e-mail for Dr Humbert, so no request sent for further information.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Table of random numbers.

Humbert 1988 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two and four dropouts in treatment and control groups accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funder not reported.
Intent to treat analysis	Low risk	Although dropouts noted, denominators in paper were all randomised patients.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Ichikawa 2010

Methods	Randomised trial comparing the use of a late-evening snack of a branched-chain amino acid-enriched supplement to no supplement in cirrhotic patients.
Participants	21 patients (12 treatment, 9 controls) with compensated cirrhosis (documented by laboratory data and imaging). Exclusion criteria - hepatocellular carcinoma, overt encephalopathy, chronic renal failure, use of BCAA supplements, alcohol use, or albumin infusions.
Interventions	Experimental group received a commercial supplement (Aminoleban EN - 13.5 gm protein [enriched with BCAAs] and 210 kcal energy in 50 gm pack) ingested at night for 8 weeks. The control group did not receive any nutrition therapy but consumed food (rice ball containing 210 kcal energy and 9 gm protein) as nocturnal snack.
Outcomes	Sleepiness (assessed by Epworth Sleepiness Scale), symptoms (assessed by cirrhosis symptom score), development encephalopathy, mortality (inferred), need for hospitalization, serum bilirubin, BMI.
Category of study	Supplements/Medical.
Sample size calculation	None reported.
Full paper or abstract only	Full paper.
Notes	Request for further information sent via e-mail on September 18, 2011 (ichikawa@net.nagasaki-u.ac.jp and Shige-ygc@umin.ac.jp). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"After balancing both groups for sex, age, Child-{ugh score (CPS), cirrhotic symptom score (CSS) and albumin level, patients were randomised…"

Ichikawa 2010 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No information provided indicating if or how allocation was concealed.
Blinding (performance bias and detection bias) All outcomes	High risk	No blinding performed.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	Low risk	Mortality and onset encephalopathy (morbidity) reported or inferred (data presented for 8 week evaluation on 21 patients, suggesting that there were no deaths).
Other bias	Unclear risk	Unclear funding; authors had published other paper employing this preparation (Takeshita 2009 below).
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No difference in variety of baseline characteristics.
Early stopping?	Unclear risk	No sample size calculation provided and not clear why trial included 21 patients.

Ishikawa 2010

Methods	Randomised trial comparing preoperative branched-chain amino acid-enriched supplements to usual diet in patients subsequently undergoing partial hepatectomy for the resection of benign or malignant tumours.
Participants	Patients with benign or malignant tumours.
Interventions	Intervention group received a commercial supplement (Aminoleban EN) twice daily for two weeks preoperatively and for 1 to 7 days postoperatively; the control group only consumed normal diet.
Outcomes	Mortality, duration of operation/hospitalization, intraoperative blood loss, postoperative complications including "clinical and biologic signs of hepatic dysfunction".
Category of study	Supplements/Surgical.
Sample size calculation	None reported if done.
Full paper or abstract only	Full paper.
Notes	14 patients excluded form analysis because of reasons that became apparent at the time of surgery; since the trial began 2 weeks earlier, these had to be excluded after randomisation (although that fact was not explicitly stated in the paper). Trial presented at Digestive Disease Week 2009 where additional information was available. Request for further information sent to Drs Ishikawa and Tajiri via e-mail (martinishikawa@nms.ac.jp and tajirit@nms.ac.jp) on September 19, 2011. No response has been received as of March 20, 2012.
Risk of bias	

Ishikawa 2010 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Patients "randomly assigned", but no further details.
Allocation concealment (selection bias)	Unclear risk	At time of presentation of paper at national meeting, stated that sealed envelopes employed, but unclear if opaque and serially numbered.
Blinding (performance bias and detection bias) All outcomes	High risk	No placebo solution employed.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Reasons for exclusion stated, but large number of dropouts (14 of original 38).
Selective reporting (reporting bias)	High risk	Explicitly stated in Methods section that lengths of stay data would be collected, but this outcome was not reported quantitatively or qualitatively.
Other bias	Unclear risk	Funder not reported.
Intent to treat analysis	High risk	14 participants unaccounted for.
Baseline imbalance?	Low risk	There were no differences in the remaining 24 patients with regard to baseline features.
Early stopping?	Unclear risk	No sample size calculation reported and there was no explanation as to why the trial was stopped when it was.

Kearns 1992

Methods	Randomised trial comparing enteral nutrition to no enteral nutrition in patients hospitalised with alcoholic liver disease. Geographical location: San Jose, California, USA. Paper published 1992.
Participants	Inclusion criteria: Clinical diagnosis of alcoholic liver disease, bilirubin > 51 micromol/l, one of the following: albumin < 3gm%, PT > 4 secs above control, ascites on examination. Exclusion criteria: None cited. 31 hospitalized patients (21 male/10 female, mean age 44).
Interventions	Intervention group received enteral nutrition through nasoduodenal tube (commercial formulation [Isocal HCN, Mead Johnson] with 167 kj/kg, 1.5 gm/kg protein/day) + regular diet. Control group given regular diet. Duration of therapy 28 days.
Outcomes	Mortality, appearance/resolution hepatic encephalopathy, bilirubin, serious/non-serious adverse events, body weight, nitrogen balance. Appearance/resolution of ascites and gastrointestinal bleeding noted to be comparable, but no numerical data. Anmthrometic measurements noted not to be different, but no numerical data. Duration hospitalization provided as mean, but no standard deviation or standard error.
Category of study	Enteral nutrition/Medical.
Sample size calculation	Planned to enrol 25 patients in each arm, but did not achieve those numbers.
Full paper or abstract only	Full paper.

Kearns 1992 *(Continued)*

Notes	31 patients described and 6 dropouts; unclear if original randomisation included 37, or if only 25 completed trial; for purposes of analysis, assumed 31 patients reported. Morlality data estimated from Kaplan-Meier curve. Request for further information sent via e-mail on September 16, 2011 (pj.kearns@med.stanford.edu). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Six dropouts (3 from each group, but unclear reasons).
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	High risk	Partial funding by industry.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	High risk	Stopped after 31 patients completed trial without any preplanned intention to do so.

Kobashi 2006

Methods	Randomised trial comparing supplements (branched chain amino acids) to no supplements in outpatients with cirrhosis and hepatocellular carcinoma. Geographical location Japan. Paper published 2006
Participants	Inclusion criteria: Cirrhotic patients with hepatocellular carcinoma. Exclusion criteria: None cited. 233 patients (159 men/74 women, mean age 69).
Interventions	Intervention group received nutritional supplement (Commercial supplement [Amionleban® - 40.5 gm protein (18.3 gm BCAA), 630 kcal/day); Controls did not receive supplement. Duration therapy three years.
Outcomes	Mortality, appearance hepatic encephalopathy. Quality of life information collected but not presented in usable format.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.

Kobashi 2006 *(Continued)*

Full paper or abstract only	Abstract.
Notes	Data for mortality and hepatic encephalopathy obtained at poster presentation by RK; numbers of hepatic encephalopathy episodes presented as total, and, for purposes of meta-analysis, assumed to be one per patient. Request for further information sent via e-mail to Dr Kobashi on September 19, 2011 (hkobashi@md.okayama-u.ac.jp); email address failed. Letter via US mail sent same day (Department of Gastroenterology and Hepatology, Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama University, Okayama, Japan). Response received via e-mail (kobashi0584@gmail.com) informing us 1) that randomisation performed with computer software by study center, 2) that, while no formal mechanism in place to provide concealment of allocation, the assignment was accomplished by fax from the study center, 3) that a sample size was calculated (but no number provided), 4) that there were no significant differences between the 2 groups as for age, sex, viral markers (HBV or HCV), serum ammonia, total bilirubin, prothrombin-time, BTR, ascites, or Child-Pugh class, but serum albumin was significantly lower and encephalopathy significantly higher in the BCAA group, and 5) that the trial was not funded (unclear what he meant, but possibly by industry). He also informed us that both ascites and encephalopathy were present in 31 patients at the beginning of the trial and newly occurred in 54 but that he did not have any data regarding how many had resolution of either during the trial, that 9 patients developed bleeding during the trial, that the serum bilirubin levels in the treated/control arms was 1.29 (0.77 SD)/1.15 (0.078 SD), there were no infections, that quality of life data were obtained (and he sent a spread sheet with numerical scores but no standard deviations), and that no data were obtained regarding costs, lengths of stay, nutritional outcomes, or adverse events. An email was sent back to Dr Kobashi on October 14, 2011, inquiring about the exact sample size calculation, the numbers in each group who had new ascites and encephalopathy, how many in each arm bled, and whether the bilirubin values were baseline or end of study values. On October 17, Dr Kobashi replied with data regarding ascites (16/100 versus 27 [+ 1 pleural effusion]/102 developed it, 3/19 versus 7/12 with ascites deteriorated, but no information provided regarding numbers with ascites who improved), encephalopathy (12/108 versus 16/113 developed it, and no apparent worsening in the 11/1 individuals who had it at the beginning, but no data regarding improvement in this small group of patients), and bleeding (7 [4 varices, 2 without endoscopy, 1 biliary]/5 [2 varices, 3 gastric ulcers] had bleeding, but the 2 without endoscopy and 1 with biliary bleeding were excluded). Also informed us that trial was not funded. While the mortality data was noted on the poster to be not significant, the analyses indicated that the 95% confidence interval did not overlap the line of equivalence; a subsequent e-mail was sent to him and he responded that the numbers that RK had copied were correct. Dr Kobashi also informed us that the trial has not been published in full paper form to date for the following reason: "Sorry to say we have not yet published the full paper of this study. I have some difficulties in the authorship, and the priority for the full authorship of this study belongs to another person (my colleague)." He indicated that this other investigator has some reason not to publish it in a full paper.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See comment in notes.
Allocation concealment (selection bias)	Low risk	See comment in notes.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcomes of all 233 patients at point in time reported.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.

Kobashi 2006 *(Continued)*

Other bias	Low risk	See comment in notes re: funding.
Intent to treat analysis	Low risk	All patients accounted for.
Baseline imbalance?	High risk	No data provided in abstract; data from email indicated that most characteristics similar, but BCAA group had lower albumin and more encephalopathy (suggesting that there was an imbalance in the degree of illness between the two groups).
Early stopping?	Unclear risk	Information from author indicated that he estimated need for 150 to 200 patients per group, but statistician did do sample size calculation. However, do not know what the exact number was and < 150 in each arm.

LeCornu 2000

Methods	Randomised trial comparing branched chain amino acid supplement to no supplement in malnourished outpatients with cirrhosis who were awaiting liver transplant at time of entry and who subsequently received a transplant. Geographical location: Birmingham, UK. Paper published 2000.
Participants	Inclusion criteria: Adult patients with end-stage liver disease on liver transplantation and waiting as outpatients, mid-arm muscle circumference < 25 percentile. Exclusion criteria: midarm muscle circumference > 25th percentile, fulminant/subacute liver failure (need for urgent transplantation), malignant disease, fluid restriction (< 500 ml/d), regrafts, multiple organ failure, celiac disease. 82 patients (60 male/22 female [1 patient in each of the treatment and control groups subsequently dropped out], median age 51).
Interventions	Intervention group received 500 cc daily of a specially prepared supplement (20 gm protein, 33.5 gm fat, minerals, 750 kcal/day) + usual diet; Control group received the usual diet. Duration of therapy until transplantation (median 77 days in treatment group, 45 days in control group). All patients received postoperative immunosuppression.
Outcomes	Mortality, bilirubin, triceps skinfold thickness, midarm muscle circumference, midarm circumference. Methods section described all of the postoperative information that was to be collected (infections, duration of stay in intensive care unit/hospital, postoperative total complications) but the only mention of it was a terse statement that there were no differences; mild rejection in 14/39 versus 10/32 and severe rejection in 15/39 versus 16/32.
Category of study	Supplements/Surgery.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for further information sent to Dr LeCornu via email (kate.lecornu@nnuh.nhs.uk) on September 19, 2011. Subsequent responses in October 4, 2011, provided details about sample size calculation, concealment of allocation, and funding, as well as some outcome data (LOS in hospital and ICU); another response on October 28, 2011, indicated that further information was not available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomisation to either the intervention group or control group".

LeCornu 2000 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Sealed envelopes selected by someone other than trial coordinator (but not stated re: opaque, numbered, or if person associated with investigators).
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One dropout in each arm accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported (mostly qualitatively).
Other bias	High risk	Authors have prior publication showing association between malnutrition and poor outcome in transplant patients; industry supplied product.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences in per protocol groups.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Meng 1999

Methods	Randomised trial comparing the use of postoperative branched chain amino acid supplement to no supplement in patients who underwent surgery for an attempted curative resection for hepatocellular carcinoma. Geographical location: Hong Kong. Paper published 1999.
Participants	Inclusion criteria: Patients with cirrhosis undergoing attempted curative resection of hepatocellular carcinoma. Exclusion criteria: Palliative resection, benign nodular hyperplasia, adenoma. 44 patients (37 male/7 female [4 other dropouts], median age 52).
Interventions	Intervention group received branched chain amino acid supplement (Aminoleban EN®) - 3 packs/day (? 50 gm packs); Control group received isocaloric, isonitrogenous diet. Duration of therapy 12 weeks.
Outcomes	Mortality, appearance gastrointestinal bleeding/hepatic encephalopathy, infections, duration hospitalization postoperative total complications (total number, not number of patients with complications)/intra-abdominal complications/wound infections/pneumonia/major complications (not predefined outcome). Paper indicates that serum bilirubin better in treatment group, but no usable numerical data. Paper indicated that there were no differences in body weight, triceps skinfold thickness, midarm circumference, but no numerical data.
Category of study	Supplements/Surgery.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for further information sent to Drs Meng and Lau via e-mail (mengcs@ha.org.hk and josephlau@cuhk.edu.hk) on September 19, 2011. No response has been received as of March 20, 2012.
Risk of bias	

Meng 1999 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence.
Allocation concealment (selection bias)	Unclear risk	Closed envelopes, but not stated if opaque, serially numbered.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Four dropouts from treatment group, 2 dropouts from control group accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	High risk	Funded by industry.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences in per protocol groups.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Mikagi 2011

Methods	Randomised trial comparing use of preoperative supplements to standard care. Geographical location Japan. Paper published in 2011.
Participants	Inclusion criteria: Patients undergoing segmentectomy or more extensive hepatectomy not including biliary tract reconstruction for liver tumors (HCC, cholangiocellular carcinoma, metastatic liver cancer, carcinoid) between 2/05 and 12/08 Exclusion criteria: Marked renal dysfunction (creatinine clear < 30 ml/min), severe diabetes (requiring insulin), chemoradiotherapy within past month, inability to take oral nutrition.
Interventions	Intervention group received 750 cc/day commercial supplement (Impact®, Ajinomoto Pharm, Tokyo) + 1/2 daily diet. Control group received regular diet.
Outcomes	Primary outcomes appeared to be surrogate measures of inflammatory status (WBC count, interleukin 6 levels), "nutrition" (albumin, prealbumin), liver "function" (ALT, AST levels), and fatty acid metabolism (eicosopentaenoic acid level). Other outcomes reported included postoperative complications (including infections), duration of stay.
Category of study	Supplements/Surgical.
Sample size calculation	Not reported.
Full paper or abstract only	Full paper.

Mikagi 2011 *(Continued)*

Notes	Concern about randomisation - see comment below. E-mail sent requesting further information about trial sent to Dr Mikagi on 2/17/12 at mikagi@med.kurume-u.ac.jp. No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states that patients were randomised. However, according to the patient flow sheet, 41 patients were initially randomised, 26 to the supplement arm and 15 to the controls, and there were 15 dropouts (12 from the supplement arm).
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Since reasons for all dropouts were provided (12 dropouts from supplement arm [8 change of treatment, 3 side effects, 1 withdrew consent], 3 from control arm [2 change of treatment, 1 withdrew consent], our criteria for low risk met. However, the disproportionate number from supplement, especially for change in treatment or side effects, could have introduced bias.
Selective reporting (reporting bias)	High risk	No mortality data reported.
Other bias	Unclear risk	Unclear funder.
Intent to treat analysis	High risk	15/41 patients dropped out and no intent-to-treat analysis reported.
Baseline imbalance?	Low risk	No baseline differences in the per protocol groups.
Early stopping?	Unclear risk	No sample size provided and not clear why trial was stopped when it was.

Nakaya 2007

Methods	Randomised trial comparing supplements (branched chain amino acids) to no supplements in outpatients with cirrhosis secondary to hepatitis C. Geographical location Japan. Paper published 2005.
Participants	Inclusion criteria: Cirrhosis, anti-HCV+, albumin < 3.5 gm%. Exclusion criteria: Overt hepatic encephalopathy, uncontrolled variceal bleeding, refractory ascites, renal impairment, prior history poor compliance, hepatocellular carcinoma with overt disease, positive alpha-fetoprotein, diabetes mellitus on medications, intravenous albumin use. 48 patients (28 men/10 women [10 other dropouts], mean age 68).
Interventions	Intervention group received nutritional supplement (Commercial branched chain amino acid supplement [Amionleban EN® - 13.5 gm protein, 3.5 gm fat, trace minerals and vitamins] 210 kcal/day); Controls received food (9 gm protein, 5 gm fat, 210 kcal/day). Duration therapy 3 months.

Nakaya 2007 *(Continued)*

Outcomes	Mortality, bilirubin, body weight. Quality of life reported, but not in usable format. Triceps skinfold thickness, midarm muscle circumference, midarm circumference measured but not reported; nitrogen balance change only reported as significant for treatment group but not for control group.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for further information sent via e-mail on September 19, 2011 (nakaya@nutr.med.tokushima-u.ac.jp); e-mail address failed. Letter sent via US mail on same day (Yutaka Nakaya, MD, Department of Nutrition and Metabolism, Institute of Health Biosciences, University of Tokushima Graduate School, Tokushima, Japan). Letter dated Novenber 15, 2011 received indicating that the generation of the randomisation scheme was adequate (computer generated based on stratification for "important parameters"), concealment of allocation was adequate (central computer), no sample size calculation was performed and no explanation provided as to why trial was stopped when it was, funding was not obtained and trial conducted by interested investigators. Ascites developed in 1/16 treatment versus 1/15 controls and resolved in 2/3 versus 0/4. Hepatic encephalopathy developed in 0/19 versus 1/19; no patient was encephalopathic at the beginning of the trial. There were no episodes of GI bleeding or infections. 8 different quality of life scores were provided; there were no apparent differences. Data regarding costs and lengths of stay were not collected. There were 5/19 versus 2/19 adverse events in the two arms (in addition to nonsevere ones (fever in one versus nausea in one), there were 4 [death from cerebral bleed, bone fracture, and 2 worsening of ascites] versus 1 [worse encephalopathy] serious adverse events). The weights in the two groups at the beginning/end of the trial were 18.6 (9.0) versus 56.6 (7.7)/59.4 (9.6 SD) versus 57.1 (7.7). The arm muscle circumferences at the beginning/end of the trial were 241.3 (39.6) versus 239.7 (32.5)/244.4 (33.7) versus 243.2 (31.8). Triceps skinfold thicknesses at the beginning/end of the trial were 11.7 (4.4) versus 12.6 (4.5)/12.6 (4.5) versus 13.4 (4.5). New e-mail address also provided (yutaka-nakaya@nutr.med.tokushima-u.ac.jp).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated with stratifications for "important parameters" (information from investigator).
Allocation concealment (selection bias)	Low risk	Central randomisation and assignment (information from investigator).
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Six dropouts in treatment group, 4 dropouts in control group all accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	No external funding; trial conducted by interested investigators. (information from investigator). No sample size calculation (see below).
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences identified.

Nakaya 2007 *(Continued)*

Early stopping?	Unclear risk	No sample size calculation was performed (information from investigator) and unknown why stopped.

Naveau 1986

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in hospitalized patients with alcoholic cirrhosis. Geographical location Bicetre, France. Study published 1986.
Participants	Inclusion criteria: Alcoholic cirrhosis on biopsy or, if not possible, at least 2 our of 5 clinical characteristics (firm liver, ascites, hepatic encephalopathy, splenomegaly, varices at endoscopy) AND bilirubin > 5mg%. Exclusion criteria: Hepatocellular carcinoma, creatinine > 2mg%, sodium < 130 meq/l, septicemia, spontaneous bacterial peritonitis, gastrointestinal bleeding within 3 days, hepatic coma. 40 patients (25 men/15 women, mean age 52).
Interventions	Intervention group received intravenous formulation (20 kcal/kg glucose, 20 kcal/kg lipid, 0.2 gm nitrogen/kg, minerals, vitamins) + oral diet; Controls received oral diet (40 kcal/kg, 0.2 gm nitrogen/kg). Duration therapy 28 days. Patients in both groups received neomycin for encephalopathy.
Outcomes	Mortality, ascites resolution, development of encephalopathy, infections (sepsis), serum bilirubin, triceps skinfold thickness, midarm muscle circumference. The only adverse effects noted were four episodes of sepsis in patients receiving parenteral nutrition; no apparent attempt to look for such events in all of the patients in the trial.
Category of study	Parenteral nutrition/Medical.
Sample size calculation	Sample size based on previously reported trial (Nasrallah 1980).
Full paper or abstract only	Full paper.
Notes	Attempt made to follow patients for 2 years; decision made to confine analysis to in-hospital period. Request for further information sent to Dr Naveau via e-mail on September 11, 2011 (Address = Sylvie.naveau@abc.ap-hop-paris.fr). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated.
Allocation concealment (selection bias)	Low risk	Serially numbered, opaque, sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Three dropouts in treatment group and 2 in control group accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.

Naveau 1986 *(Continued)*

Other bias	Unclear risk	Unclear funder.
Intent to treat analysis	High risk	All information on dropouts not available, although in-hospital mortality reported.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Low risk	Achieved planned number.

Norman 2008

Methods	Randomised trial comparing enteral nutrition to no enteral nutrition in patients hospitalised with decompensated cirrhosis. Geographical location: Germany. Paper published 2008.
Participants	Inclusion criteria: Clinical diagnosis of alcoholic liver disease, bilirubin > 51 micromol/l, one of the following: albumin < 3gm%, PT > 4secs above control, ascites on examination. Exclusion criteria: None cited. 63 hospitalized patients (40 male/23 female, age not provided).
Interventions	Intervention group received enteral nutrition through nasogastric tube (only detail was "high protein formulation"); Control group given standard diet. Duration of therapy 14 days.
Outcomes	Mortality, gastrointestinal bleeding, infections, bilirubin.
Category of study	Enteral nutrition/Medical.
Sample size calculation	Not performed (information obtained from author at poster).
Full paper or abstract only	Abstract.
Notes	Much of the information obtained via discussion with author who was present at poster where study presented (Digestive Disease Week, 2008) Trial from same group as Schuetz 2006, but appears to be different trial. On September 17, 2011, emails sent to Drs Norman and Pirlich (kristina.norman@charite.de and Matthias.pirlich@charite.de) requesting information about both Norman and Schuetz trials. (Email for Dr Pirlich failed.) No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated (information obtained at poster from author).
Allocation concealment (selection bias)	Low risk	Central phone (information obtained at poster from author).
Blinding (performance bias and detection bias) All outcomes	High risk	Information obtained at poster.
Incomplete outcome data (attrition bias) All outcomes	High risk	Dropouts had to have occurred, as percentages at poster did not produce whole numbers.

Norman 2008 *(Continued)*

Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funding source not reported; trial stopped because primary investigator left institution (information obtained at poster).
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	Although no numerical data, abstract stated that there were no differences.
Early stopping?	High risk	Trial stopped early because principal investigator left institution. (Information obtained at poster.)

Poon 2004

Methods	Randomised trial comparing supplements to no supplements in outpatients with newly diagnosed hepatocellular carcinoma. Geographical location: Hong Kong. Paper published 2004.
Participants	Inclusion criteria: Newly diagnosed unresectable hepatocellular carcinoma eligible for transarterial chemoembolisation, no extrahepatic metastases, no vascular complications (hepatic artery thrombosis, main protal vein thrombosis, arteriovenous shunting), no hepatic encephalopathy, no refractory ascites, no variceal bleed within 3 months, bilirubin < 50 micromol/l, albumin > 2.5 gm%, Karnofsky score > 50. Exclusion criteria: Previous treatment for hepatocellular carcinoma, tumor rupture. 88 patients (78 male/6 female [4 additional dropouts], median age of per protocol population 59).
Interventions	Intervention group received branched chain amino acid supplement (Aminoleban EN®) - 27 gm protein (13 gm amino acids, 13 gm peptide, 1 gm casein), 420 kcal (62.1 gm dextran, 7 gm rice oil), various minerals and vitamins/day); Control group received no supplement. All patients received transarterial chemoembolization (cisplatin/Lipiodol emulsion). Duration of therapy up to one year.
Outcomes	Mortality, appearance ascites/gastrointestinal bleeding/hepatic encephalopathy, infections, quality of life score, bilirubin, body weight, triceps skinfold thickness, midarm circumference. Adverse events not reported by group. Number of readmissions to hospitalization later in study, but these were likely related to underlying disease and not to supplement therapy (so data not used).
Category of study	Supplement/Medical.
Sample size calculation	Calculated need for 44 patients per arm and achieved that number.
Full paper or abstract only	Full report.
Notes	Although longer term mortality also reported, decided to use mortality that occurred by one month after transarterial chemoembolization therapy. Request for further information sent to Dr Poon (poontp@hkucc.hku.hk or poontp@hku.hk) with copy to Dr Fan (stfan@hku.hk) via e-mail on September 19, 2011. No response has been received as of March 20, 2012.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomised".

Poon 2004 *(Continued)*

Allocation concealment (selection bias)	Low risk	Consecutively numbered sealed envelopes. Not mentioned whether opaque or not, but we assume so.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Three dropouts in treatment group and 1 in control group adequately accounted for.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funder of trial not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Low risk	Achieved planned number.

Puglionisi 1985

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in patients hospitalised for elective portocaval shunt. Geographical location Rome, Italy. Study published 1995.
Participants	Inclusion criteria: Elective porto-caval shunt surgery for variceal bleeding. Exclusion criteria: None cited. 20 patients (13 men/7 women, mean age 55).
Interventions	Intervention group received parenteral nutrition (40 gm/l branched chain amino acids X 3 days, then 80 gm/l standard amino acids X 4 days; 16% dextrose [unspecified dose]) postoperatively; Controls received 6% dextrose intravenously. Duration 7 days.
Outcomes	Mortality, appearance encephalopathy.
Category of study	Parenteral nutrition/Surgical (Portocaval shunt).
Sample size calculation	None reported if done.
Full paper or abstract only	Full paper.
Notes	No address or location found for Dr Puglionisi; e-mail sent to one of co-authors (Dr Di Cera - enrico@slu.edu) on September 13, 2011. On September 17, 2011, Dr DiCera replied that he was only a medical student at the time and had no information to supply. E-mail returned to him asking if there was anyone else we could contact on September 17, 2011. Response received on September 18 indicated that Dr DiCera was no longer in Italy and that Dr Puglionisi died 20 years ago.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "20 patients divided into 2 random groups of 10".

Puglionisi 1985 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funding source not reported.
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Qiu 2009

Methods	Randomised trial comparing two different parenteral nutrition solutions (a standard one and one containing glutamine) to a control group receiving no nutritional interventions in patients undergoing liver transplantation.
Participants	Patients undergoing liver transplantation.
Interventions	One interventional group received standard parenteral nutrition (1 gm/kg amino acids as a commercial BCAA solution, 104.5 kJ/kg [dextrose and MCT/LCT combination 20% solution in a 2:1 ratio of carbohydrate to fat]) and a second intervention group receiving an isocaloric, isonitrogenous solution containing glutamine. Treatment was provided for 7 days postoperatively. The control arm received only standard intravenous fluids (5% dextrose and minerals).
Outcomes	Mortality (both short term and long term), duration of hospitalization, a variety of lab tests (including parameters of the Prognostic Nutritional Index).
Category of study	Parenteral nutrition, Surgical.
Sample size calculation	None reported.
Full paper or abstract only	Full paper.
Notes	For purposes of this analysis, the short-term mortality was employed (since this was a surgical trial and the therapy was all done during that hospitalization). Both treatment groups were combined and compared to the control arm. For bilirubin outcome, we used the calculated mean of two treatment groups and the lower standard deviation (since no significant difference between the two groups) and compared to the control group. Attempt to send e-mails to both Dr Qiu (Yudongqui510@hotmail.com and Yudongqiu510@hotmail.com) and Dr Ding (yitaoding@hotmail.com) on September 13/14, 2011 failed; both returned. Letter sent to Dr Ding on September 14, 2011 (Dr Yitao Ding, Department of Hepatobiliary Surgery, Affiliated Drum Tower Hospital, Medical School of Nanjing University, Zhongshang Road 321, Nanjing 210008, China). No response has been received as of March 20, 2012.

Qiu 2009 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only stated that the patients were "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details provided.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No placebo intravenous solution provided, although it was stated that the two treatment arms could not be distinguished.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent dropouts (One patient excluded for graft dysfunction, but it was assumed that that was the reason for the liver transplantation that was responsible for the patient being considered for the trial.)
Selective reporting (reporting bias)	High risk	No hepatic or postoperative morbidity data provided.
Other bias	Unclear risk	Funding source not disclosed.
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No differences in the baseline features.
Early stopping?	Unclear risk	No explanation provided regarding why the trial was stopped when it was.

Reilly 1990

Methods	Randomised trial comparing two different parenteral nutrition solutions (standard or branched-chain amino acids) to no parenteral nutrition in patients hospitalized for liver transplant. Geographical location Pittsburgh, Pennsylvania, USA. Study published 1999.
Participants	Inclusion criteria: Immediately postoperative after successful liver transplantation. Exclusion criteria: None cited. 28 patients (13 men/15 women, mean age 49).
Interventions	Intervention group received parenteral nutrition (1.5 gm/d standard or branched chain amino acids, 35 kcal/kg/d [carbohydrate and lipid]); Controls received standard dextrose solutions intravenously. Duration 7 days. All patients received cyclosporine and steroids.
Outcomes	Mortality, serum bilirubin, duration intensive care unit and total hospitalization, cost, nitrogen balance
Category of study	Parenteral nutrition/Surgical (liver transplant).
Sample size calculation	None reported if done.
Full paper or abstract only	Full paper.
Notes	For bilirubin outcome, we used the calculated mean of two treatment groups and the lower standard deviation (since no significant difference between the two groups) and compared to the control group. Unable to find address or location for Dr Reilly; e-mail sent to coauthor, Dr Leonard Makowka (Lmakowka@ITFGP.com) on September 13 failed; letter then sent by US mail (Leonard Makowka, M.D.,

Reilly 1990 *(Continued)*

	ITF Global Partners. 181 Hudson Street, PH, New York, NY 10013). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomised".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	High risk	Serum bilirubin not useful, as patients had liver transplant as confounding factor; no postoperative morbidity reported, so no morbidity data at all reported.
Other bias	Unclear risk	Funding source not reported.
Intent to treat analysis	Low risk	No dropouts.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

San-In Group 1997

Methods	Randomised trial comparing supplements to no supplements in outpatients who had had an attempted curative resection for hepatocellular carcinoma 2 to 3 weeks earlier. Geographical location: Izumo, Japan. Paper published 1997.
Participants	Inclusion criteria: Patients 2 to 3 weeks after attempted curative resection for HCC. Exclusion criteria: None cited. 150 patients (109 male/23 female [18 additional dropouts], median age of per protocol population 50 to 70).
Interventions	Intervention group received branched chain amino acid supplement (Aminoleban EN®) - 27 gm protein (13 gm amino acids, 13 gm peptide, 1 gm casein), 420 kcal (62.1 gm dextran, 7 gm rice oil), various minerals and vitamins/day); Control group received no supplement. Duration of therapy 1 year.
Outcomes	Mortality, bilirubin, body weight. Outcomes of ascites and encephalopathy reported as percentages, but not clear what denominators were, so the data could not be used in the meta-analyses.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.

San-In Group 1997 *(Continued)*

Notes	No e-mail address available for corresponding author (Dr N Nagasue); letters sent to two different addresses that were found (N Nagasue, MD, Department of Digestive and General Surgery, Shimane University School of Medicine, Izumo 693-8501, Japan and N Nagasue, MD, Department of Surgery, Kawasaki Hospital, Higashiyama-cho 3-3-1, Hyogo-ku, Kobe, Hyogo 652-0042, Japan) on September 19, 2011. Latter letter returned as being undeliverable and not able to forward. No other response received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomised".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Eight dropouts in treatment group, 10 dropouts in control group all adequately accounted for.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All dropouts accounted for.
Selective reporting (reporting bias)	Low risk	Outcomes of ascites and encephalopathy reported as percentages, but not clear what denominators were. Thus, while the data could not be used in the meta-analyses, the outcomes were reported.
Other bias	Unclear risk	Funder of trial not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Schuetz 2006

Methods	Randomised trial comparing enteral nutrition to no enteral nutrition in patients hospitalized with cirrhosis and encephalopathy. Geographical location: Germany. Paper published 2006.
Participants	Inclusion criteria: Hospitalized patients with cirrhosis and hepatic encephalopathy. Exclusion criteria: None cited. 22 hospitalised patients (16 male/6 female, mean age 60).
Interventions	Intervention group received enteral nutrition through nasogastric tube (only detail was "high protein formulation"); Control group given standard diet. Duration of therapy 14 days.
Outcomes	Appearance of hepatic encephalopathy.
Category of study	Enteral nutrition/Medical.
Sample size calculation	Not reported if performed.

Schuetz 2006 *(Continued)*

Full paper or abstract only	Abstract.
Notes	Trial from same group as Norman 2008, but appears to be different trial. Abstract states no change in encephalopathy and all patients appeared to have subclinical encephalopathy at beginning, so assumed no frank encephalopathy developed. On September 17, 2011, e-mails sent to Drs Norman and Pirlich (kristina.norman@charite.de and Matthias.pirlich@charite.de) requesting information about both Norman and Schuetz trials. (E-mail for Dr Pirlich failed.) No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	22 patients presented, but unclear if they were the only ones randomised.
Selective reporting (reporting bias)	High risk	No mortality data.
Other bias	Unclear risk	Funding source not reported.
Intent to treat analysis	Unclear risk	22 patients reported but unknown if other patients enrolled in trial.
Baseline imbalance?	Unclear risk	Only Childs-Pugh scores at baseline presented.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Sievert 1999

Methods	Randomised trial comparing supplements (standard or branched-chain amino acids) to "placebo" in malnourished outpatients with cirrhosis. Geographical location: Melbourne, Australia. Abstract published 1999.
Participants	Inclusion criteria: Malnourished cirrhotic patients expected to survive for 4 months. Exclusion criteria: None cited. 95 patients (80 male/15 female, no data regarding age) in three groups, but no information about sex distribution in each of those groups.
Interventions	Intervention group received standard amino acid supplement (40 gm protein [20% BCAA] 400 kcal, vitamins, minerals/day) or branched chain amino acid supplement (40 gm protein [45% BCAA], 400 kcal, vitamins, minerals/day); Control group received placebo (only vitamins and minerals). Duration of therapy 4 months.
Outcomes	Appearance hepatic encephalopathy, infections, non-serious adverse events, body weight. Quality of life data allegedly collected, but not reported.

Sievert 1999 *(Continued)*

Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Abstract.
Notes	In meta-analyses, data treated as if intent to treat (all patients counted in denominator). Data regarding appearance hepatic encephalopathy, infections, non-serious adverse events obtained from poster at meeting of AASLD in 1999. Request for further information sent via e-mail to Drs Sievert and Strauss (william.sievert@monash.edu and Boyd.Strauss@monash.edu) on September 19, 2011.No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomised".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No description of placebo.
Incomplete outcome data (attrition bias) All outcomes	High risk	7 dropouts from trial, but no information regarding which group or reason.
Selective reporting (reporting bias)	High risk	No mortality data and quality of life not reported (even though it was planned to be collected).
Other bias	Unclear risk	Funding source not reported.
Intent to treat analysis	Unclear risk	Not clear if data from all patients or just those who completed trial.
Baseline imbalance?	Low risk	Although no data presented in abstract, it is stated that there were no differences.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Simko 1983

Methods	Randomised trial comparing supplements to "placebo" in outpatients who had chronic (alcoholic) liver disease with past history of encephalopathy but were currently no worse that Grade I. Geographical location: Cincinatti, Ohio, USA. Paper published 1983.
Participants	Inclusion criteria: Biopsy-proven chronic liver disease (all alcoholic, either cirrhosis or alcoholic hepatitis) with past history of hepatic encephalopathy but currently no worse than Grade 1. Exclusion criteria: None cited. 15 patients (5 male/5 female [5 additional dropouts], median age of per protocol population 51).
Interventions	Intervention group received branched-chain amino acid supplement (Hepatic-Aid®) containing increased amounts branched-chain amino acids/decreased amounts aromatic amino acids, sucrose, maltodextrins (69.9%) and fat (19/7%) to tolerance or total supplement intake of 60 gm protein;

Simko 1983 *(Continued)*

	Control group received placebo. Duration of therapy 3 months.
Outcomes	Appearance hepatic encephalopathy, bilirubin, body weight, triceps skinfold thickness, midarm muscle circumference.
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Disproportionate number randomised to treatment group with no explanation. We assumed no hepatic encephalopathy since serum ammonia and trailmaking did not deteriorate in either group. On Google, found address for Vlado Simko (VA NY Harbor Healthcare System, 800 Poly Place, Brooklyn, NY 11209) and report of paper published by a Dr Vlado Simko from the GI unit at the University of Cincinnati in same time period when paper written; letter sent to him on September 19, 2011. No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "all patients were randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	No description of placebo.
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 dropouts accounted for; 4 were in treatment group and one in control group (unknown which reason caused dropout in the control group, however).
Selective reporting (reporting bias)	High risk	No mortality data.
Other bias	High risk	Five control patients older than 5 treatment patients; partial funding by industry.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	High risk	Controls older than treated patients (at least in those that completed the trial).
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Simon 1988

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in hospitalized patients with alcoholic hepatitis. Geographical location Atlanta, Georgia. Study published 1988.
Participants	Inclusion criteria: >80 gm alcohol intake for at least 2 years, right hepatic lobe enlargement, severe alcoholic hep (bilirubin >5 mg% and either primary hepatic encephalopathy or prothrombin time at least

Simon 1988 *(Continued)*

	5 sec > control) or moderate alcoholic hepatitis (albumin < 2.9gm% and one of the three criteria for severe hepatitis), and either biopsy-proven alcoholic hepatitis or, if no biopsy possible, AST <350 IU/l, AST/ALT >2, and actively consuming alcohol at time of admission. Exclusion criteria: Acute pancreatitis, insulin-dependent diabetes mellitus, positive test for hepatitis B surface antigen, malignancy, hypotension, congestive heart failure, sepsis, severe chronic obstructive pulmonary disease, recent severe trauma or surgery. 34 patients in the full paper, but 69 in a subsequent abstract (age and sex only available for 22 patients in the original paper (7 men/15 women, mean age 41).
Interventions	Intervention group received intravenous formulation (35 gm AA, 5% dextrose, minerals, MVI/liter, 2 liters/day, 0.5 liter 10% lipid solution/day) and oral intake offered to control patients; Controls received oral diet (2400 kcal and 100 gm protein) and 1 can Ensure with each meal, 1 mg folic acid/day, multivitamins. Duration therapy 28 days.
Outcomes	Mortality (in abstract with 69 patients), appearance/resolution of ascites or hepatic encephalopathy (only for severe subgroup), bilirubin (only for severe subgroup).
Category of study	Parenteral nutrition/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	A couple of the numbers in the abstract describing the 69 patients were inconsistent with the original paper, and the data from the larger group were accepted. Address and location not identified for Dr Simon; letter sent to Dr Galambos (John T Galambos, MD, 95 Collier Road, Suite 4075, Atlanta, Georgia 30309) on September 12, 2011. No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomised".
Allocation concealment (selection bias)	Unclear risk	Sealed envelope noted, but not mentioned if opaque and/or serially numbered.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Two dropouts in trial reported in full paper; one from each group in those with moderate alcoholic hepatitis, but not stated which reason for which group. No information regarding subsequent report of 69 patients provided as abstract.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.
Other bias	Unclear risk	Funding source not reported.
Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences identified.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Takeshita 2009

Methods	Randomised trial comparing the use of a late-evening snack of a branched-chain amino acid-enriched supplement to no supplement in patients undergoing transarterial chemoembolization for hepatocellular carcinoma.
Participants	Patients undergoing transarterial chemoembolisation for hepatocellular carcinoma.
Interventions	Experimental group received a commercial supplement (Aminoleban EN - 878.64 kJ energy in 50 gram pack) ingested at night (10 PM) beginning one day before the procedure and lasting for two weeks afterward. The control group did not receive any nutrition therapy.
Outcomes	Mortality, duration of hospitalization (for the chemoembolization procedure), lab tests, adverse events, body mass index.
Category of study	Supplements/Medical.
Sample size calculation	None reported.
Full paper or abstract only	Full paper.
Notes	Request for further information sent via e-mail on September 18, 2011 (ichikawa@net.nagasaki-u.ac.jp and Shige-ygc@umin.ac.jp). No response has been received as of March 20, 2012.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"patients were randomly placed into 2 groups".
Allocation concealment (selection bias)	Unclear risk	No details provided.
Blinding (performance bias and detection bias) All outcomes	High risk	No placebo solution provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts.
Selective reporting (reporting bias)	High risk	Although explicitly stated to be a secondary outcome, no hepatocellular carcinoma recurrence rates provided. No morbidity data reported.
Other bias	Unclear risk	Differences in white and red blood cell, platelet counts and total serum cholesterol between the two groups; funding not reported.
Intent to treat analysis	Low risk	All patients accounted for.
Baseline imbalance?	High risk	Controls had more abnormal hemograms and other laboratory tests.
Early stopping?	Unclear risk	No sample size calculation presented and no explanation regarding why trial stopped when it was.

Tangkijvanich 2000

Methods	Randomised trial comparing branched chain amino acid supplement to no supplement in outpatients with cirrhosis. Geographical location: Bangkok, Thailand. Abstract published 2000.
Participants	Inclusion criteria: Patients with cirrhosis documented by biopsy and/or "clear cut evidence"; no current hepatic encephalopathy, gastrointestinal bleeding, uncontrolled ascites, spontaneous bacterial peritonitis, hepatocellular carcinoma. Exclusion criteria: Diabetes mellitus, renal failure, severe cardiopulmonary disease. 30 patients (22 male/8 female [1 other dropout], mean age 53).
Interventions	Intervention group received branched-chain amino acid supplement (Aminoleban EN®) containing 150 gm protein plus 40 gm protein/2000 kcal diet; Control group received standard 80 gram protein/2000 kcal diet. Duration of therapy 4 weeks.
Outcomes	Appearance gastrointestinal bleeding/hepatic encephalopathy, bilirubin, body weight, midarm muscle circumference. Probably no mortality but not explicitly stated. Data regarding infections limited to episodes of spontaneous bacterial peritonitis, but this probably did not include all infections and not used in meta-analysis. Data regarding duration of stay in hospital/intensive care unit collected but not specifically reported; data regarding septic morbidity, six-month survival (after transplant), major non-infectious complications all supposed to be collected similarly not specifically reported (other than noting no difference).
Category of study	Supplements/Medical.
Sample size calculation	Not reported if done.
Full paper or abstract only	Full paper.
Notes	Request for further information sent to senior author (Dr. Willayalertpanya) via e-mail (wsupeech@pioneer.chula.ac.th) on September 19, 2011. E-mail address failed and letter sent on September 26, 2011 to Assoc Prof Supeecha Wittayalertpanya, Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. Response 10/16/11 stated that Dr Tangkijvanich was contacted but that he had no recollection of any details about trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "patients were randomised".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One dropout from treatment group accounted for.
Selective reporting (reporting bias)	High risk	No mortality data. Other data that were supposed to be collected were not available (see note in Outcomes above.)
Other bias	Unclear risk	Funder of trial not reported. Company acknowledged for supplying supplements, but this alone not sufficient to judge this parameter as inadequate.

Tangkijvanich 2000 *(Continued)*

Intent to treat analysis	High risk	Could not be done.
Baseline imbalance?	Low risk	No differences in per protocol groups.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

Zheng 2003

Methods	Randomised trial comparing parenteral nutrition to no parenteral nutrition in patients with chronic liver disease hospitalized for surgery. Geographical location Wuhan, China. Study published 2003.
Participants	Inclusion criteria: Patients with chronic liver damage (Childs B or C, need for at least 7 days nutritional support postoperatively. Exclusion criteria: Presence of factors that affect metabolism other than those related to underlying disease. 70 patients (no sex or age data provided).
Interventions	Intervention group received parenteral nutrition (30 kcal/kg [carbohydrate and lipid], 0.16 gm/kg nitrogen per day for at least 7 days postoperatively); Controls received no nutritional support. Duration ≥ 7 days.
Outcomes	Mortality, appearance ascites, bilirubin, weight, midarm circumference, nitrogen balance.
Category of study	Parenteral nutrition/Surgical (postoperative).
Sample size calculation	None reported if done.
Full paper or abstract only	Full paper.
Notes	E-mail sent to Dr Hu on September 14, 2011 (mailbox_1@163.net) after one sent to Dr Zheng on September 13, 2011 (zhenggichang@yahoo.cn) failed; the former failed as well. Letter sent to Dr Hu by US mail on September 14, 2011 (Dr Qing-Gang Hu, Department of Surgery, Xiehe Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, Hubei Province, China). No response has been received as of March 20, 2012.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Only states "randomly assigned".
Allocation concealment (selection bias)	Unclear risk	No details.
Blinding (performance bias and detection bias) All outcomes	High risk	Not blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers somewhat disparate in paper.
Selective reporting (reporting bias)	Low risk	Mortality and morbidity outcomes reported.

Zheng 2003 *(Continued)*

Other bias	Unclear risk	Funding source not reported.
Intent to treat analysis	Unclear risk	Somewhat disparate numbers reported in paper.
Baseline imbalance?	Low risk	Superficially adequate.
Early stopping?	Unclear risk	No sample size calculation and unknown why stopped.

gm = gram.
ckal = (EU) kilocalories; (U.S) calories.
cc = cum cibo (with food).
HCC = hepatocellular carcinoma.

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

Study	Reason for exclusion
Abad Lacruz 1990	Randomized trial comparing enteral to parenteral nutrition; no untreated control group.
Adams 2011	Only a protein supplement was assessed (not a complete supplement).
Akoglu 2008	Randomized trial assessing folic acid.
Al Mardini 2006	Not randomized trial.
Alvarez 2004	BCAA solution compared to casein; no complete nutritional formula.
Andreone 2001	Randomized trial assessing vitamin E.
Awad 2010	Randomized trial comparing an Incomplete formulation immediately post op (for only 2 doses on days 0 and 1).
Badalamenti 1995	Randomized trial comparing fish oil to standard oil.
Baldermann 1988	Randomized trial comparing two parenteral formulations with different lipid constituents.
Barle 1997	Randomized trial in patients undergoing cholecystectomy (no liver disease) who only received 8 hours of parenteral nutrition; no clinical outcomes reported.
Bartels 2004	Randomized trial comparing vitamin E to placebo; no complete nutrient formulation.
Bernardi 1981	Review article.
Bianchi 1993	Randomized trial comparing animal to vegetable protein; no artificial nutrition formulation.
Bories 1994	Not randomized trial; no control group.
Brans 1987	Randomized trial comparing different doses of lipid.
Bresci 1993	Randomized trial comparing zinc to no zinc.
Buchmiller 1993	Randomized trial comparing two different parenteral nutrition formulations; no untreated control group.

Study	Reason for exclusion
Cabre 2000	Randomized trial comparing enteral nutrition to steroids in patients with alcoholic hepatitis; no untreated control group.
Campo 1997	Randomized trial comparing oral BCAAs to oral casein (no artificial nutrition); no clinical data.
Cao 2007	Randomized trial comparing growth hormone to no growth hormone; both groups received parenteral nutrition.
Cerra 1983	Randomized trial comparing BCAA solution to neomycin; both groups received parenteral nutrition.
Cerra 1985	Randomized trial comparing BCAA solution to neomycin; both groups received parenteral nutrition.
Cerwenka 1998	Randomized trial comparing antioxidants.
Chelarescu 2003	Randomized trial comparing enteral to parenteral nutrition.
Chin 1992	Randomized crossover trial comparing BCAA and standard amino acid solution.
Christie 1985	Randomized trial comparing BCAAs to casein; both arms received artifical nutrition.
Clarke 2004	Two different enteral nutrition formulas compared; no untreated group.
Conti 1971	Not randomized trial.
Cortez Pinto 1990	No indication that trial was randomized.
Cunha 2004	Uncontrolled observational study.
Córdoba	Comparison of branched-chain amino acids versus maltodextrin added to meals; no nutrition support to either group.
Córdoba 2004	Randomized trial comparing low protein to standard protein diet.
De Antoni 1984	No evidence that trial was randomized.
de la Maza 1995	Randomized trial comparing vitamin E to placebo.
de Luis 2010	Randomized trial comparing two different diets in patients with fatty liver disease.
De-Fang 2011	Both arms received enteral nutrition.
Di Cecco 1997	Randomized trial comparing BCAA solution to casein.
Diehl 1985	Controls received same intravenous infusion as treated group except no amino acids, so trial actually only compared the use of an infused amino acid formulation.
Dionigi 1984	Randomized trial comparing different amino acid solutions; all patients received parenteral nutrition.
Egberts 1981	Randomized trial comparing two different parenteral nutrition formulations; no untreated group.
Egberts 1985	Randomized trial comparing BCAAs to casein; neither treatment group received artificial nutrition.

Study	Reason for exclusion
Egberts 1988	Randomized trial of BCAA solution; no artificial nutrition provided.
Eriksson 1982	Randomized trial comparing BCAAs to placebo; neither treatment group received artificial nutrition.
Ferenci 1981	Randomized trial comparing BCAAs to keto acids; no artificial nutrition.
Fiaccadori 1984	Randomized trial BCAA vs lactulose; both arms received hypertonic glucose.
Fiaccadori 1988	Randomized trial oral BCAAs versus casein; neither group received artificial nutrition.
Freeman 1983	Randomized trial BCAA vs no BCAA; neither treatment group received artificial nutrition.
Fukushima 2003	Nocturnal branched-chain ingestion compared to daytime ingestion; no nutrition support program and no untreated control group.
Galloway 1987	Randomized trial comparing two different parenteral nutrition formulations; no untreated control group.
Gavazzl 1999	Not a controlled trial.
Glynn 1988	Randomized trial comparing lipid to no lipid; all patients received parenteral nutrition.
Grungreiff 1993	Randomized trial comparing BCAAs versus BCAAs and valine; no untreated control patients.
Grungreiff 2001	Randomized trial of l-ornithine l-aspartate for encephalopathy.
Guarnieri 1982	Randomized trial comparing BCAA-rich amino acid solution to equicaloric glucose (1120 calories).
Guarnieri 1984	Supplements containing BCAAs compared to lactulose in patients with encephalopathy; no true untreated control group.
Habu 2003	BCAAs compared to no treatment; no artificial nutrition provided to any patients.
Habu 2009	Only branched-chain amino acids assessed; no complete formulation employed.
Haji 2008	No clinical outcomes reported.
Hayaishi 2011	Retrospective study (not randomized).
Hayashi 2007	BCAAs with or without zinc compared; no artificial nutrition provided to any patients.
Herlong 1980	Randomized trial comparing BCAAs to ornithine salts of BCAAs; no artificial nutrition provided to either group.
Hernandez-Guerra 2006	Trial compared ascorbic acid to no ascorbic acid; no artificial nutrition provided.
Holdsworth 1984	Different BCAA solutions in 10% dextrose compared to 10% dextrose in patients receiving enteral nutrition; no clinical data.
Holm 1981	Randomized trial comparing two different amino acid supplements; no artificial nutrition provided.
Holm 1984	Study in healthy people; no control group.
Holm 2000	No clinical data.

Study	Reason for exclusion
Horst 1984	Randomized trial comparing BCAA supplements to increasing protein intake; no true control group given 'standard' diet.
Huisman 2011	Most of the patients in the 'preventive' group only received dietary advice.
Hwang 1988	Randomized trial assessing BCAA solution with 10% dextrose, but only 500 cc provided daily; no group received artificial nutrition.
Ichida 1995	Not randomized trial.
Ikegami 2012	Not a randomized trial.
Ilan 2000	Trial compared different diets; no artificial nutrition provided.
Itou 2009	Not randomized trial.
Itou 2011	Supplements only provided on evening before procedure.
Jentschura 1996	Not randomized trial.
Jiang 2001	Randomized trial comparing standard to specialized.
Jiang 2007	Two parenteral nutrition formulations compared; no true control group.
Jonung 1987	Trial compared animal to vegetable protein; no artificial nutrition provided to either group.
Kaido 2010	Not randomized trial.
Kakumitsu 1998	Randomized trial comparing arginine infusion to no arginine infusion; no artificial nutrition provided.
Kanematsu 1988	Randomized trial comparing BCAA-based to standard amino acid-based parenteral nutrition; no untreated control group.
Katsumi 2005	Three different supplements compared; no untreated control group.
Kawaguchi 2008	Trial only assessed one dose of supplement prior to endoscopy.
Kawamura 2009	BCAAs compared to no amino acids; no artificial nutrition provided to either group.
Keshavarzian 1984	Trial comparing two different protein diets; no artificial nutrition provided to either group.
Kircheis 1997	Trial comparing l-ornithine l-aspartate to no such treatment; no artificial nutrition provided to either group.
Kobayashi 2008	BCAA granules compared to no treatment; no artificial nutrition provided to either group.
Krasnoff 2006	Randomized trial of dietary counseling and exercise; no artificial nutrition provided to any patients.
Kuroda 2010	Trial not randomized; patients chose the group into which they were placed.
Kuse 1990	Randomized trial of the use of different lipids in patients receiving parenteral nutrition; no untreated control group.

Study	Reason for exclusion
Kuse 2002	Randomized trial comparing two different parenteral nutrition formulations; no untreated control group.
Labadie 1994	Randomized trial comparing zinc to no zinc; no artificial nutrition provided to either group.
LaTerre 2007	Parenteral nutrition compared to enteral nutrition; no untreated control group.
Leon 2009	Editorial commentary.
Les 2011	Randomized trial comparing BCAA compound to maltodextrin; supplement incomplete.
Luntz 2005	Randomized trial comparing glycine to no glycine after liver transplantation.
Mager 2006	Trial comparing different doses of BCAAs.
Makay 2007	Randomized trial comparing early to delayed parenteral nutrition; no untreated control group.
Malaguarnera 2009	All patients received branched chain amino acids, but no calories (no artificial nutrition); patients randomized to receiving or not receiving l-acetycarnitine.
Mangiante 2002	Randomized trial comparing parenteral to enteral nutrition.
Manguso 2005	Randomized trial comparing two different diets; no artificial nutrition provided to any patients.
Marchesini 1980	Not randomized trial.
Marchesini 1990	Trial comparing BCAA to protein; no artificial nutrition provided to either group.
Marchesini 2003	Randomized trial comparing BCAAs to placebo; no artificial nutrition provided to either group.
Marchini 1983	Randomized trial comparing two different intragastric formulations to controls who received solid food; the patients were chronic alcoholics, but most of them did not have liver disease.
Marra 1998	Randomized trial comparing two different fatty acids.
McGhee 1983	Randomized trial comparing two different supplements; no untreated control group.
Mendenhall 1985	Not randomized trial.
Mendenhall 1993	Randomized trial comparing supplement plus oxandrolone to placebo; treated group received more than just supplements.
Mezey 1991	Controls received same intravenous infusion as treated group except no amino acids, so trial actually only compared the use of an infused amino acid formulation.
Michel 1985	Randomized trial comparing two different parenteral nutrition formulations; no untreated control group.
Mochizuki 2000	Retrospective study.
Moreno 2010	Both groups received enteral nutrition; variable changed was receipt or non-receipt of n-acetycysteine.
Morioka 1983	No clinical data; unclear if randomized or not.

Study	Reason for exclusion
Muto 1984	Randomized trial comparing BCAA supplements; no artificial nutrition provided.
Muto 1991	Trial compared BCAAs to diet; no artificial nutrition provided to either group.
Muto 2005	Randomized trial assessing BCAAs alone; neither group received artificial nutrition.
Nagayama 1989	Randomized trial comparing lipid-based to carbohydrate-based parenteral nutrition; no untreated control group.
Nasrallah 1980	Randomized trial comparing solution containing amino acids and other nutrients to a solultion containing the other nutrients (only compared amino acid solution).
Ndraha 2011	Randomized trial comparing l-ornithine l-aspartate to no treatment in patients with hepatic encephalopathy.
Nickkholgh 2007	Although trial only in protocol stage, is ineligible because both arms received oral supplements; no true control group.
Nielsen 1995	Uncontrolled study.
Nishiguchi 2004	Randomized trial BCAA granules versus no granules; no artificial nutrition provided to patients.
Nishizaki 1996	Patients in both arms received intravenous amino acids.
Nordenstrom 1995	Two different lipid formulations compared; no clinical outcomes.
O'Keefe 1987	Trial compared enteral and parenteral nutrition; no untreated control group.
Okabayashi 2008	Not randomized; retrospective analysis.
Okabayashi 2010	Patients in both arms received parenteral nutrition postoperatively.
Okita 1985	Comparison of different diets; no artificial nutrition provided; non-randomized crossover randomized.
Okuno 1985	Trial comparing two different parenteral nutrition formulations; no untreated group.
Olde Damink 2007	Trial comparing isoleucine to no isoleucine; artificial nutrition not provided to either group.
Panella 1987	BCAA compared to casein; no artificial nutrition provided to either group.
Pierrugus	Some control patients received parenteral nutrition.
Plank 2005	Not randomized.
Plank 2008	Randomized trial comparing daytime to nocturnal supplements; no untreated control group.
Plauth 1993	Randomized crossover trial assessing BCAAs only; no artificial nutrition provided.
Protheroe 1996	Two different feeding formulations compared.
Puglionisi 1984	Only branched chain amino acids infused (no nutrition support program).
Rakette 1981	No evidence that trial randomized.

Study	Reason for exclusion
Rayes 2005	Trial comparing different formulations; all patients received enteral nutrition.
Riederer 1980	No clinical data provided; unclear if trial randomized.
Rifai 2006	All patients received parenteral nutrition; randomization to bile acid or not.
Riggio 1984	Trial comparing BCAAs to lactulose; no artificial nutrition provided.
Rocchi 1985	Trial comparing two different amino acid formulations; all patients received hypertonic glucose.
Rossi Fanelli 1986	BCAA-based parenteral nutrition compared to lactulose; no untreated control group.
Sakaida 2004	Randomized trial of two different BCAA-based supplements; no untreated control group.
Sato 2005	Randomized trial comparing Aminoleben® to BCAAs alone; no untreated control arm.
Schafer 1981	Randomized trial comparing BCAA to other diets; no artificial nutrition provided.
Shirabe 1997	Trial comparing enteral to parenteral nutrition; no untreated control group.
Shirabe 2011	Not randomized trial, but retrospective study.
Sieg 1983	Crossover trial BCAAs versus placebo; no artificial nutrition provided to patients.
Soriano	No nutrition support; all patients received branched-chain amino acids and randomized to exercise or no exercise.
Strauss 1986	BCAA-based parenteral nutrition compared to neomycin; no untreated control group.
Striebel 1979	No evidence that trial randomized.
Sugawara 2011	Not randomized trial.
Suzuki 2004	Review article.
Swart 1981	Randomized trial comparing different amino acid preparations; no artificial nutrition provided.
Swart 1989	Randomized crossover trial of three meals versus 4 to6 meals; no artificial nutrition provided.
Tai 2011	Enteral nutrition compared to group that received supplements; no true control group.
Tang 2007	Trial assessing glutamine and/or growth hormone; all patients received parenteral nutrition.
Tayek	Trial identified on Clionical Trials.gov; is in process, but is only assessing utility of arginine.
Togo 2005	Randomized trial of BCAAs versus no BCAAs; no artificial nutrition provided.
Tomiya 2002	Trial comparing BCAAs to increased protein in diet; no artificial nutrition provided and no clinical data.
Tschepe 1985	Randomized crossover trial of BCAAs versus protein; no artificial nutrition provided.
Tsuchiya 2007	Trial comparing BCAAs with diet compared to equicaloric/equinitrogenous diet; no artificial nutrition provided and trial may not have been randomized.

Study	Reason for exclusion
Uribe 1982	Crossover trial comparing animal and vegetable protein; no artificial nutrition provided.
Valdivieso 1989	BCAA-based versus standard amino acid-based parenteral nutrition; no untreated control group and no clinical outcomes reported.
Vilar-Gomez 2009	Randomized trial comparing 'supplement' containing amino acids, vitamins, and minerals to no supplement; supplement was not complete.
Vilstrup 1990	BCAA-based parenteral nutrition compared to hypertonic glucose; no untreated control group.
Wahren 1983	Randomized trial comparing BCAAs to glucose; all patients received intravenous glucose and lipid, so no true untreated control group.
Walker 1982	Randomized crossover trial comparing keto-analogs of BCAAs versus placebo; no artificial nutrition provided.
Wang 2011	Two different parenteral nutrition formulations compared; no untreated control group.
Watanabe 1983	Non-randomized crossover trial.
Watanabe 1995	Trial comparing different forms of rice; no artificial nutrition provided.
Weber 1990	Trial comparing two different amino acid solutions; unclear if randomized and no clinical outcomes reported.
Wicks 1994	Trial comparing enteral to parenteral nutrition; all patients received artificial nutrition.
Yamamoto 2005	Trial comparing BCAAs to placebo; no artificial nutrition provided.
Yamana-Okumuru 2010	Randomized trial comparing an additional amount of food at night to no treatment.
Yang 2011	Randomized trial comparing two different parenteral nutrition formulations; no untreated control group.
Yoshiji 2011	Only branched-chain amino acids were assessed; no complete nutritional formulation employed.
Yu 2007	Randomized trial comparing growth hormone to no growth hormone; all patients received artificial nutrition.
Zhang 2003	Two different amino acid preparations compared; no clinical outcomes reported.
Zhang 2005	Randomized trial comparing enteral to parenteral nutrition.
Zheng EN	Some of the enteral nutrition patients received parenteral nutrition.
Zhuang 2003	Randomized trial comparing growth hormone to no growth hormone; all patients received parenteral nutrition.

BCAA = branched chain amino acid

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

Caballera Rovira 1987

Methods

Caballera Rovira 1987 *(Continued)*

Participants	
Interventions	
Outcomes	
Notes	Paper published in Spanish, and information in English abstract inadequate to use, as could not even determine if the trial is randomised. Requires translation.

Chen 2011

Methods	
Participants	
Interventions	
Outcomes	
Notes	Study presented at conference in Bangkok, and only information was citation identified in EMBASE search; no quantitative data.

Fink 1978

Methods	
Participants	
Interventions	
Outcomes	
Notes	Paper published in German and need translation.

Hartung 1989

Methods	
Participants	
Interventions	
Outcomes	
Notes	Abstract or very short paper published in German; no English abstract and need translation.

Khlynov 2009

Methods	
Participants	
Interventions	
Outcomes	
Notes	Paper published in Russian and information in English abstract inadequate for inclusion. Requires translation.

Korenaga 2011

Methods	
Participants	
Interventions	
Outcomes	
Notes	No clinical data provided in abstract nor was it clear how the branched-chain amino acids were formulated or delivered

Leweling 1980

Methods	
Participants	
Interventions	
Outcomes	
Notes	Paper published in German and information in brief English abstract inadequate for inclusion; unclear if even randomised. Requires translation.

Macias-Rosales 2010

Methods	
Participants	
Interventions	
Outcomes	
Notes	Only abstract available and unclear how control group treated; no quantitative data.

Zhu-ming 2001

Methods	
Participants	
Interventions	
Outcomes	
Notes	Paper published in Chinese and information in English abstract largely described biochemical outcomes; needs translation.

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

Mao

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Trial identified on ClinicalTrials.gov; no apparent publication yet.

Pirlich

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Trial identified on ClinicalTrials.gov; no apparent publication yet.

Seguin

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Trial identified on ClinicalTrials.gov; no apparent publication yet.

Van Erpecum

Trial name or title	
Methods	
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	Trial identified on ClinicalTrials.gov; no apparent publication yet.

DATA AND ANALYSES

Comparison 1. Mortality

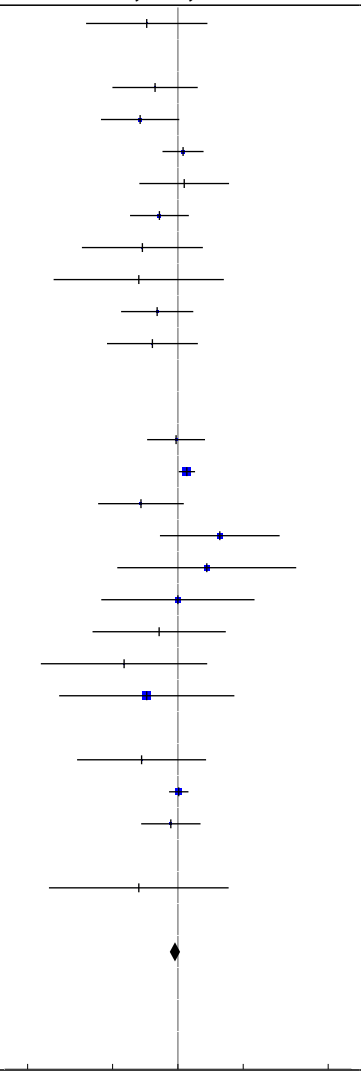
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	28	1668	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.75, 1.08]
2 Parenteral nutrition	9	465	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.29, 0.98]
2.1 Medical trials	4	158	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.28, 1.62]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2.2 Surgical trials	5	307	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.18, 1.02]
3 Enteral nutrition	6	275	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.47, 1.20]
3.1 Medical trials	5	215	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.50, 1.33]
3.2 Surgical trials	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.03, 2.41]
4 Supplements	13	928	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.84, 1.27]
4.1 Medical trials	9	710	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.87, 1.33]
4.2 Surgical trials	4	218	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.25, 1.65]
5 Medical trials	18	1083	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.82, 1.20]
5.1 Parenteral nutrition	4	158	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.28, 1.62]
5.2 Enteral nutrition	5	215	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.50, 1.33]
5.3 Supplements	9	710	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.87, 1.33]
6 Surgical trials	10	585	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.27, 0.89]
6.1 Parenteral nutrition	5	307	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.18, 1.02]
6.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.03, 2.41]
6.3 Supplements	4	218	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.25, 1.65]
7 Alcoholic hepatitis	7	300	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.50, 1.21]
7.1 Parenteral nutrition	3	118	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.25, 1.62]
7.2 Enteral nutrition	2	95	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.61, 1.99]
7.3 Supplements	2	87	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.18, 1.23]
8 Cirrhosis	9	349	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.28, 0.97]
8.1 Parenteral nutrition	2	60	Risk Ratio (M-H, Fixed, 95% CI)	0.6 [0.08, 4.27]
8.2 Enteral nutrition	3	120	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.19, 1.18]
8.3 Supplements	4	169	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.22, 1.39]
9 HCC	6	673	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.93, 1.42]
9.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.19, 1.47]
9.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	5	549	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.98, 1.52]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10 Abstracts excluded	25	1348	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.57, 0.92]
10.1 Medical trials - parenteral nutrition	4	158	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.28, 1.62]
10.2 Surgical trials - parenteral nutrition	5	307	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.18, 1.02]
10.3 Medical trials - enteral nutrition	4	152	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.51, 1.38]
10.4 Surgical trials - enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.03, 2.41]
10.5 Medical trials - supplements	8	477	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.60, 1.12]
10.6 Surgical trials - supplements	3	194	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.25, 1.65]
11 Surgical trials without transplant patients	7	410	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.30, 1.20]
11.1 Parenteral nutrition	3	214	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.18, 1.17]
11.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.03, 2.41]
11.3 Supplements	3	136	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.37, 5.98]
12 Intent to treat - best-case scenario for intervention	24	1539	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.61, 0.86]
12.1 Medical trials - parenteral nutrition	4	170	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.19, 0.96]
12.2 Surgical trials - parenteral nutrition	4	268	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.10, 0.49]
12.3 Medical trials - enteral nutrition	5	215	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.50, 1.33]
12.4 Surgical trials - enteral nutrition	1	64	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.12]
12.5 Medical trials - supplements	8	690	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.74, 1.12]
12.6 Surgical trials - supplements	2	132	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.23, 1.52]
13 Intent to treat - worst-case scenario for intervention	24	1539	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.99, 1.40]
13.1 Medical trials - parenteral nutrition	4	170	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.56, 2.50]
13.2 Surgical trials - parenteral nutrition	4	268	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.63, 2.25]
13.3 Medical trials - enteral nutrition	5	215	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.50, 1.33]
13.4 Surgical trials - enteral nutrition	1	64	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.37, 4.23]
13.5 Medical trials - supplements	8	690	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [1.03, 1.56]
13.6 Surgical trials - supplements	2	132	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.50, 2.96]

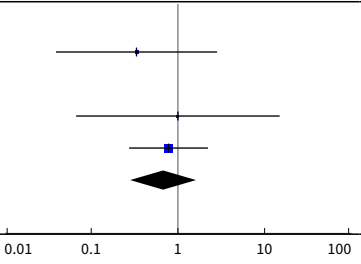
Analysis 1.1. Comparison 1 Mortality, Outcome 1 All studies.

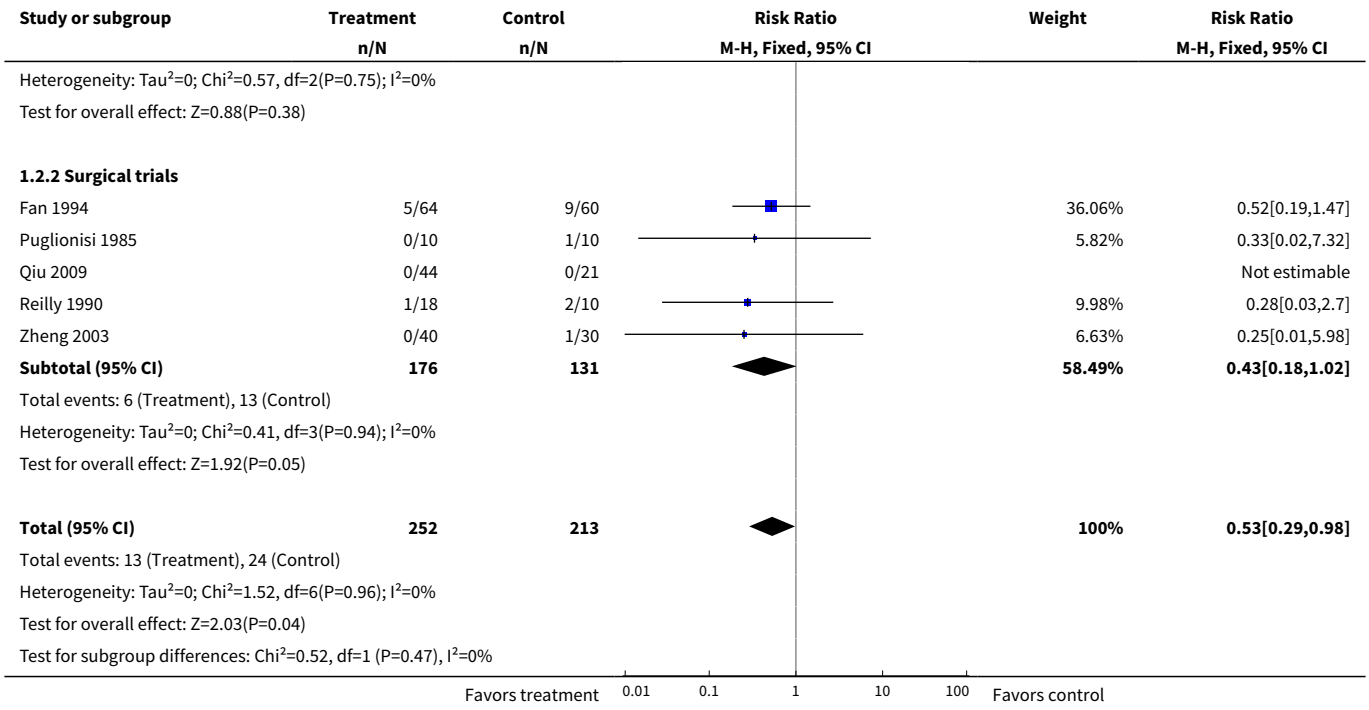
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Achord 1987	1/14	3/14		1.84%	0.33[0.04,2.83]
Bonkovsky 1991	0/9	0/12			Not estimable
Bunout 1989	2/17	5/19		2.89%	0.45[0.1,2.01]
Cabre 1990	2/16	9/19		5.04%	0.26[0.07,1.05]
Calvey 1985	16/42	7/22		5.63%	1.2[0.58,2.47]
DeLedinghen 1997	3/12	2/10		1.34%	1.25[0.26,6.07]
Fan 1994	5/64	9/60		5.69%	0.52[0.19,1.47]
Foschi 1986	1/28	4/32		2.29%	0.29[0.03,2.41]
Hendry 2010	0/30	2/38		1.36%	0.25[0.01,5.05]
Hirsch 1993	3/26	6/25		3.75%	0.48[0.13,1.72]
Humbert 1988	2/27	4/22		2.7%	0.41[0.08,2.02]
Ichikawa 2010	0/12	0/9			Not estimable
Ishikawa 2010	0/11	0/13			Not estimable
Kearns 1992	5/16	5/15		3.16%	0.94[0.34,2.6]
Kobashi 2006	63/119	44/114		27.54%	1.37[1.03,1.83]
LeCornu 2000	2/42	7/40		4.39%	0.27[0.06,1.23]
Meng 1999	4/21	1/23		0.58%	4.38[0.53,36.13]
Nakaya 2007	1/25	0/23		0.32%	2.77[0.12,64.76]
Naveau 1986	1/20	1/20		0.61%	1[0.07,14.9]
Norman 2008	1/31	2/32		1.21%	0.52[0.05,5.41]
Poon 2004	0/41	3/43		2.09%	0.15[0.01,2.81]
Puglionisi 1985	0/10	1/10		0.92%	0.33[0.02,7.32]
Qiu 2009	0/44	0/21			Not estimable
Reilly 1990	1/18	2/10		1.58%	0.28[0.03,2.7]
San-In Group 1997	34/67	32/65		19.91%	1.03[0.73,1.45]
Simon 1988	5/33	7/36		4.1%	0.78[0.27,2.22]
Takeshita 2009	0/28	0/28			Not estimable
Zheng 2003	0/40	1/30		1.05%	0.25[0.01,5.98]
Total (95% CI)	**863**	**805**		**100%**	**0.9[0.75,1.08]**
Total events: 152 (Treatment), 157 (Control)					
Heterogeneity: Tau^2=0; Chi^2=27.9, df=22(P=0.18); I^2=21.15%					
Test for overall effect: Z=1.11(P=0.27)					



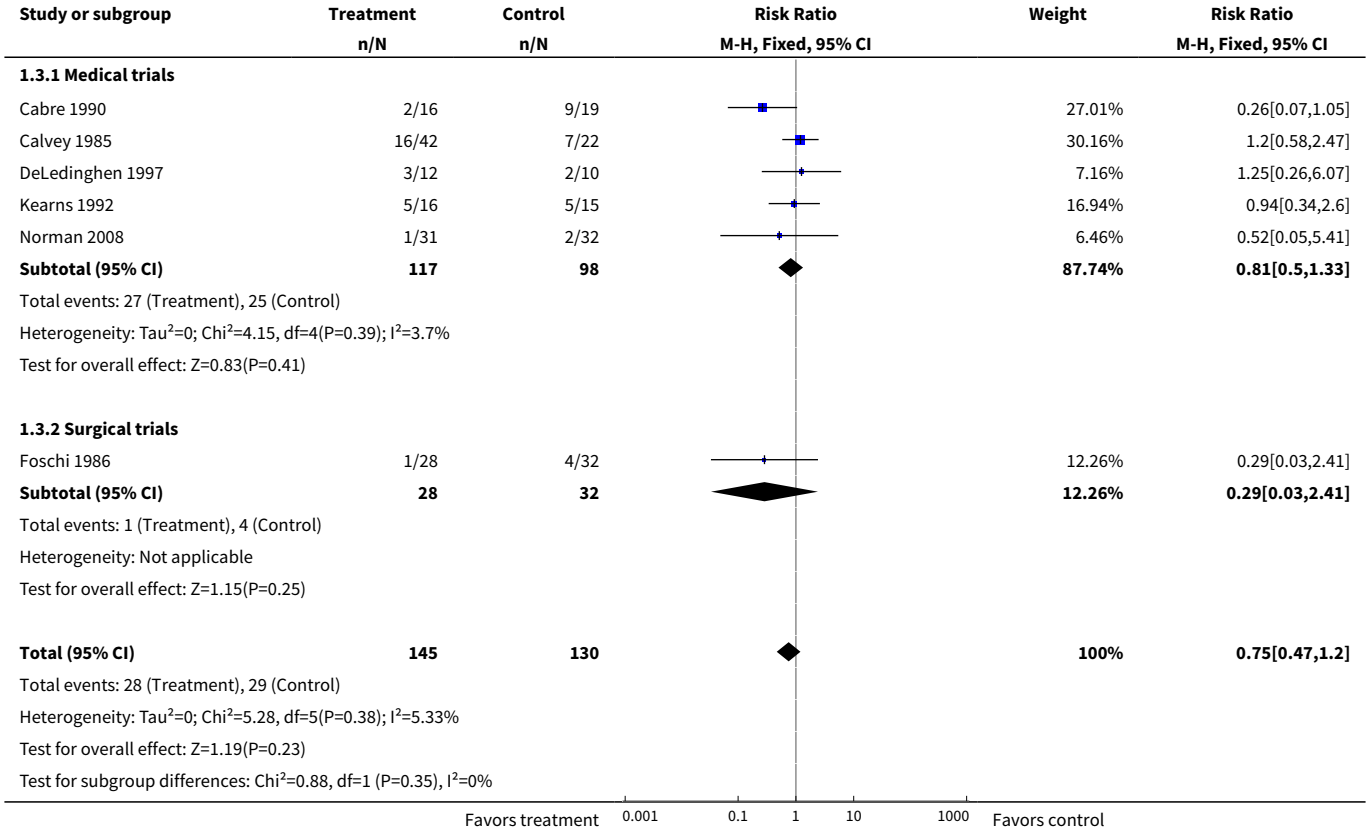
Analysis 1.2. Comparison 1 Mortality, Outcome 2 Parenteral nutrition.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Medical trials					
Achord 1987	1/14	3/14		11.64%	0.33[0.04,2.83]
Bonkovsky 1991	0/9	0/12			Not estimable
Naveau 1986	1/20	1/20		3.88%	1[0.07,14.9]
Simon 1988	5/33	7/36		25.99%	0.78[0.27,2.22]
Subtotal (95% CI)	**76**	**82**		**41.51%**	**0.67[0.28,1.62]**
Total events: 7 (Treatment), 11 (Control)					



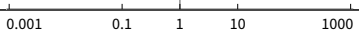


Analysis 1.3. Comparison 1 Mortality, Outcome 3 Enteral nutrition.



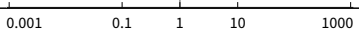
Analysis 1.4. Comparison 1 Mortality, Outcome 4 Supplements.

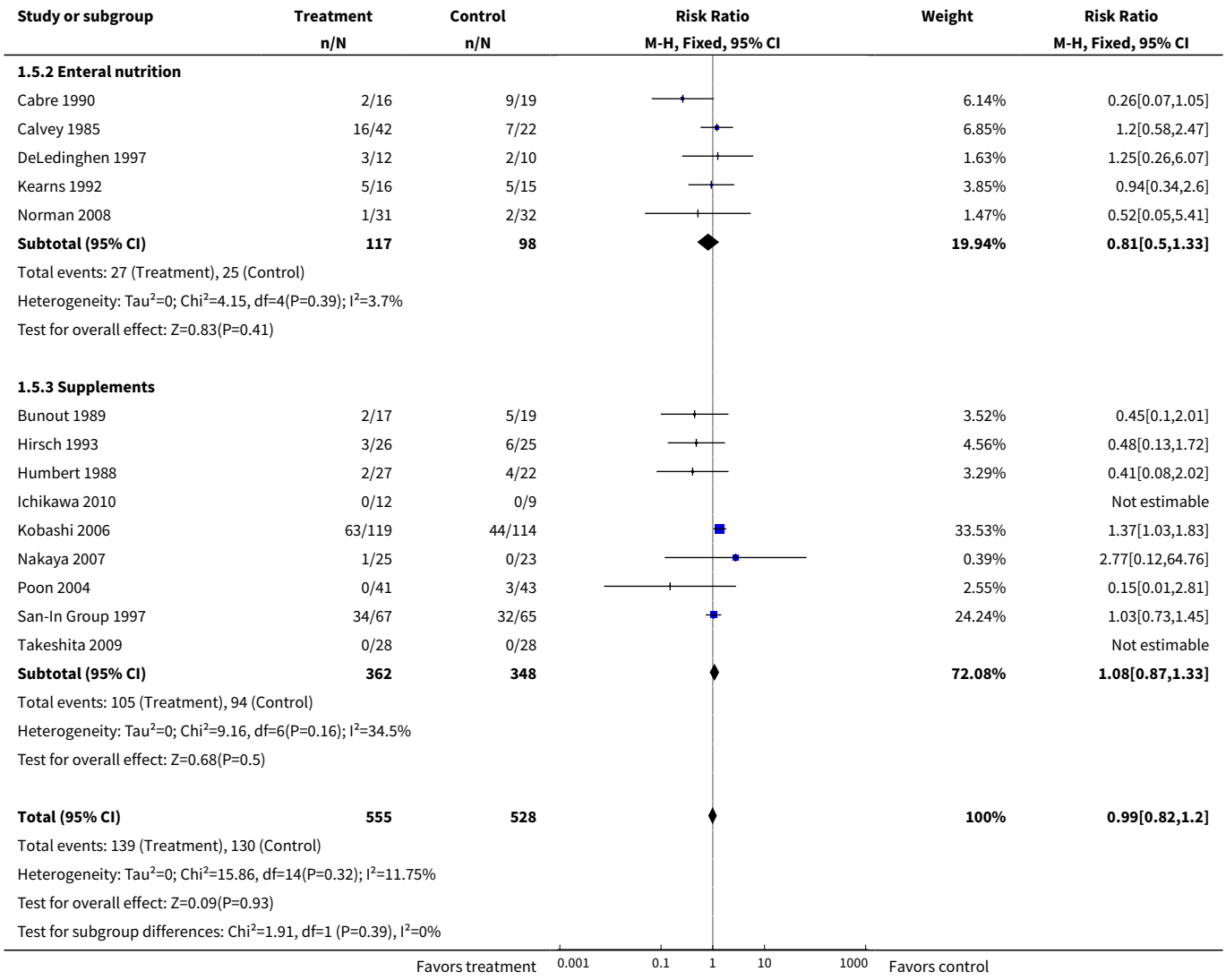
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.4.1 Medical trials					
Bunout 1989	2/17	5/19		4.42%	0.45[0.1,2.01]
Hirsch 1993	3/26	6/25		5.72%	0.48[0.13,1.72]
Humbert 1988	2/27	4/22		4.12%	0.41[0.08,2.02]
Ichikawa 2010	0/12	0/9			Not estimable
Kobashi 2006	63/119	44/114		42.02%	1.37[1.03,1.83]
Nakaya 2007	1/25	0/23		0.49%	2.77[0.12,64.76]
Poon 2004	0/41	3/43		3.2%	0.15[0.01,2.81]
San-In Group 1997	34/67	32/65		30.37%	1.03[0.73,1.45]
Takeshita 2009	0/28	0/28			Not estimable
Subtotal (95% CI)	**362**	**348**		**90.33%**	**1.08[0.87,1.33]**
Total events: 105 (Treatment), 94 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.16, df=6(P=0.16); I^2=34.5%					
Test for overall effect: Z=0.68(P=0.5)					
1.4.2 Surgical trials					
Hendry 2010	0/30	2/38		2.07%	0.25[0.01,5.05]
Ishikawa 2010	0/11	0/13			Not estimable
LeCornu 2000	2/42	7/40		6.7%	0.27[0.06,1.23]
Meng 1999	4/21	1/23		0.89%	4.38[0.53,36.13]
Subtotal (95% CI)	**104**	**114**		**9.67%**	**0.65[0.25,1.65]**
Total events: 6 (Treatment), 10 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.8, df=2(P=0.09); I^2=58.34%					
Test for overall effect: Z=0.91(P=0.36)					
Total (95% CI)	**466**	**462**		**100%**	**1.03[0.84,1.27]**
Total events: 111 (Treatment), 104 (Control)					
Heterogeneity: Tau^2=0; Chi^2=15.3, df=9(P=0.08); I^2=41.19%					
Test for overall effect: Z=0.32(P=0.75)					
Test for subgroup differences: Chi^2=1.07, df=1 (P=0.3), I^2=6.95%					



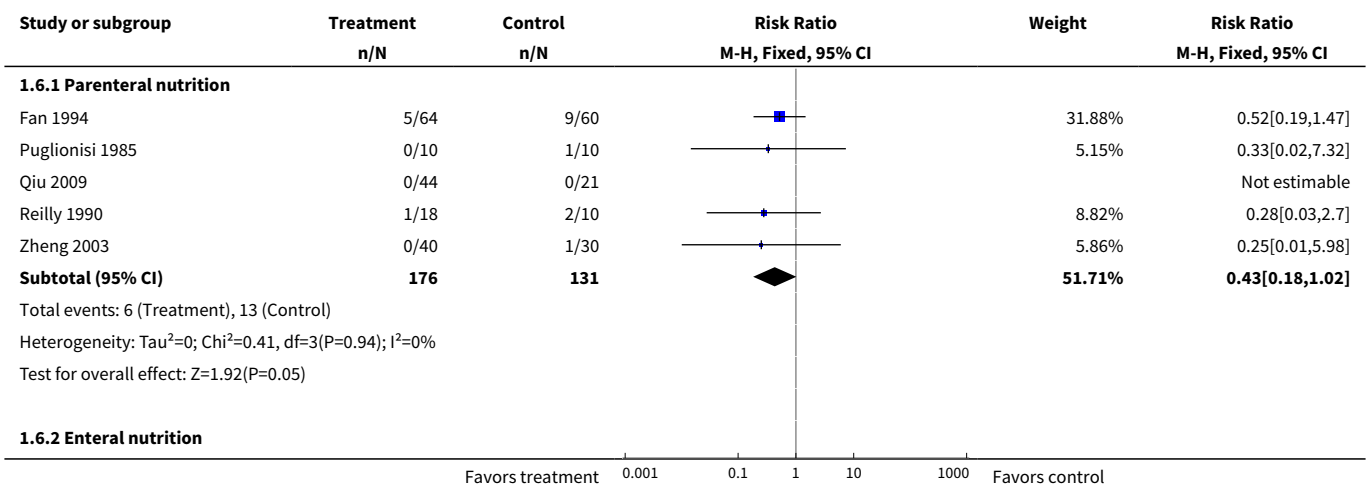
Analysis 1.5. Comparison 1 Mortality, Outcome 5 Medical trials.

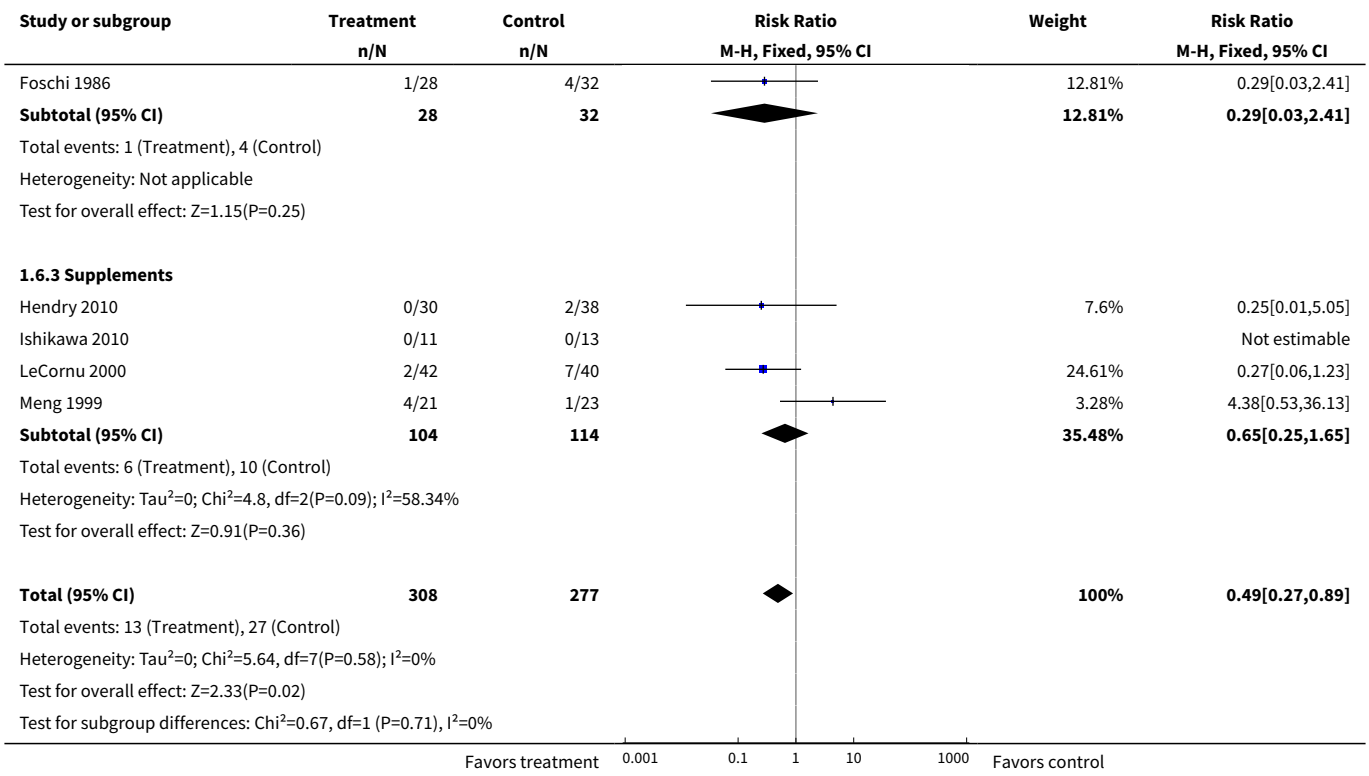
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.5.1 Parenteral nutrition					
Achord 1987	1/14	3/14		2.24%	0.33[0.04,2.83]
Bonkovsky 1991	0/9	0/12			Not estimable
Naveau 1986	1/20	1/20		0.75%	1[0.07,14.9]
Simon 1988	5/33	7/36		5%	0.78[0.27,2.22]
Subtotal (95% CI)	**76**	**82**		**7.98%**	**0.67[0.28,1.62]**
Total events: 7 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.57, df=2(P=0.75); I^2=0%					
Test for overall effect: Z=0.88(P=0.38)					



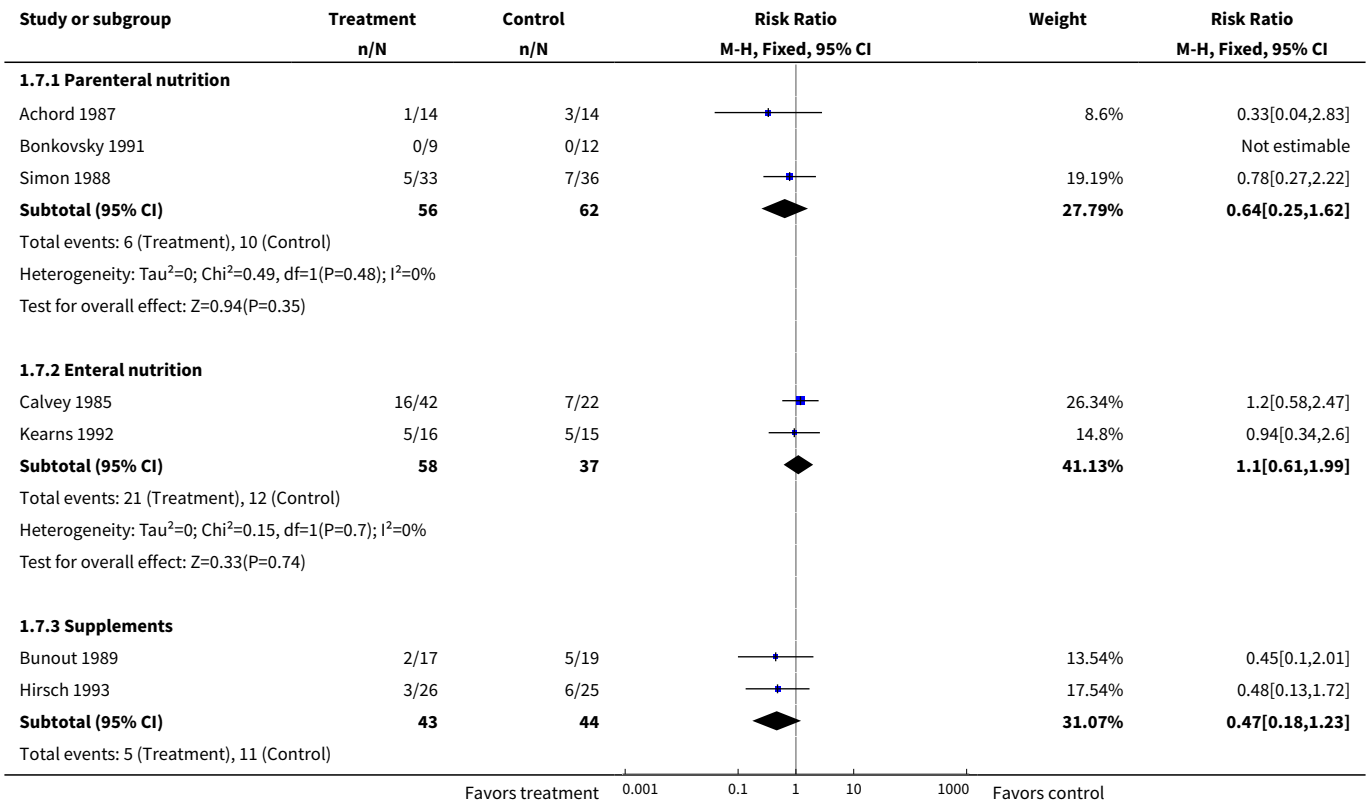


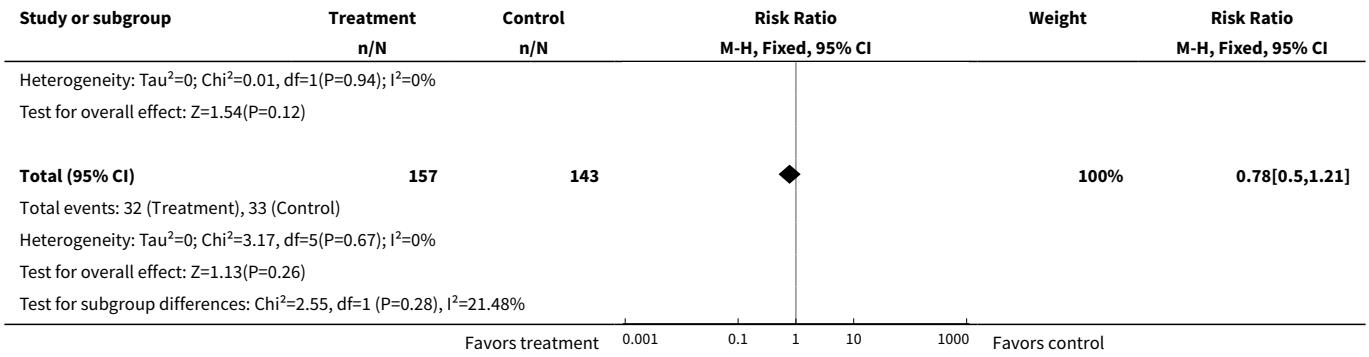
Analysis 1.6. Comparison 1 Mortality, Outcome 6 Surgical trials.



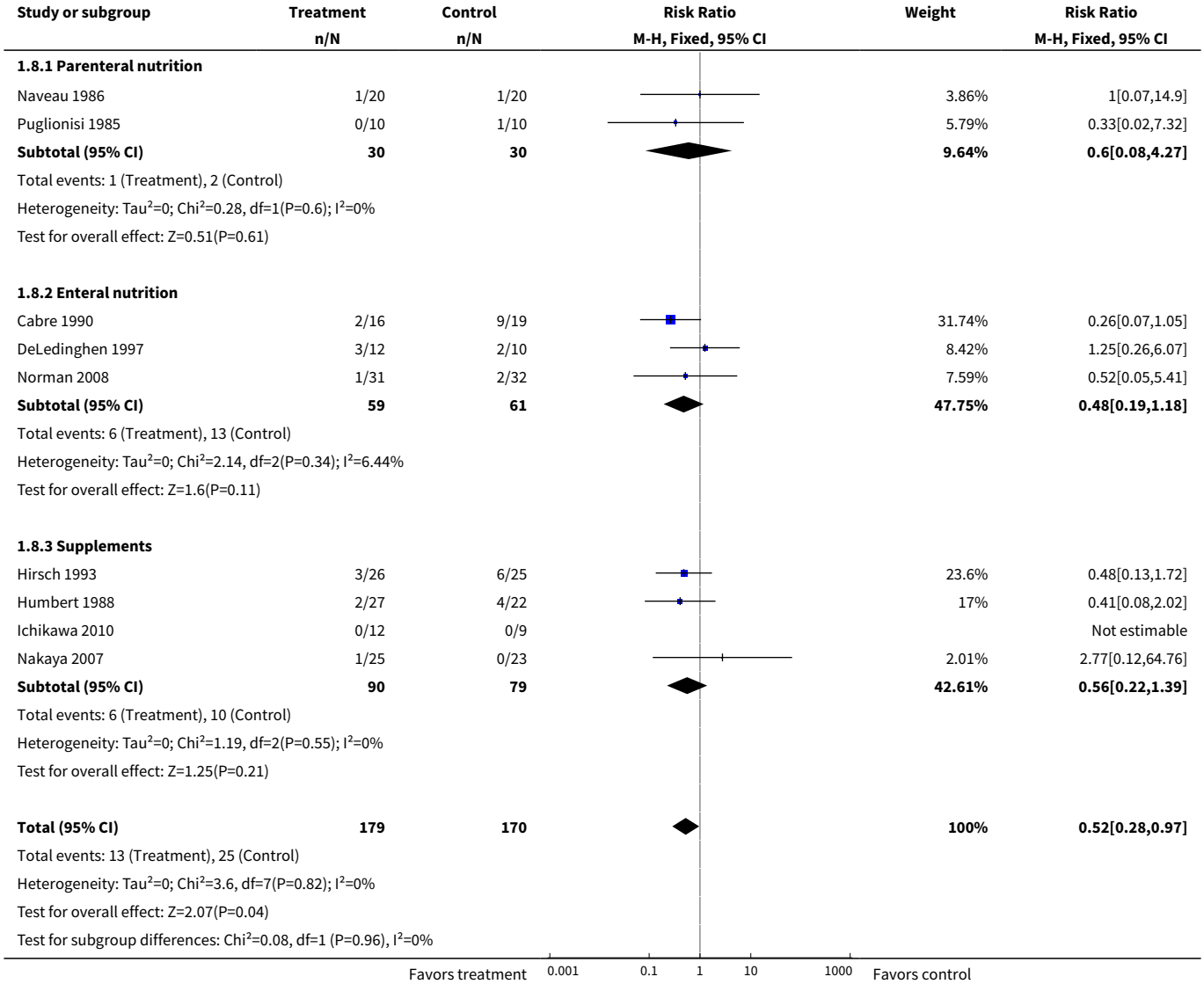


Analysis 1.7. Comparison 1 Mortality, Outcome 7 Alcoholic hepatitis.





Analysis 1.8. Comparison 1 Mortality, Outcome 8 Cirrhosis.

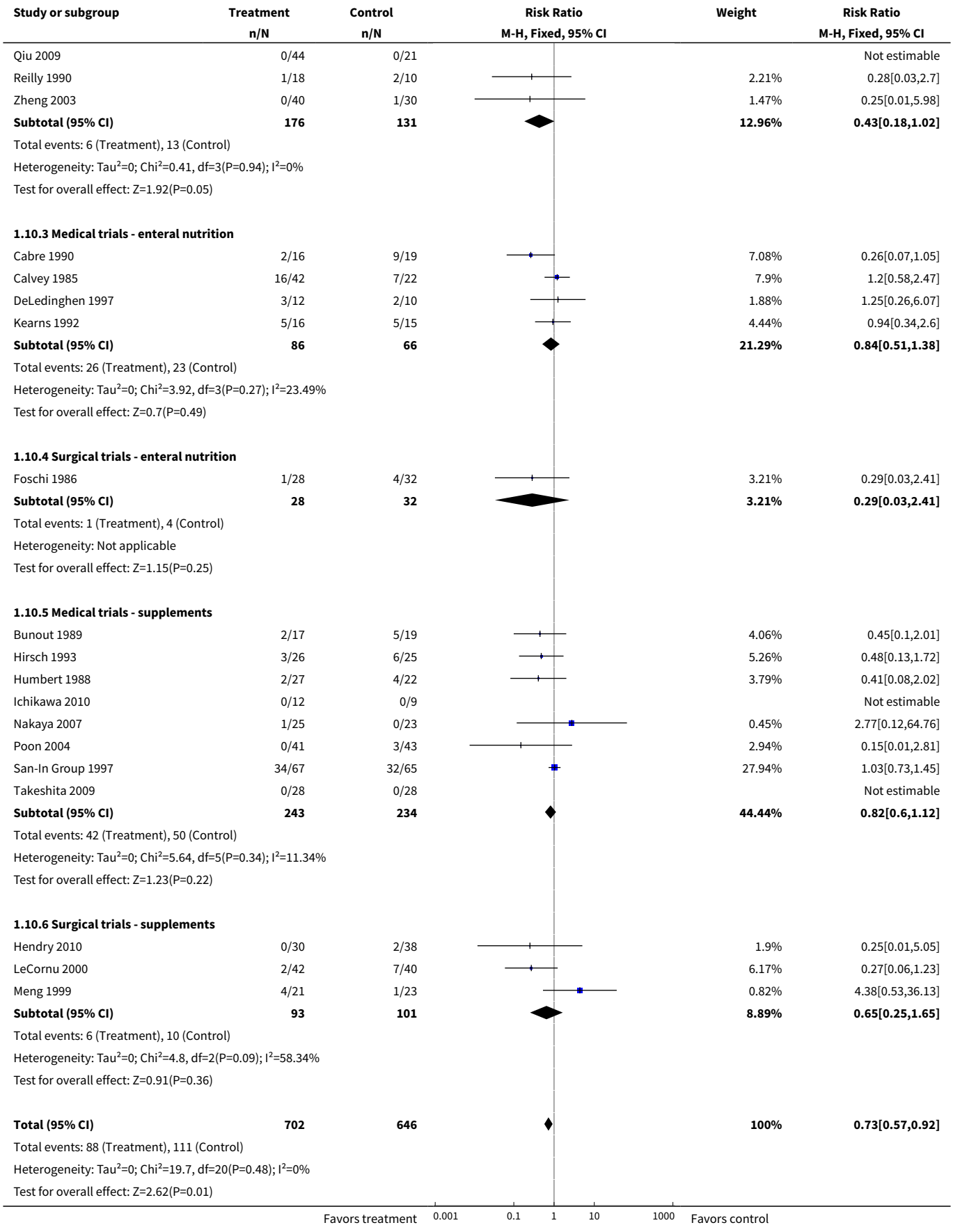


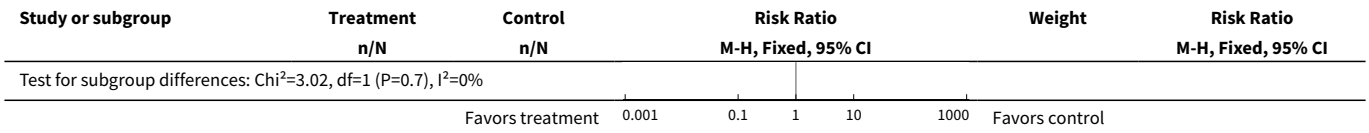
Analysis 1.9. Comparison 1 Mortality, Outcome 9 HCC.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.1 Parenteral nutrition					
Fan 1994	5/64	9/60		10.2%	0.52[0.19,1.47]
Subtotal (95% CI)	**64**	**60**		**10.2%**	**0.52[0.19,1.47]**
Total events: 5 (Treatment), 9 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.24(P=0.22)					
1.9.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.9.3 Supplements					
Kobashi 2006	63/119	44/114		49.34%	1.37[1.03,1.83]
Meng 1999	4/21	1/23		1.05%	4.38[0.53,36.13]
Poon 2004	0/41	3/43		3.75%	0.15[0.01,2.81]
San-In Group 1997	34/67	32/65		35.66%	1.03[0.73,1.45]
Takeshita 2009	0/28	0/28			Not estimable
Subtotal (95% CI)	**276**	**273**		**89.8%**	**1.22[0.98,1.52]**
Total events: 101 (Treatment), 80 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.95, df=3(P=0.18); I^2=39.43%					
Test for overall effect: Z=1.79(P=0.07)					
Total (95% CI)	**340**	**333**		**100%**	**1.15[0.93,1.42]**
Total events: 106 (Treatment), 89 (Control)					
Heterogeneity: Tau^2=0; Chi^2=7.5, df=4(P=0.11); I^2=46.66%					
Test for overall effect: Z=1.27(P=0.2)					
Test for subgroup differences: Chi^2=2.49, df=1 (P=0.11), I^2=59.84%					

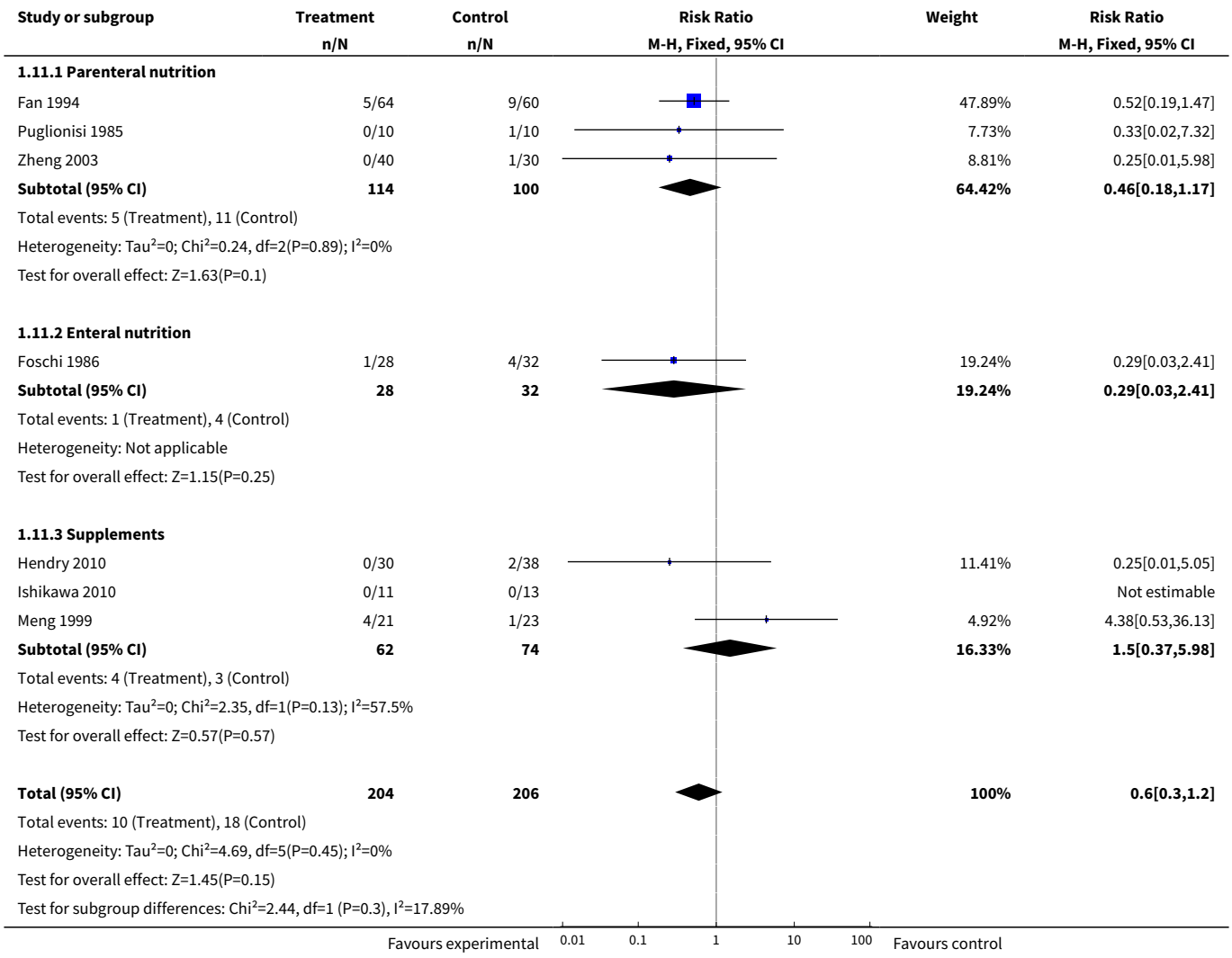
Analysis 1.10. Comparison 1 Mortality, Outcome 10 Abstracts excluded.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 Medical trials - parenteral nutrition					
Achord 1987	1/14	3/14		2.58%	0.33[0.04,2.83]
Bonkovsky 1991	0/9	0/12			Not estimable
Naveau 1986	1/20	1/20		0.86%	1[0.07,14.9]
Simon 1988	5/33	7/36		5.76%	0.78[0.27,2.22]
Subtotal (95% CI)	**76**	**82**		**9.2%**	**0.67[0.28,1.62]**
Total events: 7 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.57, df=2(P=0.75); I^2=0%					
Test for overall effect: Z=0.88(P=0.38)					
1.10.2 Surgical trials - parenteral nutrition					
Fan 1994	5/64	9/60		7.99%	0.52[0.19,1.47]
Puglionisi 1985	0/10	1/10		1.29%	0.33[0.02,7.32]

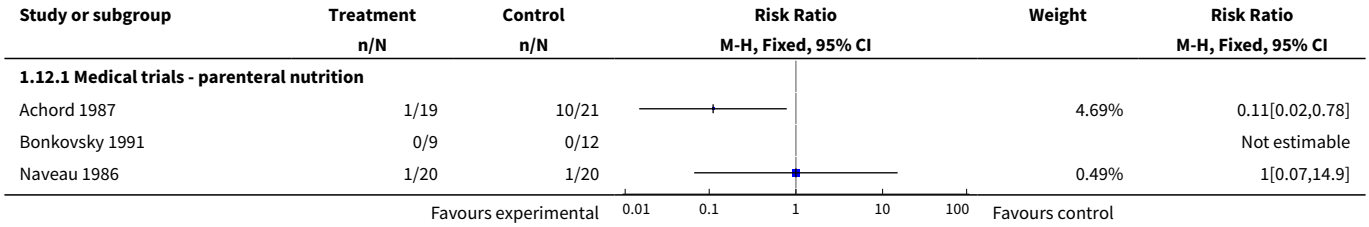


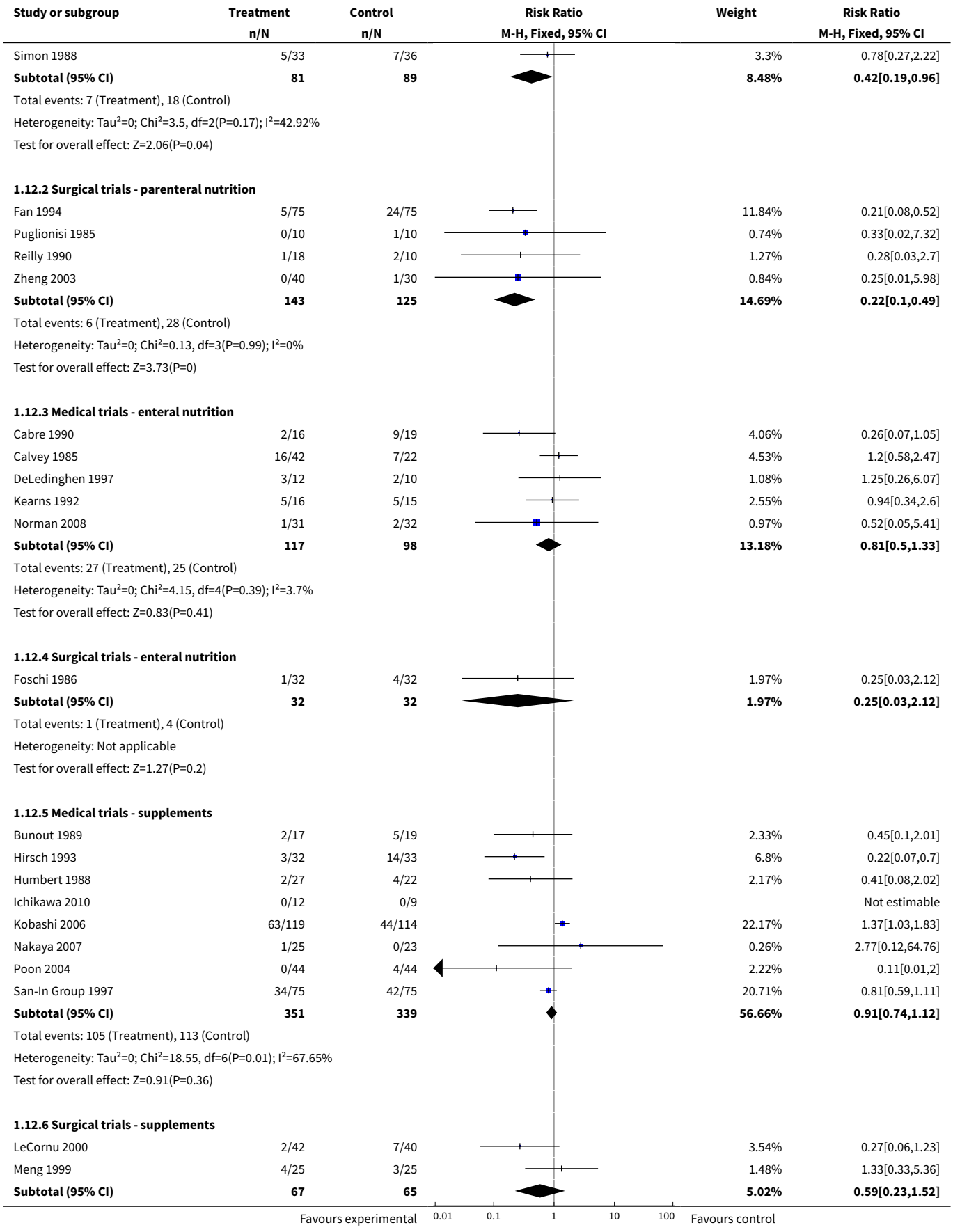


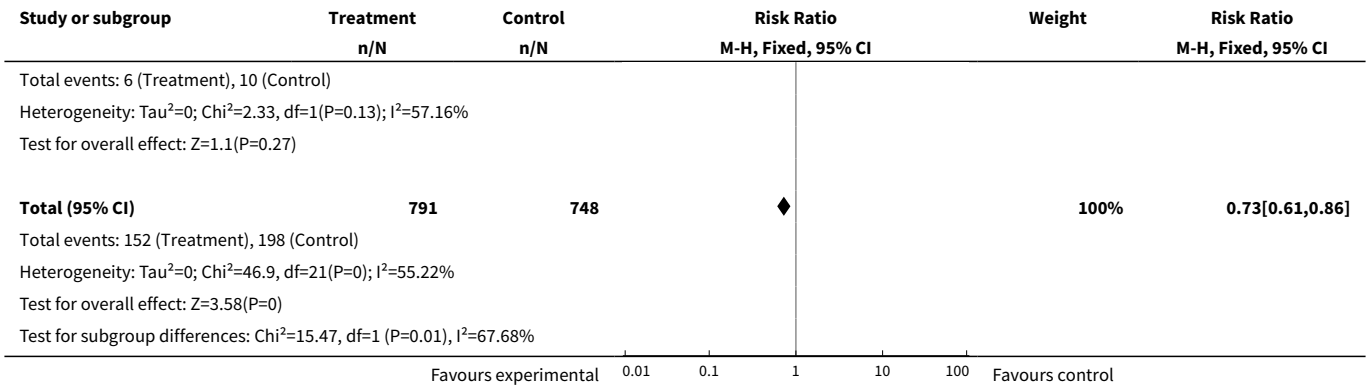
Analysis 1.11. Comparison 1 Mortality, Outcome 11 Surgical trials without transplant patients.



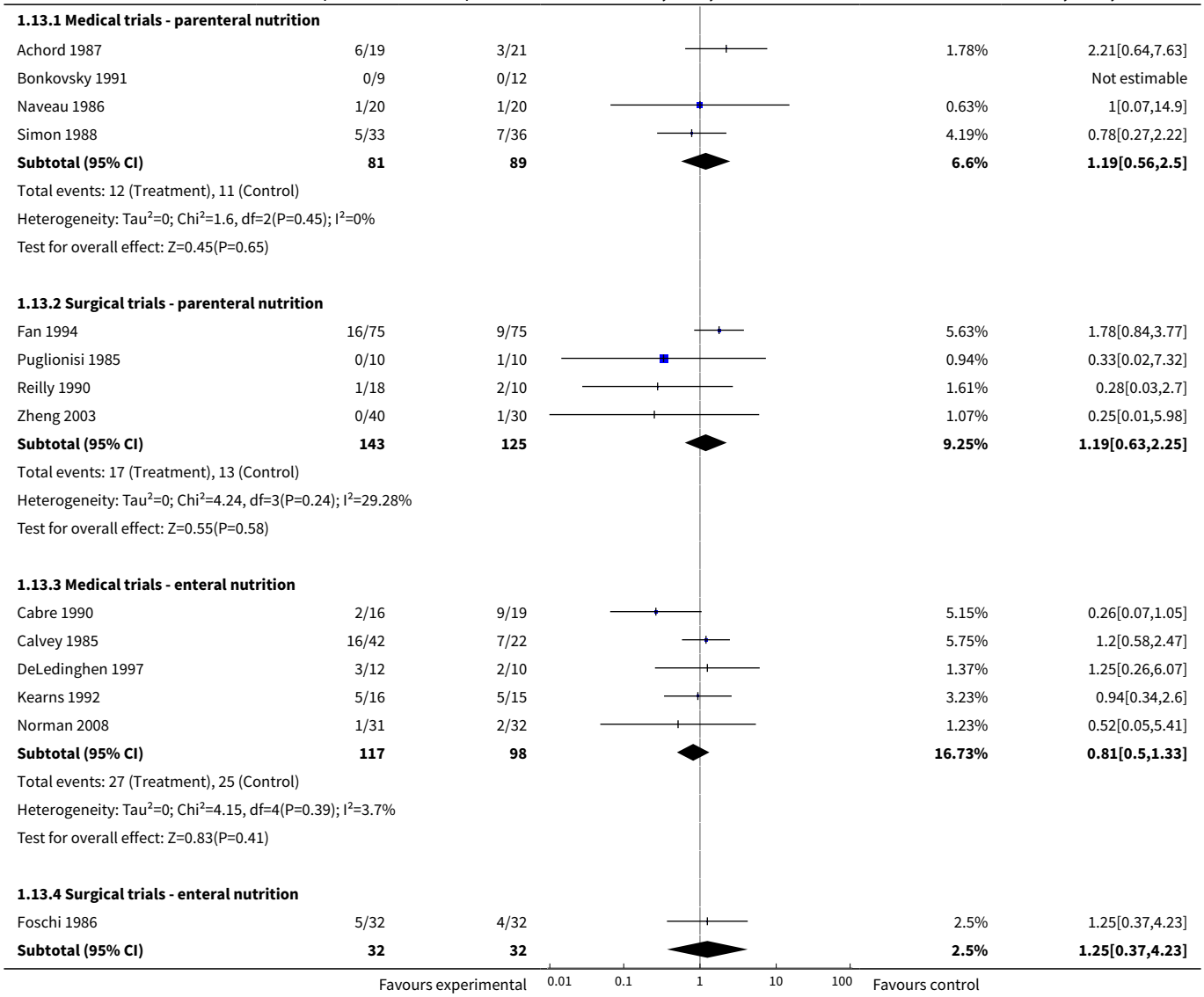
Analysis 1.12. Comparison 1 Mortality, Outcome 12 Intent to treat - best-case scenario for intervention.

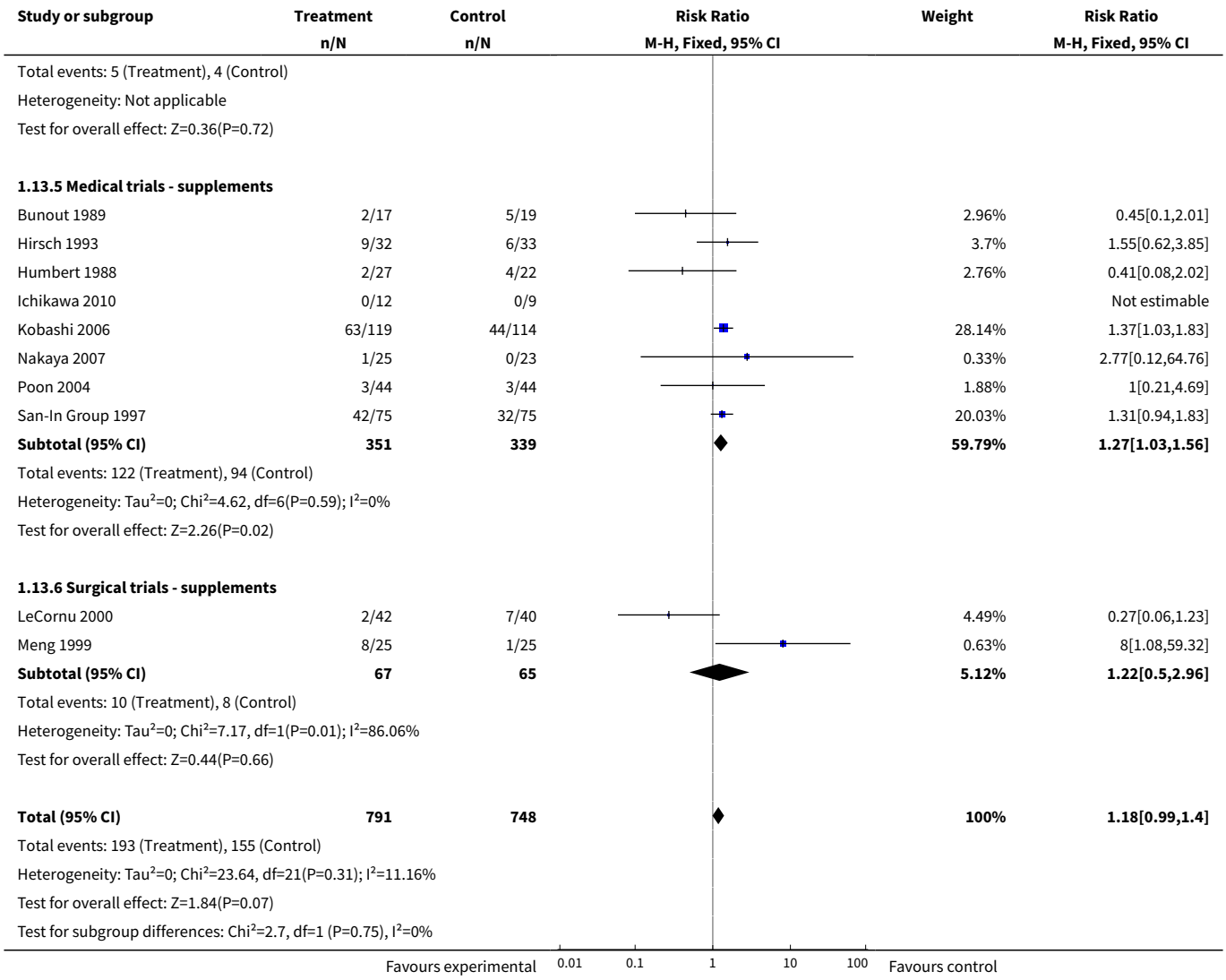






Analysis 1.13. Comparison 1 Mortality, Outcome 13 Intent to treat - worst-case scenario for intervention.





Comparison 2. Appearance of ascites

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	8	582	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.47, 0.77]
2 Parenteral nutrition	4	214	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.39, 1.08]
2.1 Medical trials	2	26	Risk Ratio (M-H, Random, 95% CI)	0.23 [0.01, 3.97]
2.2 Surgical trials	2	188	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.39, 1.15]
3 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.1 Medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	4	368	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.38, 0.87]
4.1 Medical trials	4	368	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.38, 0.87]
4.2 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Medical trials	6	394	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.37, 0.84]
5.1 Parenteral nutrition	2	26	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.01, 3.97]
5.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Supplements	4	368	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.38, 0.87]
6 Surgical trials	2	188	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.87]
6.1 Parenteral nutrition	2	188	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.87]
6.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Alcoholic hepatitis	3	77	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.31, 1.26]
7.1 Parenteral nutrition	2	26	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.01, 3.97]
7.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Supplements	1	51	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.34, 1.45]
8 Cirrhosis	2	82	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.36, 1.46]
8.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Supplements	2	82	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.36, 1.46]
9 HCC	2	286	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.32, 0.87]
9.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	2	286	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.32, 0.87]
10 Abstracts excluded	7	380	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.46, 0.79]
10.1 Parenteral nutrition - medical trials	2	26	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.01, 3.97]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
10.2 Parenteral nutrition - surgical trials	2	188	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.87]
10.3 Enteral nutrition - medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.4 Enteral nutrition = surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.5 Supplements - medical trials	3	166	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.29, 1.00]
10.6 Supplements - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Surgical trials without transplant	2	188	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.87]
11.1 Parenteral nutrition	2	188	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.48, 0.87]
11.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Intent to treat - best-case scenario for in-tervention	8	626	Risk Ratio (M-H, Fixed, 95% CI)	0.50 [0.39, 0.64]
12.1 Parenteral nutrition - medical trials	2	26	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.01, 3.97]
12.2 Parenteral nutrition - surgical trials	2	214	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.39, 0.70]
12.3 Enteral nutrition - medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	4	386	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.33, 0.73]
12.6 Supplements - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Intent to treat - worst-case scenario for intervention	8	626	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.65, 1.02]
13.1 Parenteral nutrition - medical trials	2	26	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.01, 3.97]
13.2 Parenteral nutrition - surgical trials	2	214	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.66, 1.15]
13.3 Enteral nutrition - medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.4 Enteral nutrition = surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.5 Supplements - medical trials	4	386	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.53, 1.11]
13.6 Supplements - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

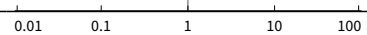
Analysis 2.1. Comparison 2 Appearance of ascites, Outcome 1 All studies.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Achord 1987	0/9	0/6			Not estimable
Fan 1994	16/64	30/60		29.45%	0.5[0.31,0.82]
Hirsch 1993	8/26	11/25		10.67%	0.7[0.34,1.45]
Kobashi 2006	16/100	27/102		25.43%	0.6[0.35,1.05]
Nakaya 2007	1/16	1/15		0.98%	0.94[0.06,13.68]
Poon 2004	3/41	10/43		9.28%	0.31[0.09,1.06]
Simon 1988	0/5	2/6		2.19%	0.23[0.01,3.97]
Zheng 2003	23/37	20/27		21.99%	0.84[0.6,1.17]
Total (95% CI)	**298**	**284**		**100%**	**0.6[0.47,0.77]**
Total events: 67 (Experimental), 101 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.04, df=6(P=0.42); I^2=0.7%					
Test for overall effect: Z=4(P<0.0001)					

Favours experimental — Favours control

Analysis 2.2. Comparison 2 Appearance of ascites, Outcome 2 Parenteral nutrition.

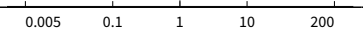
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 Medical trials					
Achord 1987	0/9	0/6			Not estimable
Simon 1988	0/5	2/6		3.12%	0.23[0.01,3.97]
Subtotal (95% CI)	**14**	**12**		**3.12%**	**0.23[0.01,3.97]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.01(P=0.31)					
2.2.2 Surgical trials					
Fan 1994	16/64	30/60		42.65%	0.5[0.31,0.82]
Zheng 2003	23/37	20/27		54.24%	0.84[0.6,1.17]
Subtotal (95% CI)	**101**	**87**		**96.88%**	**0.67[0.39,1.15]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau^2=0.11; Chi^2=3.38, df=1(P=0.07); I^2=70.37%					
Test for overall effect: Z=1.46(P=0.14)					
Total (95% CI)	**115**	**99**		**100%**	**0.65[0.39,1.08]**
Total events: 39 (Experimental), 52 (Control)					
Heterogeneity: Tau^2=0.1; Chi^2=4.14, df=2(P=0.13); I^2=51.7%					
Test for overall effect: Z=1.67(P=0.09)					
Test for subgroup differences: Chi^2=0.51, df=1 (P=0.48), I^2=0%					



Favours experimental — Favours control

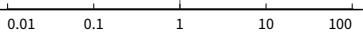
Analysis 2.4. Comparison 2 Appearance of ascites, Outcome 4 Supplements.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 Medical trials					
Hirsch 1993	8/26	11/25		23.01%	0.7[0.34,1.45]
Kobashi 2006	16/100	27/102		54.84%	0.6[0.35,1.05]
Nakaya 2007	1/16	1/15		2.12%	0.94[0.06,13.68]
Poon 2004	3/41	10/43		20.03%	0.31[0.09,1.06]
Subtotal (95% CI)	**183**	**185**		**100%**	**0.58[0.38,0.87]**
Total events: 28 (Experimental), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.38, df=3(P=0.71); I^2=0%					
Test for overall effect: Z=2.64(P=0.01)					
2.4.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**183**	**185**		**100%**	**0.58[0.38,0.87]**
Total events: 28 (Experimental), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.38, df=3(P=0.71); I^2=0%					
Test for overall effect: Z=2.64(P=0.01)					
Test for subgroup differences: Not applicable					



Analysis 2.5. Comparison 2 Appearance of ascites, Outcome 5 Medical trials.

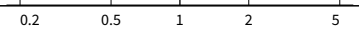
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 Parenteral nutrition					
Achord 1987	0/9	0/6			Not estimable
Simon 1988	0/5	2/6		4.52%	0.23[0.01,3.97]
Subtotal (95% CI)	**14**	**12**		**4.52%**	**0.23[0.01,3.97]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.01(P=0.31)					
2.5.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.5.3 Supplements					
Hirsch 1993	8/26	11/25		21.97%	0.7[0.34,1.45]
Kobashi 2006	16/100	27/102		52.37%	0.6[0.35,1.05]
Nakaya 2007	1/16	1/15		2.02%	0.94[0.06,13.68]
Poon 2004	3/41	10/43		19.12%	0.31[0.09,1.06]
Subtotal (95% CI)	**183**	**185**		**95.48%**	**0.58[0.38,0.87]**
Total events: 28 (Experimental), 49 (Control)					



Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=1.38, df=3(P=0.71); I²=0%					
Test for overall effect: Z=2.64(P=0.01)					
Total (95% CI)	**197**	**197**		**100%**	**0.56[0.37,0.84]**
Total events: 28 (Experimental), 51 (Control)					
Heterogeneity: Tau²=0; Chi²=1.8, df=4(P=0.77); I²=0%					
Test for overall effect: Z=2.8(P=0.01)					
Test for subgroup differences: Chi²=0.38, df=1 (P=0.54), I²=0%					

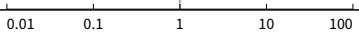
Analysis 2.6. Comparison 2 Appearance of ascites, Outcome 6 Surgical trials.

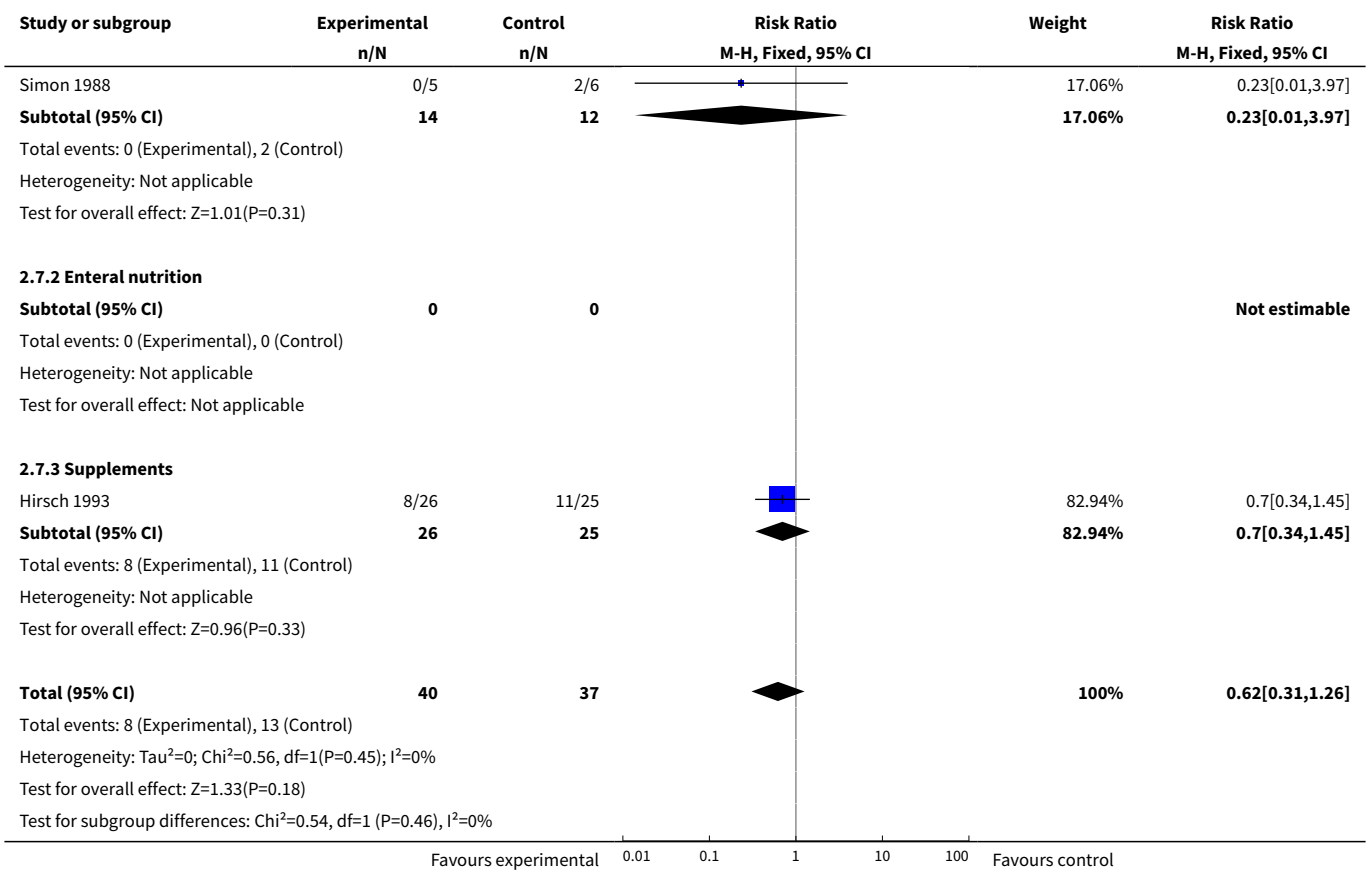
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.6.1 Parenteral nutrition					
Fan 1994	16/64	30/60		57.25%	0.5[0.31,0.82]
Zheng 2003	23/37	20/27		42.75%	0.84[0.6,1.17]
Subtotal (95% CI)	**101**	**87**		**100%**	**0.65[0.48,0.87]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau²=0; Chi²=3.38, df=1(P=0.07); I²=70.37%					
Test for overall effect: Z=2.88(P=0)					
2.6.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.6.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**101**	**87**		**100%**	**0.65[0.48,0.87]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau²=0; Chi²=3.38, df=1(P=0.07); I²=70.37%					
Test for overall effect: Z=2.88(P=0)					
Test for subgroup differences: Chi²=0, df=1 (P<0.0001), I²=100%					



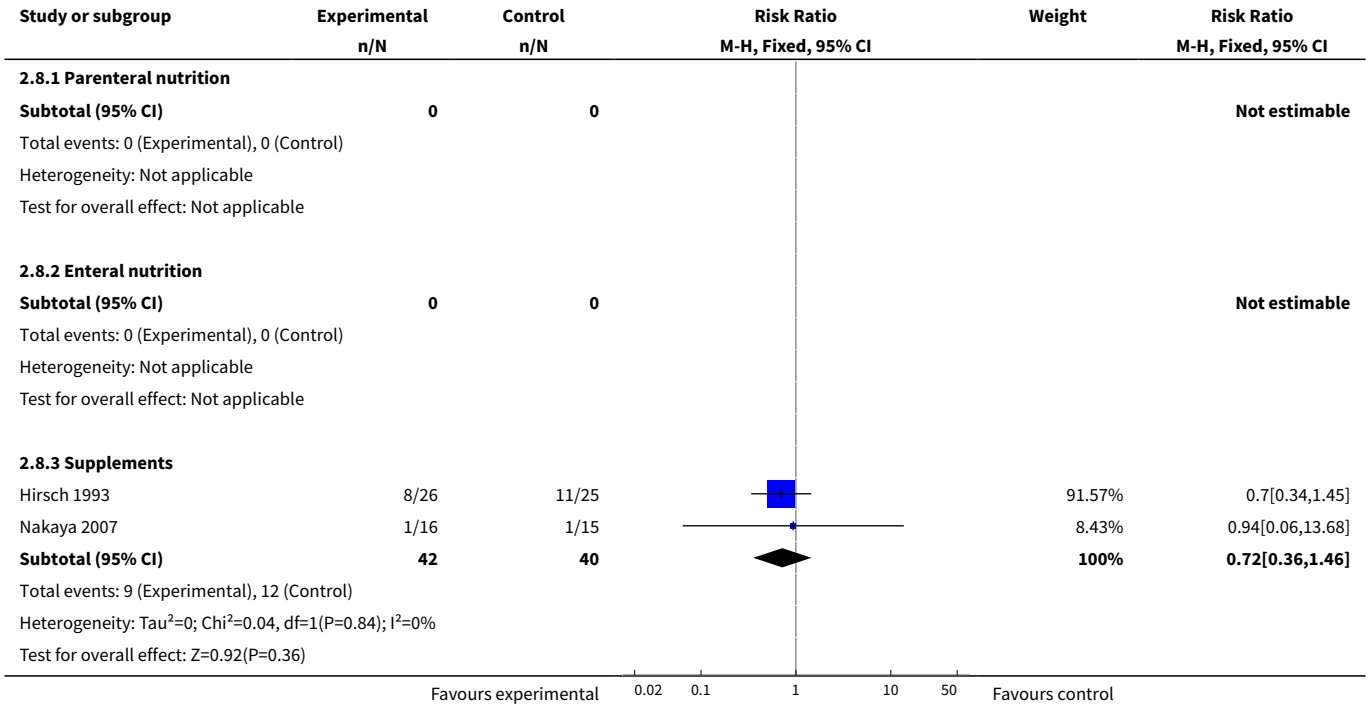
Analysis 2.7. Comparison 2 Appearance of ascites, Outcome 7 Alcoholic hepatitis.

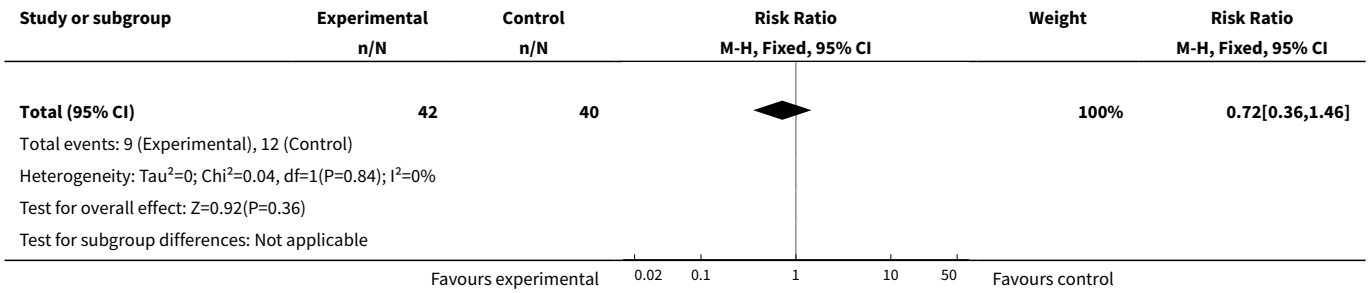
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.7.1 Parenteral nutrition					
Achord 1987	0/9	0/6			Not estimable



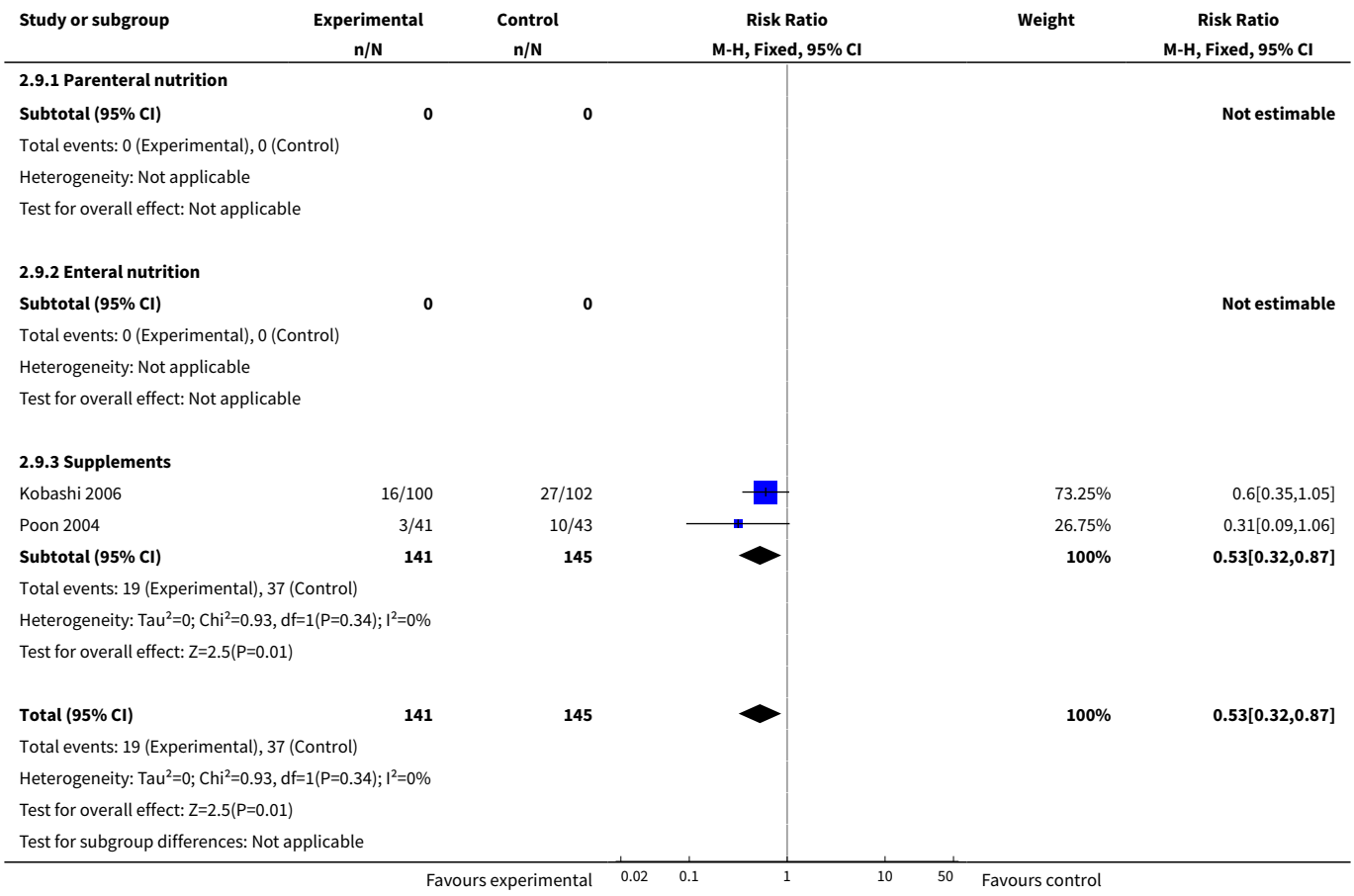


Analysis 2.8. Comparison 2 Appearance of ascites, Outcome 8 Cirrhosis.

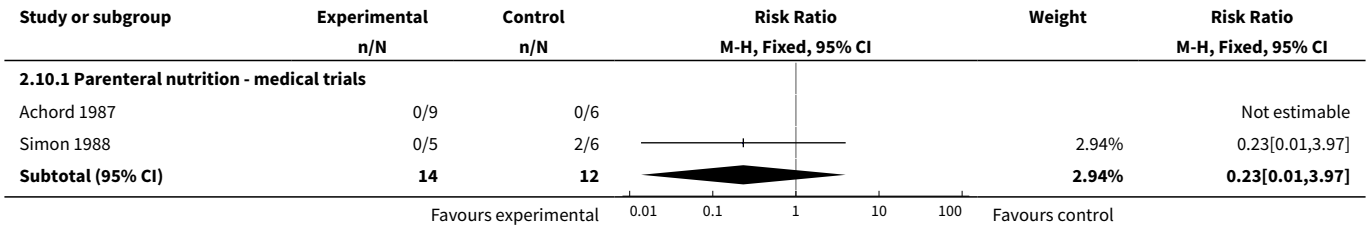


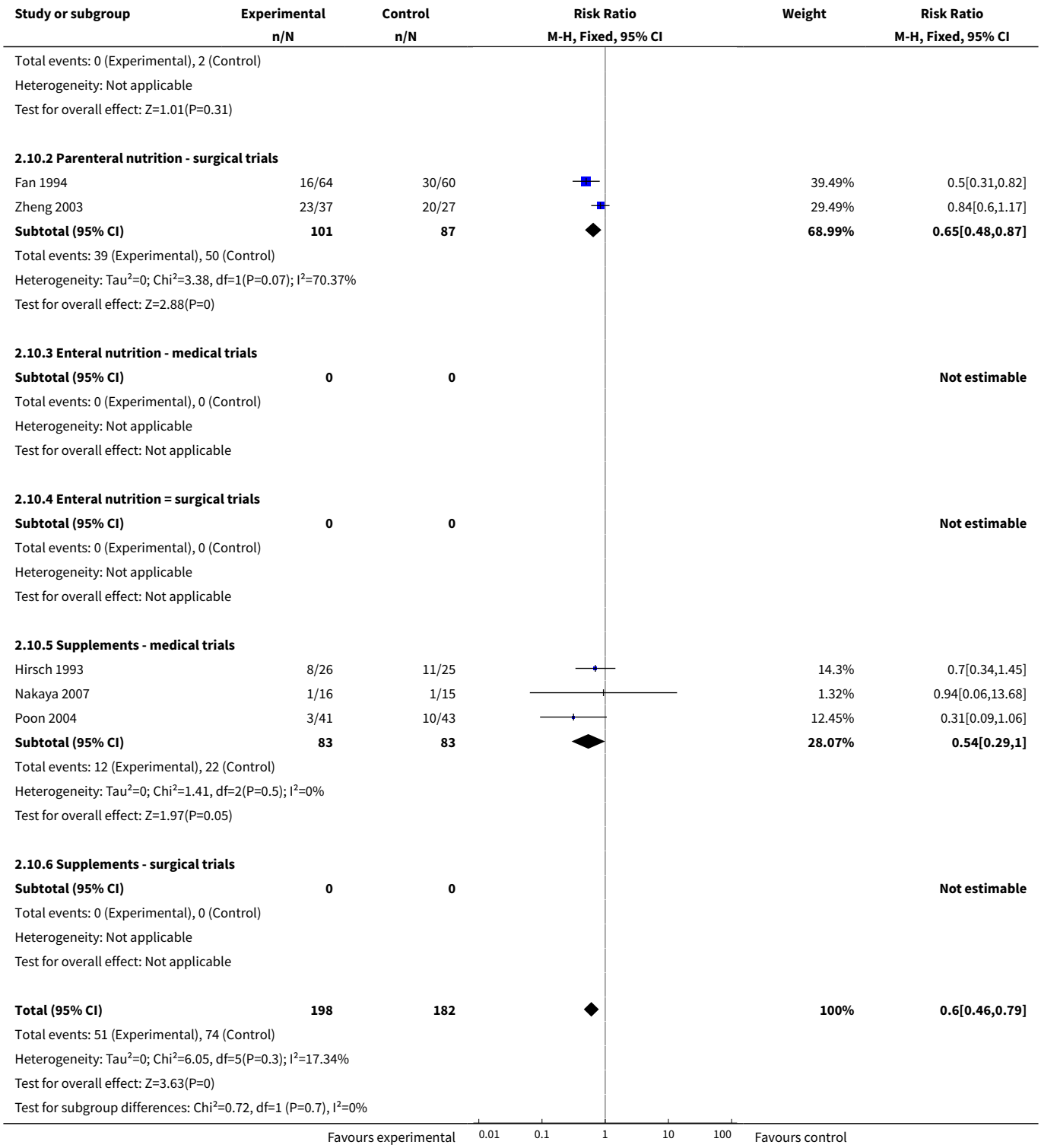


Analysis 2.9. Comparison 2 Appearance of ascites, Outcome 9 HCC.



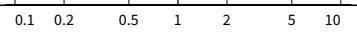
Analysis 2.10. Comparison 2 Appearance of ascites, Outcome 10 Abstracts excluded.





Analysis 2.11. Comparison 2 Appearance of ascites, Outcome 11 Surgical trials without transplant.

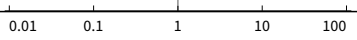
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.11.1 Parenteral nutrition					
Fan 1994	16/64	30/60		57.25%	0.5[0.31,0.82]
Zheng 2003	23/37	20/27		42.75%	0.84[0.6,1.17]
Subtotal (95% CI)	**101**	**87**		**100%**	**0.65[0.48,0.87]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.38, df=1(P=0.07); I^2=70.37%					
Test for overall effect: Z=2.88(P=0)					
2.11.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.11.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**101**	**87**		**100%**	**0.65[0.48,0.87]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.38, df=1(P=0.07); I^2=70.37%					
Test for overall effect: Z=2.88(P=0)					
Test for subgroup differences: Chi^2=0, df=1 (P<0.0001), I^2=100%					



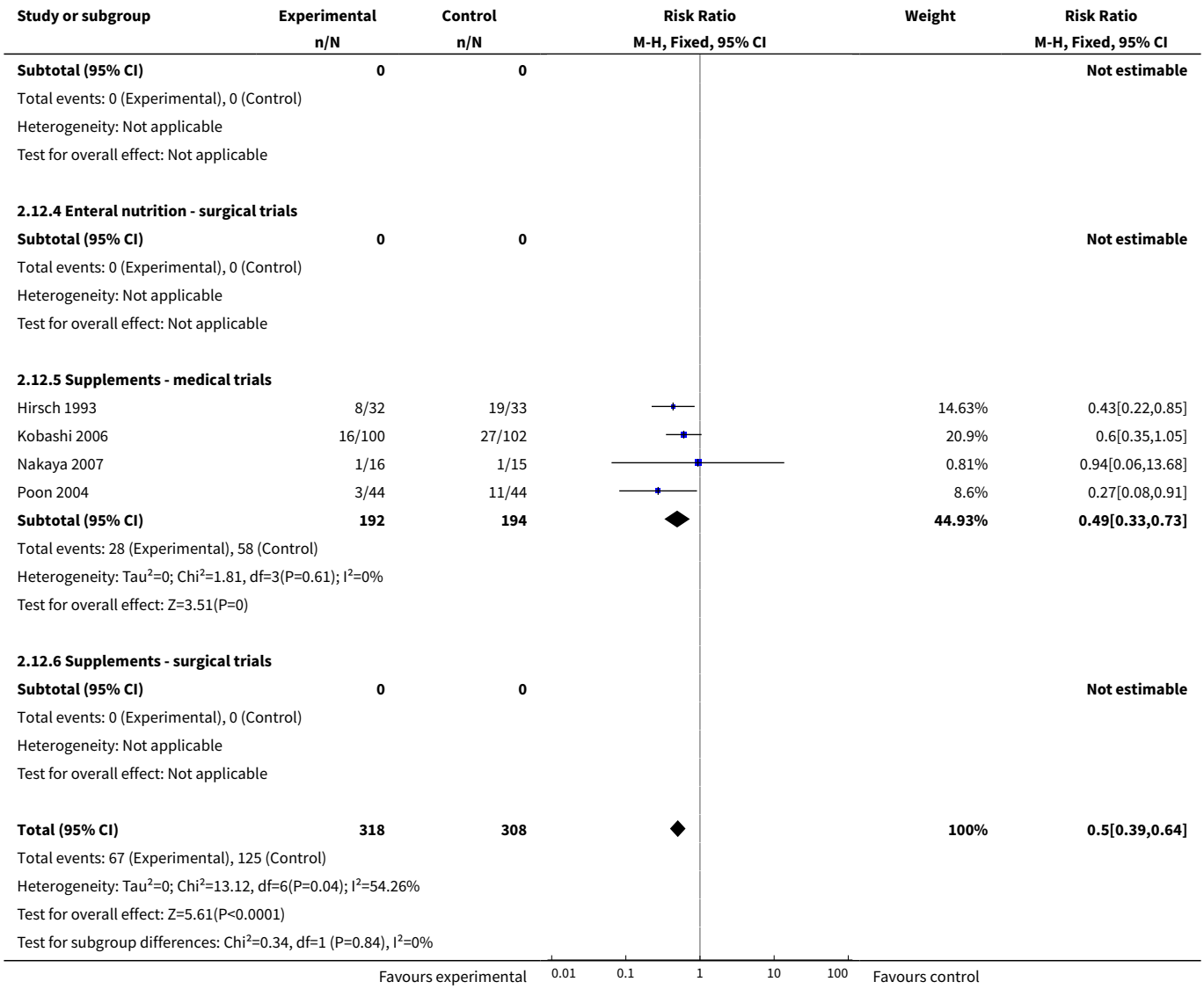
Favours experimental — Favours control

Analysis 2.12. Comparison 2 Appearance of ascites, Outcome 12 Intent to treat - best-case scenario for intervention.

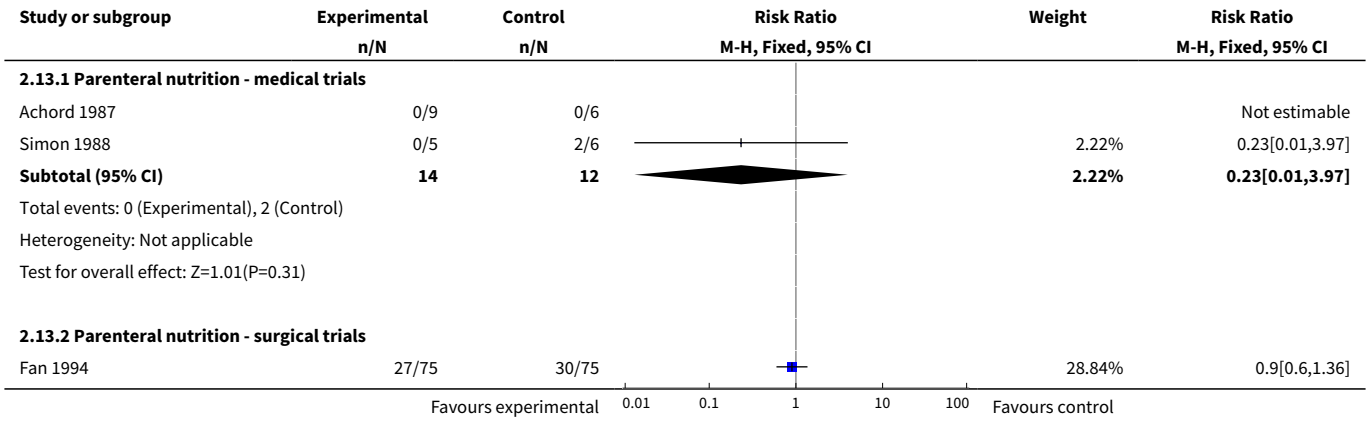
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.12.1 Parenteral nutrition - medical trials					
Achord 1987	0/9	0/6			Not estimable
Simon 1988	0/5	2/6		1.8%	0.23[0.01,3.97]
Subtotal (95% CI)	**14**	**12**		**1.8%**	**0.23[0.01,3.97]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.01(P=0.31)					
2.12.2 Parenteral nutrition - surgical trials					
Fan 1994	16/75	45/75		35.18%	0.36[0.22,0.57]
Zheng 2003	23/37	20/27		18.08%	0.84[0.6,1.17]
Subtotal (95% CI)	**112**	**102**		**53.26%**	**0.52[0.39,0.7]**
Total events: 39 (Experimental), 65 (Control)					
Heterogeneity: Tau^2=0; Chi^2=10.29, df=1(P=0); I^2=90.28%					
Test for overall effect: Z=4.33(P<0.0001)					
2.12.3 Enteral nutrition - medical trials					

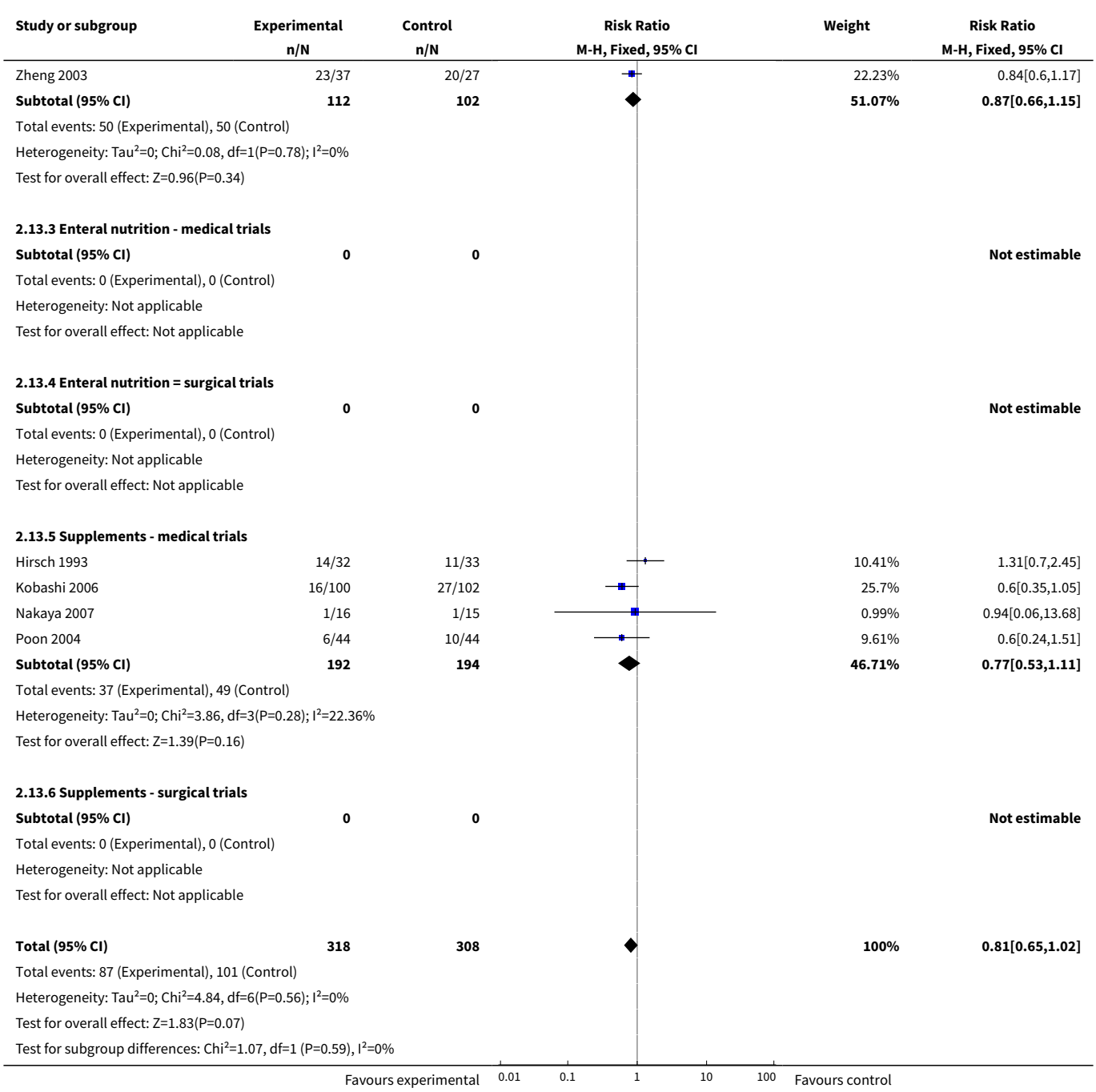


Favours experimental — Favours control



Analysis 2.13. Comparison 2 Appearance of ascites, Outcome 13 Intent to treat - worst-case scenario for intervention.





Comparison 3. Resolution of ascites

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	6	131	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.66, 1.27]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2 Parenteral nutrition	3	73	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.48, 1.05]
2.1 Medical trials	3	73	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.48, 1.05]
2.2 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Enteral nutrition	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
3.1 Medical trials	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
3.2 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]
4.1 Medical trials	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]
4.2 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Medical trials	6	131	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.66, 1.27]
5.1 Parenteral nutrition	3	73	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.48, 1.05]
5.2 Enteral nutrition	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
5.3 Supplements	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]
6 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Alcoholic hepatitis	2	40	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.46, 2.19]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7.1 Parenteral nutrition	2	40	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.46, 2.19]
7.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Cirrhosis	4	91	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.62, 1.27]
8.1 Parenteral nutrition	1	33	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.37, 0.88]
8.2 Enteral nutrition	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
8.3 Supplements	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]
9 HCC	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Abstracts excluded	6	131	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.66, 1.27]
10.1 Parenteral nutrition - medical trials	3	73	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.48, 1.05]
10.2 Parenteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Enteral nutrition - medical trials	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
10.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.5 Supplements - medical trials	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]
10.6 Supplements - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11 Surgical trials without transplant	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Intent to treat - best-case scenario for intervention - no changes made because all patients with ascites reported	6	131	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.66, 1.27]
12.1 Parenteral nutrition - medical trials	3	73	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.48, 1.05]
12.2 Parenteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Enteral nutrition - medical trials	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
12.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]
12.6 Supplements - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Intent to treat - worst case scenario for intervention - no changes made because all patients with ascites reported	6	131	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.66, 1.27]
13.1 Parenteral nutrition - medical trials	3	73	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.48, 1.05]
13.2 Parenteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 Enteral nutrition - medical trials	1	29	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.46, 1.62]
13.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.5 Supplements - medical trials	2	29	Risk Ratio (M-H, Fixed, 95% CI)	4.16 [0.87, 19.84]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
13.6 Supplements - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

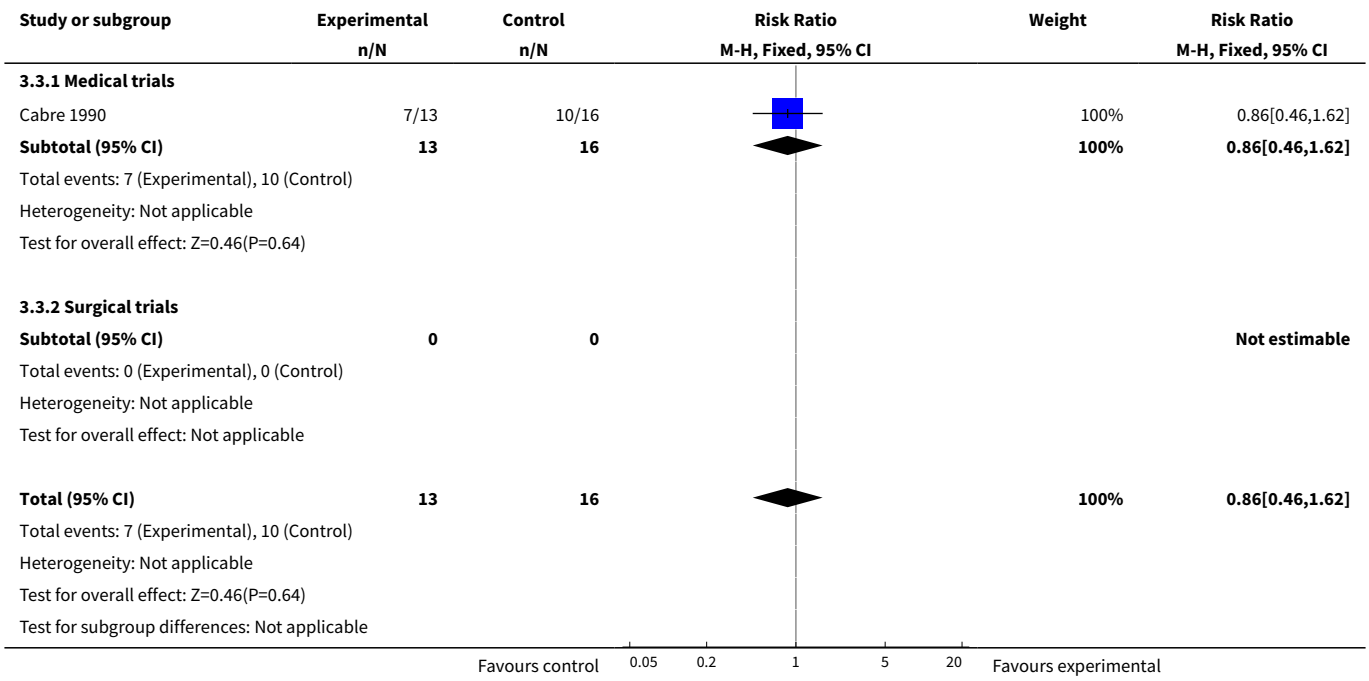
Analysis 3.1. Comparison 3 Resolution of ascites, Outcome 1 All studies.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Achord 1987	3/5	3/8		6.56%	1.6[0.51,5.03]
Cabre 1990	7/13	10/16		25.49%	0.86[0.46,1.62]
Hayashi 1991	6/14	1/8		3.62%	3.43[0.5,23.63]
Nakaya 2007	2/3	0/4		1.26%	6.25[0.4,96.5]
Naveau 1986	9/16	17/17		48.33%	0.57[0.37,0.88]
Simon 1988	4/14	5/13		14.74%	0.74[0.25,2.18]
Total (95% CI)	**65**	**66**		**100%**	**0.91[0.66,1.27]**
Total events: 31 (Experimental), 36 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.28, df=5(P=0.1); I^2=46.14%					
Test for overall effect: Z=0.53(P=0.6)					

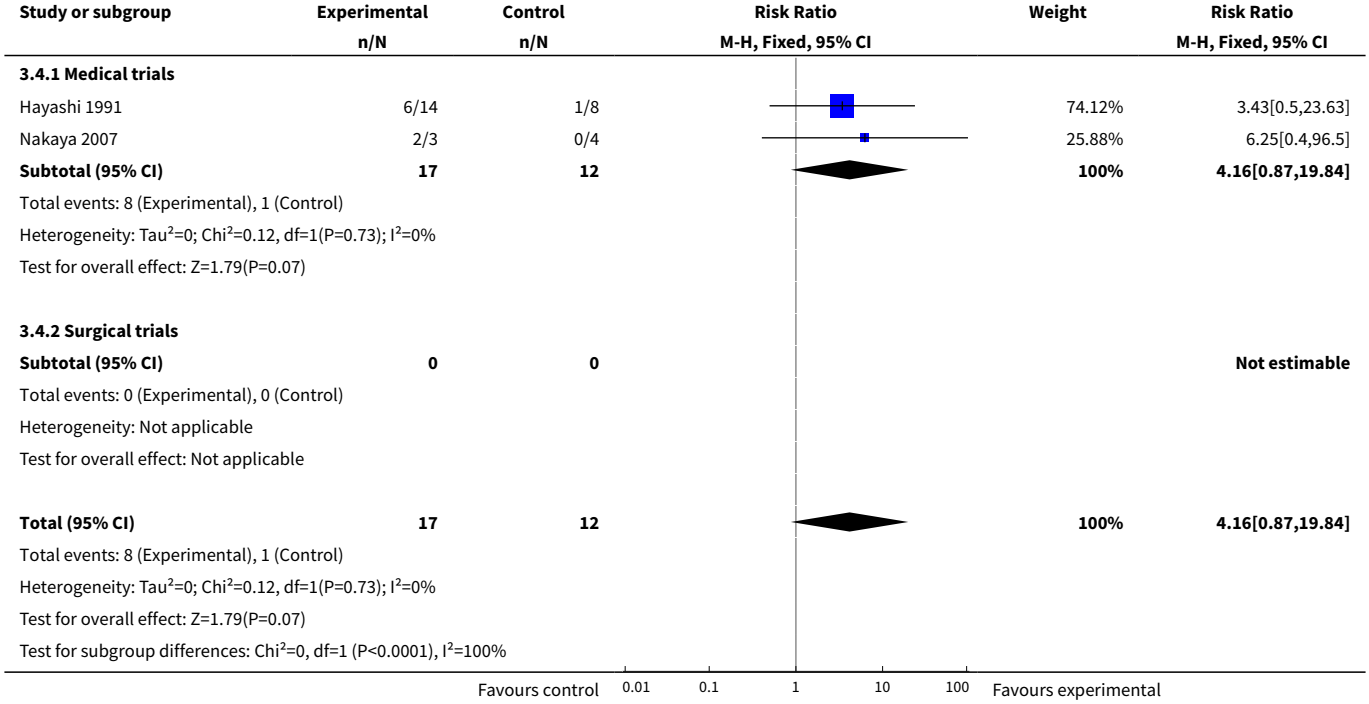
Analysis 3.2. Comparison 3 Resolution of ascites, Outcome 2 Parenteral nutrition.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.1 Medical trials					
Achord 1987	3/5	3/8		9.42%	1.6[0.51,5.03]
Naveau 1986	9/16	17/17		69.41%	0.57[0.37,0.88]
Simon 1988	4/14	5/13		21.17%	0.74[0.25,2.18]
Subtotal (95% CI)	**35**	**38**		**100%**	**0.71[0.48,1.05]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.85, df=2(P=0.24); I^2=29.89%					
Test for overall effect: Z=1.74(P=0.08)					
3.2.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**35**	**38**		**100%**	**0.71[0.48,1.05]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.85, df=2(P=0.24); I^2=29.89%					
Test for overall effect: Z=1.74(P=0.08)					
Test for subgroup differences: Not applicable					

Analysis 3.3. Comparison 3 Resolution of ascites, Outcome 3 Enteral nutrition.

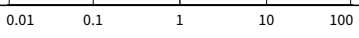


Analysis 3.4. Comparison 3 Resolution of ascites, Outcome 4 Supplements.



Analysis 3.5. Comparison 3 Resolution of ascites, Outcome 5 Medical trials.

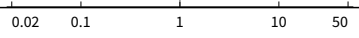
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.5.1 Parenteral nutrition					
Achord 1987	3/5	3/8		6.56%	1.6[0.51,5.03]
Naveau 1986	9/16	17/17		48.33%	0.57[0.37,0.88]
Simon 1988	4/14	5/13		14.74%	0.74[0.25,2.18]
Subtotal (95% CI)	**35**	**38**		**69.63%**	**0.71[0.48,1.05]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.85, df=2(P=0.24); I^2=29.89%					
Test for overall effect: Z=1.74(P=0.08)					
3.5.2 Enteral nutrition					
Cabre 1990	7/13	10/16		25.49%	0.86[0.46,1.62]
Subtotal (95% CI)	**13**	**16**		**25.49%**	**0.86[0.46,1.62]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					
3.5.3 Supplements					
Hayashi 1991	6/14	1/8		3.62%	3.43[0.5,23.63]
Nakaya 2007	2/3	0/4		1.26%	6.25[0.4,96.5]
Subtotal (95% CI)	**17**	**12**		**4.88%**	**4.16[0.87,19.84]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.12, df=1(P=0.73); I^2=0%					
Test for overall effect: Z=1.79(P=0.07)					
Total (95% CI)	**65**	**66**		**100%**	**0.91[0.66,1.27]**
Total events: 31 (Experimental), 36 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.28, df=5(P=0.1); I^2=46.14%					
Test for overall effect: Z=0.53(P=0.6)					
Test for subgroup differences: Chi^2=4.71, df=1 (P=0.09), I^2=57.53%					



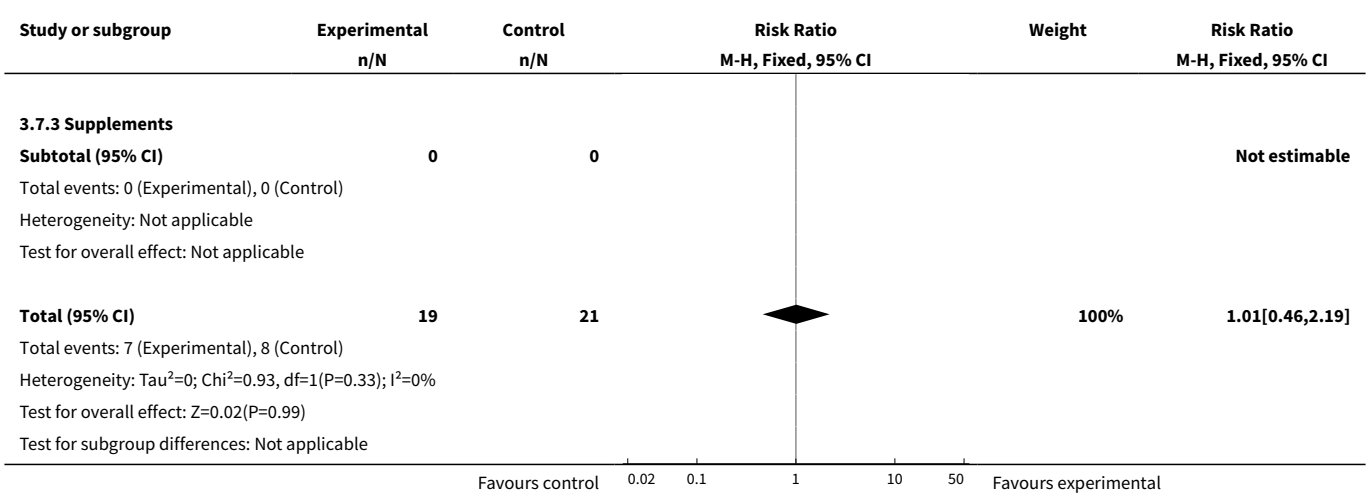
Favours control — Favours experimental

Analysis 3.7. Comparison 3 Resolution of ascites, Outcome 7 Alcoholic hepatitis.

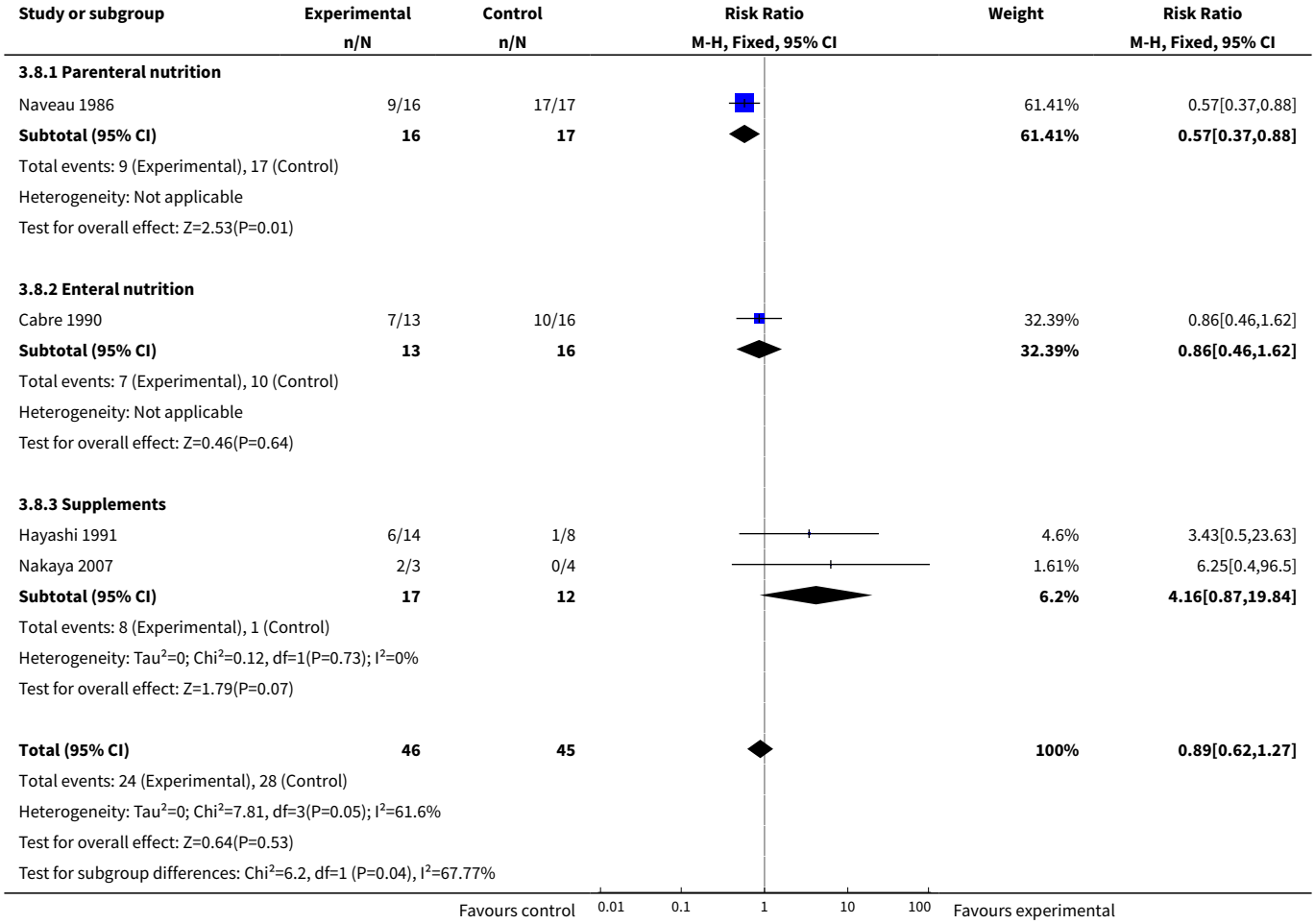
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.7.1 Parenteral nutrition					
Achord 1987	3/5	3/8		30.8%	1.6[0.51,5.03]
Simon 1988	4/14	5/13		69.2%	0.74[0.25,2.18]
Subtotal (95% CI)	**19**	**21**		**100%**	**1.01[0.46,2.19]**
Total events: 7 (Experimental), 8 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.93, df=1(P=0.33); I^2=0%					
Test for overall effect: Z=0.02(P=0.99)					
3.7.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Favours control — Favours experimental

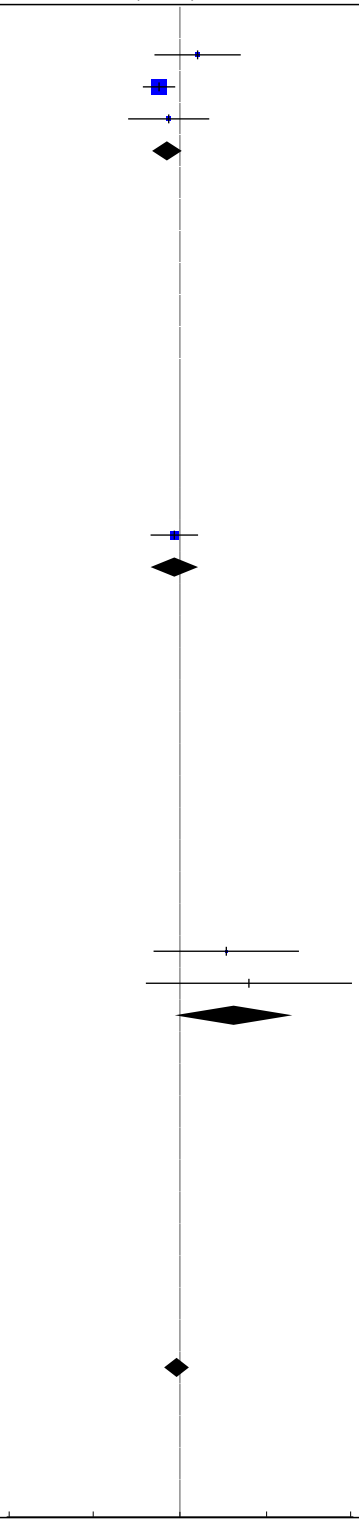


Analysis 3.8. Comparison 3 Resolution of ascites, Outcome 8 Cirrhosis.



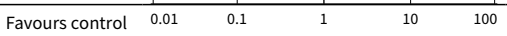
Analysis 3.10. Comparison 3 Resolution of ascites, Outcome 10 Abstracts excluded.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.10.1 Parenteral nutrition - medical trials					
Achord 1987	3/5	3/8		6.56%	1.6[0.51,5.03]
Naveau 1986	9/16	17/17		48.33%	0.57[0.37,0.88]
Simon 1988	4/14	5/13		14.74%	0.74[0.25,2.18]
Subtotal (95% CI)	**35**	**38**		**69.63%**	**0.71[0.48,1.05]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.85, df=2(P=0.24); I^2=29.89%					
Test for overall effect: Z=1.74(P=0.08)					
3.10.2 Parenteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.10.3 Enteral nutrition - medical trials					
Cabre 1990	7/13	10/16		25.49%	0.86[0.46,1.62]
Subtotal (95% CI)	**13**	**16**		**25.49%**	**0.86[0.46,1.62]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					
3.10.4 Enteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.10.5 Supplements - medical trials					
Hayashi 1991	6/14	1/8		3.62%	3.43[0.5,23.63]
Nakaya 2007	2/3	0/4		1.26%	6.25[0.4,96.5]
Subtotal (95% CI)	**17**	**12**		**4.88%**	**4.16[0.87,19.84]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.12, df=1(P=0.73); I^2=0%					
Test for overall effect: Z=1.79(P=0.07)					
3.10.6 Supplements - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**65**	**66**		**100%**	**0.91[0.66,1.27]**
Total events: 31 (Experimental), 36 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.28, df=5(P=0.1); I^2=46.14%					
Test for overall effect: Z=0.53(P=0.6)					
Test for subgroup differences: Chi^2=4.71, df=1 (P=0.09), I^2=57.53%					



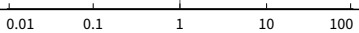
Analysis 3.12. Comparison 3 Resolution of ascites, Outcome 12 Intent to treat - best-case scenario for intervention - no changes made because all patients with ascites reported.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.12.1 Parenteral nutrition - medical trials					
Achord 1987	3/5	3/8		6.56%	1.6[0.51,5.03]
Naveau 1986	9/16	17/17		48.33%	0.57[0.37,0.88]
Simon 1988	4/14	5/13		14.74%	0.74[0.25,2.18]
Subtotal (95% CI)	**35**	**38**		**69.63%**	**0.71[0.48,1.05]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.85, df=2(P=0.24); I^2=29.89%					
Test for overall effect: Z=1.74(P=0.08)					
3.12.2 Parenteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.12.3 Enteral nutrition - medical trials					
Cabre 1990	7/13	10/16		25.49%	0.86[0.46,1.62]
Subtotal (95% CI)	**13**	**16**		**25.49%**	**0.86[0.46,1.62]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					
3.12.4 Enteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.12.5 Supplements - medical trials					
Hayashi 1991	6/14	1/8		3.62%	3.43[0.5,23.63]
Nakaya 2007	2/3	0/4		1.26%	6.25[0.4,96.5]
Subtotal (95% CI)	**17**	**12**		**4.88%**	**4.16[0.87,19.84]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.12, df=1(P=0.73); I^2=0%					
Test for overall effect: Z=1.79(P=0.07)					
3.12.6 Supplements - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**65**	**66**		**100%**	**0.91[0.66,1.27]**
Total events: 31 (Experimental), 36 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.28, df=5(P=0.1); I^2=46.14%					
Test for overall effect: Z=0.53(P=0.6)					
Test for subgroup differences: Chi^2=4.71, df=1 (P=0.09), I^2=57.53%					



Analysis 3.13. Comparison 3 Resolution of ascites, Outcome 13 Intent to treat - worst case scenario for intervention - no changes made because all patients with ascites reported.

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.13.1 Parenteral nutrition - medical trials					
Achord 1987	3/5	3/8		6.56%	1.6[0.51,5.03]
Naveau 1986	9/16	17/17		48.33%	0.57[0.37,0.88]
Simon 1988	4/14	5/13		14.74%	0.74[0.25,2.18]
Subtotal (95% CI)	**35**	**38**		**69.63%**	**0.71[0.48,1.05]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.85, df=2(P=0.24); I^2=29.89%					
Test for overall effect: Z=1.74(P=0.08)					
3.13.2 Parenteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.13.3 Enteral nutrition - medical trials					
Cabre 1990	7/13	10/16		25.49%	0.86[0.46,1.62]
Subtotal (95% CI)	**13**	**16**		**25.49%**	**0.86[0.46,1.62]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					
3.13.4 Enteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.13.5 Supplements - medical trials					
Hayashi 1991	6/14	1/8		3.62%	3.43[0.5,23.63]
Nakaya 2007	2/3	0/4		1.26%	6.25[0.4,96.5]
Subtotal (95% CI)	**17**	**12**		**4.88%**	**4.16[0.87,19.84]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.12, df=1(P=0.73); I^2=0%					
Test for overall effect: Z=1.79(P=0.07)					
3.13.6 Supplements - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**65**	**66**		**100%**	**0.91[0.66,1.27]**
Total events: 31 (Experimental), 36 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.28, df=5(P=0.1); I^2=46.14%					
Test for overall effect: Z=0.53(P=0.6)					
Test for subgroup differences: Chi^2=4.71, df=1 (P=0.09), I^2=57.53%					



Favours control — Favours experimental

Comparison 4. Appearance of gastrointestinal bleeding

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	11	783	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.85, 1.96]
2 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	2.82 [0.12, 67.80]
2.1 Medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Surgical trials	1	124	Risk Ratio (M-H, Fixed, 95% CI)	2.82 [0.12, 67.80]
3 Enteral nutrition (all medical)	4	180	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.78, 2.86]
3.1 Medical trials	4	180	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.78, 2.86]
3.2 Surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	6	479	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.62, 1.89]
4.1 Medical trials	5	435	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.61, 1.91]
4.2 Surgical trials	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.07, 16.43]
5 Medical trials	9	615	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [0.82, 1.94]
5.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 Enteral nutrition	4	180	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.78, 2.86]
5.3 Supplements	5	435	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.61, 1.91]
6 Surgical trials	2	168	Risk Ratio (M-H, Fixed, 95% CI)	1.70 [0.23, 12.73]
6.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	2.82 [0.12, 67.80]
6.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

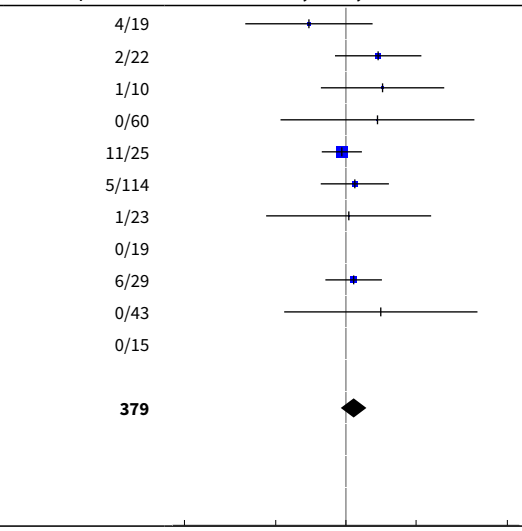
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
6.3 Supplements	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.07, 16.43]
7 Alcoholic hepatitis	1	64	Risk Ratio (M-H, Fixed, 95% CI)	2.88 [0.70, 11.87]
7.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Enteral nutrition	1	64	Risk Ratio (M-H, Fixed, 95% CI)	2.88 [0.70, 11.87]
7.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Cirrhosis	6	234	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.62, 1.67]
8.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Enteral nutrition	3	116	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.55, 2.43]
8.3 Supplements	3	118	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.45, 1.69]
9 HCC	2	317	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.53, 4.26]
9.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Eneral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	2	317	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.53, 4.26]
10 Abstracts excluded	9	491	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [0.76, 2.13]
10.1 Parenteral nutrition - medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 Parenteral nutrition - surgical trials	1	124	Risk Ratio (M-H, Fixed, 95% CI)	2.82 [0.12, 67.80]
10.3 Enteral nutrition - medical trials	3	121	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.68, 4.10]
10.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.5 Supplements - medical trials	4	202	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.51, 1.84]
10.6 Supplements - surgical trials	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.07, 16.43]
11 Surgical trials without transplant patients (no trials with transplant patients)	2	168	Risk Ratio (M-H, Fixed, 95% CI)	1.70 [0.23, 12.73]
11.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	2.82 [0.12, 67.80]
11.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Supplements	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.07, 16.43]
12 Intent to treat - best-case scenario for intervention	11	838	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.47, 0.97]
12.1 Parenteral nutrition - medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 Parenteral nutrition - surgical trials	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.01, 0.49]
12.3 Enteral nutrition - medical trials	4	184	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.69, 2.30]
12.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	5	454	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.42, 1.16]
12.6 Supplements - surgical trials	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.04, 2.99]
13 Intent to treat - worst-case scenario for intervention	11	838	Risk Ratio (M-H, Fixed, 95% CI)	2.14 [1.46, 3.15]
13.1 Parenteral nutrition - medical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Parenteral nutrition - surgical trials	1	150	Risk Ratio (M-H, Fixed, 95% CI)	25.0 [1.51, 414.73]
13.3 Enteral nutrition - medical trials	4	184	Risk Ratio (M-H, Fixed, 95% CI)	1.61 [0.85, 3.07]
13.4 Enteral nutrition - surgical trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
13.5 Supplements - medical trials	5	454	Risk Ratio (M-H, Fixed, 95% CI)	1.72 [1.02, 2.88]
13.6 Supplements - surgical trials	1	50	Risk Ratio (M-H, Fixed, 95% CI)	5.0 [0.63, 39.79]

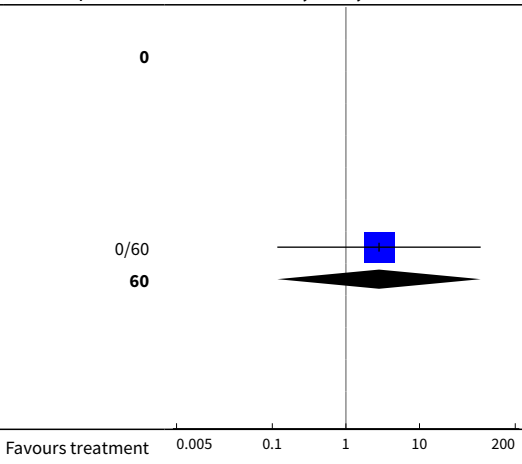
Analysis 4.1. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 1 All studies.

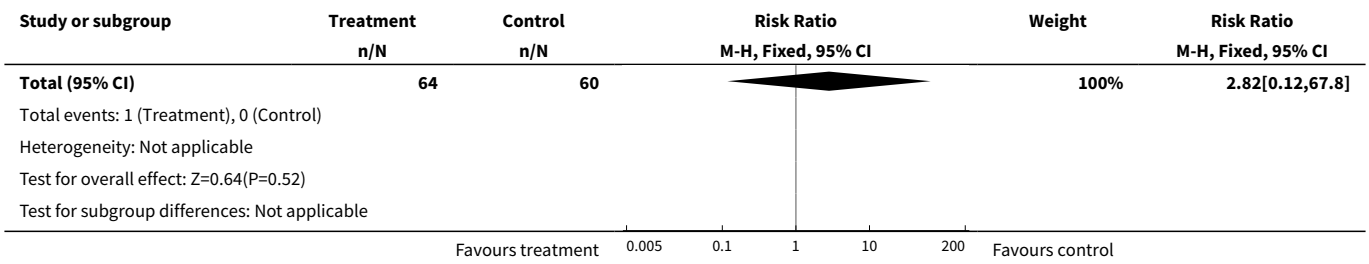
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Cabre 1990	1/16	4/19		11.52%	0.3[0.04,2.4]
Calvey 1985	11/42	2/22		8.27%	2.88[0.7,11.87]
DeLedinghen 1997	4/12	1/10		3.44%	3.33[0.44,25.23]
Fan 1994	1/64	0/60		1.62%	2.82[0.12,67.8]
Hirsch 1993	10/26	11/25		35.32%	0.87[0.45,1.69]
Kobashi 2006	7/119	5/114		16.08%	1.34[0.44,4.1]
Meng 1999	1/21	1/23		3.01%	1.1[0.07,16.43]
Nakaya 2007	0/19	0/19			Not estimable
Norman 2008	8/30	6/29		19.21%	1.29[0.51,3.26]
Poon 2004	1/41	0/43		1.54%	3.14[0.13,75.02]
Tangkijvanich 2000	0/14	0/15			Not estimable
Total (95% CI)	**404**	**379**		**100%**	**1.29[0.85,1.96]**
Total events: 44 (Treatment), 30 (Control)					
Heterogeneity: Tau²=0; Chi²=5.87, df=8(P=0.66); I²=0%					
Test for overall effect: Z=1.17(P=0.24)					



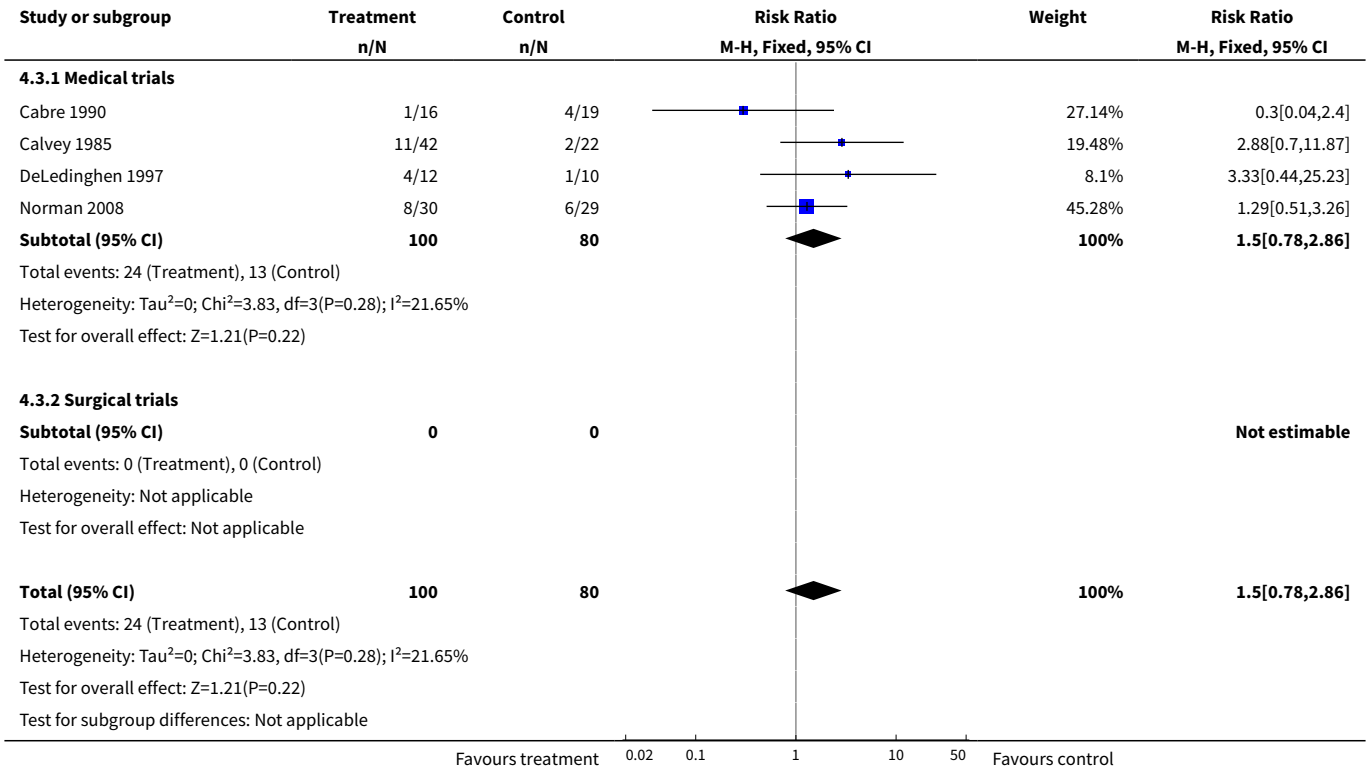
Analysis 4.2. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 2 Parenteral nutrition.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 Medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.2.2 Surgical trials					
Fan 1994	1/64	0/60		100%	2.82[0.12,67.8]
Subtotal (95% CI)	**64**	**60**		**100%**	**2.82[0.12,67.8]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.64(P=0.52)					

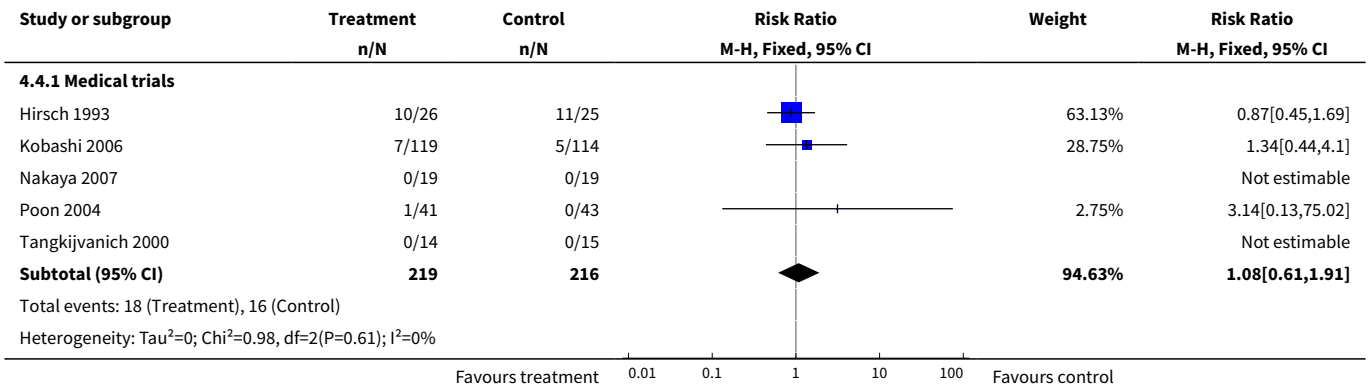


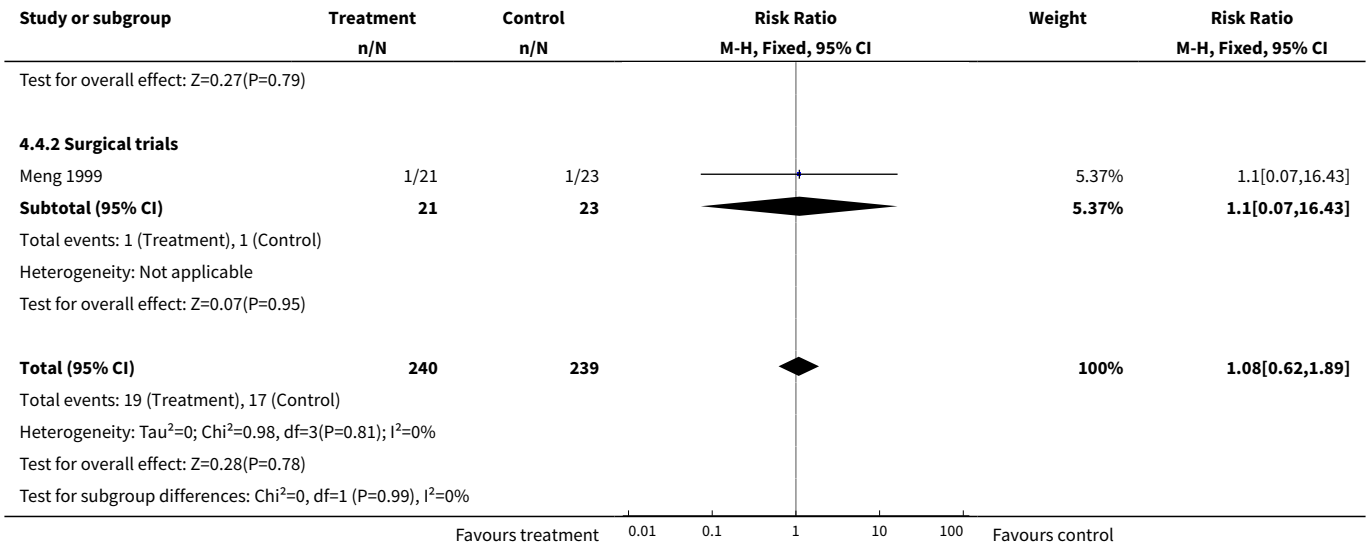


Analysis 4.3. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 3 Enteral nutrition (all medical).

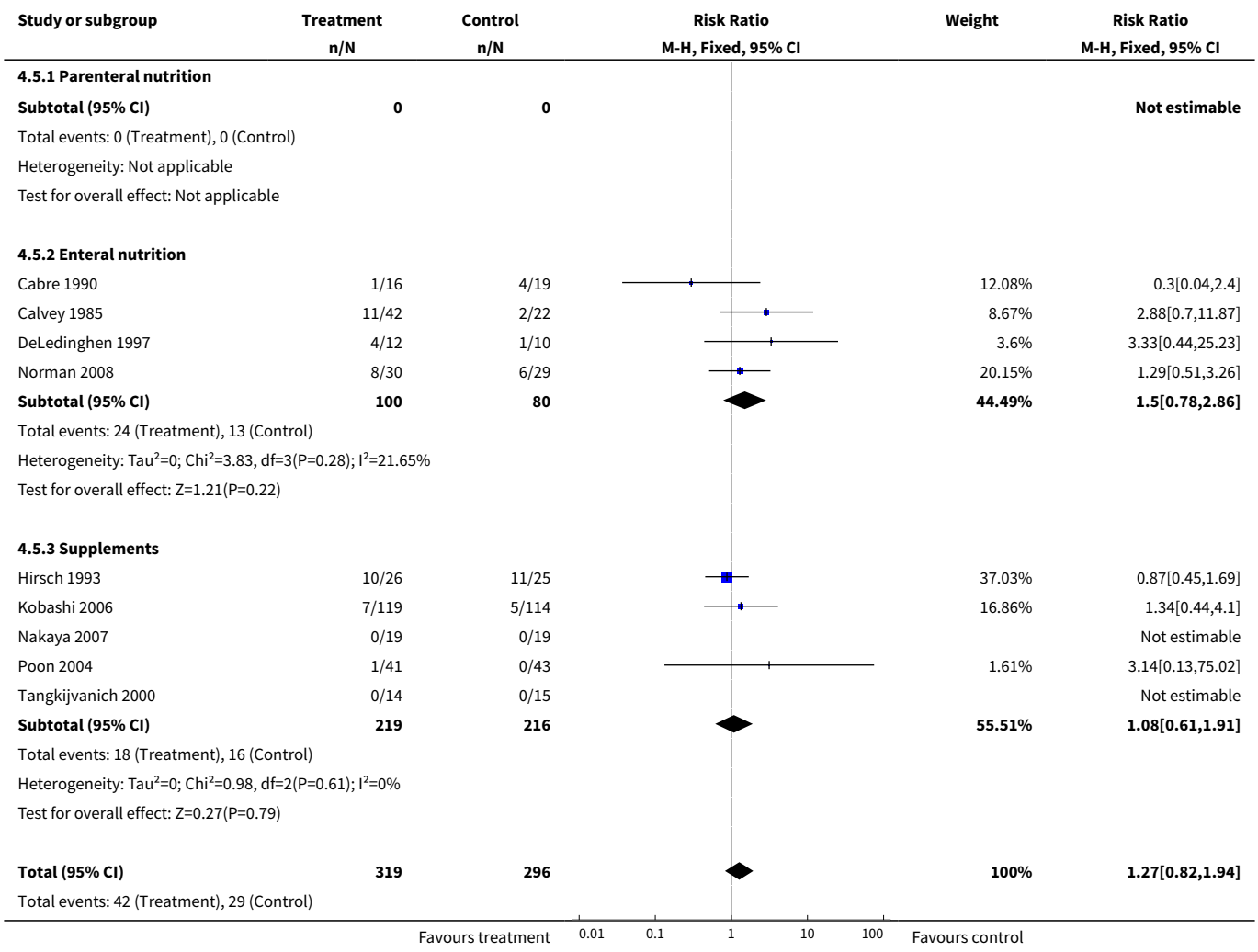


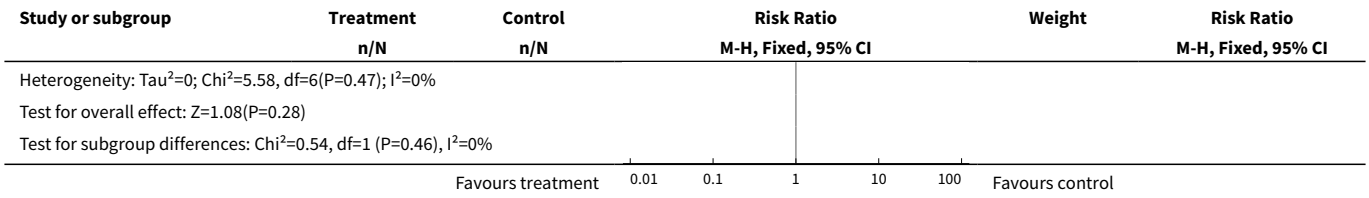
Analysis 4.4. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 4 Supplements.



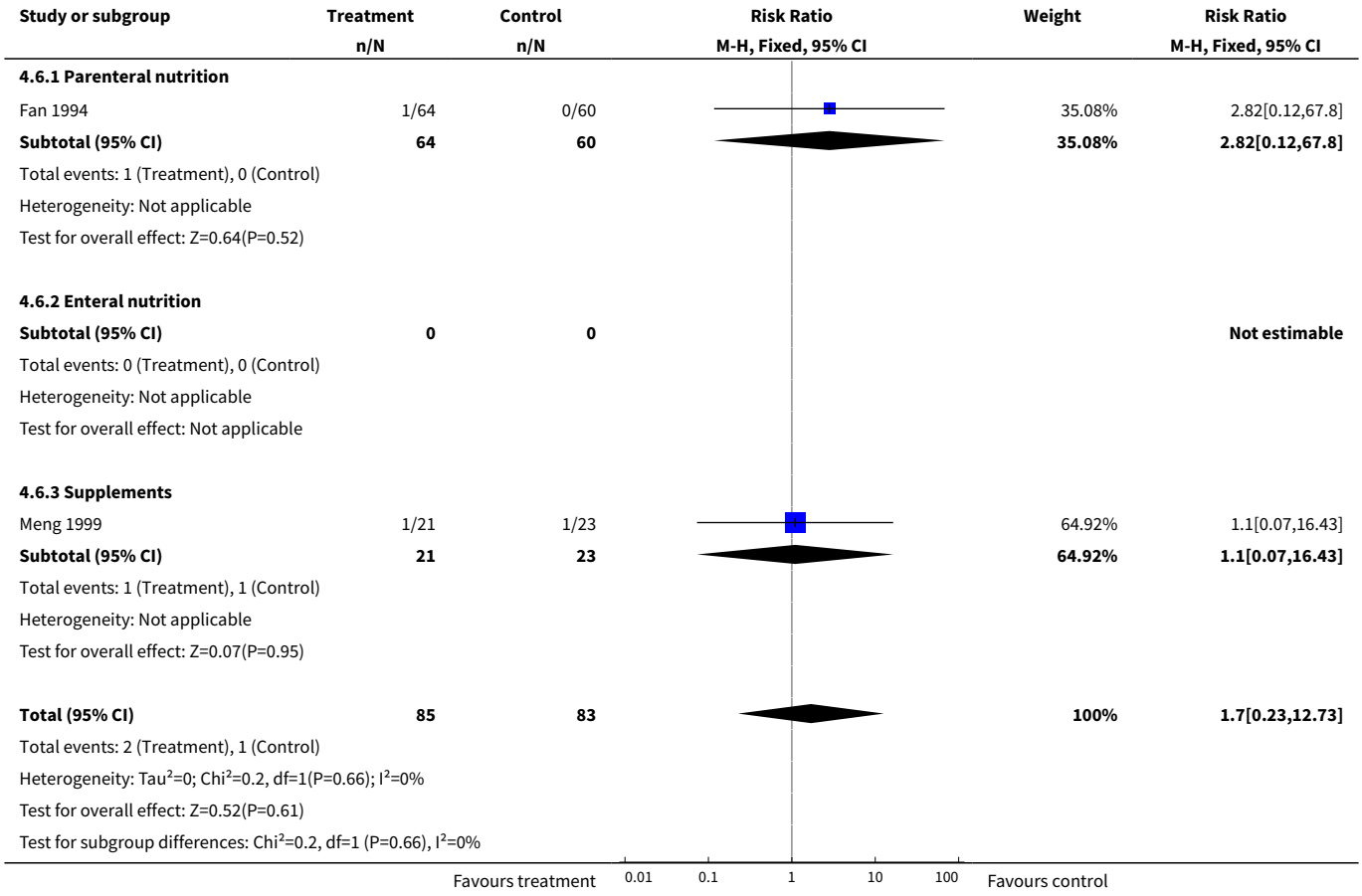


Analysis 4.5. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 5 Medical trials.

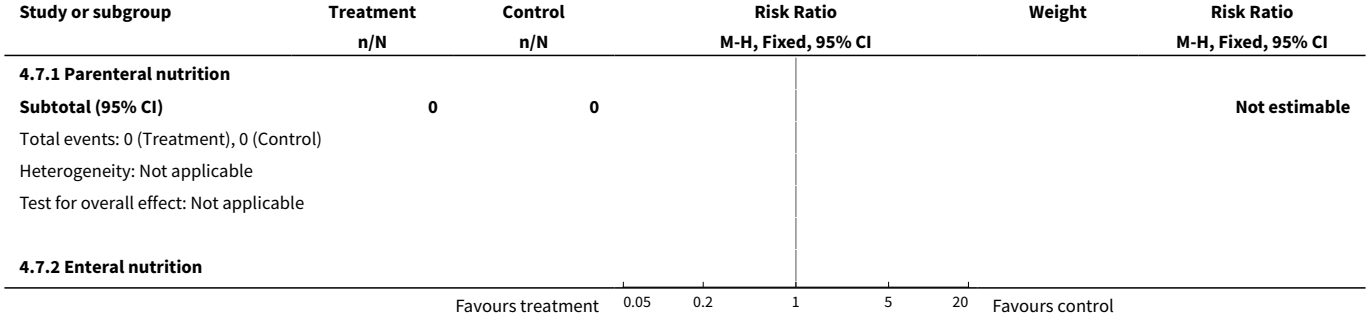


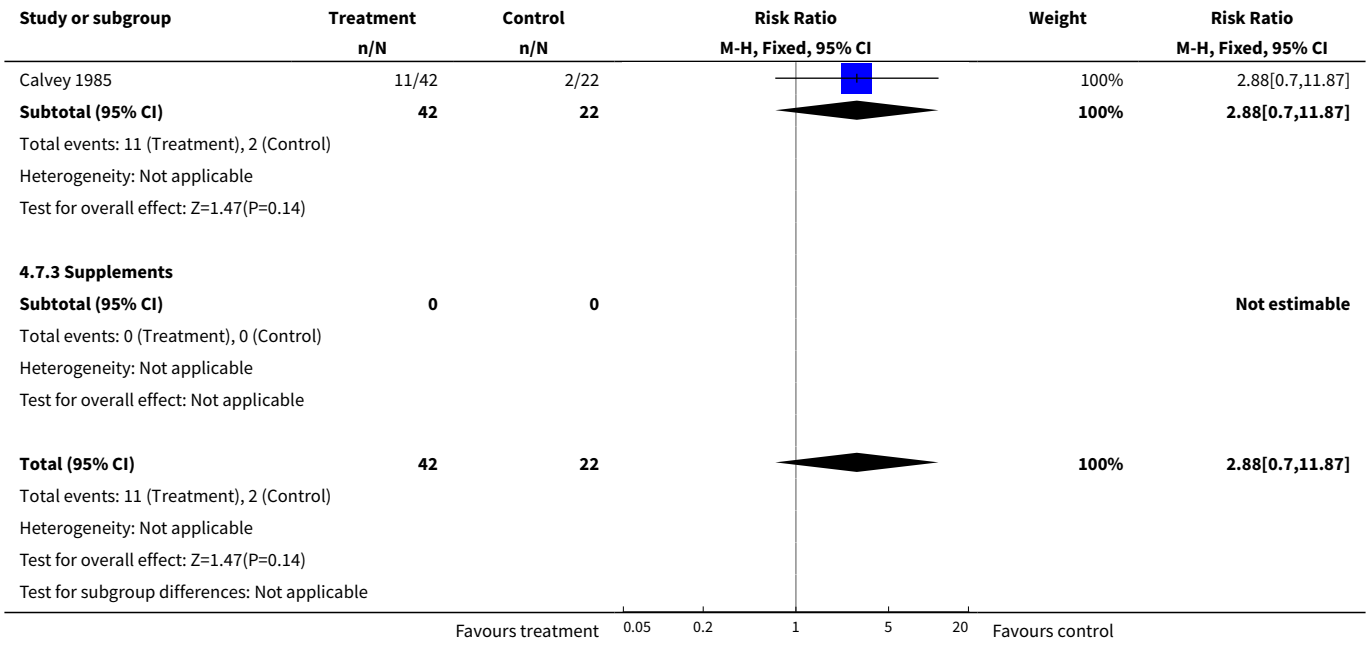


Analysis 4.6. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 6 Surgical trials.

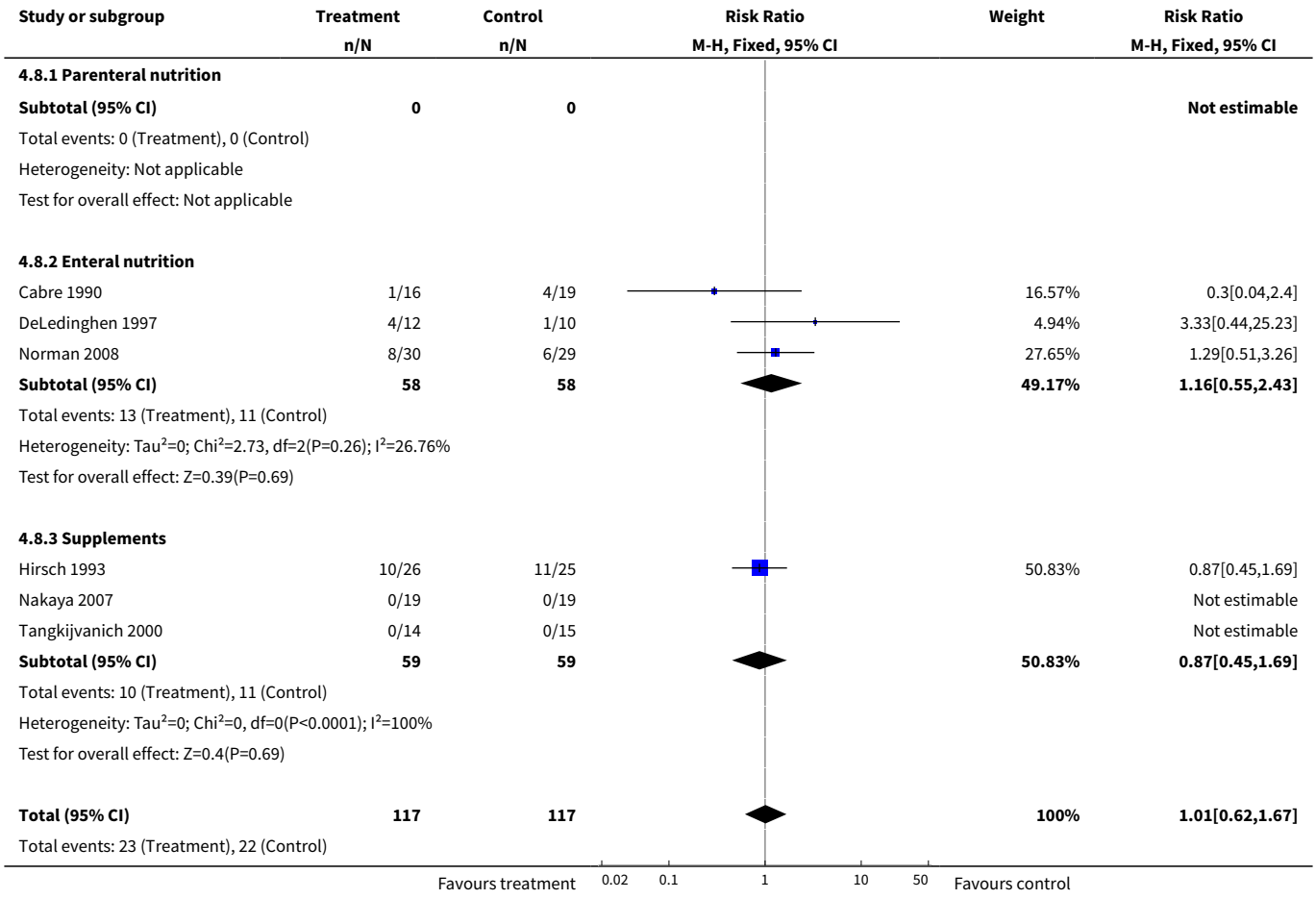


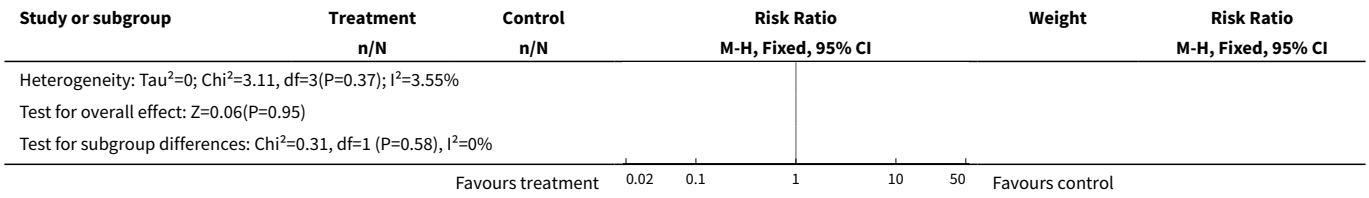
Analysis 4.7. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 7 Alcoholic hepatitis.



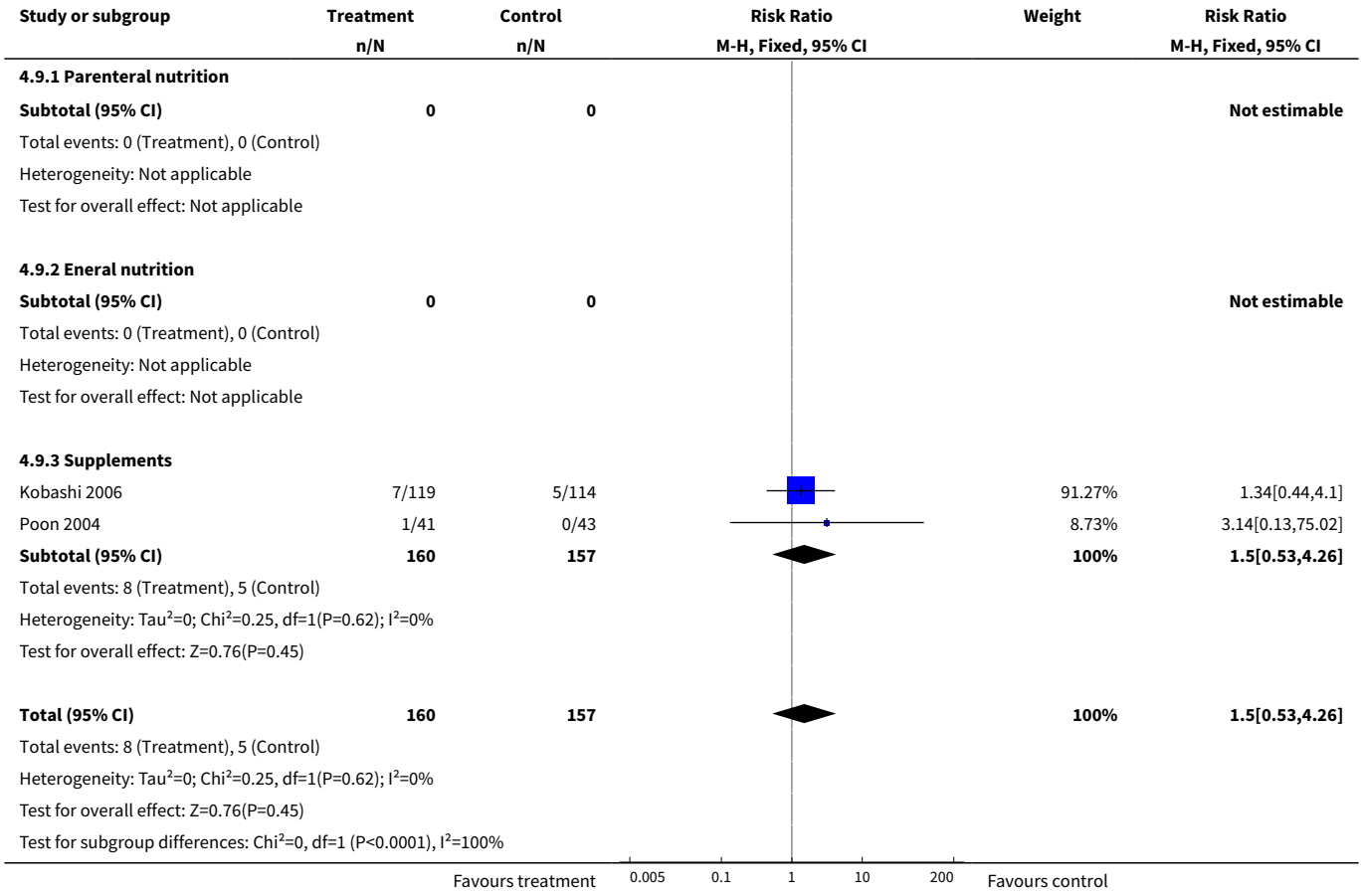


Analysis 4.8. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 8 Cirrhosis.

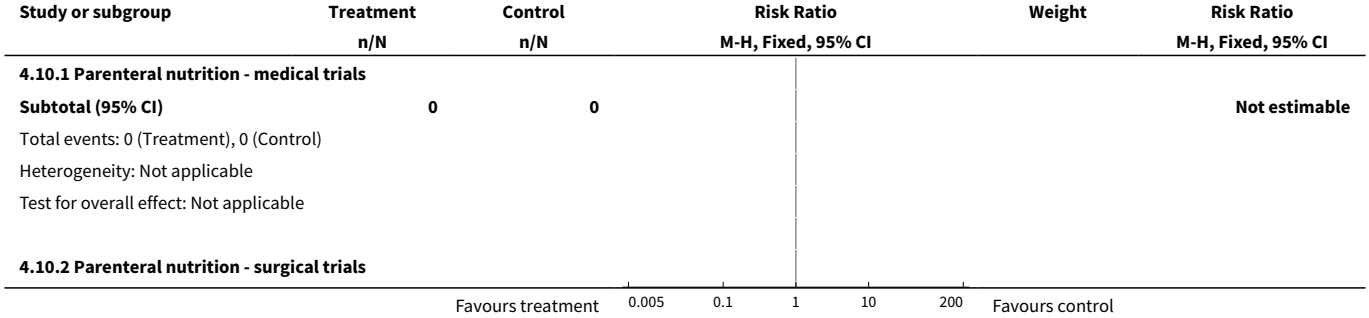


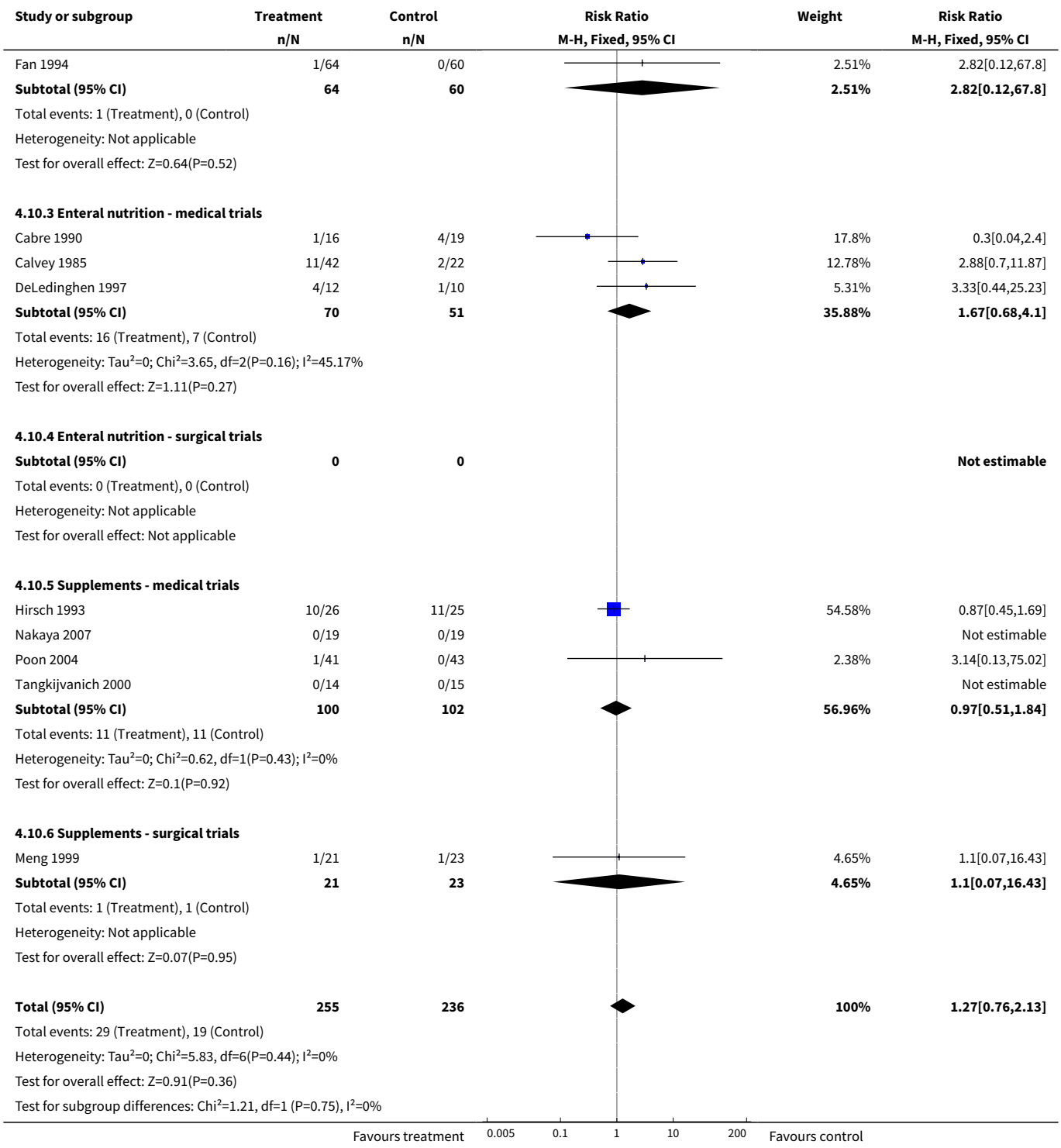


Analysis 4.9. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 9 HCC.



Analysis 4.10. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 10 Abstracts excluded.

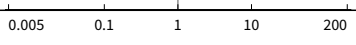




Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Fan 1994	1/64	0/60		2.51%	2.82[0.12,67.8]
Subtotal (95% CI)	**64**	**60**		**2.51%**	**2.82[0.12,67.8]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.64(P=0.52)					
4.10.3 Enteral nutrition - medical trials					
Cabre 1990	1/16	4/19		17.8%	0.3[0.04,2.4]
Calvey 1985	11/42	2/22		12.78%	2.88[0.7,11.87]
DeLedinghen 1997	4/12	1/10		5.31%	3.33[0.44,25.23]
Subtotal (95% CI)	**70**	**51**		**35.88%**	**1.67[0.68,4.1]**
Total events: 16 (Treatment), 7 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.65, df=2(P=0.16); I^2=45.17%					
Test for overall effect: Z=1.11(P=0.27)					
4.10.4 Enteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.10.5 Supplements - medical trials					
Hirsch 1993	10/26	11/25		54.58%	0.87[0.45,1.69]
Nakaya 2007	0/19	0/19			Not estimable
Poon 2004	1/41	0/43		2.38%	3.14[0.13,75.02]
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**100**	**102**		**56.96%**	**0.97[0.51,1.84]**
Total events: 11 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.62, df=1(P=0.43); I^2=0%					
Test for overall effect: Z=0.1(P=0.92)					
4.10.6 Supplements - surgical trials					
Meng 1999	1/21	1/23		4.65%	1.1[0.07,16.43]
Subtotal (95% CI)	**21**	**23**		**4.65%**	**1.1[0.07,16.43]**
Total events: 1 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.07(P=0.95)					
Total (95% CI)	**255**	**236**		**100%**	**1.27[0.76,2.13]**
Total events: 29 (Treatment), 19 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.83, df=6(P=0.44); I^2=0%					
Test for overall effect: Z=0.91(P=0.36)					
Test for subgroup differences: Chi^2=1.21, df=1 (P=0.75), I^2=0%					

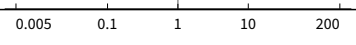
Analysis 4.11. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 11 Surgical trials without transplant patients (no trials with transplant patients).

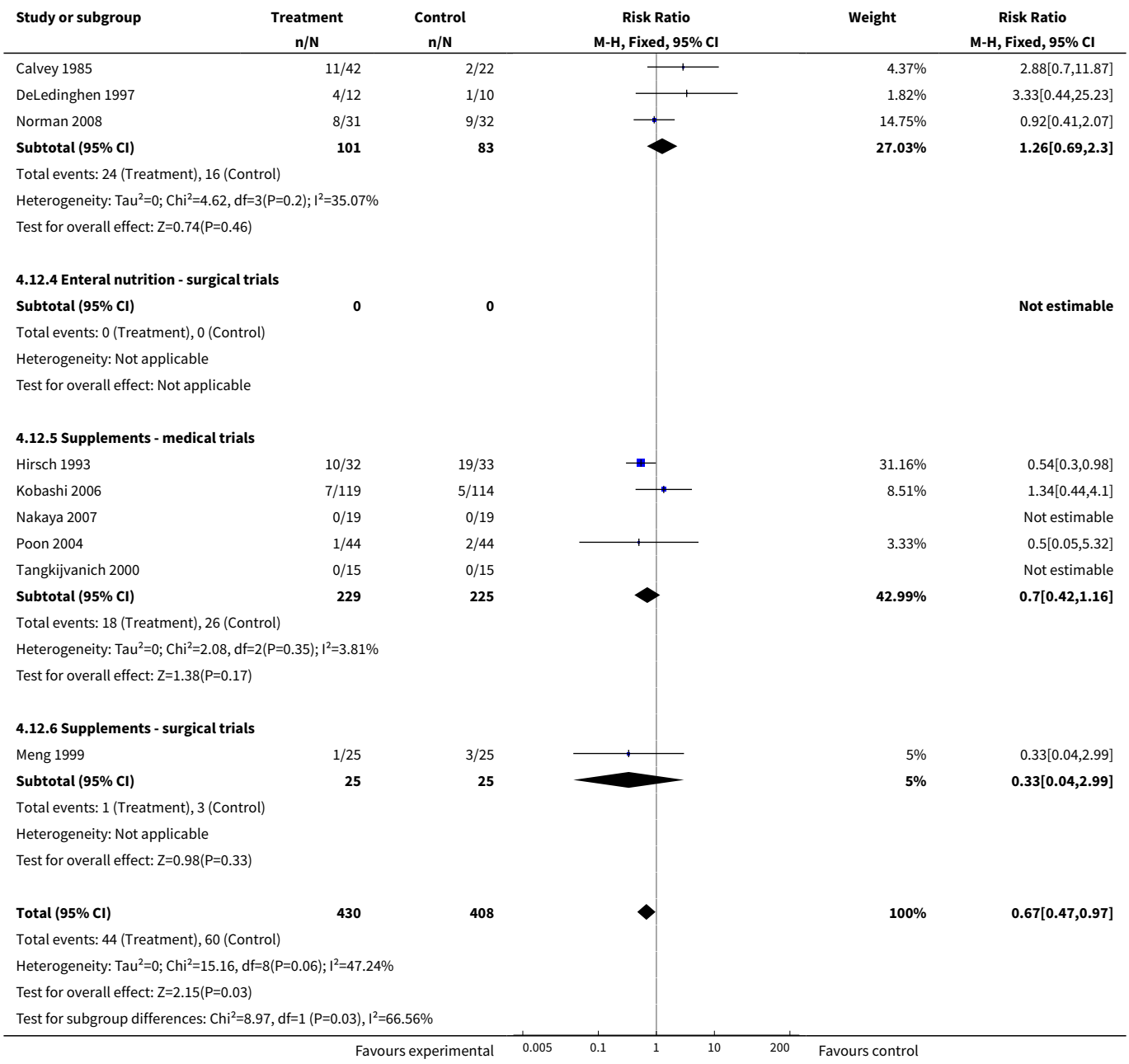
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.11.1 Parenteral nutrition					
Fan 1994	1/64	0/60		35.08%	2.82[0.12,67.8]
Subtotal (95% CI)	**64**	**60**		**35.08%**	**2.82[0.12,67.8]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.64(P=0.52)					
4.11.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.11.3 Supplements					
Meng 1999	1/21	1/23		64.92%	1.1[0.07,16.43]
Subtotal (95% CI)	**21**	**23**		**64.92%**	**1.1[0.07,16.43]**
Total events: 1 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.07(P=0.95)					
Total (95% CI)	**85**	**83**		**100%**	**1.7[0.23,12.73]**
Total events: 2 (Treatment), 1 (Control)					
Heterogeneity: Tau²=0; Chi²=0.2, df=1(P=0.66); I²=0%					
Test for overall effect: Z=0.52(P=0.61)					
Test for subgroup differences: Chi²=0.2, df=1 (P=0.66), I²=0%					



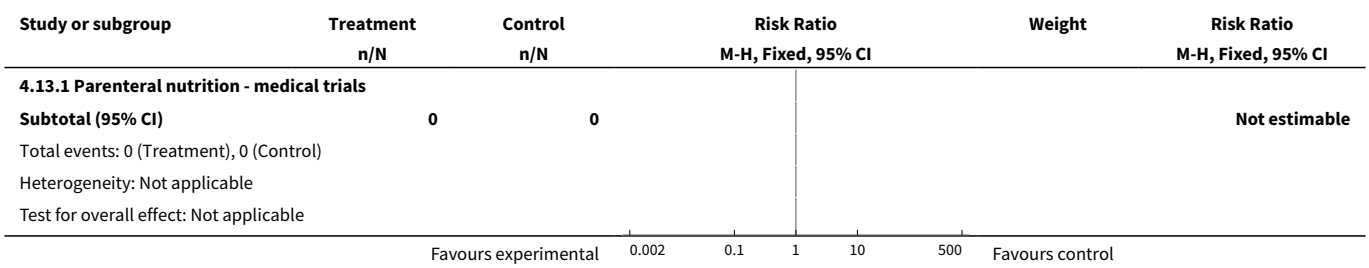
Analysis 4.12. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 12 Intent to treat - best-case scenario for intervention.

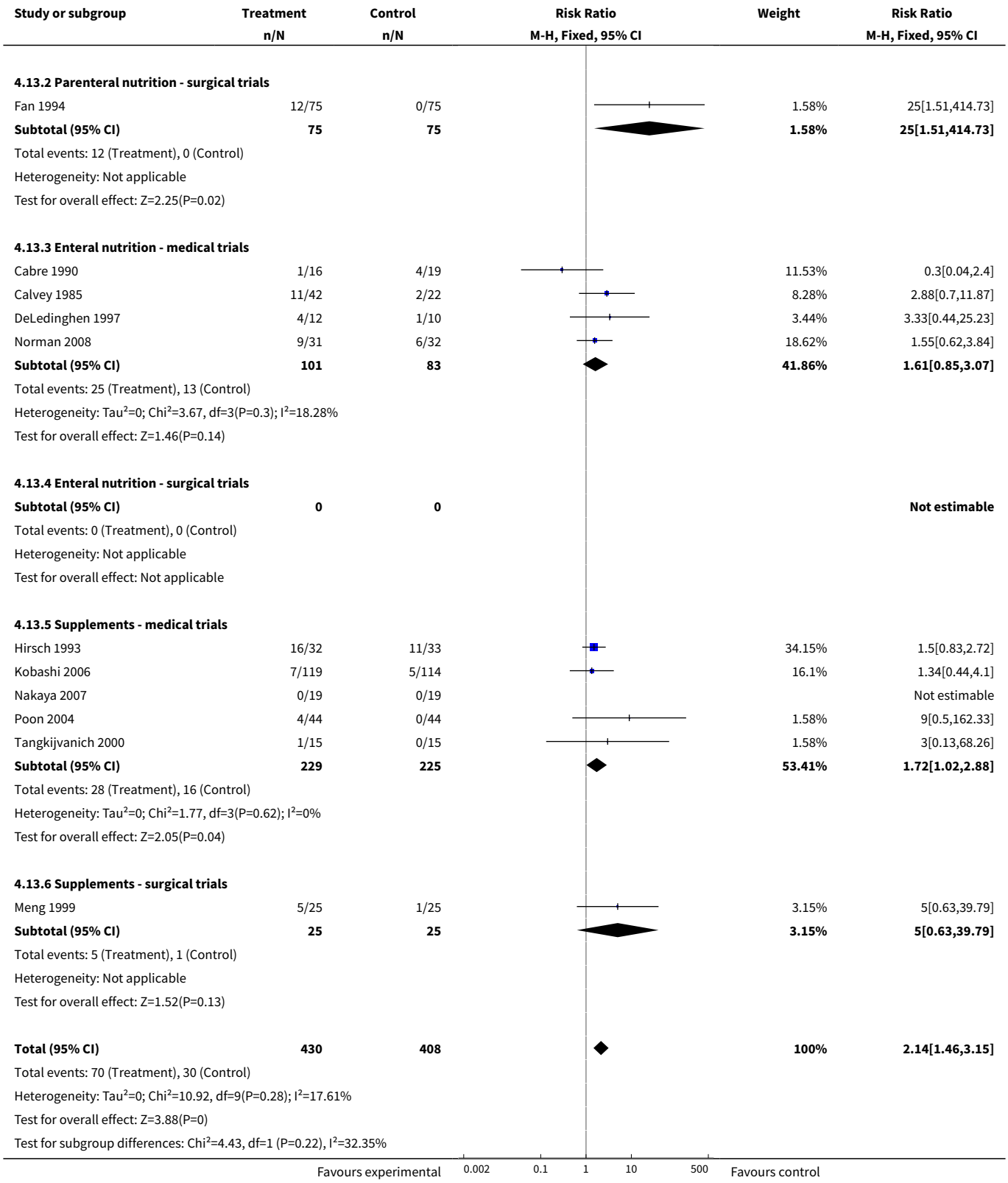
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.12.1 Parenteral nutrition - medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.12.2 Parenteral nutrition - surgical trials					
Fan 1994	1/75	15/75		24.98%	0.07[0.01,0.49]
Subtotal (95% CI)	**75**	**75**		**24.98%**	**0.07[0.01,0.49]**
Total events: 1 (Treatment), 15 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.66(P=0.01)					
4.12.3 Enteral nutrition - medical trials					
Cabre 1990	1/16	4/19		6.09%	0.3[0.04,2.4]





Analysis 4.13. Comparison 4 Appearance of gastrointestinal bleeding, Outcome 13 Intent to treat - worst-case scenario for intervention.





Comparison 5. Appearance of encephalopathy - all studies

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 All studies	23		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 All trials	23	1062	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.65, 1.08]
1.2 Standard amino acids	11	339	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.50, 1.48]
1.3 BCAAs	15	772	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.63, 1.09]
2 Parenteral nutrition - all trials	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 All trials	5	231	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.21, 1.25]
2.2 Standard amino acids	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
2.3 BCAAs	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
3 Parenteral nutrition - medical trials	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 All trials	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
3.2 Standard amino acids	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
3.3 BCAAs	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Parenteral nutrition - surgical trials	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 All trials	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
4.2 Standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 BCAAs	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
5 Enteral nutrition - all studies	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Standard amino acids	4	91	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [0.67, 4.45]
5.2 BCAAs	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
6 Enteral nutrition - medical trials	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 All studies	4	102	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [0.52, 3.44]
6.2 Standard amino acids	4	91	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [0.67, 4.45]
6.3 BCAAs	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
7 Enteral nutrition - surgical trials	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 All trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7.3 BCAAs	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Supplements	14		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 All trials	14	734	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.61, 1.05]
8.2 Standard amino acids -medical trials	4	170	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.31, 1.57]
8.3 BCAAs - medical trials	10	536	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.60, 1.05]
8.4 All supplements - medical	12	666	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.61, 1.05]
8.5 All surgical	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Medical trials all trials	19	846	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.66, 1.11]
9.1 Parenteral nutrition	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
9.2 Enteral nutrition	4	102	Risk Ratio (M-H, Fixed, 95% CI)	1.85 [0.75, 4.56]
9.3 Supplements	12	657	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.61, 1.06]
10 Medical trials - standard amino acids	11	339	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.50, 1.48]
10.1 Parenteral nutrition	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
10.2 Enteral nutrition	4	91	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [0.67, 4.45]
10.3 Supplements	4	161	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.32, 1.67]
11 Medical trials - BCAAs	11	560	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.64, 1.12]
11.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Enteral nutrition	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
11.3 Supplements	10	536	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.60, 1.05]
12 Surgical trials - all studies	4	212	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
12.1 Parenteral nutrition	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
12.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Supplements	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Surgical trials - standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
14 Surgical trials - BCAAs	4	212	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
14.1 Parenteral nutrition	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
14.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 Supplements	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Alcoholic hepatitis - all studies	6	172	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.53, 2.68]
15.1 Parenteral nutrition	2	47	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.01, 3.52]
15.2 Enteral nutrition	2	48	Risk Ratio (M-H, Fixed, 95% CI)	1.95 [0.57, 6.69]
15.3 Supplements	2	77	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.32, 4.56]
16 Alcoholic hepatitis - standard amino acids	6	161	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.45, 2.50]
16.1 Parenteral nutrition	2	47	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.01, 3.52]
16.2 Enteral nutrition	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.75 [0.45, 6.70]
16.3 Supplements	2	77	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.32, 4.56]
17 Alcoholic hepatitis - BCAA	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
17.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 Enteral nutrition	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
17.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Cirrhosis - all studies	12	420	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.64, 1.08]
18.1 Parenteral nutrition	1	40	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.10, 2.43]
18.2 Enteral nutrition	2	54	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.46, 6.44]
18.3 Supplements	9	326	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.62, 1.04]
19 Cirrhosis - standard amino acids	6	229	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.53, 1.72]
19.1 Parenteral nutrition	1	40	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.10, 2.43]
19.2 Enteral nutrition	2	54	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.46, 6.44]
19.3 Supplements	3	135	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.44, 1.97]
20 Cirrhosis - BCAAs	8	231	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.63, 1.04]
20.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

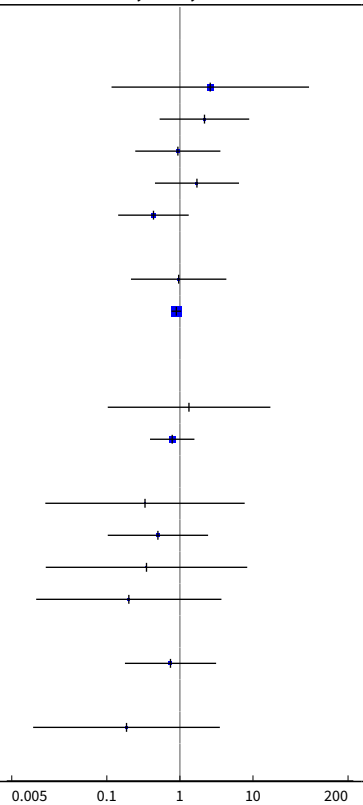
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
20.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 Supplementss	8	231	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.63, 1.04]
21 HCC - all studies	2	305	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.38, 1.48]
21.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.3 Supplements	2	305	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.38, 1.48]
22 HCC - standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 HCC - BCAAs	2	305	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.38, 1.48]
23.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 Supplements	2	305	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.38, 1.48]
24 Abstracts excluded	18		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
24.1 All trials	18	659	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.64, 1.13]
24.2 Standard amino acids	7	201	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.42, 1.86]
24.3 BCAAs	12	471	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.67, 1.16]
24.4 Parenteral nutrition all	5	231	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.21, 1.25]
24.5 Parenteral nutrition - SAAs	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
24.6 Parenteral nutrition - BCAAs	2	144	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.21, 2.12]
24.7 Enteral nutrition all	2	48	Risk Ratio (M-H, Fixed, 95% CI)	1.95 [0.57, 6.69]
24.8 Enteral nutrition - SAAs	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.75 [0.45, 6.70]
24.9 Enteral nutrition - BCAAs	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
24.10 Supplements all	11	380	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.68, 1.13]
24.11 Supplements - SAAs	2	77	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.32, 4.56]
24.12 Supplements - BCAAs	9	303	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.68, 1.03]

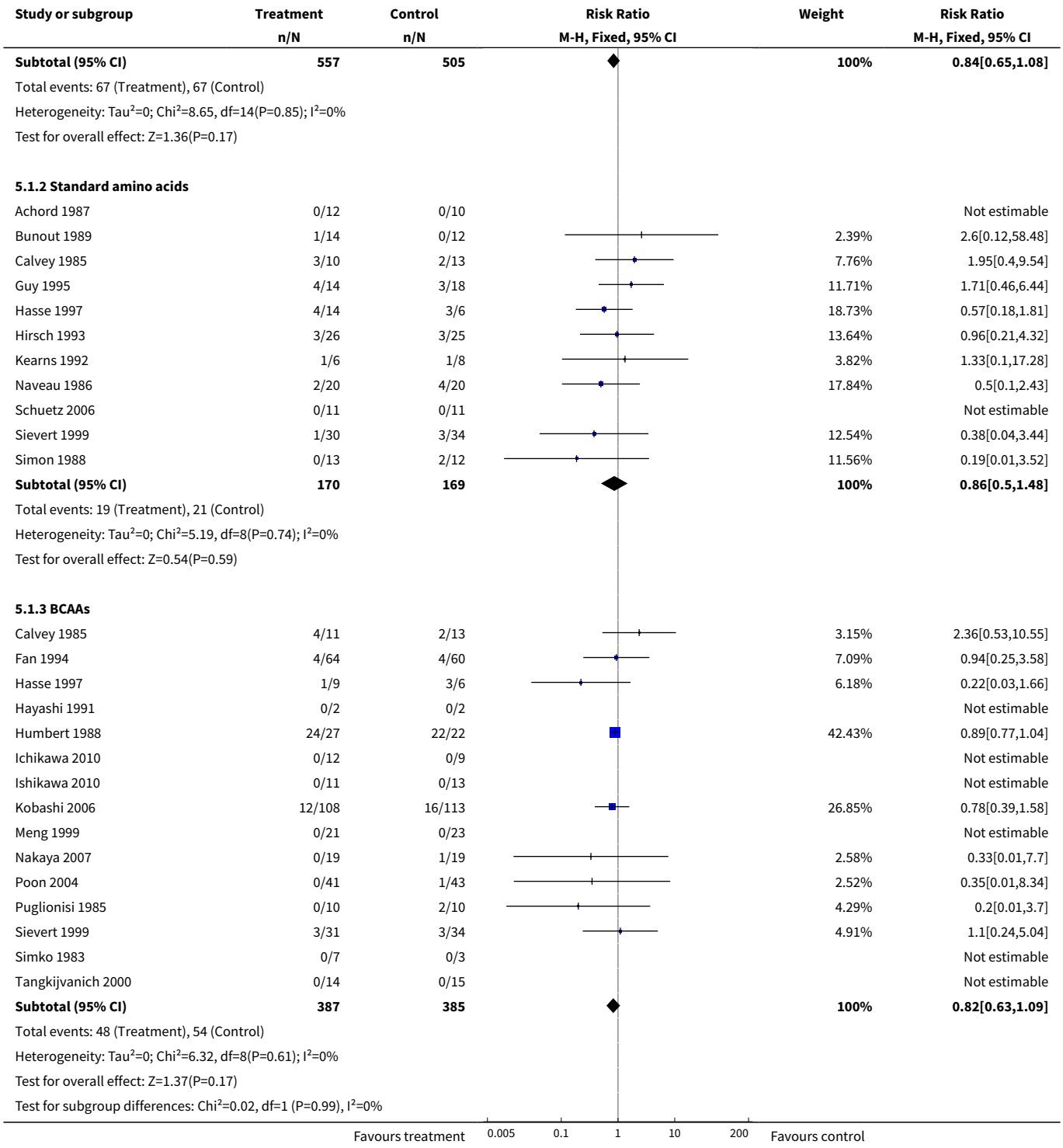
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
25 Surgical trials - transplant trials eliminated	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
25.1 All trials	3	192	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.25, 3.58]
25.2 Standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 BCAAs	3	192	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.25, 3.58]
26 ITT - Parenteral nutrition - best-case scenario	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
26.1 All trials	5	257	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.11, 0.55]
26.2 Standard amino acids	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
26.3 BCAAs	2	170	Risk Ratio (M-H, Fixed, 95% CI)	0.21 [0.08, 0.55]
27 ITT - Parenteral nutrition - worst-case scenario	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
27.1 All trials	5	257	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.70, 2.71]
27.2 Standard amino acids	3	87	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.48]
27.3 BCAAs	2	170	Risk Ratio (M-H, Fixed, 95% CI)	2.38 [0.99, 5.73]
28 ITT - Enteral nutrition - best-case scenario	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
28.1 All trials	4	112	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.53, 2.74]
28.2 Standard amino acids	4	101	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.45, 2.52]
28.3 BCAAs	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
29 ITT - Enteral nutrition - worst-case scenario	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
29.1 All trials	4	112	Risk Ratio (M-H, Fixed, 95% CI)	2.77 [1.23, 6.26]
29.2 Standard amino acids	4	101	Risk Ratio (M-H, Fixed, 95% CI)	2.78 [1.19, 6.48]
29.3 BCAAs	1	24	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.53, 10.55]
30 ITT- Supplements - best-case scenario	14		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
30.1 All trials	14	782	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.47, 0.79]
30.2 Standard amino acids -medical trials	4	191	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.18, 0.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
30.3 BCAAs - medical trials	10	559	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.52, 0.90]
30.4 All supplements - medical	12	707	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.48, 0.81]
30.5 All surgical	2	74	Risk Ratio (M-H, Fixed, 95% CI)	0.2 [0.01, 3.97]
31 ITT - Supplements - worst-case scenario	14		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
31.1 All trials	14	781	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.90, 1.54]
31.2 Standard amino acids -medical trials	4	191	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.79, 3.13]
31.3 BCAAs - medical trials	10	559	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.78, 1.35]
31.4 All supplements - medical	12	707	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.85, 1.45]
31.5 All surgical	2	74	Risk Ratio (M-H, Fixed, 95% CI)	9.0 [0.51, 158.85]

Analysis 5.1. Comparison 5 Appearance of encephalopathy - all studies, Outcome 1 All studies.

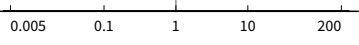
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.1.1 All trials					
Achord 1987	0/12	0/10			Not estimable
Bunout 1989	1/14	0/12		0.72%	2.6[0.12,58.48]
Calvey 1985	7/21	2/13		3.31%	2.17[0.53,8.88]
Fan 1994	4/64	4/60		5.53%	0.94[0.25,3.58]
Guy 1995	4/14	3/18		3.51%	1.71[0.46,6.44]
Hasse 1997	5/23	3/6		6.37%	0.43[0.14,1.32]
Hayashi 1991	0/2	0/6			Not estimable
Hirsch 1993	3/26	3/25		4.1%	0.96[0.21,4.32]
Humbert 1988	24/27	22/22		33.08%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Ishikawa 2010	0/11	0/13			Not estimable
Kearns 1992	1/6	1/8		1.15%	1.33[0.1,17.28]
Kobashi 2006	12/108	16/113		20.94%	0.78[0.39,1.58]
Meng 1999	0/21	0/23			Not estimable
Nakaya 2007	0/19	1/19		2.01%	0.33[0.01,7.7]
Naveau 1986	2/20	4/20		5.36%	0.5[0.1,2.43]
Poon 2004	0/41	1/43		1.96%	0.35[0.01,8.34]
Puglionisi 1985	0/10	2/10		3.35%	0.2[0.01,3.7]
Schuetz 2006	0/11	0/11			Not estimable
Sievert 1999	4/61	3/34		5.16%	0.74[0.18,3.13]
Simko 1983	0/7	0/3			Not estimable
Simon 1988	0/13	2/12		3.47%	0.19[0.01,3.52]
Tangkijvanich 2000	0/14	0/15			Not estimable





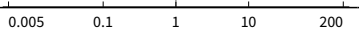
Analysis 5.2. Comparison 5 Appearance of encephalopathy - all studies, Outcome 2 Parenteral nutrition - all trials.

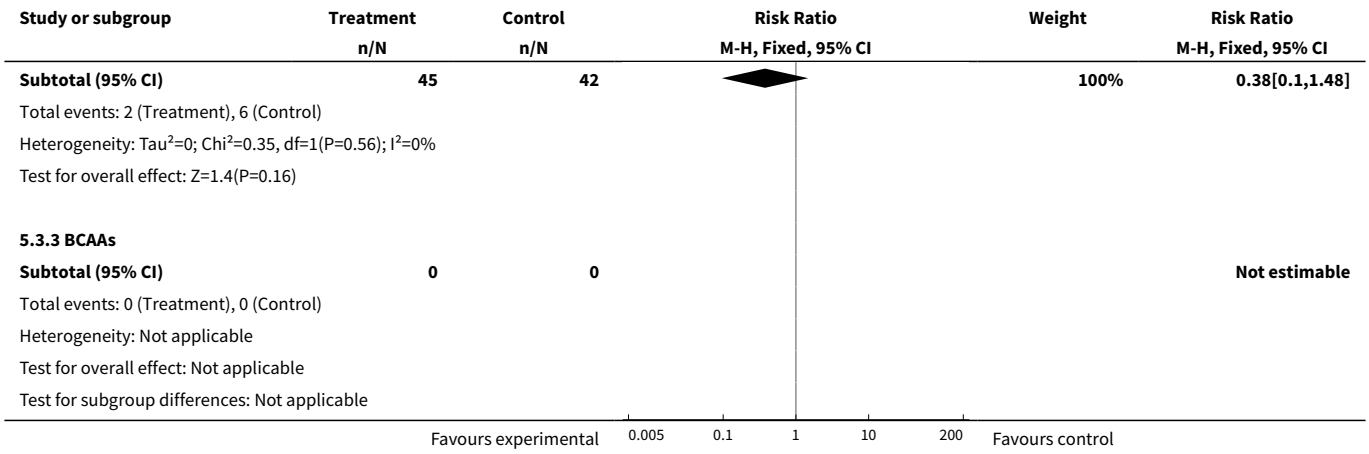
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.2.1 All trials					
Achord 1987	0/12	0/10			Not estimable
Fan 1994	4/64	4/60		31.23%	0.94[0.25,3.58]
Naveau 1986	2/20	4/20		30.25%	0.5[0.1,2.43]
Puglionisi 1985	0/10	2/10		18.91%	0.2[0.01,3.7]
Simon 1988	0/13	2/12		19.61%	0.19[0.01,3.52]
Subtotal (95% CI)	**119**	**112**		**100%**	**0.52[0.21,1.25]**
Total events: 6 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.63, df=3(P=0.65); I^2=0%					
Test for overall effect: Z=1.46(P=0.14)					
5.2.2 Standard amino acids					
Achord 1987	0/12	0/10			Not estimable
Naveau 1986	2/20	4/20		60.67%	0.5[0.1,2.43]
Simon 1988	0/13	2/12		39.33%	0.19[0.01,3.52]
Subtotal (95% CI)	**45**	**42**		**100%**	**0.38[0.1,1.48]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.35, df=1(P=0.56); I^2=0%					
Test for overall effect: Z=1.4(P=0.16)					
5.2.3 BCAAs					
Fan 1994	4/64	4/60		62.29%	0.94[0.25,3.58]
Puglionisi 1985	0/10	2/10		37.71%	0.2[0.01,3.7]
Subtotal (95% CI)	**74**	**70**		**100%**	**0.66[0.21,2.12]**
Total events: 4 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.91, df=1(P=0.34); I^2=0%					
Test for overall effect: Z=0.7(P=0.48)					
Test for subgroup differences: Chi^2=0.37, df=1 (P=0.83), I^2=0%					



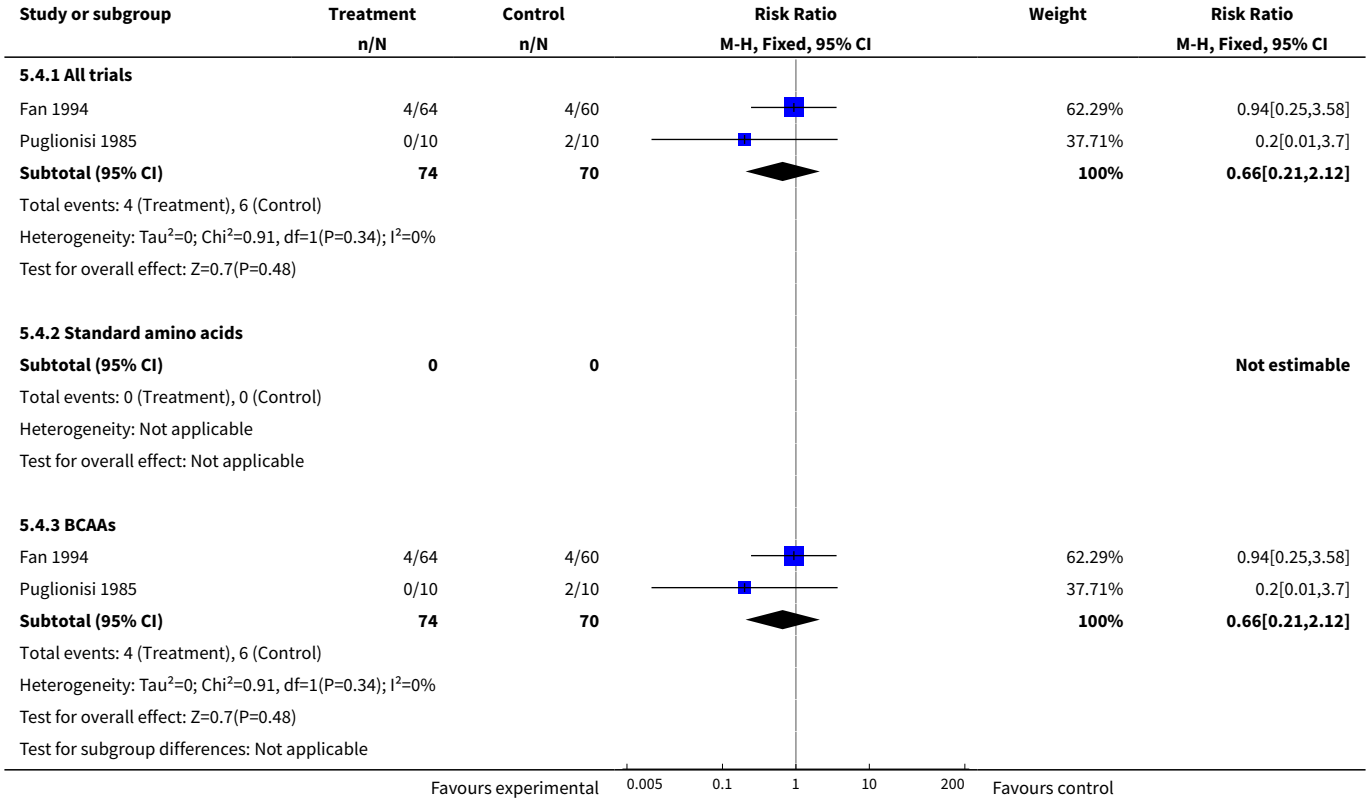
Analysis 5.3. Comparison 5 Appearance of encephalopathy - all studies, Outcome 3 Parenteral nutrition - medical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.3.1 All trials					
Achord 1987	0/12	0/10			Not estimable
Naveau 1986	2/20	4/20		60.67%	0.5[0.1,2.43]
Simon 1988	0/13	2/12		39.33%	0.19[0.01,3.52]
Subtotal (95% CI)	**45**	**42**		**100%**	**0.38[0.1,1.48]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.35, df=1(P=0.56); I^2=0%					
Test for overall effect: Z=1.4(P=0.16)					
5.3.2 Standard amino acids					
Achord 1987	0/12	0/10			Not estimable
Naveau 1986	2/20	4/20		60.67%	0.5[0.1,2.43]
Simon 1988	0/13	2/12		39.33%	0.19[0.01,3.52]

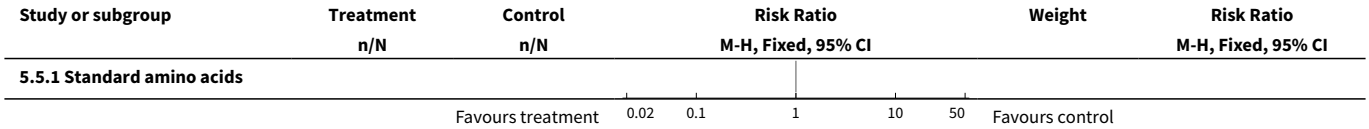


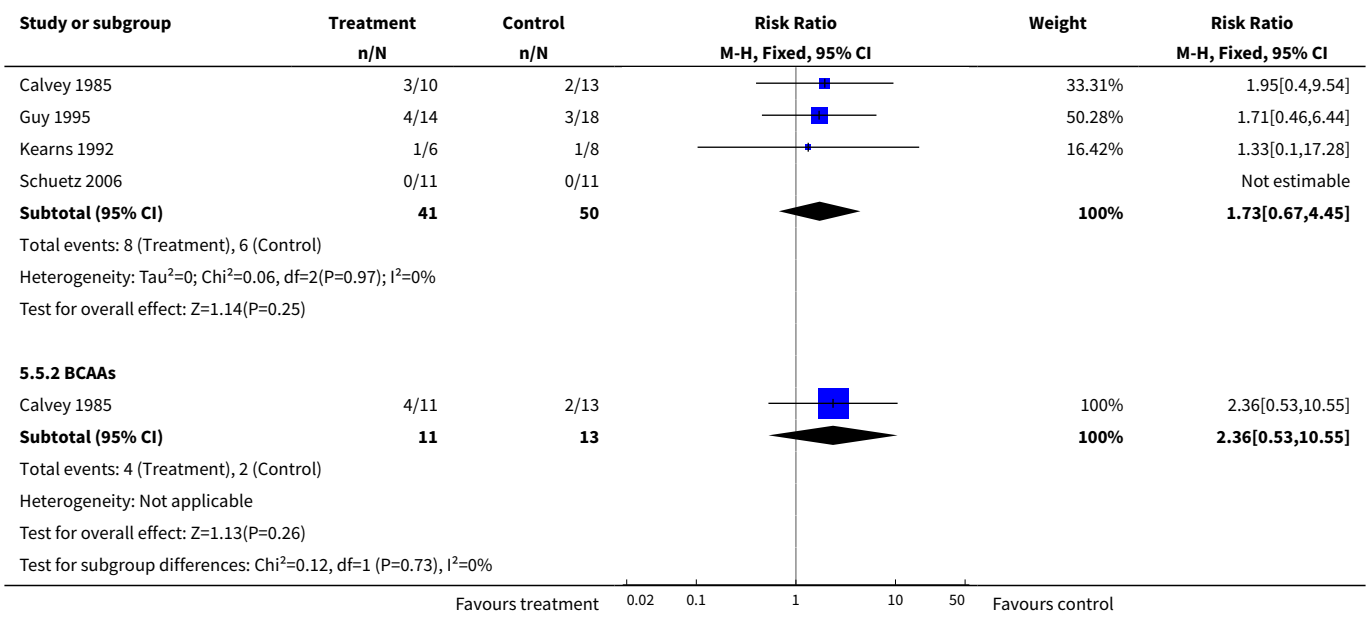


Analysis 5.4. Comparison 5 Appearance of encephalopathy - all studies, Outcome 4 Parenteral nutrition - surgical trials.

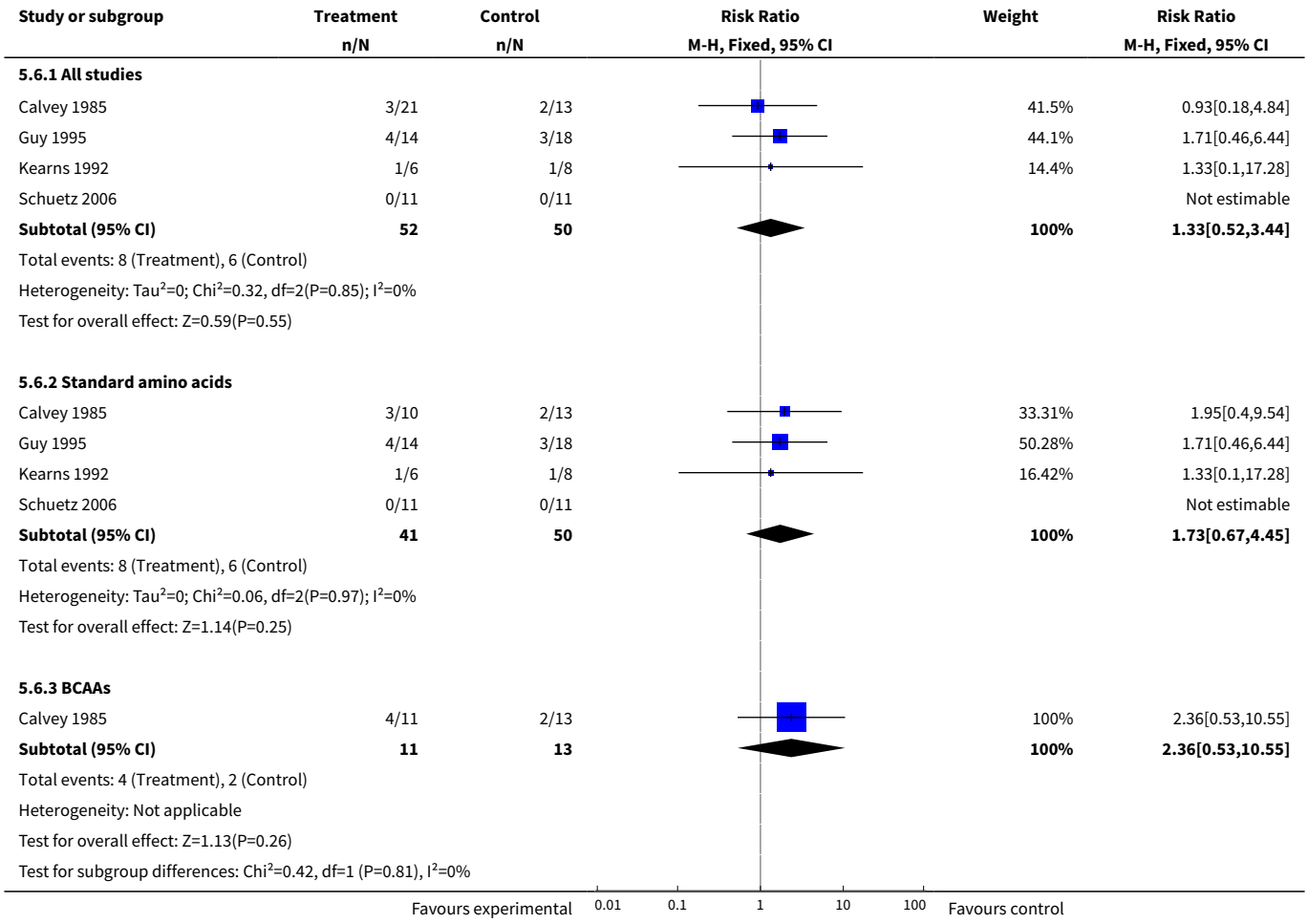


Analysis 5.5. Comparison 5 Appearance of encephalopathy - all studies, Outcome 5 Enteral nutrition - all studies.



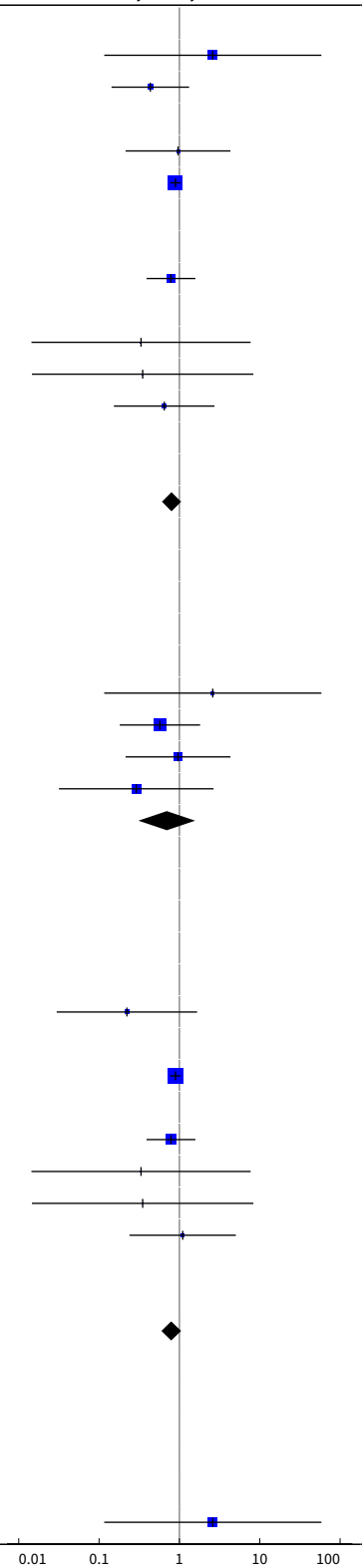


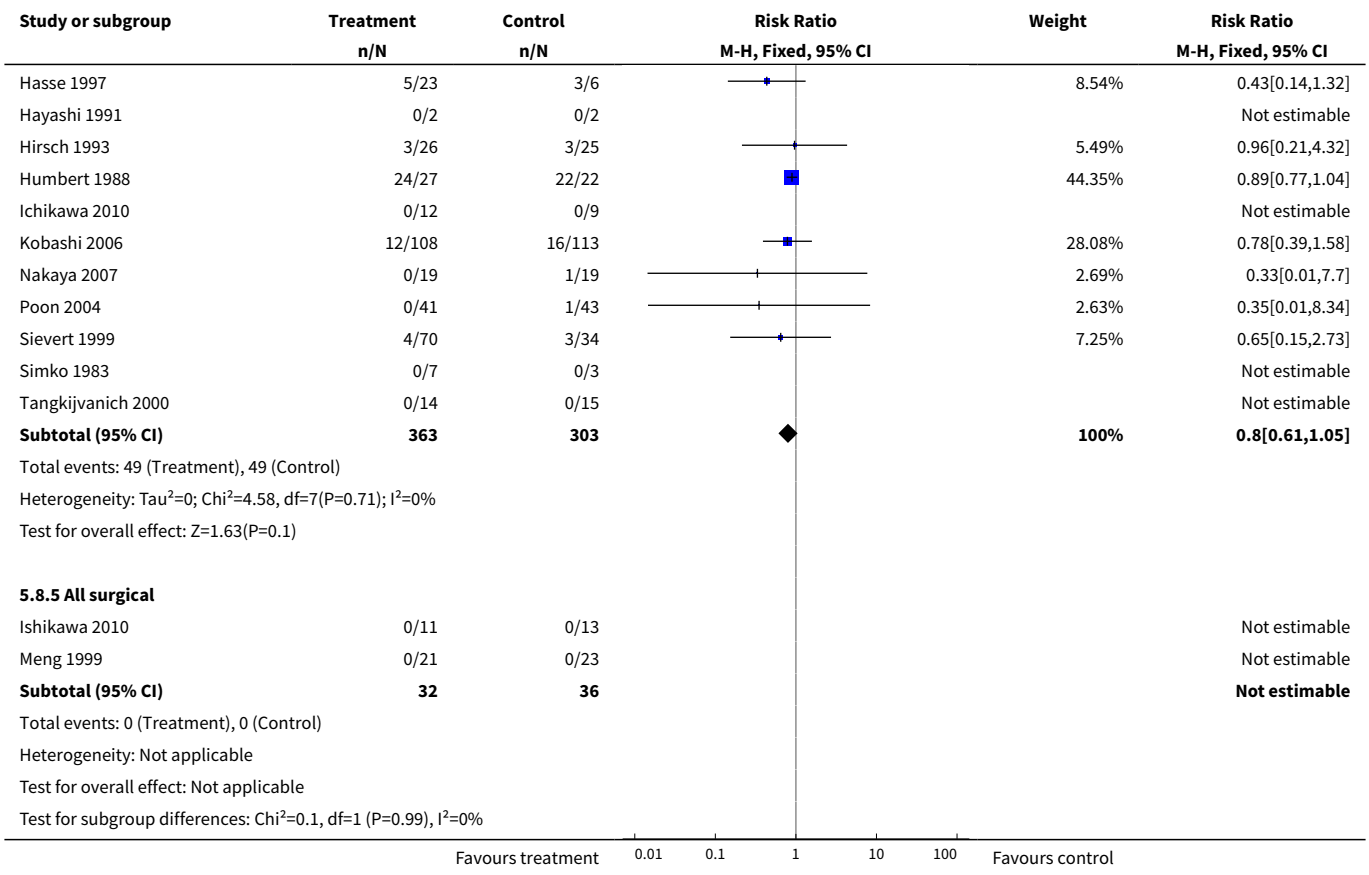
Analysis 5.6. Comparison 5 Appearance of encephalopathy - all studies, Outcome 6 Enteral nutrition - medical trials.



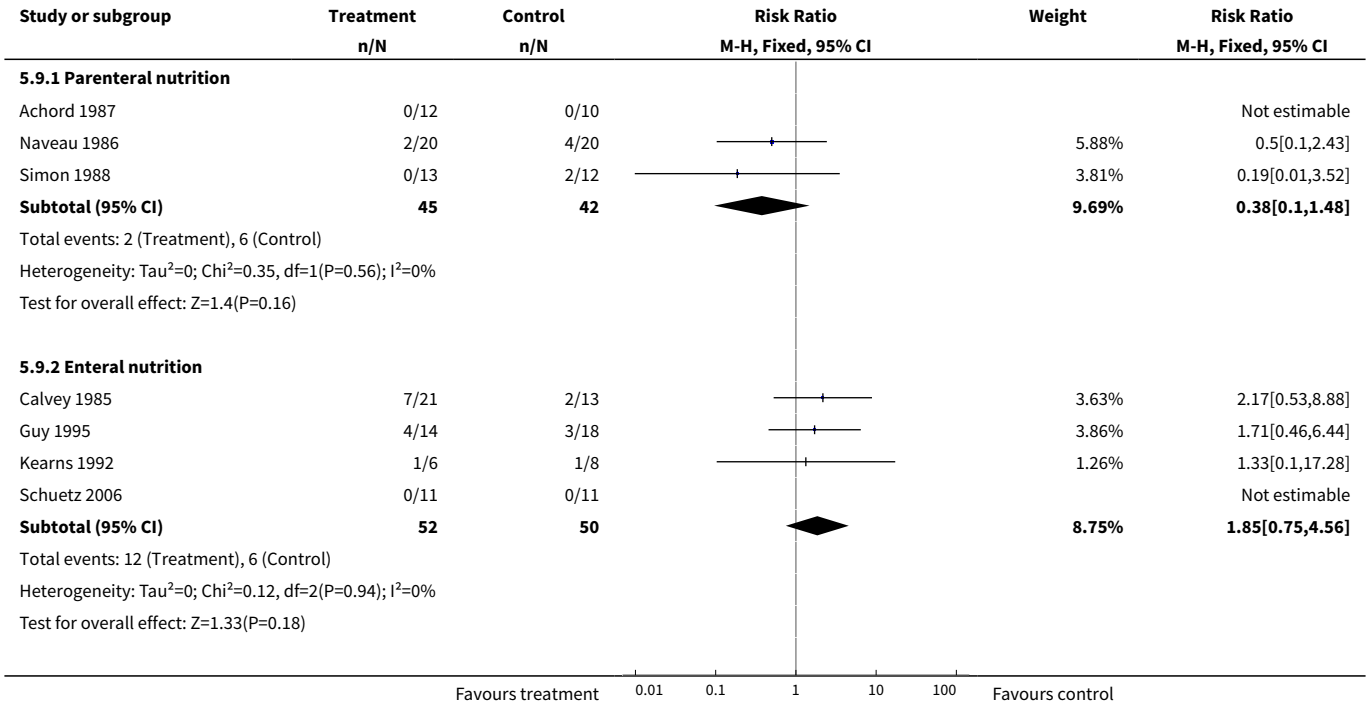
Analysis 5.8. Comparison 5 Appearance of encephalopathy - all studies, Outcome 8 Supplements.

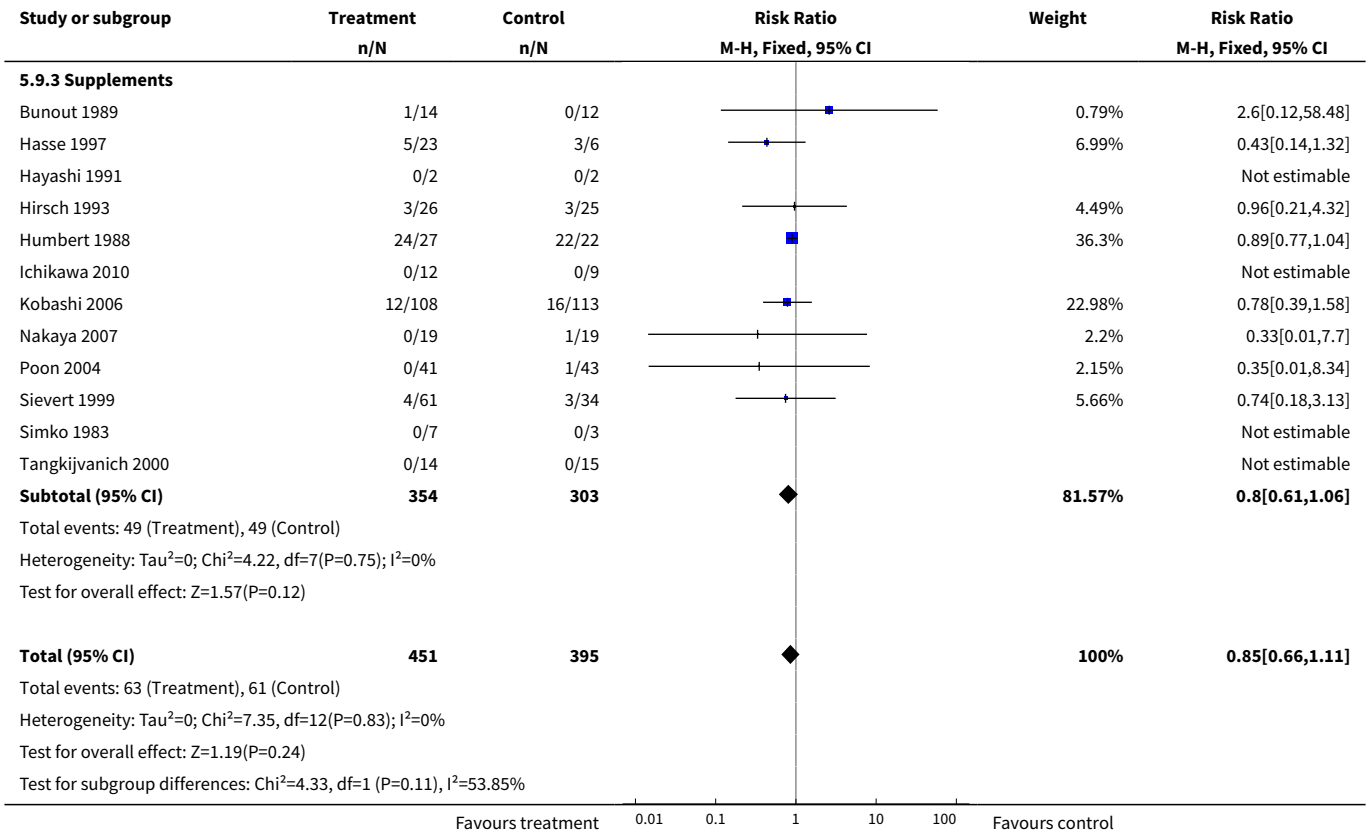
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.8.1 All trials					
Bunout 1989	1/14	0/12		0.96%	2.6[0.12,58.48]
Hasse 1997	5/23	3/6		8.54%	0.43[0.14,1.32]
Hayashi 1991	0/2	0/2			Not estimable
Hirsch 1993	3/26	3/25		5.49%	0.96[0.21,4.32]
Humbert 1988	24/27	22/22		44.35%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Ishikawa 2010	0/11	0/13			Not estimable
Kobashi 2006	12/108	16/113		28.08%	0.78[0.39,1.58]
Meng 1999	0/21	0/23			Not estimable
Nakaya 2007	0/19	1/19		2.69%	0.33[0.01,7.7]
Poon 2004	0/41	1/43		2.63%	0.35[0.01,8.34]
Sievert 1999	4/70	3/34		7.25%	0.65[0.15,2.73]
Simko 1983	0/7	0/3			Not estimable
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**395**	**339**		**100%**	**0.8[0.61,1.05]**
Total events: 49 (Treatment), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.58, df=7(P=0.71); I^2=0%					
Test for overall effect: Z=1.63(P=0.1)					
5.8.2 Standard amino acids -medical trials					
Bunout 1989	1/14	0/12		4.87%	2.6[0.12,58.48]
Hasse 1997	4/14	3/6		38.18%	0.57[0.18,1.81]
Hirsch 1993	3/26	3/25		27.81%	0.96[0.21,4.32]
Sievert 1999	1/39	3/34		29.14%	0.29[0.03,2.66]
Subtotal (95% CI)	**93**	**77**		**100%**	**0.7[0.31,1.57]**
Total events: 9 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.58, df=3(P=0.66); I^2=0%					
Test for overall effect: Z=0.87(P=0.38)					
5.8.3 BCAAs - medical trials					
Hasse 1997	1/9	3/6		7.23%	0.22[0.03,1.66]
Hayashi 1991	0/2	0/2			Not estimable
Humbert 1988	24/27	22/22		49.64%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Kobashi 2006	12/108	16/113		31.42%	0.78[0.39,1.58]
Nakaya 2007	0/19	1/19		3.01%	0.33[0.01,7.7]
Poon 2004	0/41	1/43		2.94%	0.35[0.01,8.34]
Sievert 1999	3/31	3/34		5.75%	1.1[0.24,5.04]
Simko 1983	0/7	0/3			Not estimable
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**270**	**266**		**100%**	**0.79[0.6,1.05]**
Total events: 40 (Treatment), 46 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.79, df=5(P=0.44); I^2=0%					
Test for overall effect: Z=1.64(P=0.1)					
5.8.4 All supplements - medical					
Bunout 1989	1/14	0/12		0.96%	2.6[0.12,58.48]



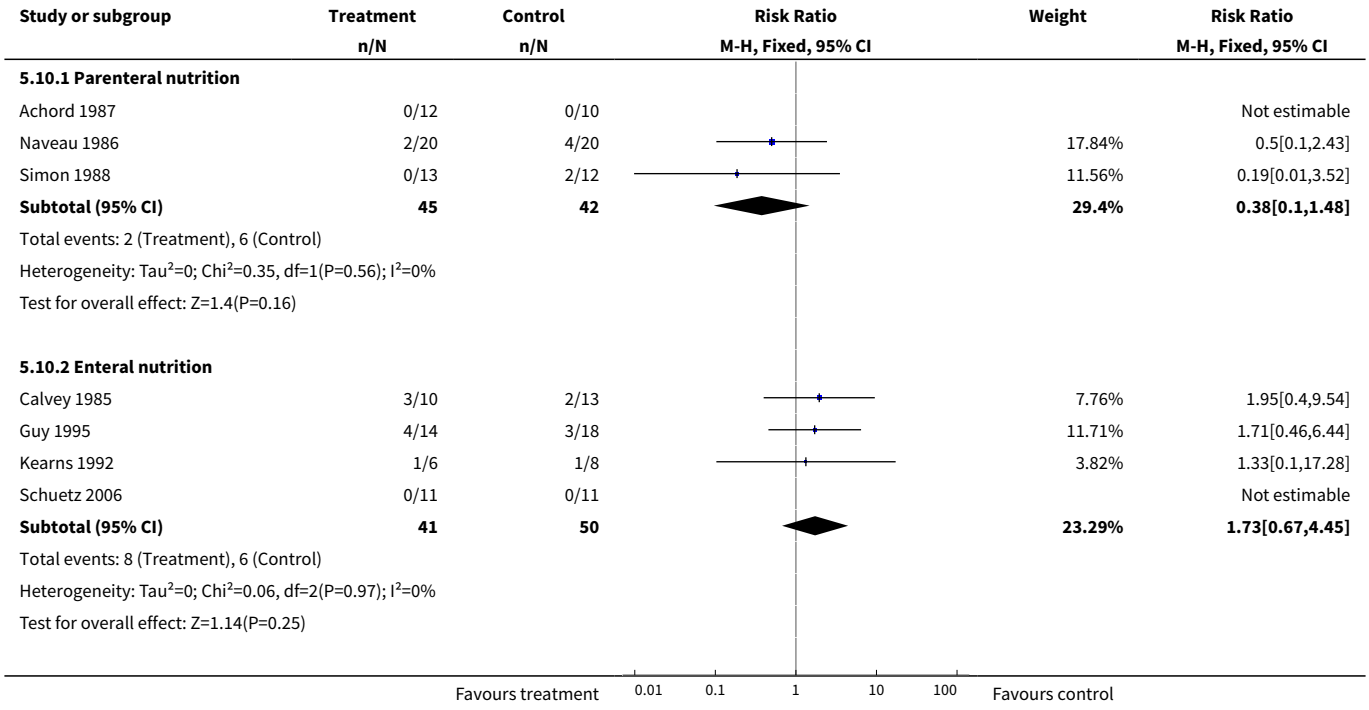


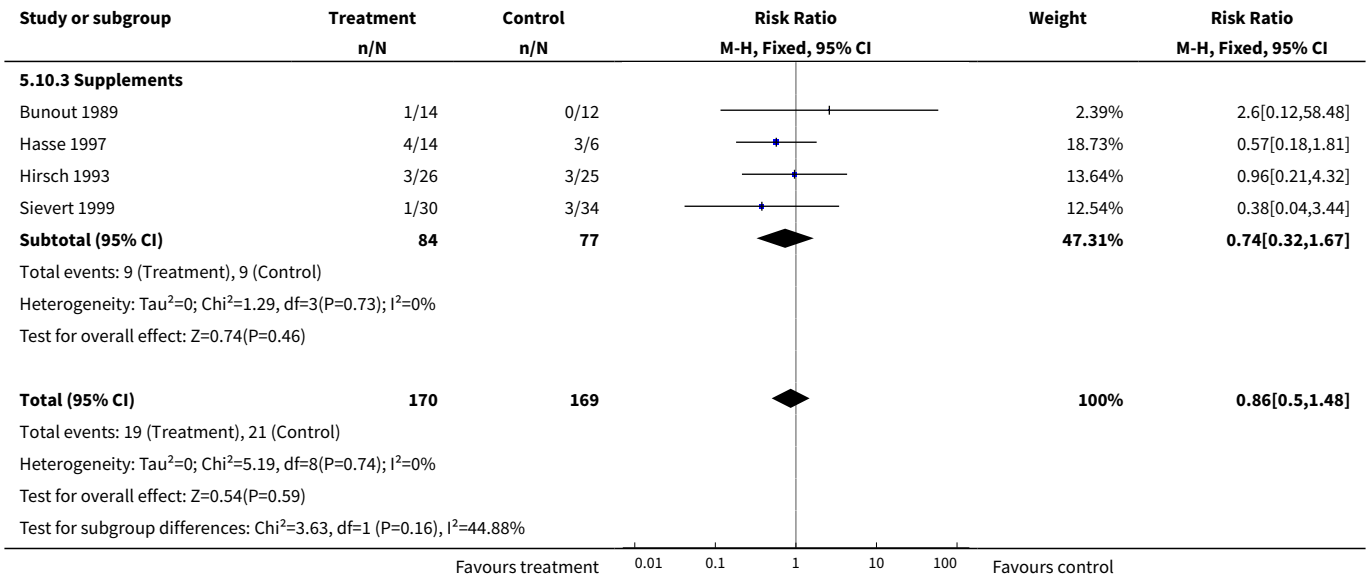
Analysis 5.9. Comparison 5 Appearance of encephalopathy - all studies, Outcome 9 Medical trials all trials.



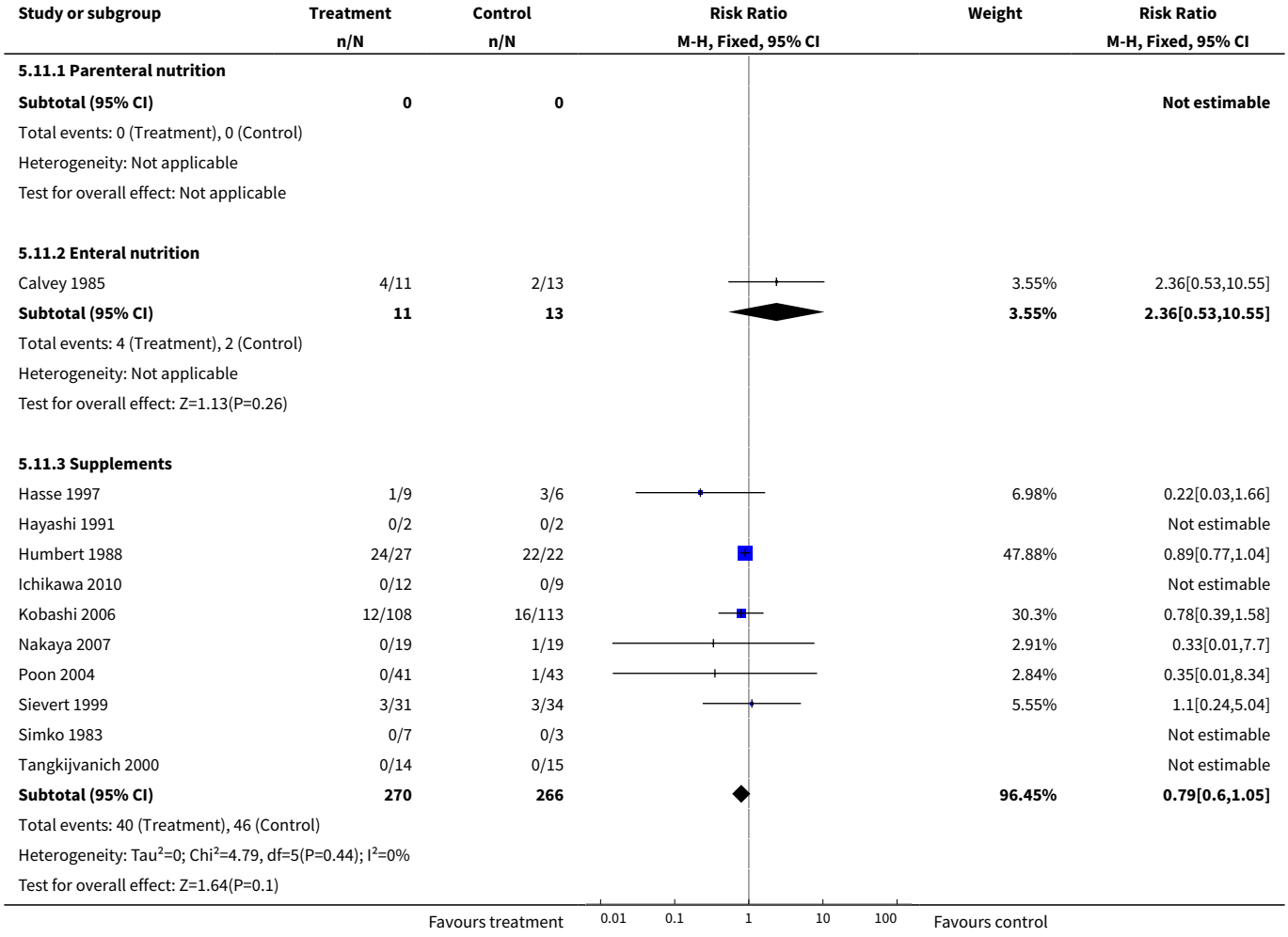


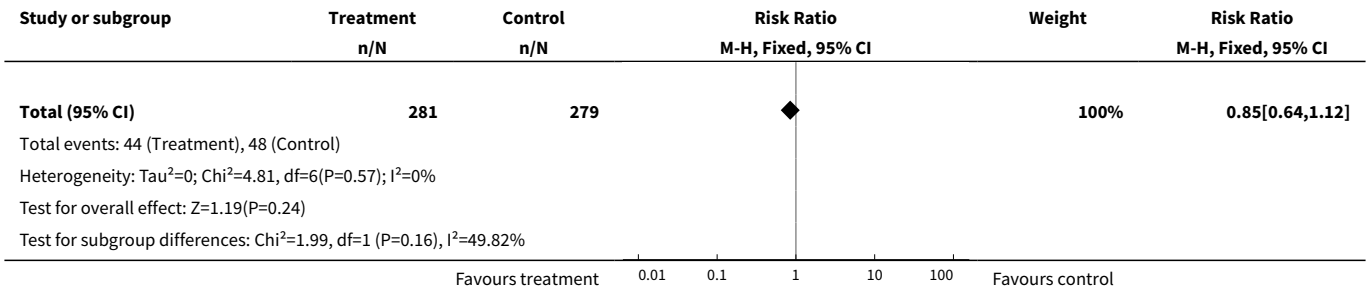
Analysis 5.10. Comparison 5 Appearance of encephalopathy - all studies, Outcome 10 Medical trials - standard amino acids.



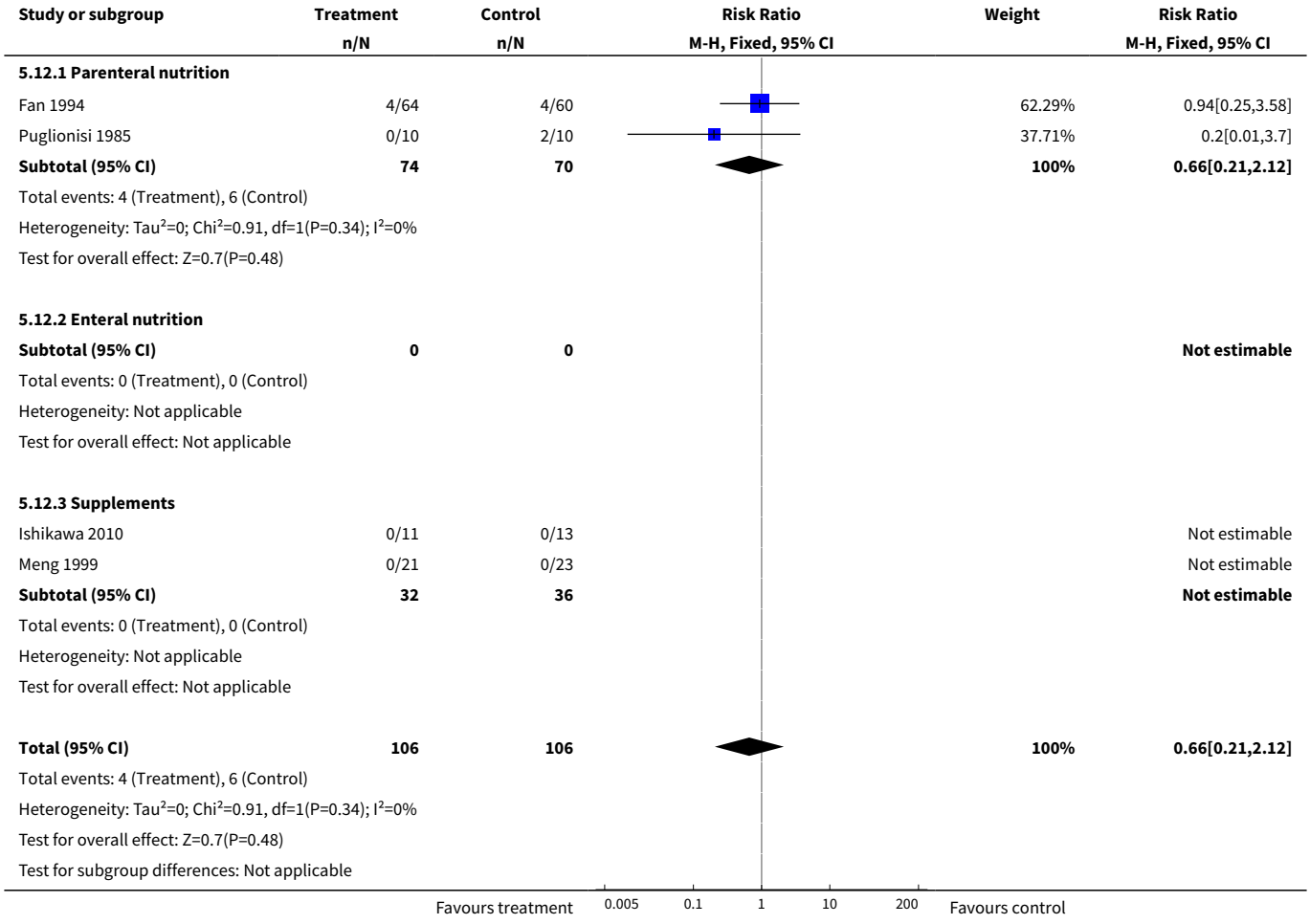


Analysis 5.11. Comparison 5 Appearance of encephalopathy - all studies, Outcome 11 Medical trials - BCAAs.

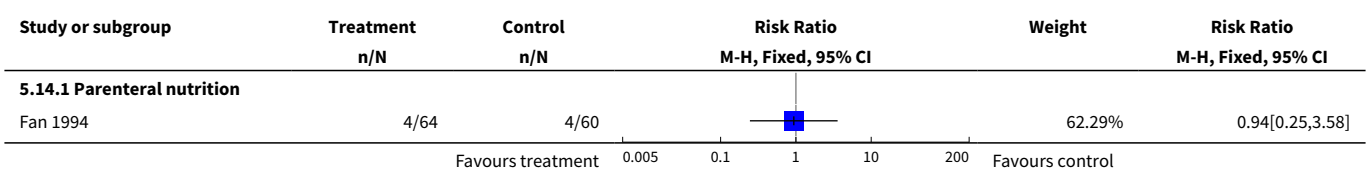


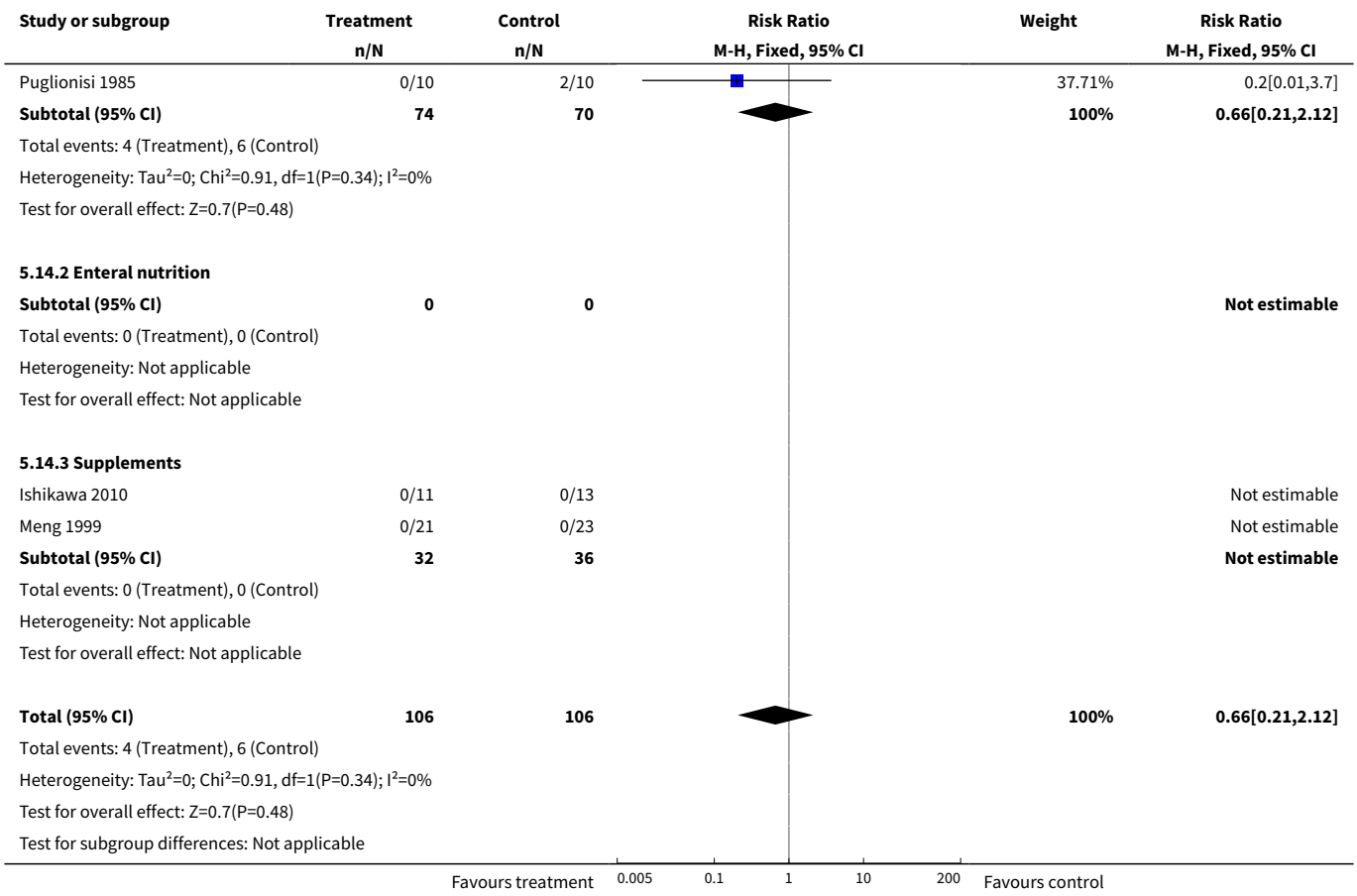


Analysis 5.12. Comparison 5 Appearance of encephalopathy - all studies, Outcome 12 Surgical trials - all studies.

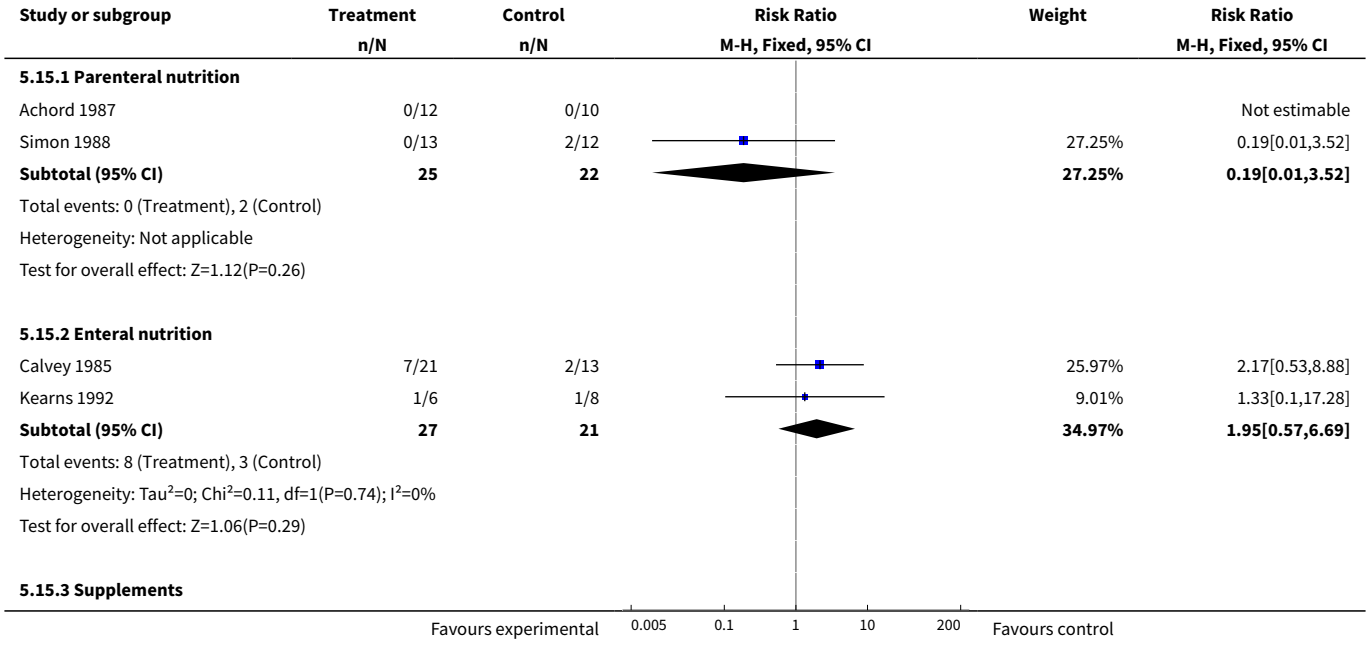


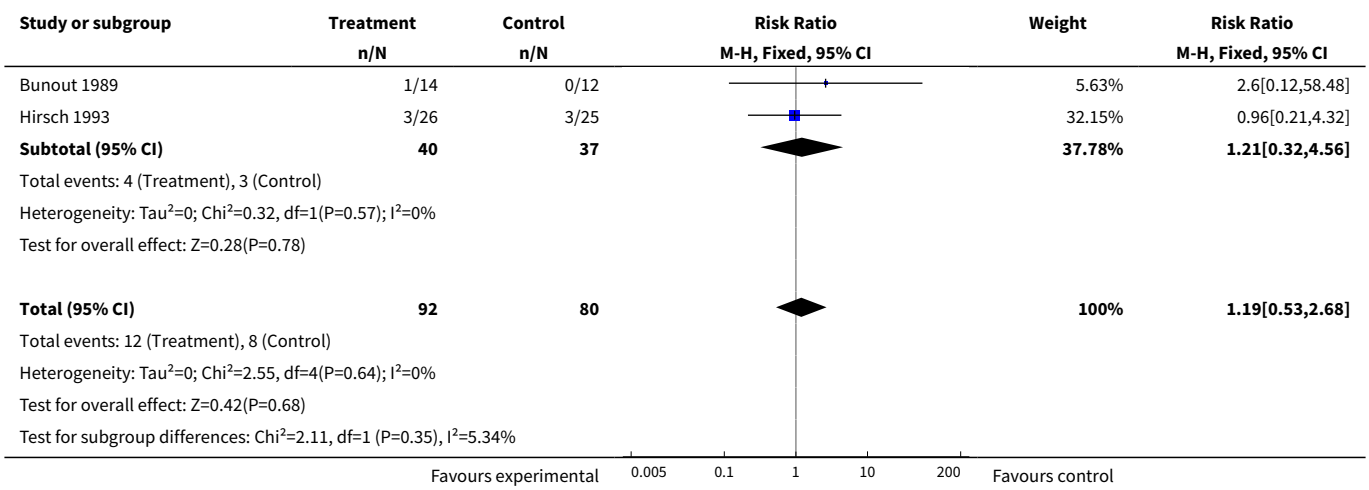
Analysis 5.14. Comparison 5 Appearance of encephalopathy - all studies, Outcome 14 Surgical trials - BCAAs.



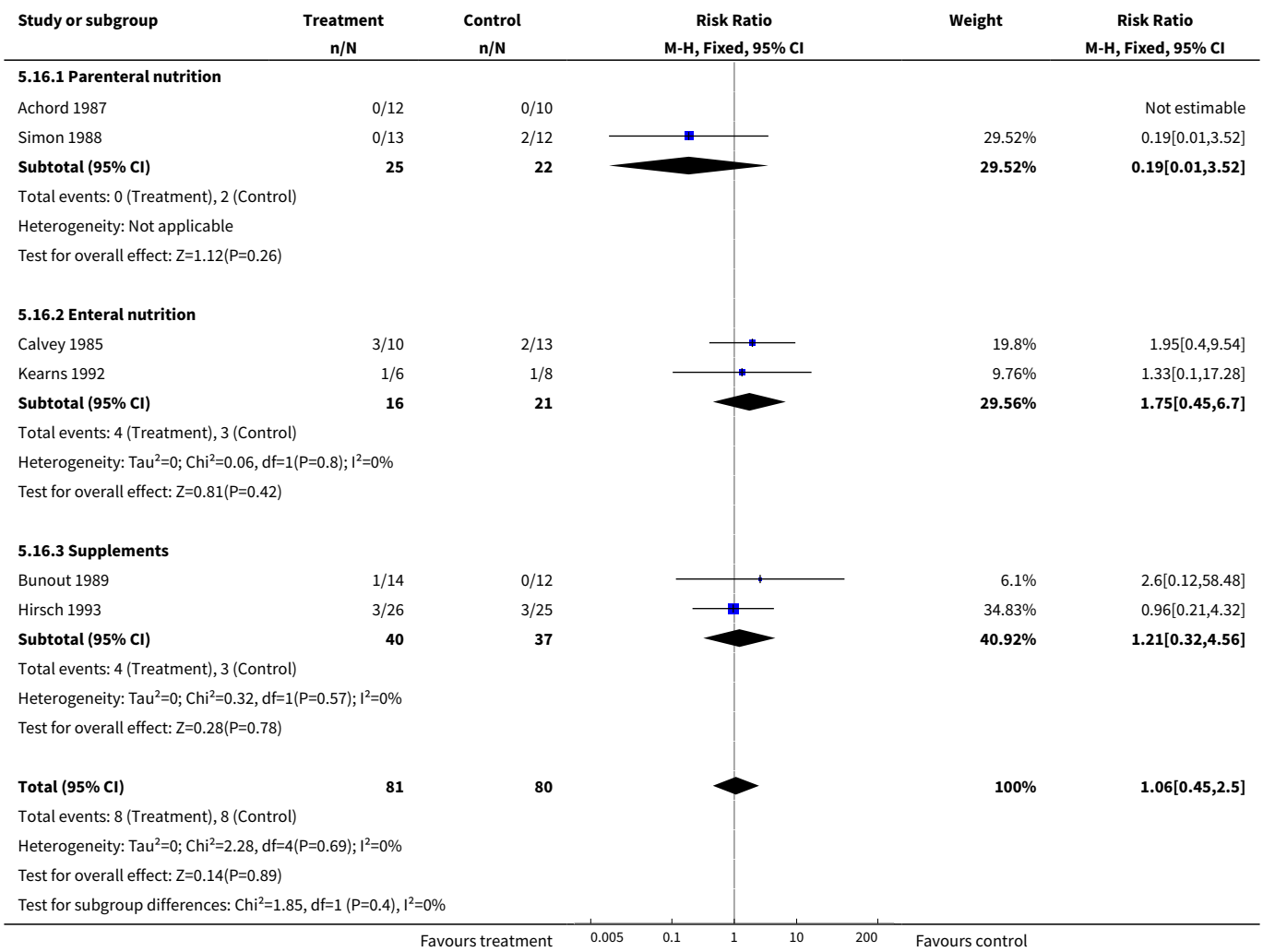


Analysis 5.15. Comparison 5 Appearance of encephalopathy - all studies, Outcome 15 Alcoholic hepatitis - all studies.



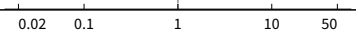


Analysis 5.16. Comparison 5 Appearance of encephalopathy - all studies, Outcome 16 Alcoholic hepatitis - standard amino acids.



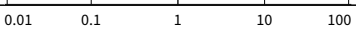
Analysis 5.17. Comparison 5 Appearance of encephalopathy - all studies, Outcome 17 Alcoholic hepatitis - BCAA.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.17.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.17.2 Enteral nutrition					
Calvey 1985	4/11	2/13		100%	2.36[0.53,10.55]
Subtotal (95% CI)	**11**	**13**		**100%**	**2.36[0.53,10.55]**
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.13(P=0.26)					
5.17.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**11**	**13**		**100%**	**2.36[0.53,10.55]**
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.13(P=0.26)					
Test for subgroup differences: Not applicable					

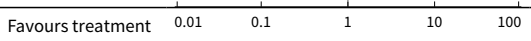


Analysis 5.18. Comparison 5 Appearance of encephalopathy - all studies, Outcome 18 Cirrhosis - all studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.18.1 Parenteral nutrition					
Naveau 1986	2/20	4/20		8.99%	0.5[0.1,2.43]
Subtotal (95% CI)	**20**	**20**		**8.99%**	**0.5[0.1,2.43]**
Total events: 2 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.86(P=0.39)					
5.18.2 Enteral nutrition					
Guy 1995	4/14	3/18		5.9%	1.71[0.46,6.44]
Schuetz 2006	0/11	0/11			Not estimable
Subtotal (95% CI)	**25**	**29**		**5.9%**	**1.71[0.46,6.44]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.8(P=0.42)					
5.18.3 Supplements					

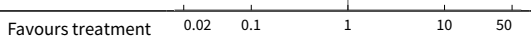


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Hasse 1997	5/23	3/6		10.69%	0.43[0.14,1.32]
Hayashi 1991	0/2	0/2			Not estimable
Hirsch 1993	3/26	3/25		6.87%	0.96[0.21,4.32]
Humbert 1988	24/27	22/22		55.52%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Nakaya 2007	0/19	1/19		3.37%	0.33[0.01,7.7]
Sievert 1999	4/61	3/34		8.66%	0.74[0.18,3.13]
Simko 1983	0/7	0/3			Not estimable
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**191**	**135**		**85.11%**	**0.8[0.62,1.04]**
Total events: 36 (Treatment), 32 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.39, df=4(P=0.49); I^2=0%					
Test for overall effect: Z=1.67(P=0.1)					
Total (95% CI)	**236**	**184**		**100%**	**0.83[0.64,1.08]**
Total events: 42 (Treatment), 39 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.13, df=6(P=0.66); I^2=0%					
Test for overall effect: Z=1.37(P=0.17)					
Test for subgroup differences: Chi^2=1.59, df=1 (P=0.45), I^2=0%					

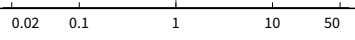


Analysis 5.19. Comparison 5 Appearance of encephalopathy - all studies, Outcome 19 Cirrhosis - standard amino acids.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.19.1 Parenteral nutrition					
Naveau 1986	2/20	4/20		23.96%	0.5[0.1,2.43]
Subtotal (95% CI)	**20**	**20**		**23.96%**	**0.5[0.1,2.43]**
Total events: 2 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.86(P=0.39)					
5.19.2 Enteral nutrition					
Guy 1995	4/14	3/18		15.72%	1.71[0.46,6.44]
Schuetz 2006	0/11	0/11			Not estimable
Subtotal (95% CI)	**25**	**29**		**15.72%**	**1.71[0.46,6.44]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.8(P=0.42)					
5.19.3 Supplements					
Hasse 1997	9/14	3/6		25.16%	1.29[0.53,3.13]
Hirsch 1993	3/26	3/25		18.32%	0.96[0.21,4.32]
Sievert 1999	1/30	3/34		16.85%	0.38[0.04,3.44]
Subtotal (95% CI)	**70**	**65**		**60.32%**	**0.93[0.44,1.97]**
Total events: 13 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.14, df=2(P=0.57); I^2=0%					
Test for overall effect: Z=0.18(P=0.86)					

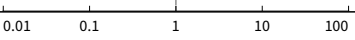


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)	**115**	**114**		**100%**	**0.95[0.53,1.72]**
Total events: 19 (Treatment), 16 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.51, df=4(P=0.64); I^2=0%					
Test for overall effect: Z=0.16(P=0.87)					
Test for subgroup differences: Chi^2=1.4, df=1 (P=0.5), I^2=0%					



Analysis 5.20. Comparison 5 Appearance of encephalopathy - all studies, Outcome 20 Cirrhosis - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.20.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.20.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.20.3 Supplementss					
Hasse 1997	1/9	3/6		11.02%	0.22[0.03,1.66]
Hayashi 1991	0/2	0/2			Not estimable
Humbert 1988	24/27	22/22		75.63%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Nakaya 2007	0/19	1/19		4.59%	0.33[0.01,7.7]
Sievert 1999	3/31	3/34		8.76%	1.1[0.24,5.04]
Simko 1983	0/7	0/3			Not estimable
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**121**	**110**		**100%**	**0.81[0.63,1.04]**
Total events: 28 (Treatment), 29 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.58, df=3(P=0.31); I^2=16.16%					
Test for overall effect: Z=1.65(P=0.1)					
Total (95% CI)	**121**	**110**		**100%**	**0.81[0.63,1.04]**
Total events: 28 (Treatment), 29 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.58, df=3(P=0.31); I^2=16.16%					
Test for overall effect: Z=1.65(P=0.1)					
Test for subgroup differences: Not applicable					

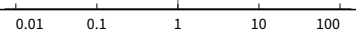


Analysis 5.21. Comparison 5 Appearance of encephalopathy - all studies, Outcome 21 HCC - all studies.

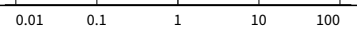
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.21.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.21.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.21.3 Supplements					
Kobashi 2006	12/108	16/113		91.43%	0.78[0.39,1.58]
Poon 2004	0/41	1/43		8.57%	0.35[0.01,8.34]
Subtotal (95% CI)	**149**	**156**		**100%**	**0.75[0.38,1.48]**
Total events: 12 (Treatment), 17 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.24, df=1(P=0.62); I^2=0%					
Test for overall effect: Z=0.84(P=0.4)					
Total (95% CI)	**149**	**156**		**100%**	**0.75[0.38,1.48]**
Total events: 12 (Treatment), 17 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.24, df=1(P=0.62); I^2=0%					
Test for overall effect: Z=0.84(P=0.4)					
Test for subgroup differences: Not applicable					

Analysis 5.23. Comparison 5 Appearance of encephalopathy - all studies, Outcome 23 HCC - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.23.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.23.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.23.3 Supplements					
Kobashi 2006	12/108	16/113		91.43%	0.78[0.39,1.58]
Poon 2004	0/41	1/43		8.57%	0.35[0.01,8.34]
Subtotal (95% CI)	**149**	**156**		**100%**	**0.75[0.38,1.48]**
Total events: 12 (Treatment), 17 (Control)					

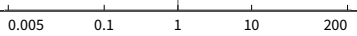


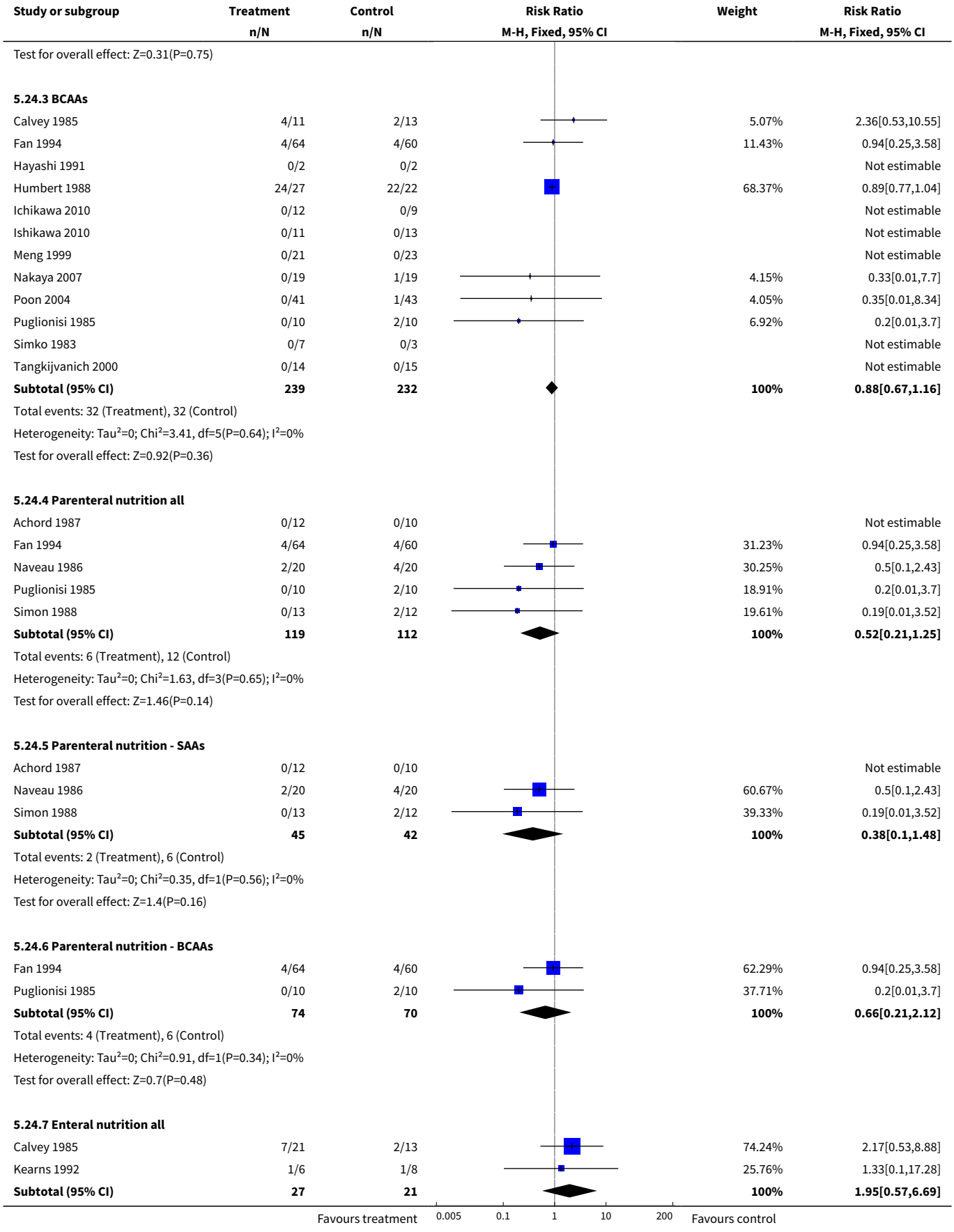
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=0.24, df=1(P=0.62); I²=0%					
Test for overall effect: Z=0.84(P=0.4)					
Total (95% CI)	**149**	**156**		**100%**	**0.75[0.38,1.48]**
Total events: 12 (Treatment), 17 (Control)					
Heterogeneity: Tau²=0; Chi²=0.24, df=1(P=0.62); I²=0%					
Test for overall effect: Z=0.84(P=0.4)					
Test for subgroup differences: Not applicable					

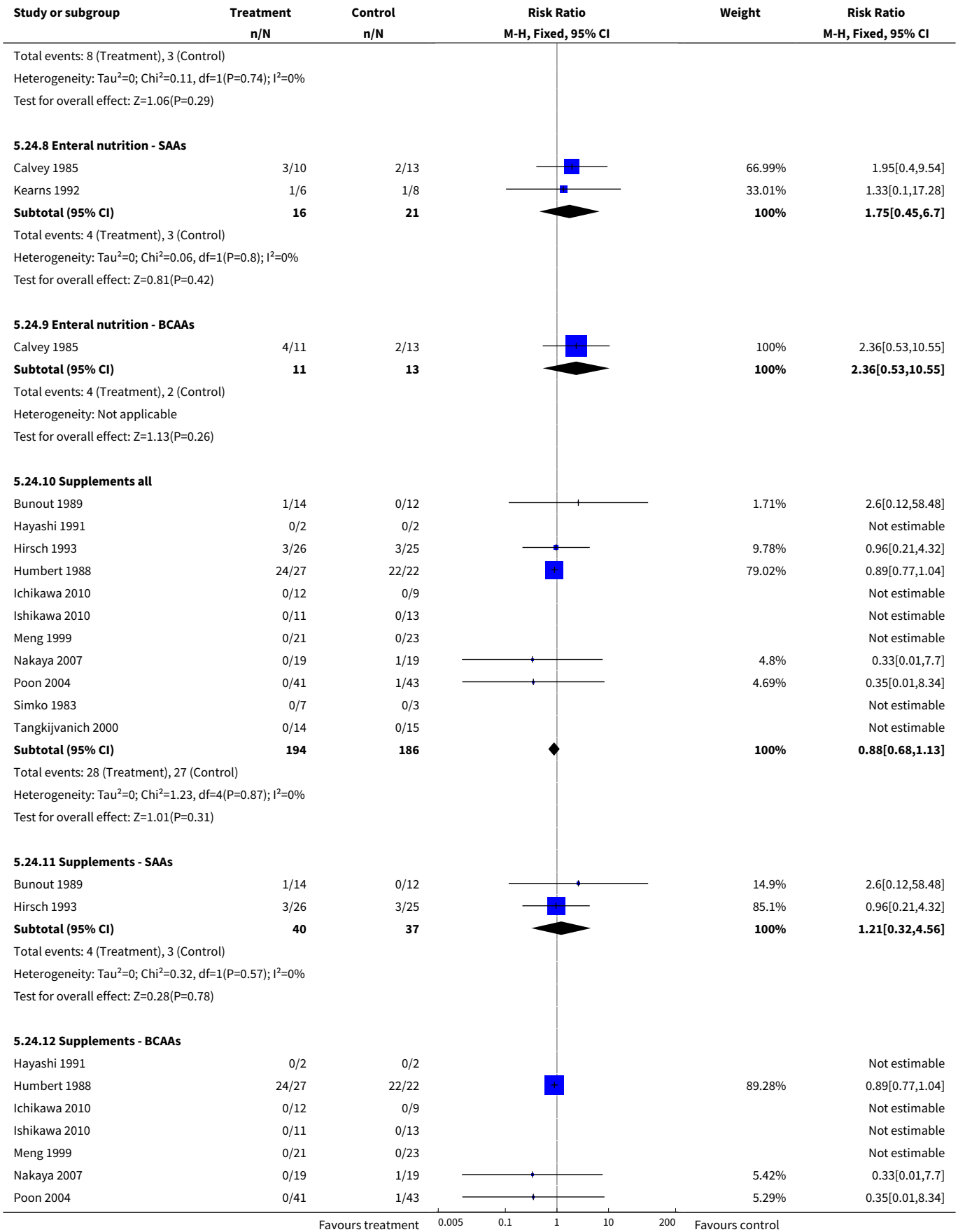


Analysis 5.24. Comparison 5 Appearance of encephalopathy - all studies, Outcome 24 Abstracts excluded.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.24.1 All trials					
Achord 1987	0/12	0/10			Not estimable
Bunout 1989	1/14	0/12		1.12%	2.6[0.12,58.48]
Calvey 1985	7/21	2/13		5.17%	2.17[0.53,8.88]
Fan 1994	4/64	4/60		8.64%	0.94[0.25,3.58]
Hayashi 1991	0/2	0/2			Not estimable
Hirsch 1993	3/26	3/25		6.4%	0.96[0.21,4.32]
Humbert 1988	24/27	22/22		51.67%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Ishikawa 2010	0/11	0/13			Not estimable
Kearns 1992	1/6	1/8		1.79%	1.33[0.1,17.28]
Meng 1999	0/21	0/23			Not estimable
Nakaya 2007	0/19	1/19		3.14%	0.33[0.01,7.7]
Naveau 1986	2/20	4/20		8.37%	0.5[0.1,2.43]
Poon 2004	0/41	1/43		3.06%	0.35[0.01,8.34]
Puglionisi 1985	0/10	2/10		5.23%	0.2[0.01,3.7]
Simko 1983	0/7	0/3			Not estimable
Simon 1988	0/13	2/12		5.42%	0.19[0.01,3.52]
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**340**	**319**		**100%**	**0.85[0.64,1.13]**
Total events: 42 (Treatment), 42 (Control)					
Heterogeneity: Tau²=0; Chi²=5.77, df=10(P=0.83); I²=0%					
Test for overall effect: Z=1.09(P=0.27)					
5.24.2 Standard amino acids					
Achord 1987	0/12	0/10			Not estimable
Bunout 1989	1/14	0/12		4.19%	2.6[0.12,58.48]
Calvey 1985	3/10	2/13		13.6%	1.95[0.4,9.54]
Hirsch 1993	3/26	3/25		23.93%	0.96[0.21,4.32]
Kearns 1992	1/6	1/8		6.71%	1.33[0.1,17.28]
Naveau 1986	2/20	4/20		31.29%	0.5[0.1,2.43]
Simon 1988	0/13	2/12		20.28%	0.19[0.01,3.52]
Subtotal (95% CI)	**101**	**100**		**100%**	**0.89[0.42,1.86]**
Total events: 10 (Treatment), 12 (Control)					
Heterogeneity: Tau²=0; Chi²=3.1, df=5(P=0.68); I²=0%					







Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Simko 1983	0/7	0/3			Not estimable
Tangkijvanich 2000	0/14	0/15			Not estimable
Subtotal (95% CI)	**154**	**149**		**100%**	**0.84[0.68,1.03]**
Total events: 24 (Treatment), 24 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.39, df=2(P=0.5); I^2=0%					
Test for overall effect: Z=1.7(P=0.09)					
Test for subgroup differences: Chi^2=7.78, df=1 (P=0.73), I^2=0%					

Favours treatment 0.005 0.1 1 10 200 Favours control

Analysis 5.25. Comparison 5 Appearance of encephalopathy - all studies, Outcome 25 Surgical trials - transplant trials eliminated.

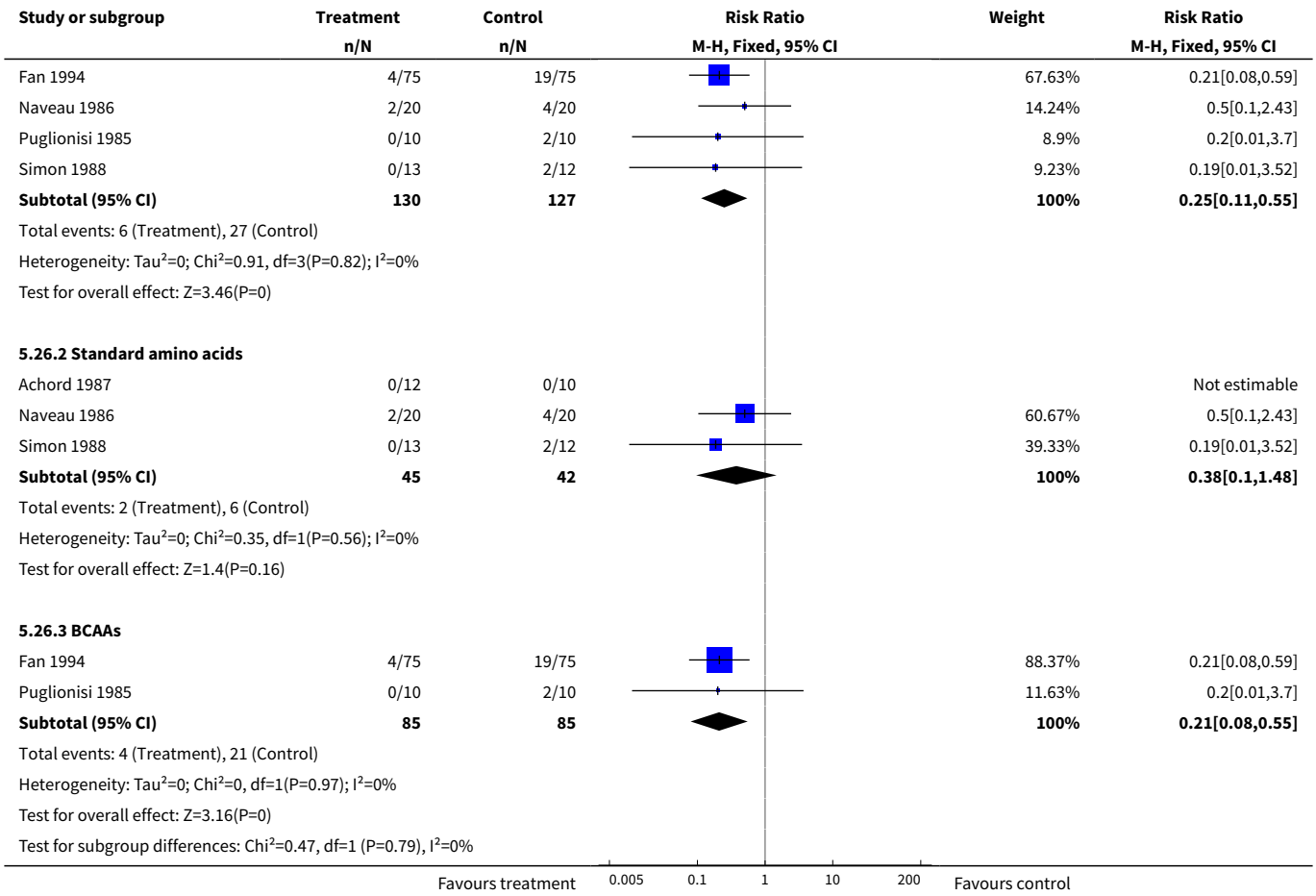
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.25.1 All trials					
Fan 1994	4/64	4/60		100%	0.94[0.25,3.58]
Ishikawa 2010	0/11	0/13			Not estimable
Meng 1999	0/21	0/23			Not estimable
Subtotal (95% CI)	**96**	**96**		**100%**	**0.94[0.25,3.58]**
Total events: 4 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.09(P=0.92)					
5.25.2 Standard amino acids					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
5.25.3 BCAAs					
Fan 1994	4/64	4/60		100%	0.94[0.25,3.58]
Ishikawa 2010	0/11	0/13			Not estimable
Meng 1999	0/21	0/23			Not estimable
Subtotal (95% CI)	**96**	**96**		**100%**	**0.94[0.25,3.58]**
Total events: 4 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.09(P=0.92)					
Test for subgroup differences: Not applicable					

Favours treatment 0.1 0.2 0.5 1 2 5 10 Favours control

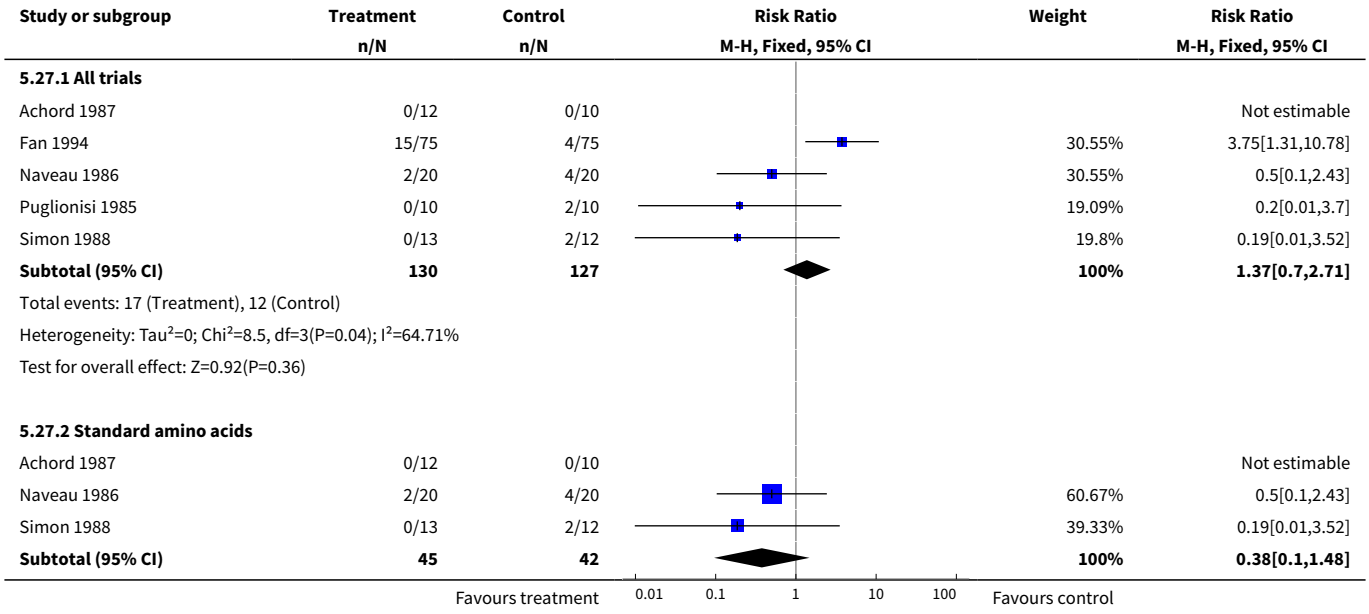
Analysis 5.26. Comparison 5 Appearance of encephalopathy - all studies, Outcome 26 ITT - Parenteral nutrition - best-case scenario.

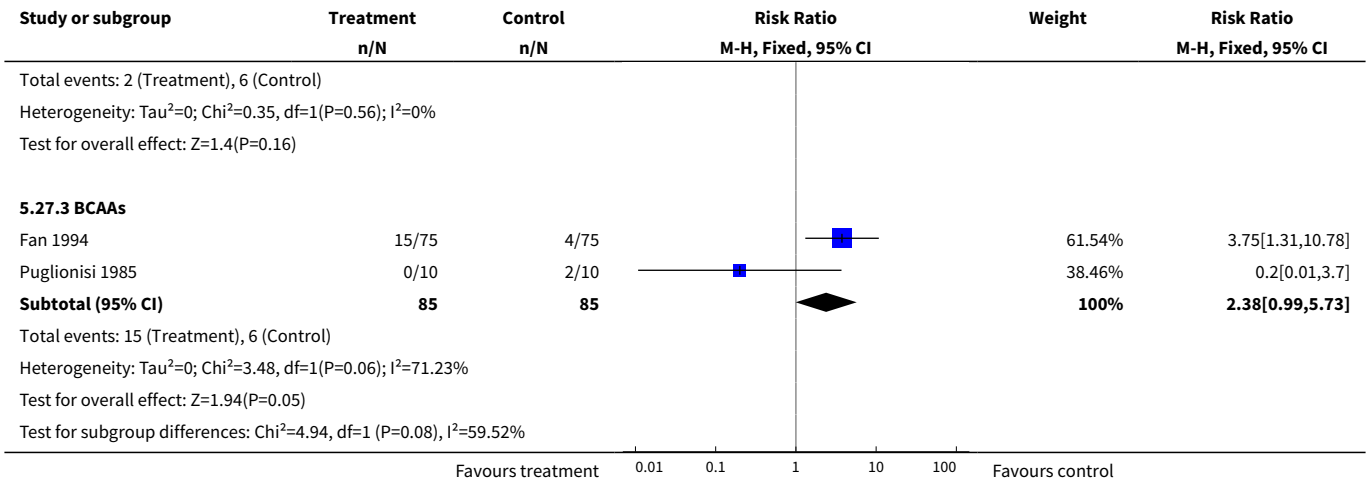
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.26.1 All trials					
Achord 1987	0/12	0/10			Not estimable

Favours treatment 0.005 0.1 1 10 200 Favours control

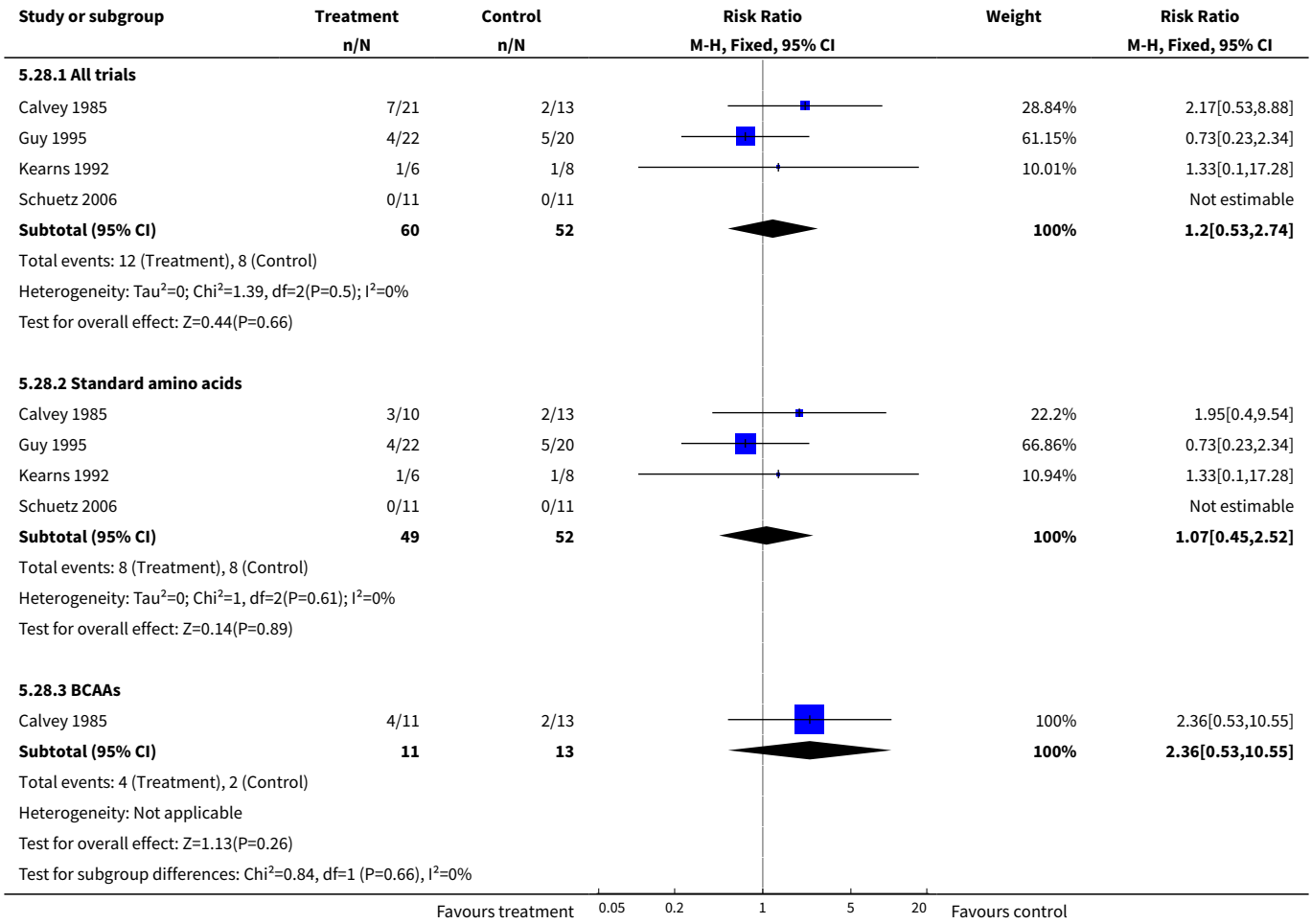


Analysis 5.27. Comparison 5 Appearance of encephalopathy - all studies, Outcome 27 ITT - Parenteral nutrition - worst-case scenario.



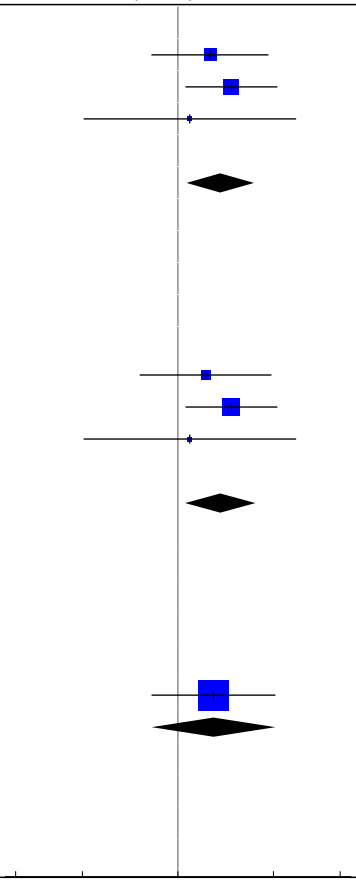


Analysis 5.28. Comparison 5 Appearance of encephalopathy - all studies, Outcome 28 ITT - Enteral nutrition - best-case scenario.



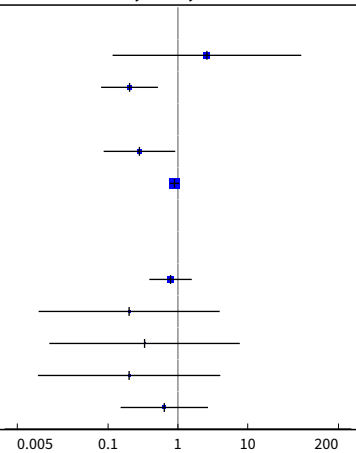
Analysis 5.29. Comparison 5 Appearance of encephalopathy - all studies, Outcome 29 ITT - Enteral nutrition - worst-case scenario.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.29.1 All trials					
Calvey 1985	7/21	2/13		38.18%	2.17[0.53,8.88]
Guy 1995	12/22	3/20		48.57%	3.64[1.2,11.04]
Kearns 1992	1/6	1/8		13.25%	1.33[0.1,17.28]
Schuetz 2006	0/11	0/11			Not estimable
Subtotal (95% CI)	**60**	**52**		**100%**	**2.77[1.23,6.26]**
Total events: 20 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.66, df=2(P=0.72); I^2=0%					
Test for overall effect: Z=2.45(P=0.01)					
5.29.2 Standard amino acids					
Calvey 1985	3/10	2/13		30.3%	1.95[0.4,9.54]
Guy 1995	12/22	3/20		54.76%	3.64[1.2,11.04]
Kearns 1992	1/6	1/8		14.94%	1.33[0.1,17.28]
Schuetz 2006	0/11	0/11			Not estimable
Subtotal (95% CI)	**49**	**52**		**100%**	**2.78[1.19,6.48]**
Total events: 16 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.73, df=2(P=0.69); I^2=0%					
Test for overall effect: Z=2.37(P=0.02)					
5.29.3 BCAAs					
Calvey 1985	4/11	2/13		100%	2.36[0.53,10.55]
Subtotal (95% CI)	**11**	**13**		**100%**	**2.36[0.53,10.55]**
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.13(P=0.26)					
Test for subgroup differences: Chi^2=0.04, df=1 (P=0.98), I^2=0%					

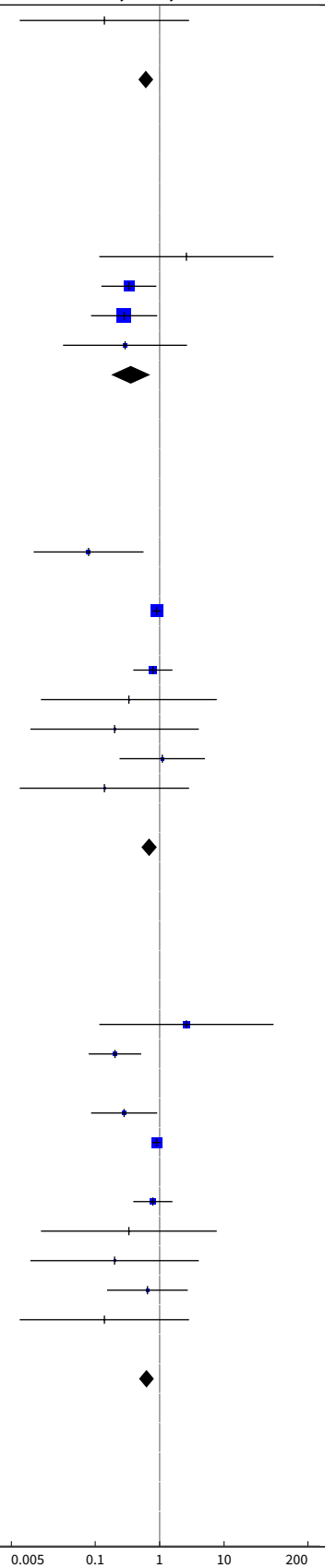


Analysis 5.30. Comparison 5 Appearance of encephalopathy - all studies, Outcome 30 ITT- Supplements - best-case scenario.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.30.1 All trials					
Bunout 1989	1/14	0/12		0.72%	2.6[0.12,58.48]
Hasse 1997	5/37	6/9		13.04%	0.2[0.08,0.52]
Hayashi 1991	0/2	0/2			Not estimable
Hirsch 1993	3/32	11/33		14.63%	0.28[0.09,0.92]
Humbert 1988	24/27	22/22		33.37%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Ishikawa 2010	0/11	0/13			Not estimable
Kobashi 2006	12/108	16/113		21.12%	0.78[0.39,1.58]
Meng 1999	0/25	2/25		3.38%	0.2[0.01,3.97]
Nakaya 2007	0/19	1/19		2.03%	0.33[0.01,7.7]
Poon 2004	0/44	2/44		3.38%	0.2[0.01,4.05]
Sievert 1999	4/71	3/34		5.48%	0.64[0.15,2.7]



Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Simko 1983	0/11	1/4		2.86%	0.14[0.01,2.86]
Tangkijvanich 2000	0/15	0/15			Not estimable
Subtotal (95% CI)	**428**	**354**		**100%**	**0.61[0.47,0.79]**
Total events: 49 (Treatment), 64 (Control)					
Heterogeneity: Tau^2=0; Chi^2=34.6, df=9(P<0.0001); I^2=73.99%					
Test for overall effect: Z=3.66(P=0)					
5.30.2 Standard amino acids -medical trials					
Bunout 1989	1/14	0/12		2.37%	2.6[0.12,58.48]
Hasse 1997	4/18	6/9		35.44%	0.33[0.13,0.89]
Hirsch 1993	3/32	11/33		47.98%	0.28[0.09,0.92]
Sievert 1999	1/39	3/34		14.2%	0.29[0.03,2.66]
Subtotal (95% CI)	**103**	**88**		**100%**	**0.36[0.18,0.72]**
Total events: 9 (Treatment), 20 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.77, df=3(P=0.62); I^2=0%					
Test for overall effect: Z=2.9(P=0)					
5.30.3 BCAAs - medical trials					
Hasse 1997	1/19	6/9		14.17%	0.08[0.01,0.56]
Hayashi 1991	0/2	0/2			Not estimable
Humbert 1988	24/27	22/22		42.99%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Kobashi 2006	12/108	16/113		27.21%	0.78[0.39,1.58]
Nakaya 2007	0/19	1/19		2.61%	0.33[0.01,7.7]
Poon 2004	0/44	2/44		4.35%	0.2[0.01,4.05]
Sievert 1999	3/31	3/34		4.98%	1.1[0.24,5.04]
Simko 1983	0/11	1/4		3.69%	0.14[0.01,2.86]
Tangkijvanich 2000	0/15	0/15			Not estimable
Subtotal (95% CI)	**288**	**271**		**100%**	**0.69[0.52,0.9]**
Total events: 40 (Treatment), 51 (Control)					
Heterogeneity: Tau^2=0; Chi^2=18.64, df=6(P=0); I^2=67.8%					
Test for overall effect: Z=2.67(P=0.01)					
5.30.4 All supplements - medical					
Bunout 1989	1/14	0/12		0.75%	2.6[0.12,58.48]
Hasse 1997	5/37	6/9		13.5%	0.2[0.08,0.52]
Hayashi 1991	0/2	0/2			Not estimable
Hirsch 1993	3/32	11/33		15.14%	0.28[0.09,0.92]
Humbert 1988	24/27	22/22		34.54%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Kobashi 2006	12/108	16/113		21.87%	0.78[0.39,1.58]
Nakaya 2007	0/19	1/19		2.1%	0.33[0.01,7.7]
Poon 2004	0/44	2/44		3.5%	0.2[0.01,4.05]
Sievert 1999	4/70	3/34		5.65%	0.65[0.15,2.73]
Simko 1983	0/11	1/4		2.96%	0.14[0.01,2.86]
Tangkijvanich 2000	0/15	0/15			Not estimable
Subtotal (95% CI)	**391**	**316**		**100%**	**0.62[0.48,0.81]**
Total events: 49 (Treatment), 62 (Control)					
Heterogeneity: Tau^2=0; Chi^2=31.41, df=8(P=0); I^2=74.53%					
Test for overall effect: Z=3.49(P=0)					
5.30.5 All surgical					

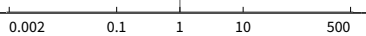


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Ishikawa 2010	0/11	0/13			Not estimable
Meng 1999	0/25	2/25		100%	0.2[0.01,3.97]
Subtotal (95% CI)	**36**	**38**		**100%**	**0.2[0.01,3.97]**
Total events: 0 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.06(P=0.29)					
Test for subgroup differences: Chi²=3.52, df=1 (P=0.48), I²=0%					

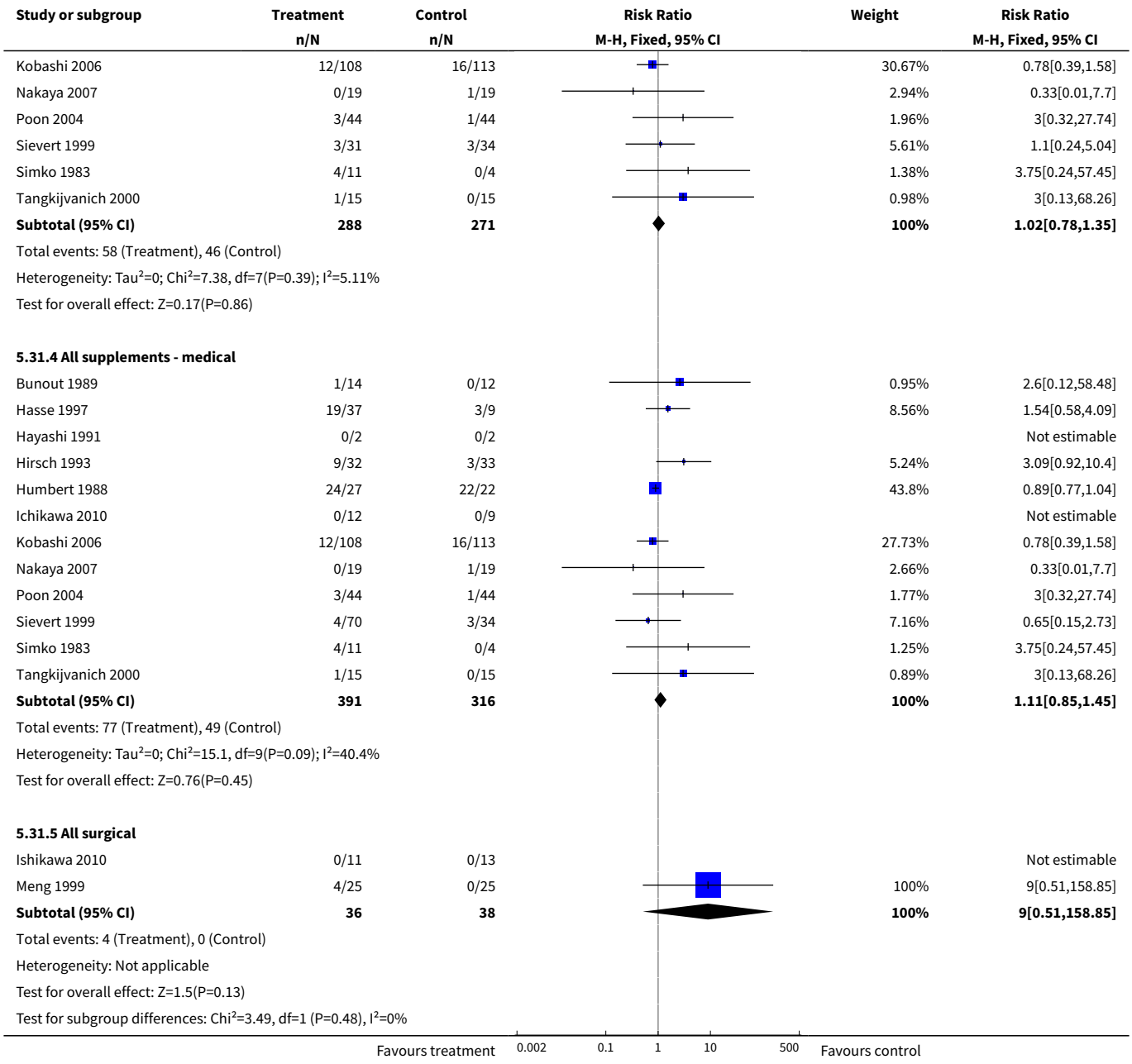
Favours treatment Favours control

Analysis 5.31. Comparison 5 Appearance of encephalopathy - all studies, Outcome 31 ITT - Supplements - worst-case scenario.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.31.1 All trials					
Bunout 1989	1/14	0/12		0.94%	2.6[0.12,58.48]
Hasse 1997	19/37	3/9		8.48%	1.54[0.58,4.09]
Hayashi 1991	0/2	0/2			Not estimable
Hirsch 1993	9/32	3/33		5.19%	3.09[0.92,10.4]
Humbert 1988	24/27	22/22		43.42%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable
Ishikawa 2010	0/11	0/13			Not estimable
Kobashi 2006	12/108	16/113		27.48%	0.78[0.39,1.58]
Meng 1999	4/25	0/25		0.88%	9[0.51,158.85]
Nakaya 2007	0/19	1/19		2.64%	0.33[0.01,7.7]
Poon 2004	3/44	1/44		1.76%	3[0.32,27.74]
Sievert 1999	4/70	3/34		7.1%	0.65[0.15,2.73]
Simko 1983	4/11	0/4		1.24%	3.75[0.24,57.45]
Tangkijvanich 2000	1/15	0/15		0.88%	3[0.13,68.26]
Subtotal (95% CI)	**427**	**354**		**100%**	**1.18[0.9,1.54]**
Total events: 81 (Treatment), 49 (Control)					
Heterogeneity: Tau²=0; Chi²=21.77, df=10(P=0.02); I²=54.07%					
Test for overall effect: Z=1.21(P=0.23)					
5.31.2 Standard amino acids -medical trials					
Bunout 1989	1/14	0/12		5.01%	2.6[0.12,58.48]
Hasse 1997	8/18	3/9		37.4%	1.33[0.46,3.84]
Hirsch 1993	9/32	3/33		27.62%	3.09[0.92,10.4]
Sievert 1999	1/39	3/34		29.97%	0.29[0.03,2.66]
Subtotal (95% CI)	**103**	**88**		**100%**	**1.57[0.79,3.13]**
Total events: 19 (Treatment), 9 (Control)					
Heterogeneity: Tau²=0; Chi²=3.62, df=3(P=0.31); I²=17.13%					
Test for overall effect: Z=1.28(P=0.2)					
5.31.3 BCAAs - medical trials					
Hasse 1997	11/19	3/9		7.99%	1.74[0.64,4.72]
Hayashi 1991	0/2	0/2			Not estimable
Humbert 1988	24/27	22/22		48.46%	0.89[0.77,1.04]
Ichikawa 2010	0/12	0/9			Not estimable



Favours treatment Favours control



Comparison 6. Resolution of encephalopathy

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 All trials	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 All studies	6	119	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.18, 3.72]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.2 Standard amino acids	5	66	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.62, 2.07]
1.3 BCAA's	2	62	Risk Ratio (M-H, Fixed, 95% CI)	7.48 [1.87, 29.94]
2 Parenteral nutrition (all medical trials)	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 All trials	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
2.2 Standard amino acids	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
2.3 BCAA's	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Enteral nutrition (all medical trials)	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 All trials	2	47	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.59, 4.13]
3.2 Standard amino acids	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.48, 3.39]
3.3 BCAA's	1	19	Risk Ratio (M-H, Fixed, 95% CI)	3.6 [0.49, 26.54]
4 Supplements (all medical trials)	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 All trials	2	53	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.06, 75.19]
4.2 Standard amino acids	1	10	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.02, 4.29]
4.3 BCAA's	1	43	Risk Ratio (M-H, Random, 95% CI)	11.30 [1.62, 78.95]
5 Medical trials - all trials	6	119	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.18, 3.72]
5.1 Parenteral nutrition	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
5.2 Enteral nutrition	2	47	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.59, 4.13]
5.3 Supplements	2	53	Risk Ratio (M-H, Fixed, 95% CI)	3.75 [1.15, 12.18]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
6 Medical trials - standard amino acids	5	66	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.62, 2.07]
6.1 Parenteral nutrition	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
6.2 Enteral nutrition	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.48, 3.39]
6.3 Supplements	1	10	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.02, 4.29]
7 Medical trials - BCAAs	2	62	Risk Ratio (M-H, Fixed, 95% CI)	7.48 [1.87, 29.94]
7.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Enteral nutrition	1	19	Risk Ratio (M-H, Fixed, 95% CI)	3.6 [0.49, 26.54]
7.3 Supplements	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]
8 Surgical trials - all trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.1 Pareneral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Surgical trials - standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Pareneral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Surgical trials - BCAAs	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.1 Pareneral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
10.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Alcoholic hepatitis - all trials	5	76	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.68, 2.31]
11.1 Parenteral nutrition	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
11.2 Enteral nutrition	2	47	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.59, 4.13]
11.3 Supplements	1	10	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.02, 4.29]
12 Alcoholic hepatitis - standard amino acids	5	66	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.62, 2.07]
12.1 Parenteral nutrition	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
12.2 Enteral nutrition	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.48, 3.39]
12.3 Supplements	1	10	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.02, 4.29]
13 Alcoholic hepatitis - BCAAs	1	19	Risk Ratio (M-H, Fixed, 95% CI)	3.6 [0.49, 26.54]
13.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Enteral nutrition	1	19	Risk Ratio (M-H, Fixed, 95% CI)	3.6 [0.49, 26.54]
13.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Cirrhosis - all	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]
14.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 Supplements	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
15 Cirrhosis - standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Cirrhosis - BCAAs	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]
16.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 Supplements	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]
17 HCC - all studies	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 HCC - standard amino acids	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 HCC - BCAAs	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

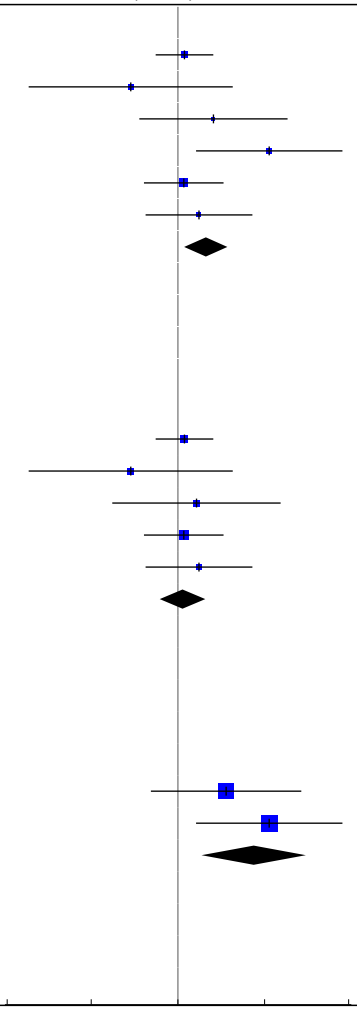
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
19.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Abstracts excluded - all trials	6	119	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.18, 3.72]
20.1 Parenteral nutrition	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
20.2 Enteral nutrition	2	47	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.59, 4.13]
20.3 Supplements	2	53	Risk Ratio (M-H, Fixed, 95% CI)	3.75 [1.15, 12.18]
21 Abstracts excluded - standard amino acids	5	66	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.62, 2.07]
21.1 Parenteral nutrition	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
21.2 Enteral nutrition	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.48, 3.39]
21.3 Supplements	1	10	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.02, 4.29]
22 Abstracts excluded - BCAAs	3	72	Risk Ratio (M-H, Random, 95% CI)	2.75 [0.40, 19.10]
22.1 Parenteral nutrition	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
22.2 Enteral nutrition	1	19	Risk Ratio (M-H, Random, 95% CI)	3.60 [0.49, 26.54]
22.3 Supplements	2	53	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.06, 75.19]
23 Surgical trials (transplant patients re-moved) - all trials	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.1 Pareneral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 Supplements	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
24 ITT - All trials - best-case scenario - no changes made because all patients reported	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
24.1 All studies	6	119	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.18, 3.72]
24.2 Standard amino acids	5	66	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.62, 2.07]
24.3 BCAA's	2	62	Risk Ratio (M-H, Fixed, 95% CI)	7.48 [1.87, 29.94]
25 ITT - Parenteral nutrition trials - best-case scenario - no changes made because all patients reported	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
25.1 All studies	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
25.2 Standard amino acids	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
25.3 BCAA's	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 ITT - Enteral trials - best-case scenario - no changes made because all patients reported	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
26.1 All studies	2	47	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.59, 4.13]
26.2 Standard amino acids	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.48, 3.39]
26.3 BCAA's	1	19	Risk Ratio (M-H, Fixed, 95% CI)	3.6 [0.49, 26.54]
27 ITT - Supplements trials - best-case scenario - no changes made because all patients reported	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
27.1 All studies	2	53	Risk Ratio (M-H, Fixed, 95% CI)	3.75 [1.15, 12.18]
27.2 Standard amino acids	1	10	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.02, 4.29]
27.3 BCAA's	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]
28 ITT - All trials - worst-case scenario - no changes made because all patients reported	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
28.1 All studies	6	119	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.18, 3.72]
28.2 Standard amino acids	5	66	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.62, 2.07]
28.3 BCAA's	2	62	Risk Ratio (M-H, Fixed, 95% CI)	7.48 [1.87, 29.94]
29 ITT - Parenteral nutrition trials - worst-case scenario - no changes made because all patients reported	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
29.1 All studies	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
29.2 Standard amino acids	2	19	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.66, 3.07]
29.3 BCAA's	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
30 ITT - Enteral nutrition trials - worst-case scenario - no changes made because all patients reported	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
30.1 All studies	2	47	Risk Ratio (M-H, Fixed, 95% CI)	1.57 [0.59, 4.13]
30.2 Standard amino acids	2	37	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.48, 3.39]
30.3 BCAA's	1	19	Risk Ratio (M-H, Fixed, 95% CI)	3.6 [0.49, 26.54]
31 ITT - Supplement trials - worst-case scenario - no changes made because all patients reported	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
31.1 All studies	2	53	Risk Ratio (M-H, Fixed, 95% CI)	3.75 [1.15, 12.18]
31.2 Standard amino acids	2	23	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.28, 3.09]
31.3 BCAA's	1	43	Risk Ratio (M-H, Fixed, 95% CI)	11.30 [1.62, 78.95]

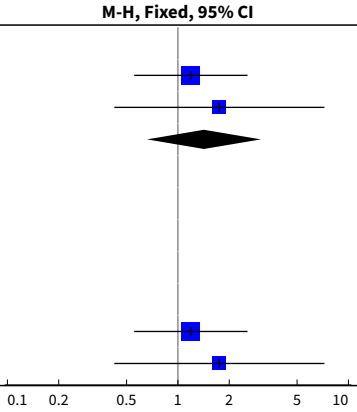
Analysis 6.1. Comparison 6 Resolution of encephalopathy, Outcome 1 All trials.

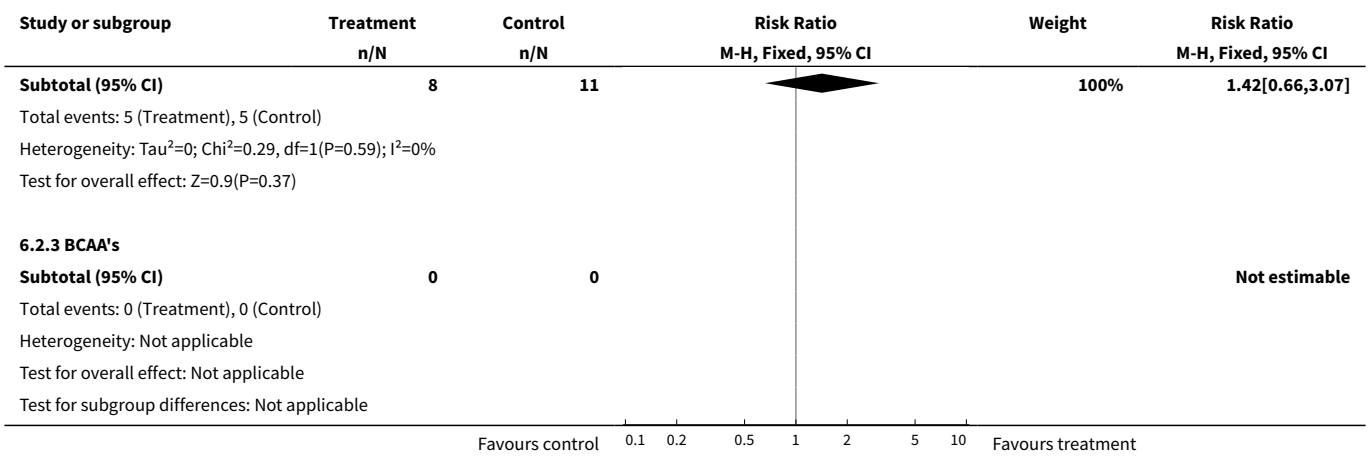
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.1.1 All studies					
Achord 1987	2/2	3/4		20.5%	1.19[0.55,2.56]
Bunout 1989	0/3	3/7		18.22%	0.29[0.02,4.29]
Calvey 1985	6/21	1/9		10.93%	2.57[0.36,18.4]
Hayashi 1991	13/23	1/20		8.36%	11.3[1.62,78.95]
Kearns 1992	5/10	3/7		27.57%	1.17[0.41,3.36]
Simon 1988	3/6	2/7		14.42%	1.75[0.42,7.23]
Subtotal (95% CI)	**65**	**54**		**100%**	**2.1[1.18,3.72]**
Total events: 29 (Treatment), 13 (Control)					
Heterogeneity: Tau²=0; Chi²=8.35, df=5(P=0.14); I²=40.12%					
Test for overall effect: Z=2.53(P=0.01)					
6.1.2 Standard amino acids					
Achord 1987	2/2	3/4		22.96%	1.19[0.55,2.56]
Bunout 1989	0/3	3/7		20.41%	0.29[0.02,4.29]
Calvey 1985	2/11	1/9		9.62%	1.64[0.18,15.26]
Kearns 1992	5/10	3/7		30.87%	1.17[0.41,3.36]
Simon 1988	3/6	2/7		16.15%	1.75[0.42,7.23]
Subtotal (95% CI)	**32**	**34**		**100%**	**1.13[0.62,2.07]**
Total events: 12 (Treatment), 12 (Control)					
Heterogeneity: Tau²=0; Chi²=1.48, df=4(P=0.83); I²=0%					
Test for overall effect: Z=0.4(P=0.69)					
6.1.3 BCAA's					
Calvey 1985	4/10	1/9		49.6%	3.6[0.49,26.54]
Hayashi 1991	13/23	1/20		50.4%	11.3[1.62,78.95]
Subtotal (95% CI)	**33**	**29**		**100%**	**7.48[1.87,29.94]**
Total events: 17 (Treatment), 2 (Control)					
Heterogeneity: Tau²=0; Chi²=0.69, df=1(P=0.41); I²=0%					
Test for overall effect: Z=2.85(P=0)					
Test for subgroup differences: Chi²=6.58, df=1 (P=0.04), I²=69.6%					



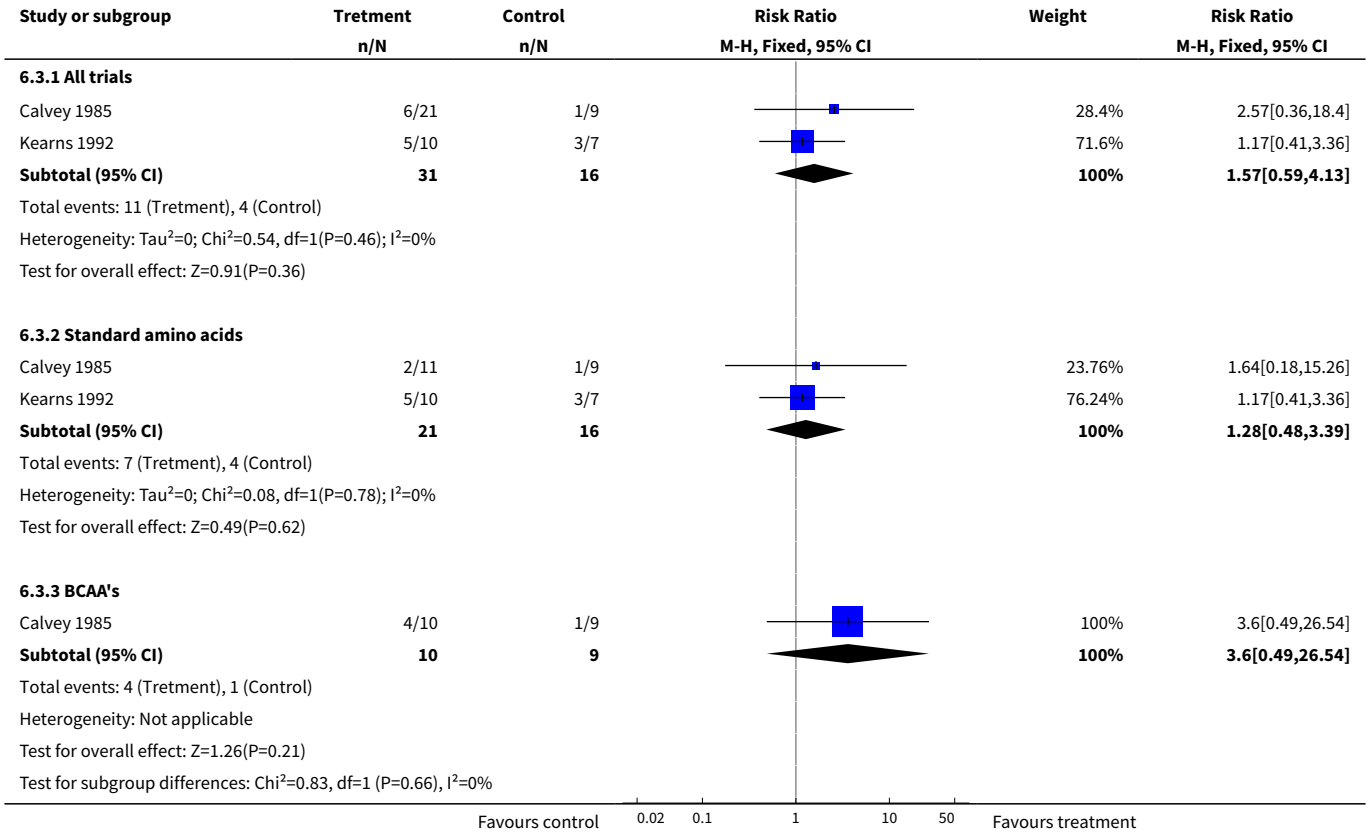
Analysis 6.2. Comparison 6 Resolution of encephalopathy, Outcome 2 Parenteral nutrition (all medical trials).

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.2.1 All trials					
Achord 1987	2/2	3/4		58.71%	1.19[0.55,2.56]
Simon 1988	3/6	2/7		41.29%	1.75[0.42,7.23]
Subtotal (95% CI)	**8**	**11**		**100%**	**1.42[0.66,3.07]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau²=0; Chi²=0.29, df=1(P=0.59); I²=0%					
Test for overall effect: Z=0.9(P=0.37)					
6.2.2 Standard amino acids					
Achord 1987	2/2	3/4		58.71%	1.19[0.55,2.56]
Simon 1988	3/6	2/7		41.29%	1.75[0.42,7.23]

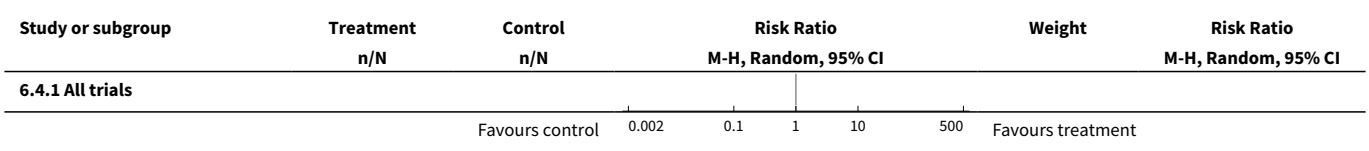


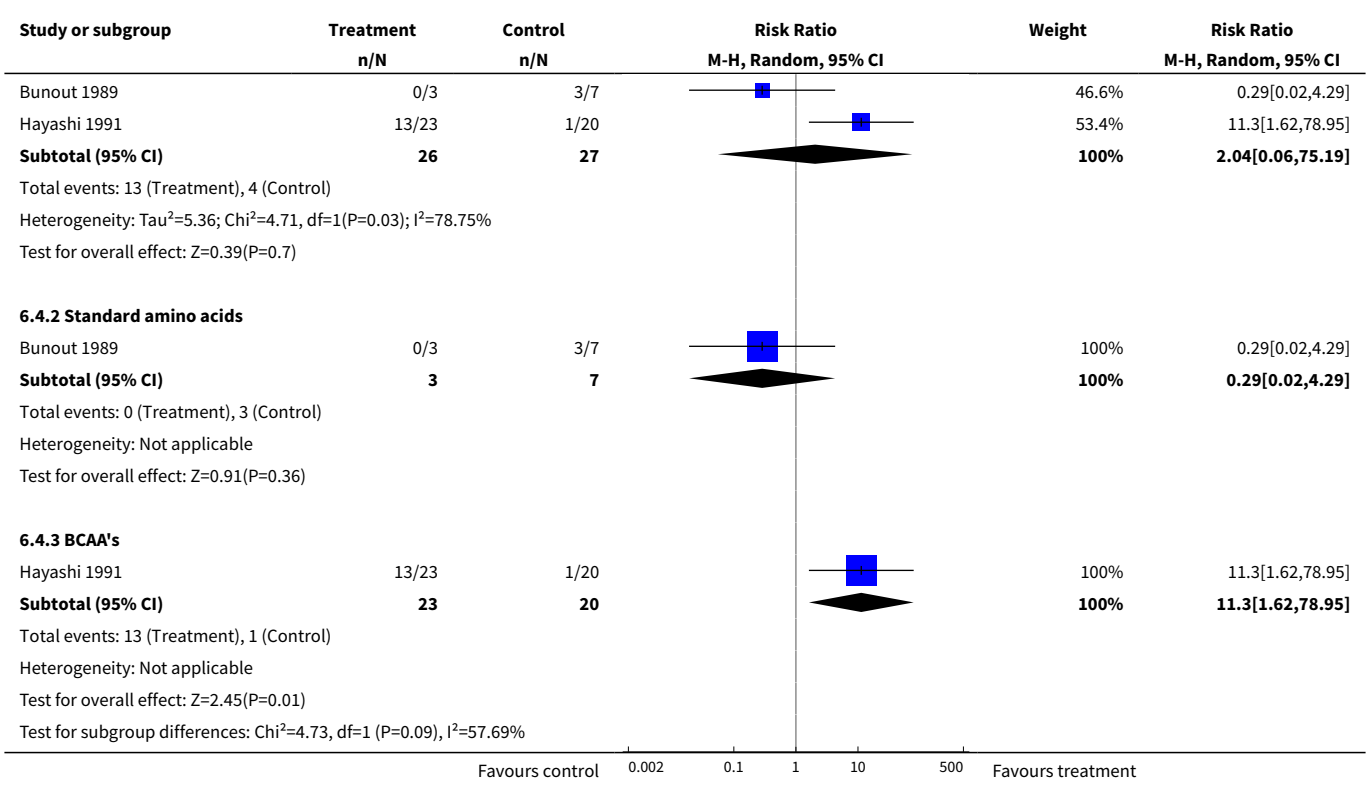


Analysis 6.3. Comparison 6 Resolution of encephalopathy, Outcome 3 Enteral nutrition (all medical trials).

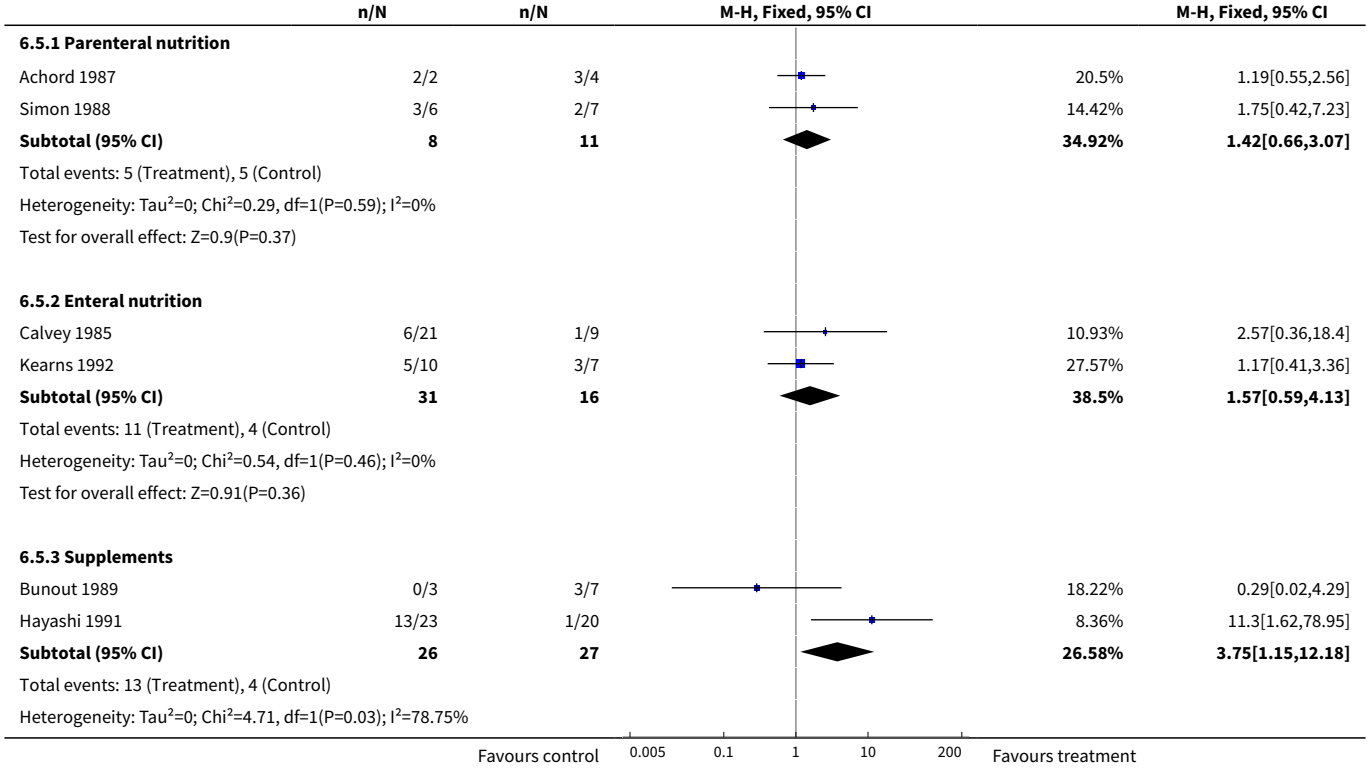


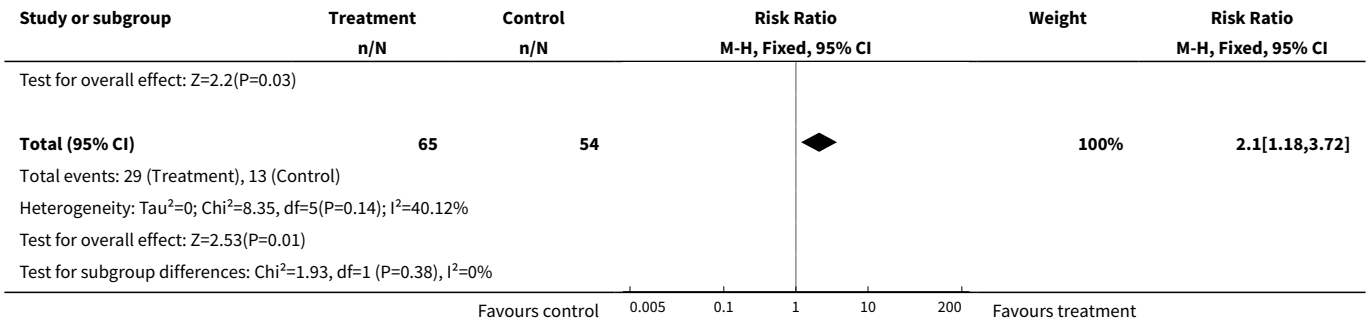
Analysis 6.4. Comparison 6 Resolution of encephalopathy, Outcome 4 Supplements (all medical trials).



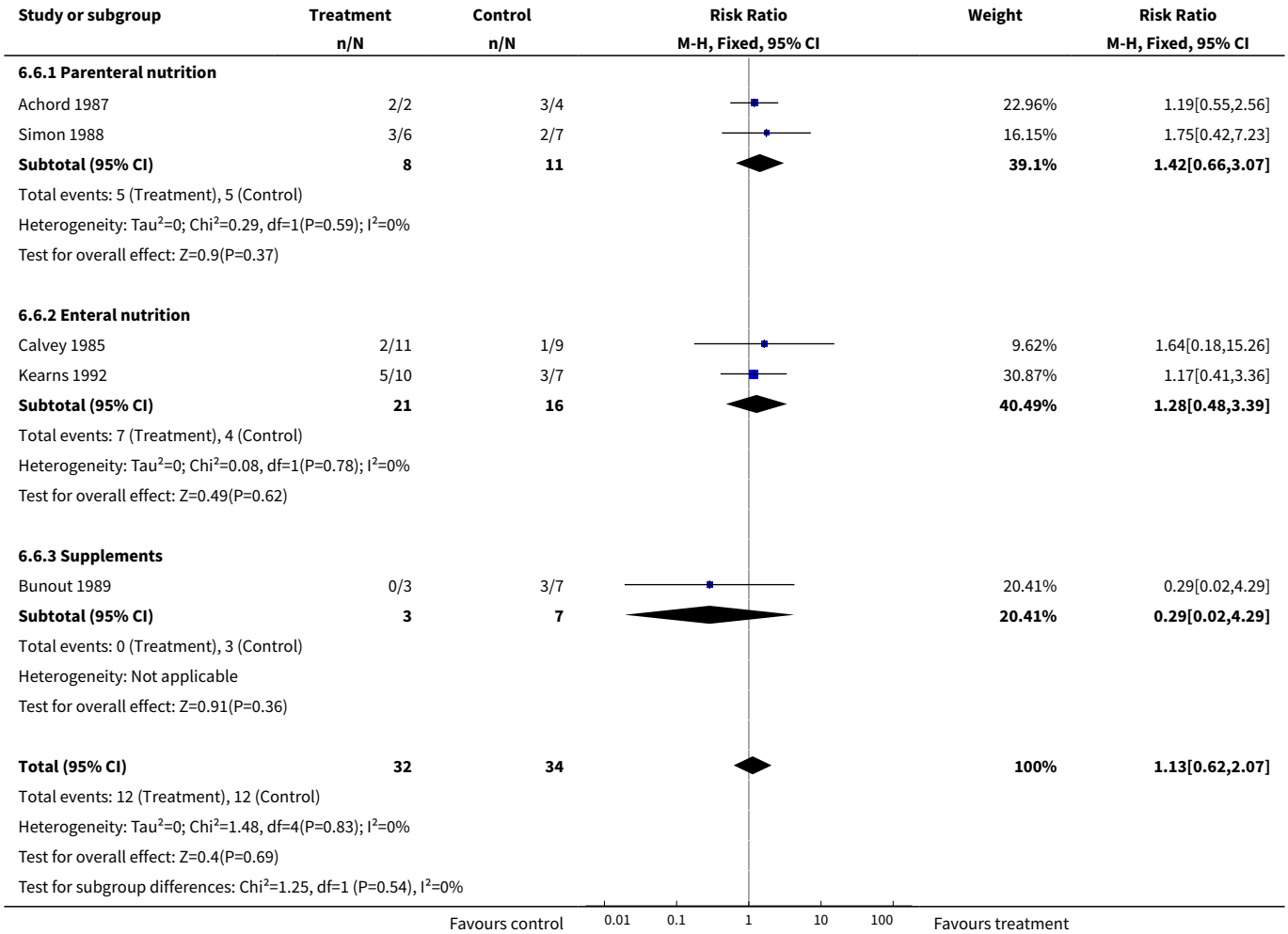


Analysis 6.5. Comparison 6 Resolution of encephalopathy, Outcome 5 Medical trials - all trials.



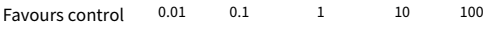


Analysis 6.6. Comparison 6 Resolution of encephalopathy, Outcome 6 Medical trials - standard amino acids.



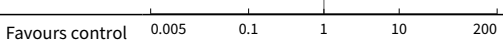
Analysis 6.7. Comparison 6 Resolution of encephalopathy, Outcome 7 Medical trials - BCAAs.

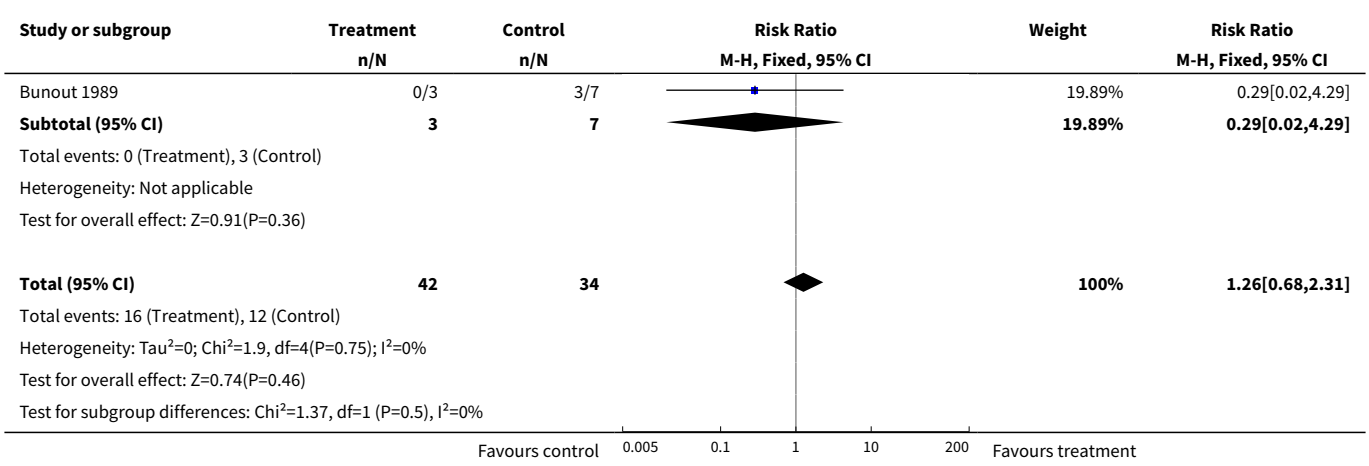
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.7.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.7.2 Enteral nutrition					
Calvey 1985	4/10	1/9		49.6%	3.6[0.49,26.54]
Subtotal (95% CI)	**10**	**9**		**49.6%**	**3.6[0.49,26.54]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.26(P=0.21)					
6.7.3 Supplements					
Hayashi 1991	13/23	1/20		50.4%	11.3[1.62,78.95]
Subtotal (95% CI)	**23**	**20**		**50.4%**	**11.3[1.62,78.95]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.45(P=0.01)					
Total (95% CI)	**33**	**29**		**100%**	**7.48[1.87,29.94]**
Total events: 17 (Treatment), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.69, df=1(P=0.41); I^2=0%					
Test for overall effect: Z=2.85(P=0)					
Test for subgroup differences: Chi^2=0.65, df=1 (P=0.42), I^2=0%					



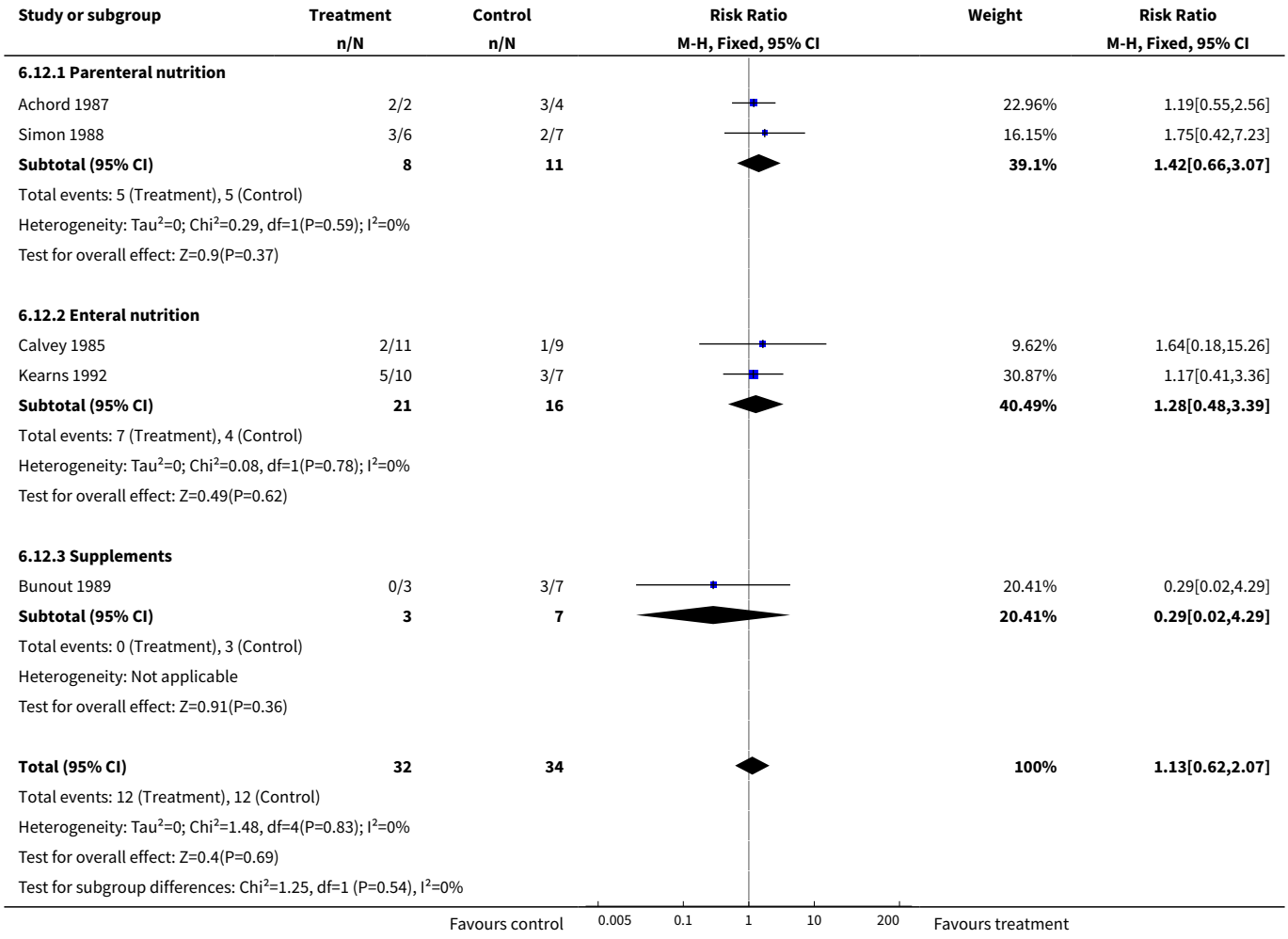
Analysis 6.11. Comparison 6 Resolution of encephalopathy, Outcome 11 Alcoholic hepatitis - all trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.11.1 Parenteral nutrition					
Achord 1987	2/2	3/4		22.37%	1.19[0.55,2.56]
Simon 1988	3/6	2/7		15.73%	1.75[0.42,7.23]
Subtotal (95% CI)	**8**	**11**		**38.1%**	**1.42[0.66,3.07]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.29, df=1(P=0.59); I^2=0%					
Test for overall effect: Z=0.9(P=0.37)					
6.11.2 Enteral nutrition					
Calvey 1985	6/21	1/9		11.93%	2.57[0.36,18.4]
Kearns 1992	5/10	3/7		30.08%	1.17[0.41,3.36]
Subtotal (95% CI)	**31**	**16**		**42.01%**	**1.57[0.59,4.13]**
Total events: 11 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.54, df=1(P=0.46); I^2=0%					
Test for overall effect: Z=0.91(P=0.36)					
6.11.3 Supplements					





Analysis 6.12. Comparison 6 Resolution of encephalopathy, Outcome 12 Alcoholic hepatitis - standard amino acids.

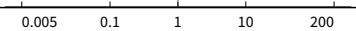


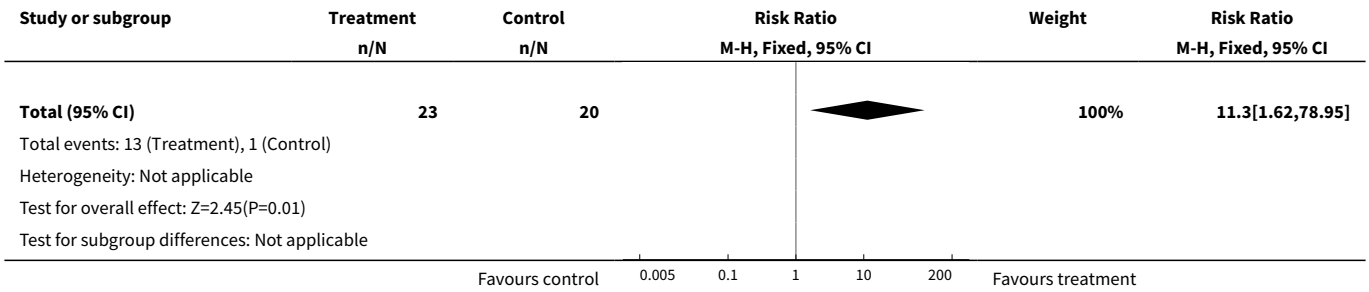
Analysis 6.13. Comparison 6 Resolution of encephalopathy, Outcome 13 Alcoholic hepatitis - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.13.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.13.2 Enteral nutrition					
Calvey 1985	4/10	1/9		100%	3.6[0.49,26.54]
Subtotal (95% CI)	**10**	**9**		**100%**	**3.6[0.49,26.54]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.26(P=0.21)					
6.13.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**10**	**9**		**100%**	**3.6[0.49,26.54]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.26(P=0.21)					
Test for subgroup differences: Not applicable					

Analysis 6.14. Comparison 6 Resolution of encephalopathy, Outcome 14 Cirrhosis - all.

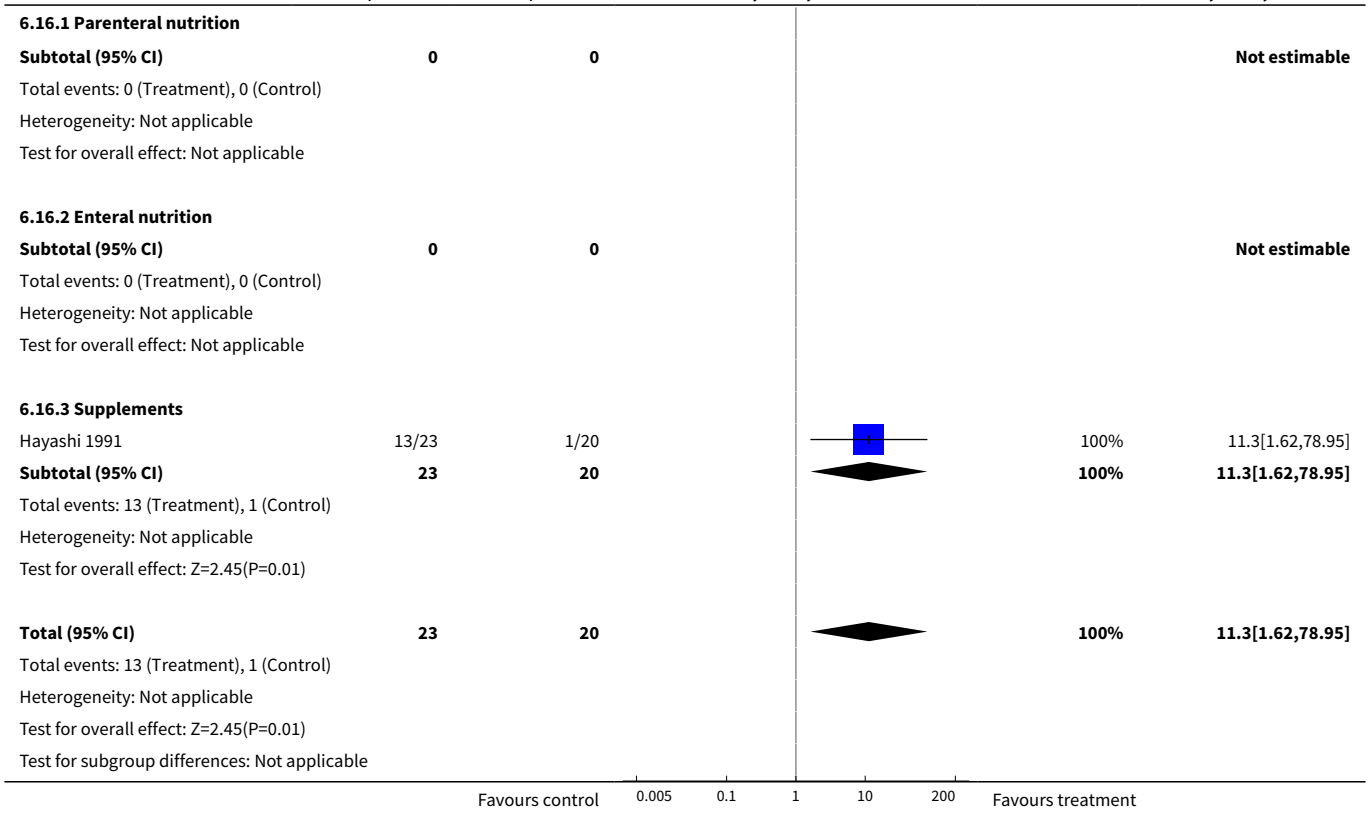
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.14.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.14.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.14.3 Supplements					
Hayashi 1991	13/23	1/20		100%	11.3[1.62,78.95]
Subtotal (95% CI)	**23**	**20**		**100%**	**11.3[1.62,78.95]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.45(P=0.01)					





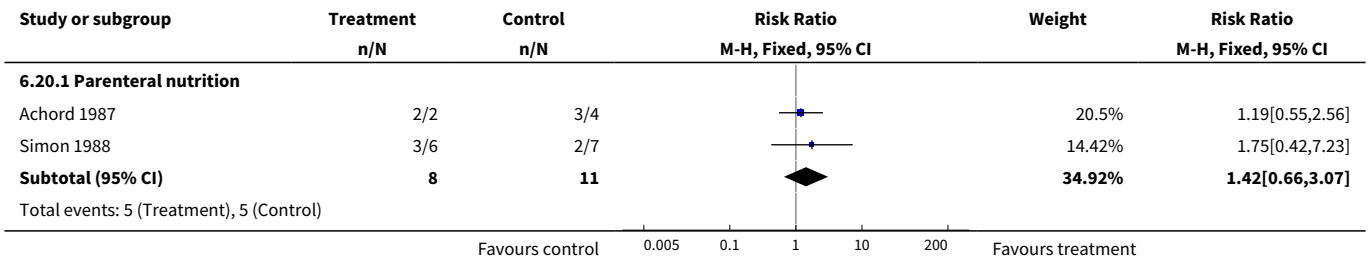
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)	**23**	**20**		**100%**	**11.3[1.62,78.95]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.45(P=0.01)					
Test for subgroup differences: Not applicable					

Analysis 6.16. Comparison 6 Resolution of encephalopathy, Outcome 16 Cirrhosis - BCAAs.

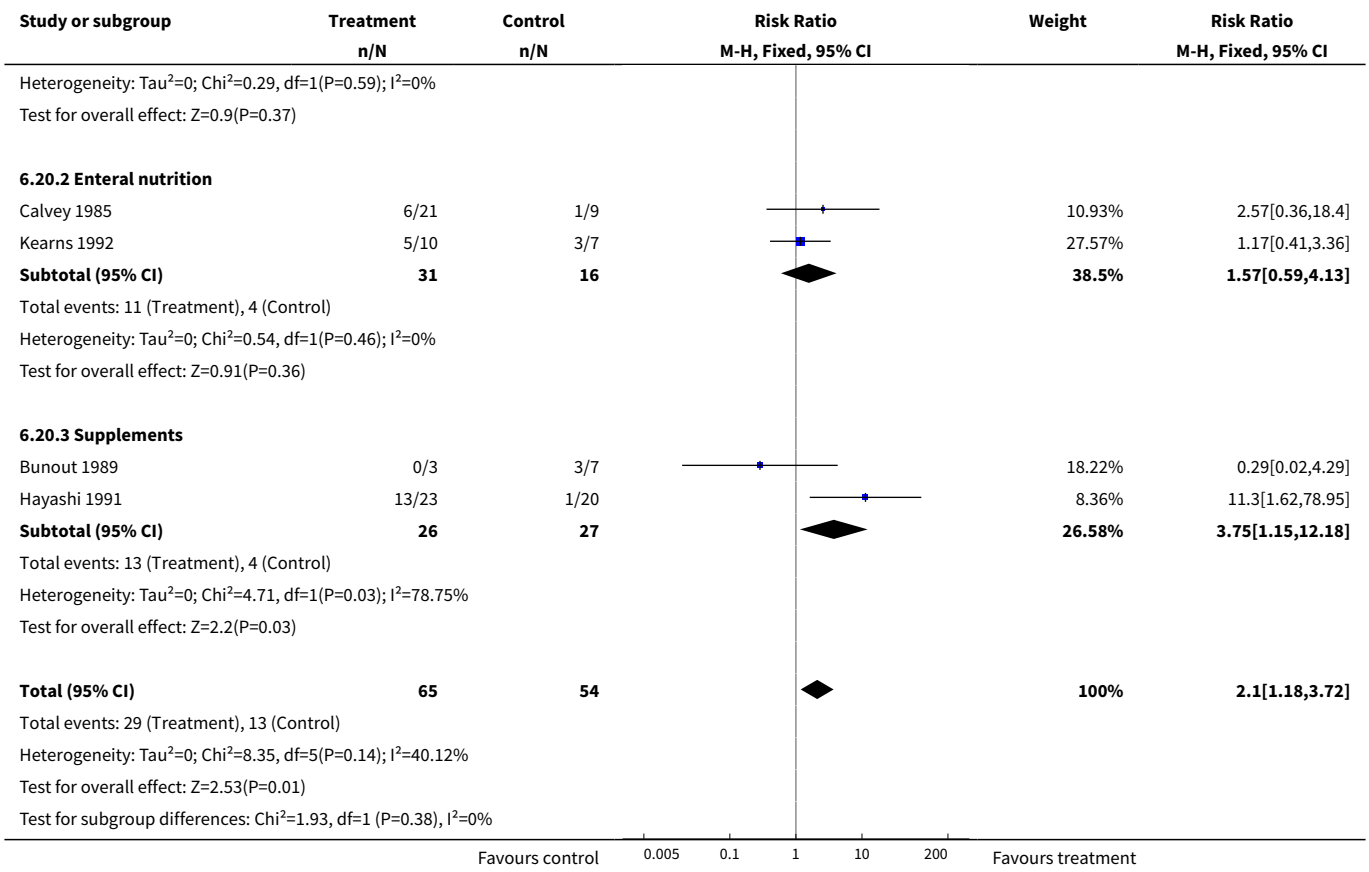


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.16.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.16.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
6.16.3 Supplements					
Hayashi 1991	13/23	1/20		100%	11.3[1.62,78.95]
Subtotal (95% CI)	**23**	**20**		**100%**	**11.3[1.62,78.95]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.45(P=0.01)					
Total (95% CI)	**23**	**20**		**100%**	**11.3[1.62,78.95]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.45(P=0.01)					
Test for subgroup differences: Not applicable					

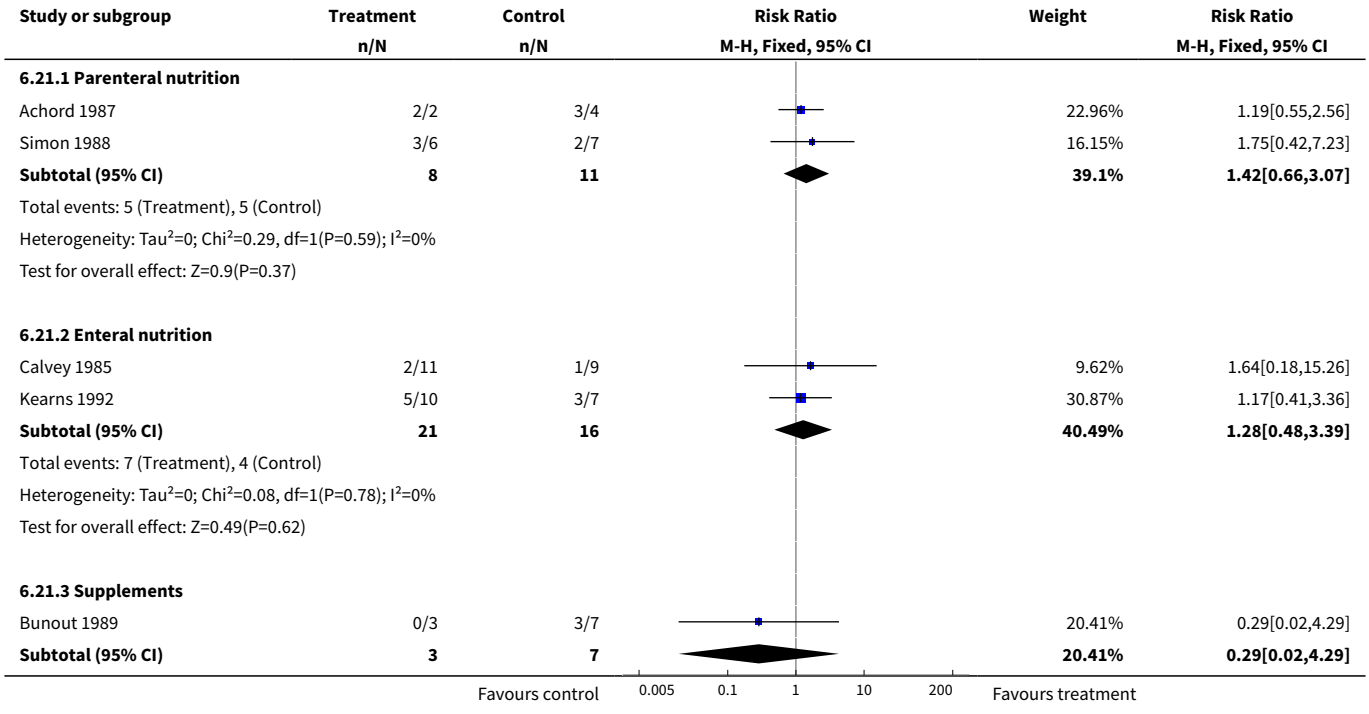
Analysis 6.20. Comparison 6 Resolution of encephalopathy, Outcome 20 Abstracts excluded - all trials.

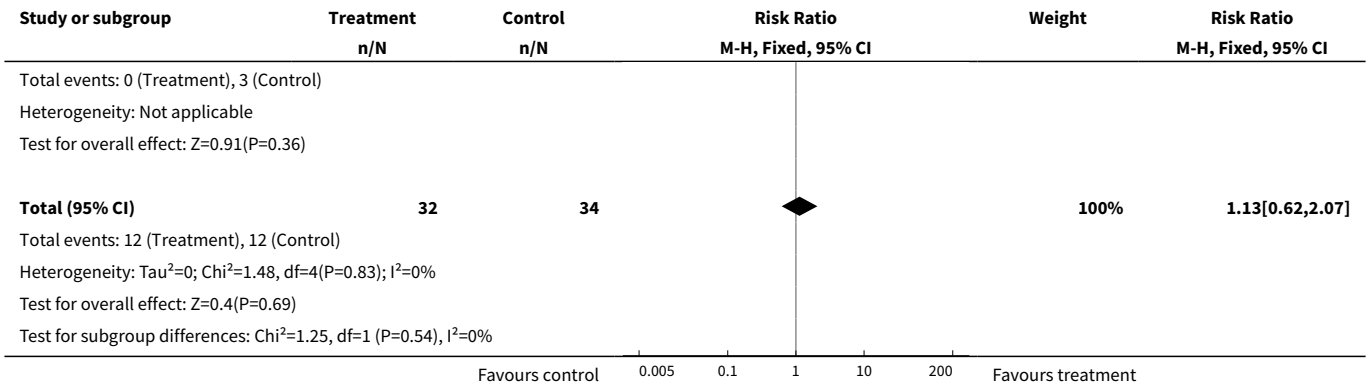


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.20.1 Parenteral nutrition					
Achord 1987	2/2	3/4		20.5%	1.19[0.55,2.56]
Simon 1988	3/6	2/7		14.42%	1.75[0.42,7.23]
Subtotal (95% CI)	**8**	**11**		**34.92%**	**1.42[0.66,3.07]**
Total events: 5 (Treatment), 5 (Control)					

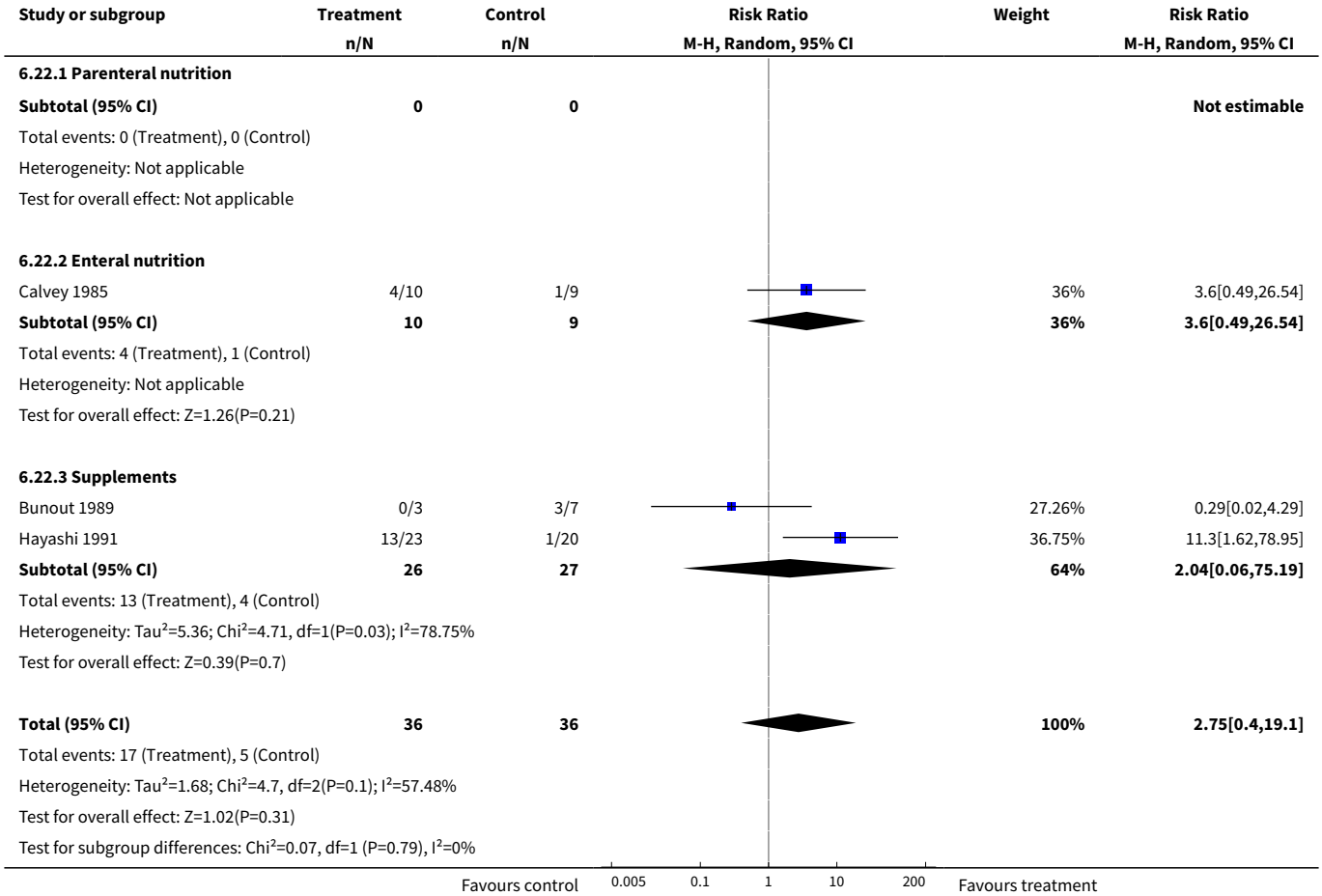


Analysis 6.21. Comparison 6 Resolution of encephalopathy, Outcome 21 Abstracts excluded - standard amino acids.



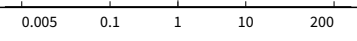


Analysis 6.22. Comparison 6 Resolution of encephalopathy, Outcome 22 Abstracts excluded - BCAAs.



Analysis 6.24. Comparison 6 Resolution of encephalopathy, Outcome 24 ITT - All trials - best-case scenario - no changes made because all patients reported.

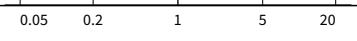
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.24.1 All studies					
Achord 1987	2/2	3/4		20.5%	1.19[0.55,2.56]
Bunout 1989	0/3	3/7		18.22%	0.29[0.02,4.29]
Calvey 1985	6/21	1/9		10.93%	2.57[0.36,18.4]
Hayashi 1991	13/23	1/20		8.36%	11.3[1.62,78.95]
Kearns 1992	5/10	3/7		27.57%	1.17[0.41,3.36]
Simon 1988	3/6	2/7		14.42%	1.75[0.42,7.23]
Subtotal (95% CI)	**65**	**54**		**100%**	**2.1[1.18,3.72]**
Total events: 29 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=8.35, df=5(P=0.14); I^2=40.12%					
Test for overall effect: Z=2.53(P=0.01)					
6.24.2 Standard amino acids					
Achord 1987	2/2	3/4		22.96%	1.19[0.55,2.56]
Bunout 1989	0/3	3/7		20.41%	0.29[0.02,4.29]
Calvey 1985	2/11	1/9		9.62%	1.64[0.18,15.26]
Kearns 1992	5/10	3/7		30.87%	1.17[0.41,3.36]
Simon 1988	3/6	2/7		16.15%	1.75[0.42,7.23]
Subtotal (95% CI)	**32**	**34**		**100%**	**1.13[0.62,2.07]**
Total events: 12 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.48, df=4(P=0.83); I^2=0%					
Test for overall effect: Z=0.4(P=0.69)					
6.24.3 BCAA's					
Calvey 1985	4/10	1/9		49.6%	3.6[0.49,26.54]
Hayashi 1991	13/23	1/20		50.4%	11.3[1.62,78.95]
Subtotal (95% CI)	**33**	**29**		**100%**	**7.48[1.87,29.94]**
Total events: 17 (Treatment), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.69, df=1(P=0.41); I^2=0%					
Test for overall effect: Z=2.85(P=0)					
Test for subgroup differences: Chi^2=6.58, df=1 (P=0.04), I^2=69.6%					



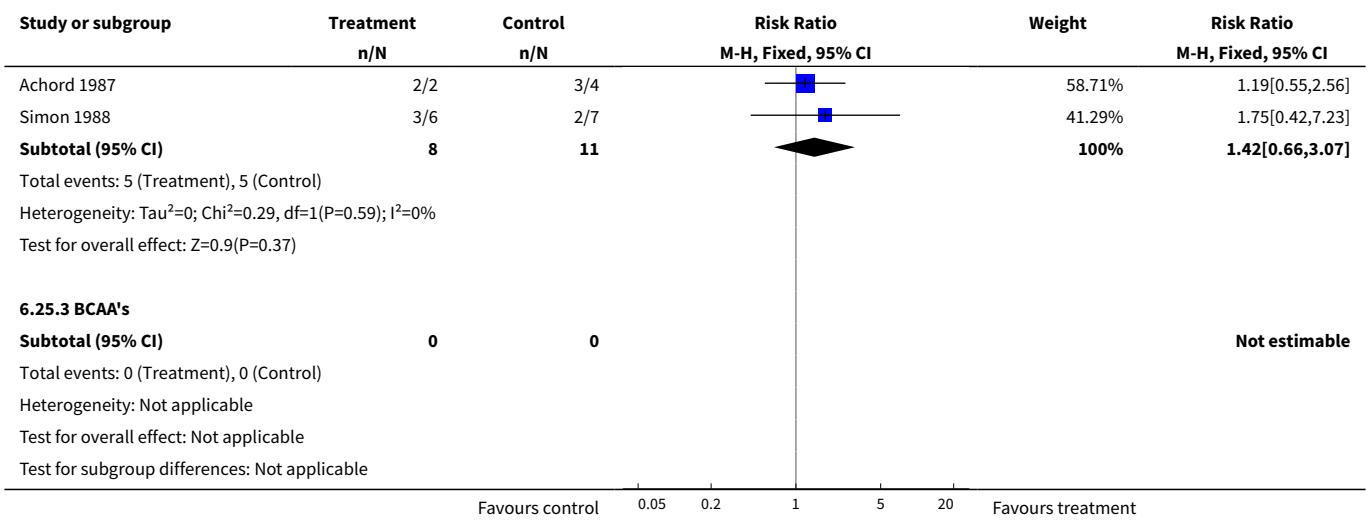
Favours control — Favours treatment

Analysis 6.25. Comparison 6 Resolution of encephalopathy, Outcome 25 ITT - Parenteral nutrition trials - best-case scenario - no changes made because all patients reported.

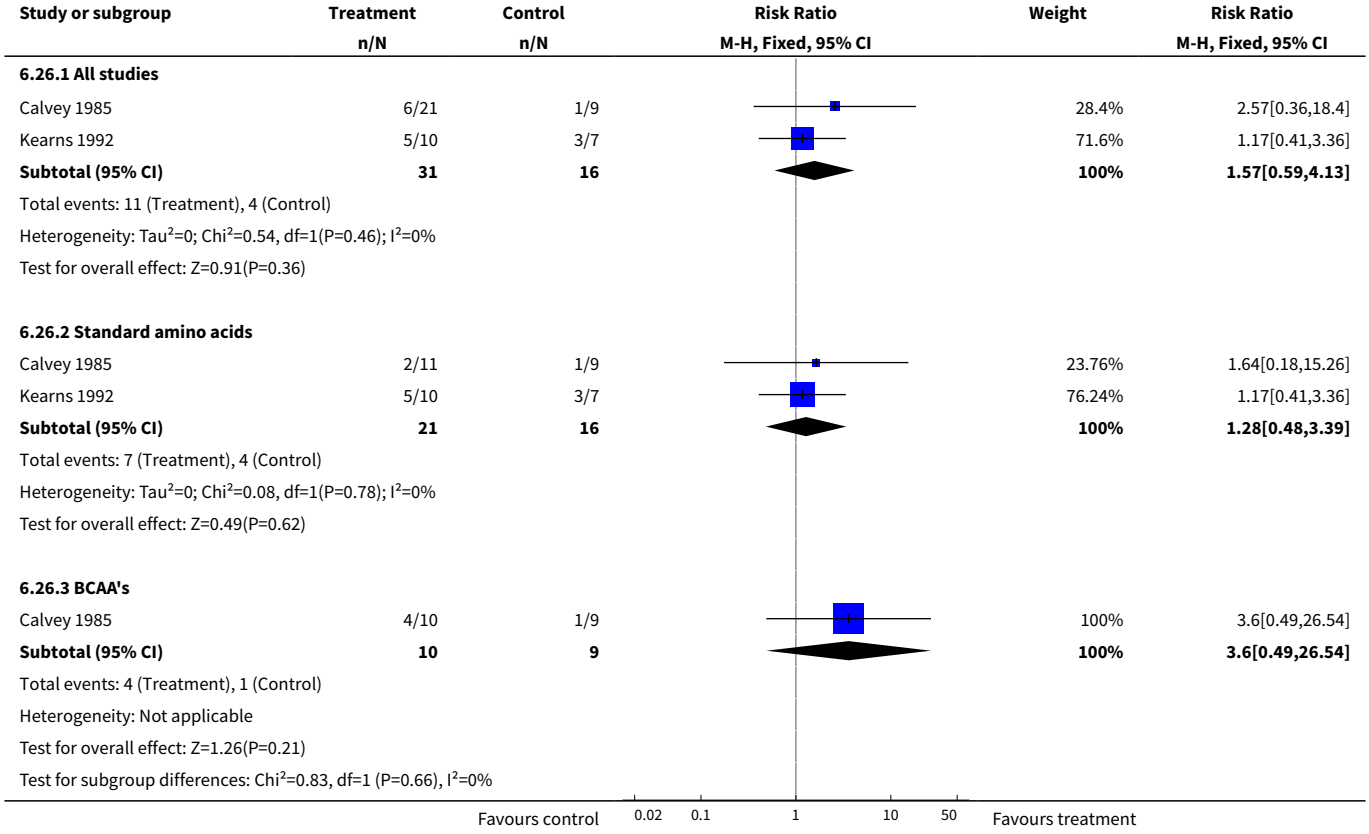
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.25.1 All studies					
Achord 1987	2/2	3/4		58.71%	1.19[0.55,2.56]
Simon 1988	3/6	2/7		41.29%	1.75[0.42,7.23]
Subtotal (95% CI)	**8**	**11**		**100%**	**1.42[0.66,3.07]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.29, df=1(P=0.59); I^2=0%					
Test for overall effect: Z=0.9(P=0.37)					
6.25.2 Standard amino acids					



Favours control — Favours treatment

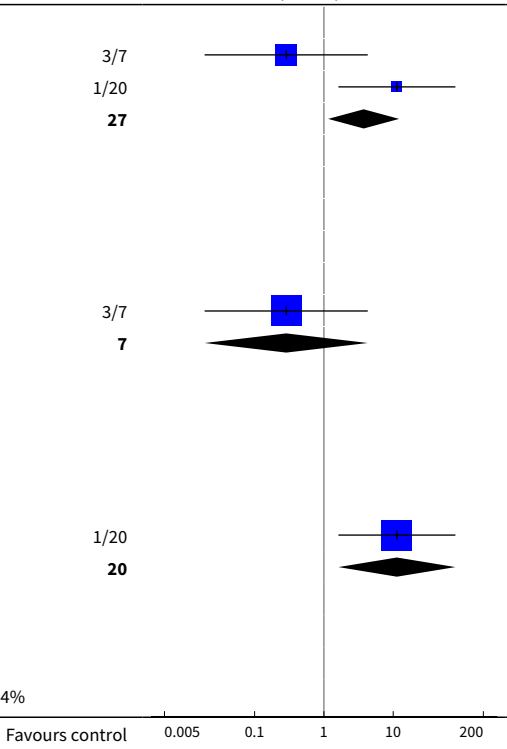


Analysis 6.26. Comparison 6 Resolution of encephalopathy, Outcome 26 ITT - Enteral trials - best-case scenario - no changes made because all patients reported.



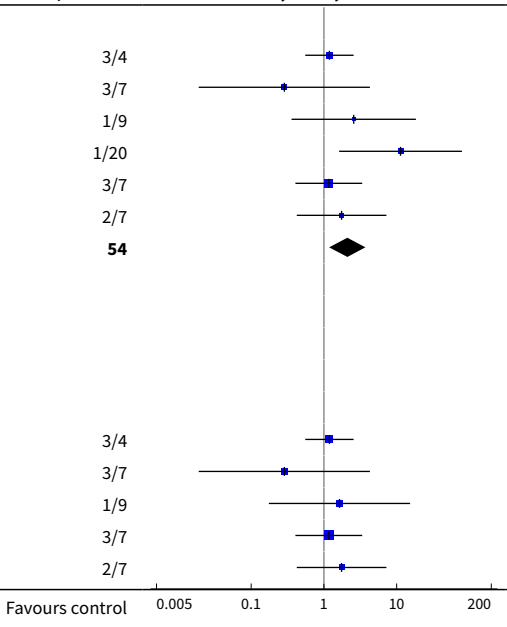
Analysis 6.27. Comparison 6 Resolution of encephalopathy, Outcome 27 ITT - Supplements trials - best-case scenario - no changes made because all patients reported.

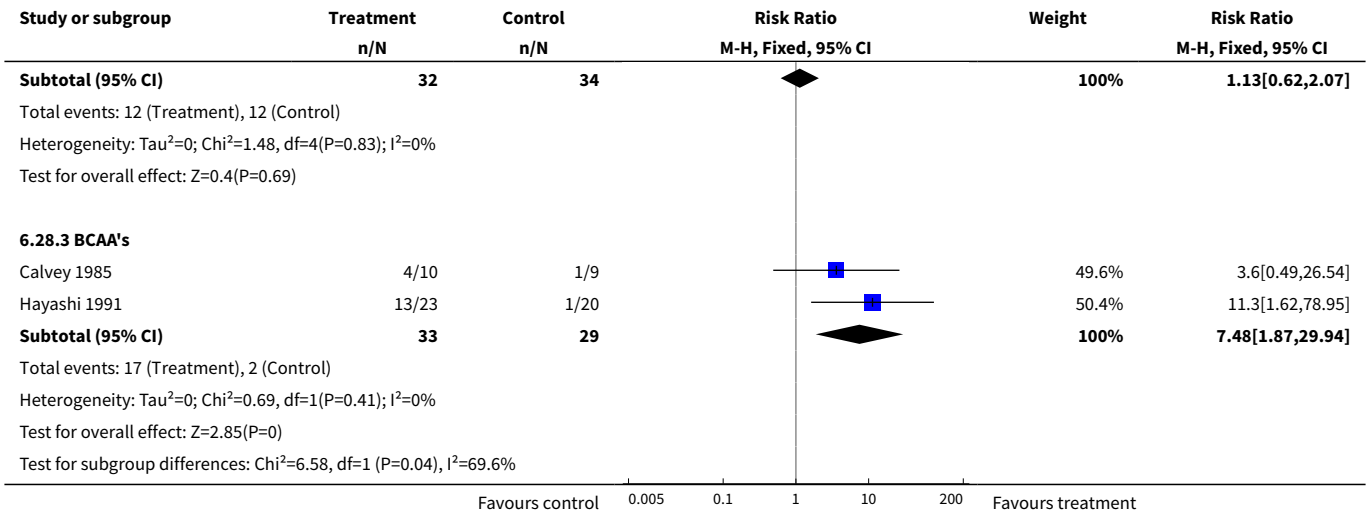
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.27.1 All studies					
Bunout 1989	0/3	3/7		68.56%	0.29[0.02,4.29]
Hayashi 1991	13/23	1/20		31.44%	11.3[1.62,78.95]
Subtotal (95% CI)	**26**	**27**		**100%**	**3.75[1.15,12.18]**
Total events: 13 (Treatment), 4 (Control)					
Heterogeneity: Tau²=0; Chi²=4.71, df=1(P=0.03); I²=78.75%					
Test for overall effect: Z=2.2(P=0.03)					
6.27.2 Standard amino acids					
Bunout 1989	0/3	3/7		100%	0.29[0.02,4.29]
Subtotal (95% CI)	**3**	**7**		**100%**	**0.29[0.02,4.29]**
Total events: 0 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.91(P=0.36)					
6.27.3 BCAA's					
Hayashi 1991	13/23	1/20		100%	11.3[1.62,78.95]
Subtotal (95% CI)	**23**	**20**		**100%**	**11.3[1.62,78.95]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.45(P=0.01)					
Test for subgroup differences: Chi²=4.7, df=1 (P=0.1), I²=57.4%					



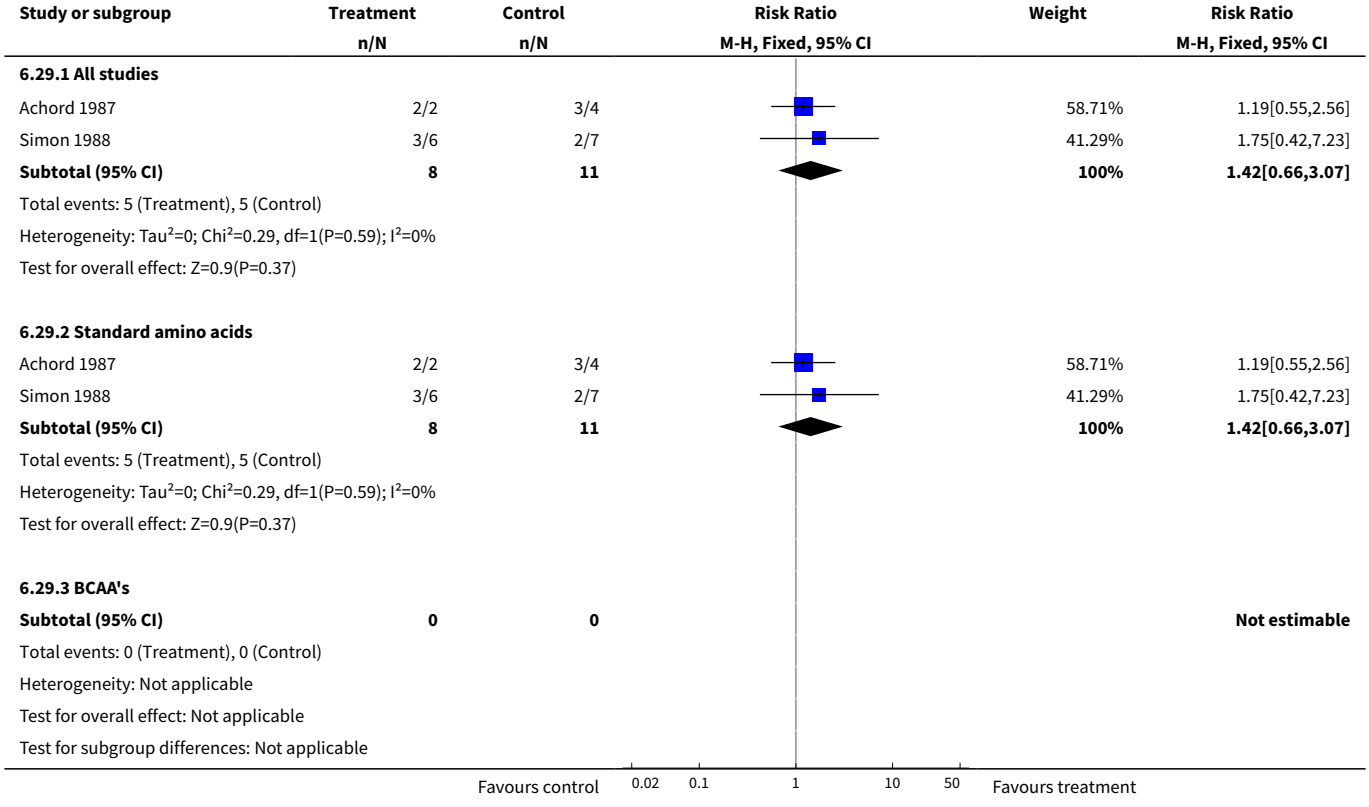
Analysis 6.28. Comparison 6 Resolution of encephalopathy, Outcome 28 ITT - All trials - worst-case scenario - no changes made because all patients reported.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.28.1 All studies					
Achord 1987	2/2	3/4		20.5%	1.19[0.55,2.56]
Bunout 1989	0/3	3/7		18.22%	0.29[0.02,4.29]
Calvey 1985	6/21	1/9		10.93%	2.57[0.36,18.4]
Hayashi 1991	13/23	1/20		8.36%	11.3[1.62,78.95]
Kearns 1992	5/10	3/7		27.57%	1.17[0.41,3.36]
Simon 1988	3/6	2/7		14.42%	1.75[0.42,7.23]
Subtotal (95% CI)	**65**	**54**		**100%**	**2.1[1.18,3.72]**
Total events: 29 (Treatment), 13 (Control)					
Heterogeneity: Tau²=0; Chi²=8.35, df=5(P=0.14); I²=40.12%					
Test for overall effect: Z=2.53(P=0.01)					
6.28.2 Standard amino acids					
Achord 1987	2/2	3/4		22.96%	1.19[0.55,2.56]
Bunout 1989	0/3	3/7		20.41%	0.29[0.02,4.29]
Calvey 1985	2/11	1/9		9.62%	1.64[0.18,15.26]
Kearns 1992	5/10	3/7		30.87%	1.17[0.41,3.36]
Simon 1988	3/6	2/7		16.15%	1.75[0.42,7.23]



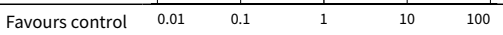


Analysis 6.29. Comparison 6 Resolution of encephalopathy, Outcome 29 ITT - Parenteral nutrition trials - worst-case scenario - no changes made because all patients reported.



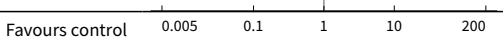
Analysis 6.30. Comparison 6 Resolution of encephalopathy, Outcome 30 ITT - Enteral nutrition trials - worst-case scenario - no changes made because all patients reported.

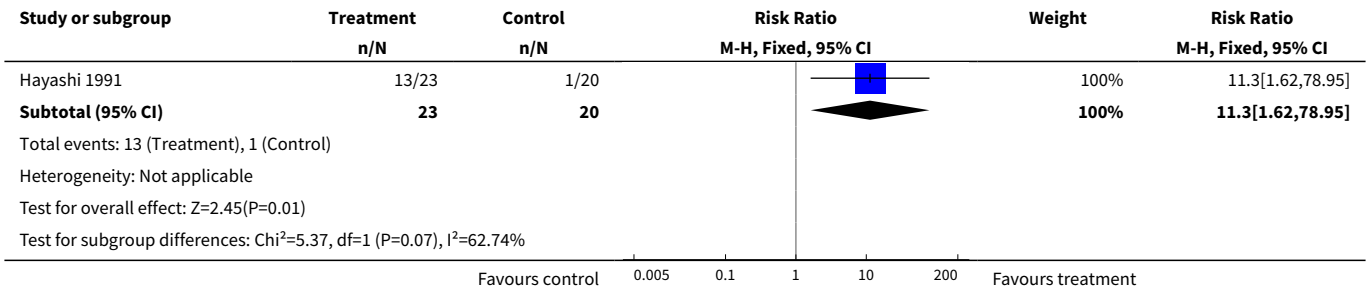
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.30.1 All studies					
Calvey 1985	6/21	1/9		28.4%	2.57[0.36,18.4]
Kearns 1992	5/10	3/7		71.6%	1.17[0.41,3.36]
Subtotal (95% CI)	**31**	**16**		**100%**	**1.57[0.59,4.13]**
Total events: 11 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.54, df=1(P=0.46); I^2=0%					
Test for overall effect: Z=0.91(P=0.36)					
6.30.2 Standard amino acids					
Calvey 1985	2/11	1/9		23.76%	1.64[0.18,15.26]
Kearns 1992	5/10	3/7		76.24%	1.17[0.41,3.36]
Subtotal (95% CI)	**21**	**16**		**100%**	**1.28[0.48,3.39]**
Total events: 7 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.08, df=1(P=0.78); I^2=0%					
Test for overall effect: Z=0.49(P=0.62)					
6.30.3 BCAA's					
Calvey 1985	4/10	1/9		100%	3.6[0.49,26.54]
Subtotal (95% CI)	**10**	**9**		**100%**	**3.6[0.49,26.54]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.26(P=0.21)					
Test for subgroup differences: Chi^2=0.83, df=1 (P=0.66), I^2=0%					



Analysis 6.31. Comparison 6 Resolution of encephalopathy, Outcome 31 ITT - Supplement trials - worst-case scenario - no changes made because all patients reported.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
6.31.1 All studies					
Bunout 1989	0/3	3/7		68.56%	0.29[0.02,4.29]
Hayashi 1991	13/23	1/20		31.44%	11.3[1.62,78.95]
Subtotal (95% CI)	**26**	**27**		**100%**	**3.75[1.15,12.18]**
Total events: 13 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.71, df=1(P=0.03); I^2=78.75%					
Test for overall effect: Z=2.2(P=0.03)					
6.31.2 Standard amino acids					
Bunout 1989	0/3	3/7		55.83%	0.29[0.02,4.29]
Simon 1988	3/6	2/7		44.17%	1.75[0.42,7.23]
Subtotal (95% CI)	**9**	**14**		**100%**	**0.93[0.28,3.09]**
Total events: 3 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.49, df=1(P=0.22); I^2=32.83%					
Test for overall effect: Z=0.11(P=0.91)					
6.31.3 BCAA's					





Comparison 7. infections

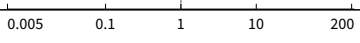
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	15	793	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.57, 0.91]
2 Trials with total numbers (Meng) excluded	14	749	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.54, 0.90]
3 Parenteral nutrition	2	164	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.37, 1.16]
3.1 Medical trials	1	40	Risk Ratio (M-H, Fixed, 95% CI)	9.0 [0.52, 156.91]
3.2 Surgical trials	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.25, 0.88]
4 Enteral nutrition	6	267	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.59, 1.09]
4.1 Medical trials	4	176	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.67, 1.30]
4.2 Surgical trials	2	91	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.22, 1.05]
5 Supplements	7	362	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.39, 1.03]
5.1 Medical trials	4	268	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.24, 0.99]
5.2 Surgical trials	3	94	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.44, 1.67]
6 Medical trials	9	484	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.63, 1.15]
7 Surgical trials	6	309	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.39, 0.85]
8 Alcoholic hepatitis	2	115	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.28, 1.13]
9 Cirrhosis	7	336	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.62, 1.17]
9.1 Parenteral nutrition	1	40	Risk Ratio (M-H, Fixed, 95% CI)	9.0 [0.52, 156.91]
9.2 Enteral nutrition	3	112	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.66, 1.31]
9.3 Supplements	3	184	Risk Ratio (M-H, Fixed, 95% CI)	0.50 [0.24, 1.03]
10 HCC	2	208	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.25, 0.86]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.25, 0.88]
10.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Supplements	1	84	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.01, 8.34]
11 Abstracts excluded	14	738	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.52, 0.93]
12 Abstracts excluded	14	738	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.52, 0.93]
12.1 Parenteral nutrition	2	164	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.37, 1.16]
12.2 Enteral nutrition	5	212	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.50, 1.24]
12.3 Supplements	7	362	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.39, 1.03]
13 Surgical trials excluding transplants	5	278	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.39, 0.90]
14 Parenteral nutrition - best-case scenario	2	190	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.24, 0.70]
14.1 Medical trials	1	40	Risk Ratio (M-H, Fixed, 95% CI)	9.0 [0.52, 156.91]
14.2 Surgical trials	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.16, 0.54]
15 Parenteral nutrition - worst-case scenario	2	190	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.73, 1.90]
15.1 Medical trials	1	40	Risk Ratio (M-H, Fixed, 95% CI)	9.0 [0.52, 156.91]
15.2 Surgical trials	1	150	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.61, 1.64]
16 Enteral nutrition - best-case scenario	6	298	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.46, 0.84]
16.1 Medical trials	4	184	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.60, 1.16]
16.2 Surgical trials	2	114	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.13, 0.60]
17 Enteral nutrition - worst-case scenario	6	298	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.85, 1.46]
17.1 Medical trials	4	184	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.76, 1.41]
17.2 Surgical trials	2	114	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.78, 2.16]
18 Supplements - best-case scenario	7	401	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.24, 0.62]
18.1 Medical trials	4	286	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.17, 0.67]
18.2 Surgical trials	3	115	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.23, 0.84]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
19 Supplements - worst-case scenario	7	401	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.77, 1.73]
19.1 Medical trials	4	286	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.55, 1.71]
19.2 Surgical trials	3	115	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [0.79, 2.55]

Analysis 7.1. Comparison 7 infections, Outcome 1 All studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		5.95%	1.19[0.53,2.67]
Calvey 1985	11/42	6/22		7.33%	0.96[0.41,2.25]
DeLedinghen 1997	2/12	1/10		1.02%	1.67[0.18,15.8]
Fan 1994	11/64	22/60		21.13%	0.47[0.25,0.88]
Foschi 1986	4/28	9/32		7.82%	0.51[0.18,1.47]
Hasse 1995	3/14	8/17		6.72%	0.46[0.15,1.4]
Hirsch 1993	2/26	9/25		8.54%	0.21[0.05,0.89]
Ishikawa 2010	2/11	3/13		2.56%	0.79[0.16,3.9]
Meng 1999	8/21	9/23		7.99%	0.97[0.46,2.05]
Mikagi 2011	0/13	1/13		1.4%	0.33[0.01,7.5]
Nakaya 2007	0/19	0/19			Not estimable
Naveau 1986	4/20	0/20		0.47%	9[0.52,156.91]
Norman 2008	16/26	22/29		19.35%	0.81[0.56,1.17]
Poon 2004	0/41	1/43		1.36%	0.35[0.01,8.34]
Sievert 1999	10/61	7/34		8.36%	0.8[0.33,1.9]
Total (95% CI)	**414**	**379**		**100%**	**0.72[0.57,0.91]**
Total events: 80 (Treatment), 105 (Control)					
Heterogeneity: Tau^2=0; Chi^2=12.58, df=13(P=0.48); I^2=0%					
Test for overall effect: Z=2.71(P=0.01)					

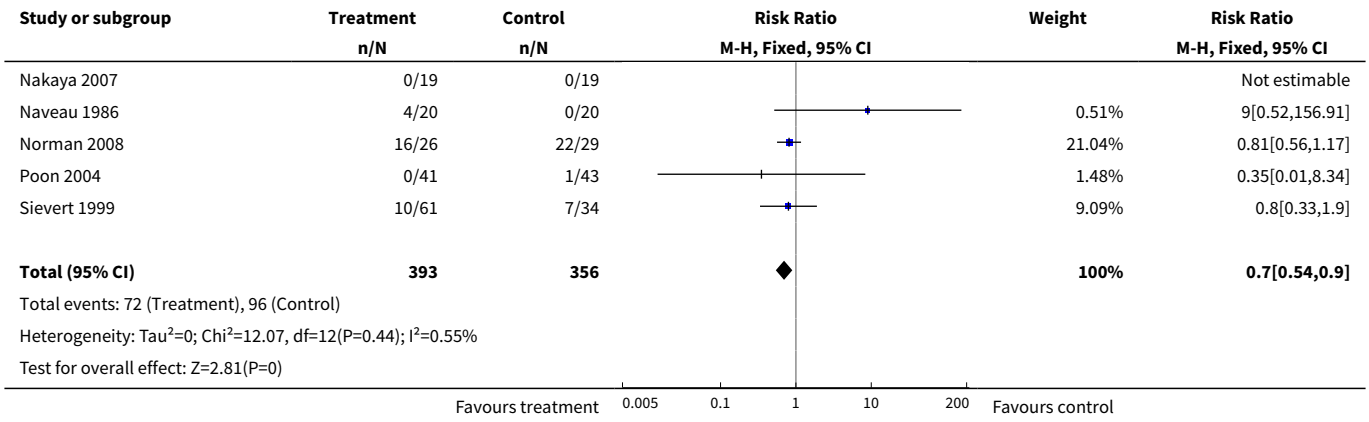


Favours treatment — Favours control

Analysis 7.2. Comparison 7 infections, Outcome 2 Trials with total numbers (Meng) excluded.

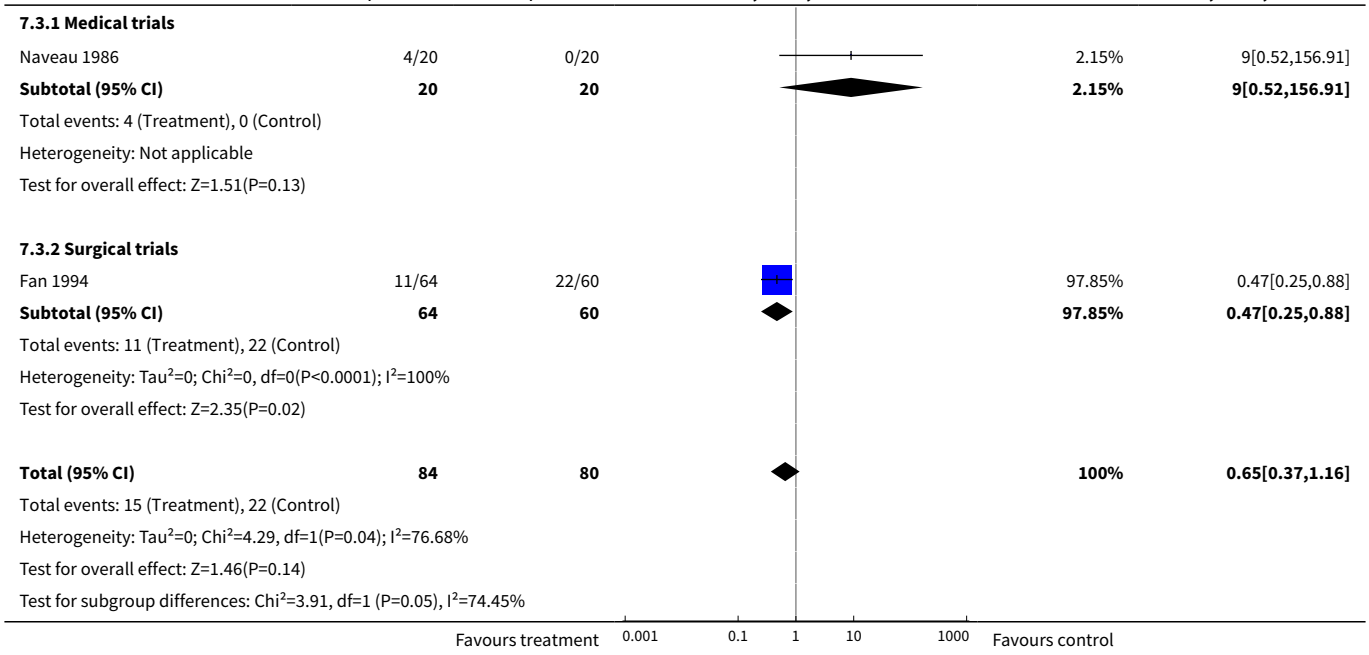
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		6.47%	1.19[0.53,2.67]
Calvey 1985	11/42	6/22		7.96%	0.96[0.41,2.25]
DeLedinghen 1997	2/12	1/10		1.1%	1.67[0.18,15.8]
Fan 1994	11/64	22/60		22.97%	0.47[0.25,0.88]
Foschi 1986	4/28	9/32		8.49%	0.51[0.18,1.47]
Hasse 1995	3/14	8/17		7.31%	0.46[0.15,1.4]
Hirsch 1993	2/26	9/25		9.28%	0.21[0.05,0.89]
Ishikawa 2010	2/11	3/13		2.78%	0.79[0.16,3.9]
Mikagi 2011	0/13	1/13		1.52%	0.33[0.01,7.5]

Favours treatment — Favours control



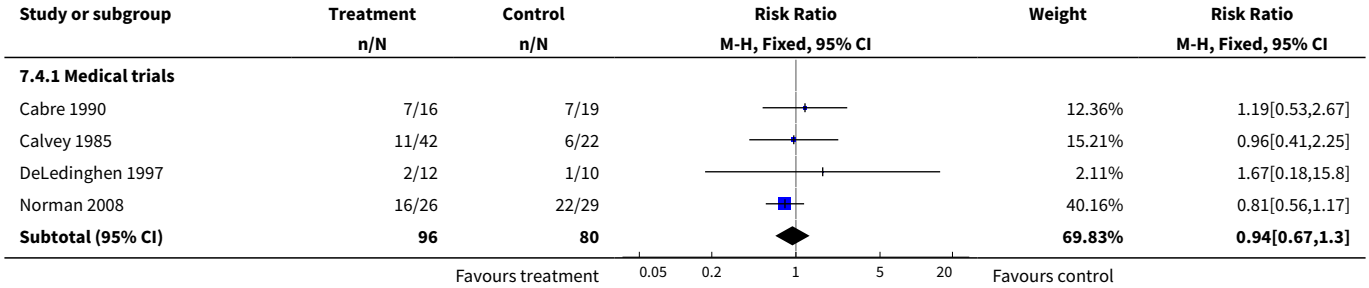
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Nakaya 2007	0/19	0/19			Not estimable
Naveau 1986	4/20	0/20		0.51%	9[0.52,156.91]
Norman 2008	16/26	22/29		21.04%	0.81[0.56,1.17]
Poon 2004	0/41	1/43		1.48%	0.35[0.01,8.34]
Sievert 1999	10/61	7/34		9.09%	0.8[0.33,1.9]
Total (95% CI)	**393**	**356**		**100%**	**0.7[0.54,0.9]**
Total events: 72 (Treatment), 96 (Control)					
Heterogeneity: Tau²=0; Chi²=12.07, df=12(P=0.44); I²=0.55%					
Test for overall effect: Z=2.81(P=0)					

Analysis 7.3. Comparison 7 infections, Outcome 3 Parenteral nutrition.

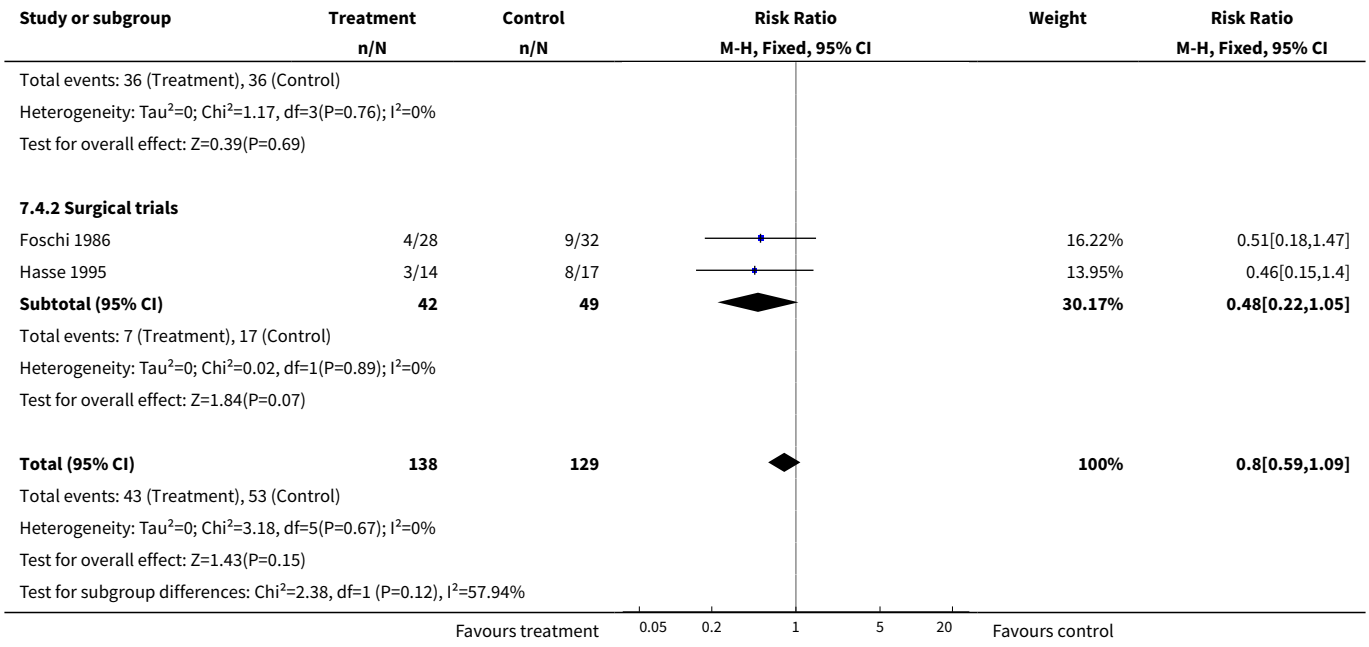


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.3.1 Medical trials					
Naveau 1986	4/20	0/20		2.15%	9[0.52,156.91]
Subtotal (95% CI)	**20**	**20**		**2.15%**	**9[0.52,156.91]**
Total events: 4 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.51(P=0.13)					
7.3.2 Surgical trials					
Fan 1994	11/64	22/60		97.85%	0.47[0.25,0.88]
Subtotal (95% CI)	**64**	**60**		**97.85%**	**0.47[0.25,0.88]**
Total events: 11 (Treatment), 22 (Control)					
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%					
Test for overall effect: Z=2.35(P=0.02)					
Total (95% CI)	**84**	**80**		**100%**	**0.65[0.37,1.16]**
Total events: 15 (Treatment), 22 (Control)					
Heterogeneity: Tau²=0; Chi²=4.29, df=1(P=0.04); I²=76.68%					
Test for overall effect: Z=1.46(P=0.14)					
Test for subgroup differences: Chi²=3.91, df=1 (P=0.05), I²=74.45%					

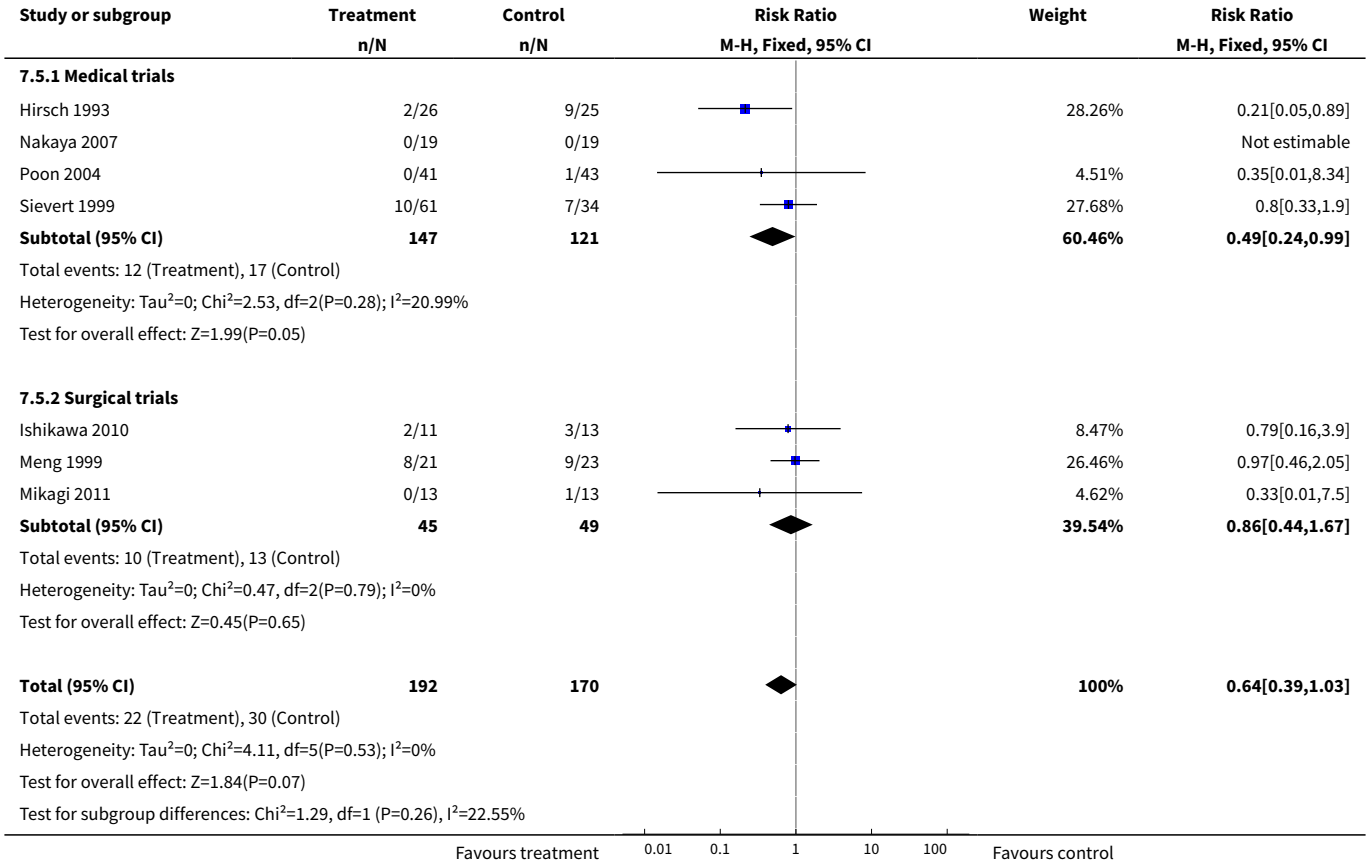
Analysis 7.4. Comparison 7 infections, Outcome 4 Enteral nutrition.



Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.4.1 Medical trials					
Cabre 1990	7/16	7/19		12.36%	1.19[0.53,2.67]
Calvey 1985	11/42	6/22		15.21%	0.96[0.41,2.25]
DeLedinghen 1997	2/12	1/10		2.11%	1.67[0.18,15.8]
Norman 2008	16/26	22/29		40.16%	0.81[0.56,1.17]
Subtotal (95% CI)	**96**	**80**		**69.83%**	**0.94[0.67,1.3]**

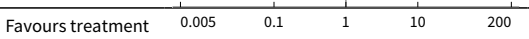


Analysis 7.5. Comparison 7 infections, Outcome 5 Supplements.



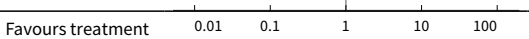
Analysis 7.6. Comparison 7 infections, Outcome 6 Medical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		11.37%	1.19[0.53,2.67]
Calvey 1985	11/42	6/22		13.99%	0.96[0.41,2.25]
DeLedinghen 1997	2/12	1/10		1.94%	1.67[0.18,15.8]
Hirsch 1993	2/26	9/25		16.3%	0.21[0.05,0.89]
Nakaya 2007	0/19	0/19			Not estimable
Naveau 1986	4/20	0/20		0.89%	9[0.52,156.91]
Norman 2008	16/26	22/29		36.95%	0.81[0.56,1.17]
Poon 2004	0/41	1/43		2.6%	0.35[0.01,8.34]
Sievert 1999	10/61	7/34		15.97%	0.8[0.33,1.9]
Total (95% CI)	**263**	**221**		**100%**	**0.85[0.63,1.15]**
Total events: 52 (Treatment), 53 (Control)					
Heterogeneity: Tau^2=0; Chi^2=7.66, df=7(P=0.36); I^2=8.67%					
Test for overall effect: Z=1.04(P=0.3)					



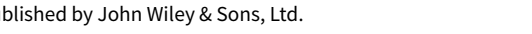
Analysis 7.7. Comparison 7 infections, Outcome 7 Surgical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Fan 1994	11/64	22/60		44.38%	0.47[0.25,0.88]
Foschi 1986	4/28	9/32		16.41%	0.51[0.18,1.47]
Hasse 1995	3/14	8/17		14.12%	0.46[0.15,1.4]
Ishikawa 2010	2/11	3/13		5.37%	0.79[0.16,3.9]
Meng 1999	8/21	9/23		16.79%	0.97[0.46,2.05]
Mikagi 2011	0/13	1/13		2.93%	0.33[0.01,7.5]
Total (95% CI)	**151**	**158**		**100%**	**0.57[0.39,0.85]**
Total events: 28 (Treatment), 52 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.81, df=5(P=0.73); I^2=0%					
Test for overall effect: Z=2.8(P=0.01)					



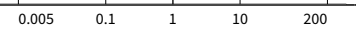
Analysis 7.8. Comparison 7 infections, Outcome 8 Alcoholic hepatitis.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Calvey 1985	11/42	6/22		46.18%	0.96[0.41,2.25]
Hirsch 1993	2/26	9/25		53.82%	0.21[0.05,0.89]
Total (95% CI)	**68**	**47**		**100%**	**0.56[0.28,1.13]**
Total events: 13 (Treatment), 15 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.29, df=1(P=0.07); I^2=69.63%					
Test for overall effect: Z=1.63(P=0.1)					



Analysis 7.9. Comparison 7 infections, Outcome 9 Cirrhosis.

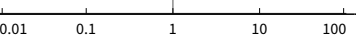
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.9.1 Parenteral nutrition					
Naveau 1986	4/20	0/20		1.06%	9[0.52,156.91]
Subtotal (95% CI)	**20**	**20**		**1.06%**	**9[0.52,156.91]**
Total events: 4 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.51(P=0.13)					
7.9.2 Enteral nutrition					
Cabre 1990	7/16	7/19		13.63%	1.19[0.53,2.67]
DeLedinghen 1997	2/12	1/10		2.32%	1.67[0.18,15.8]
Norman 2008	16/26	22/29		44.3%	0.81[0.56,1.17]
Subtotal (95% CI)	**54**	**58**		**60.25%**	**0.93[0.66,1.31]**
Total events: 25 (Treatment), 30 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.14, df=2(P=0.57); I^2=0%					
Test for overall effect: Z=0.42(P=0.68)					
7.9.3 Supplements					
Hirsch 1993	2/26	9/25		19.54%	0.21[0.05,0.89]
Nakaya 2007	0/19	0/19			Not estimable
Sievert 1999	10/61	7/34		19.14%	0.8[0.33,1.9]
Subtotal (95% CI)	**106**	**78**		**38.69%**	**0.5[0.24,1.03]**
Total events: 12 (Treatment), 16 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.45, df=1(P=0.12); I^2=59.18%					
Test for overall effect: Z=1.88(P=0.06)					
Total (95% CI)	**180**	**156**		**100%**	**0.85[0.62,1.17]**
Total events: 41 (Treatment), 46 (Control)					
Heterogeneity: Tau^2=0; Chi^2=7.28, df=5(P=0.2); I^2=31.33%					
Test for overall effect: Z=0.99(P=0.32)					
Test for subgroup differences: Chi^2=4.94, df=1 (P=0.08), I^2=59.49%					



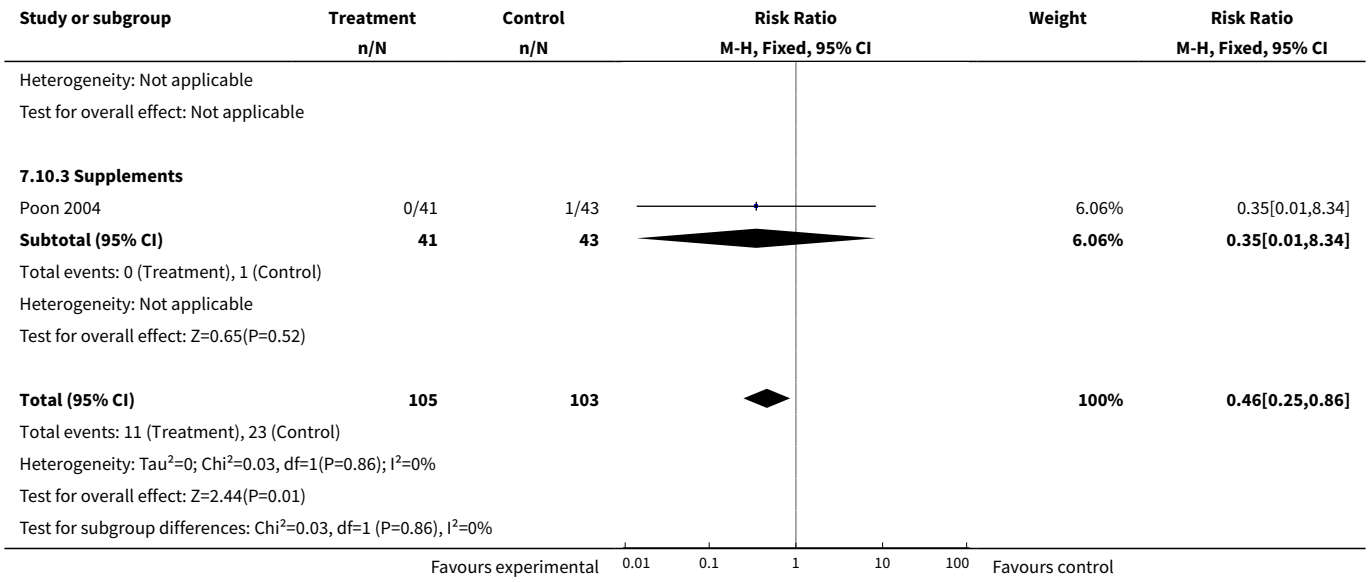
Favours experimental — Favours control

Analysis 7.10. Comparison 7 infections, Outcome 10 HCC.

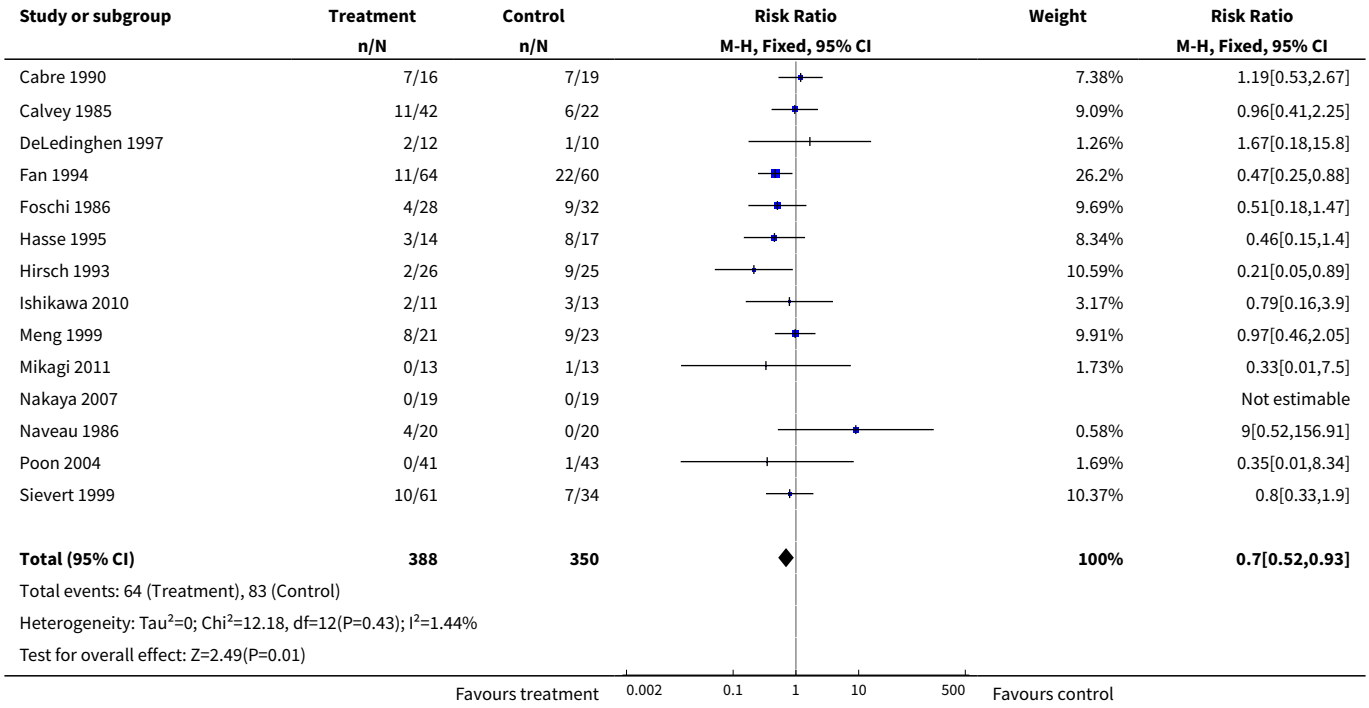
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.10.1 Parenteral nutrition					
Fan 1994	11/64	22/60		93.94%	0.47[0.25,0.88]
Subtotal (95% CI)	**64**	**60**		**93.94%**	**0.47[0.25,0.88]**
Total events: 11 (Treatment), 22 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%					
Test for overall effect: Z=2.35(P=0.02)					
7.10.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					



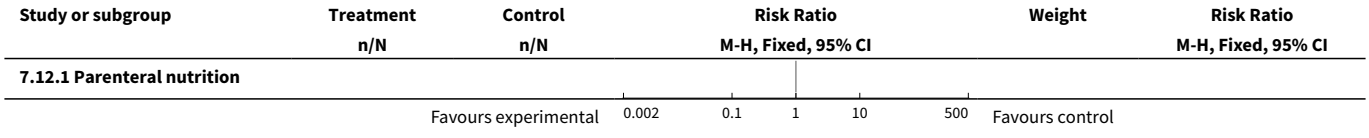
Favours experimental — Favours control

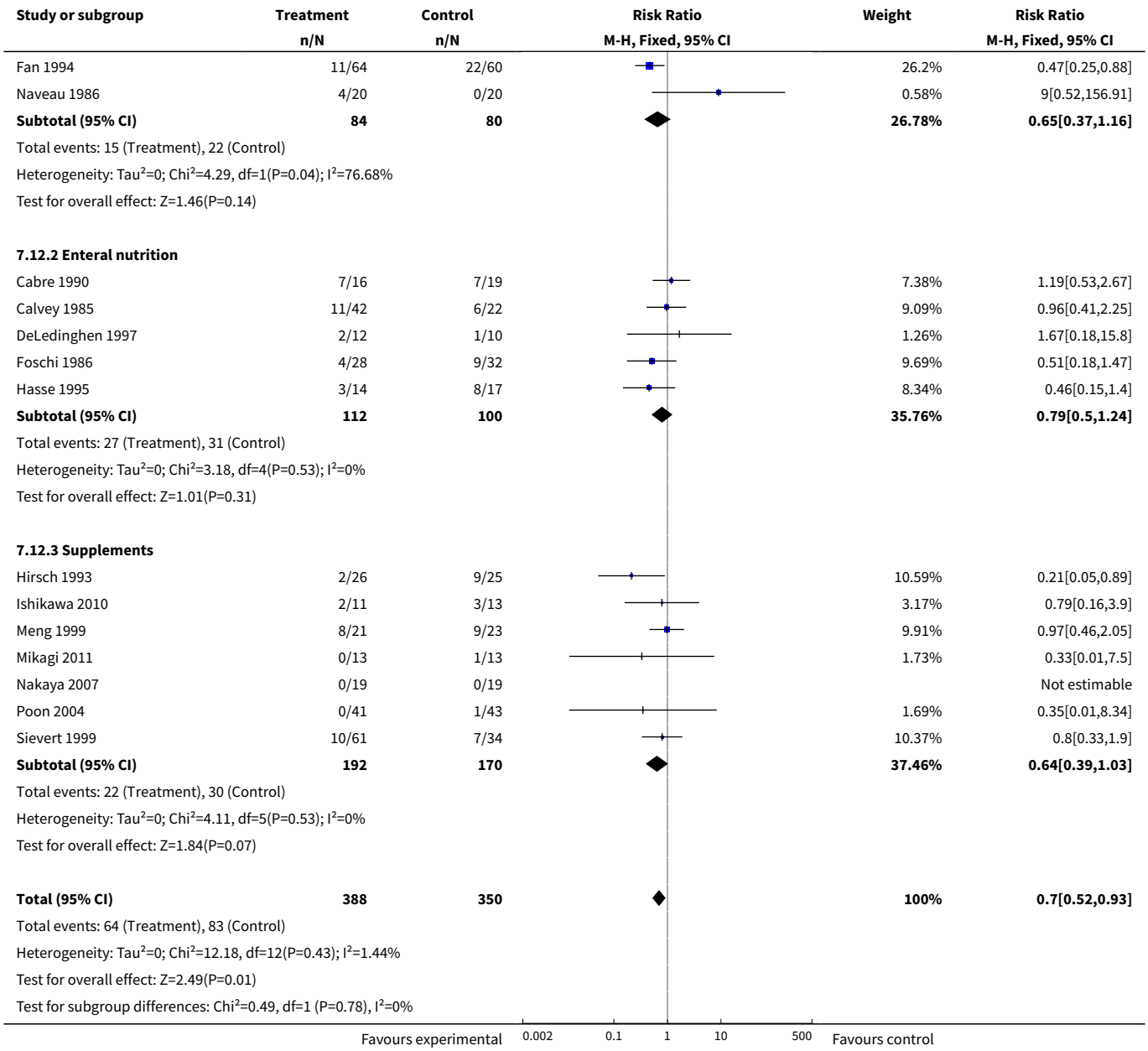


Analysis 7.11. Comparison 7 infections, Outcome 11 Abstracts excluded.

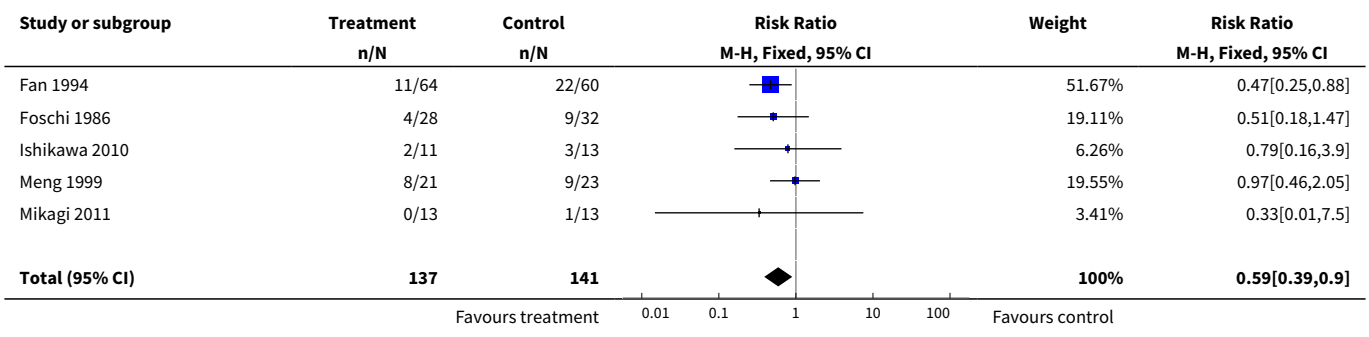


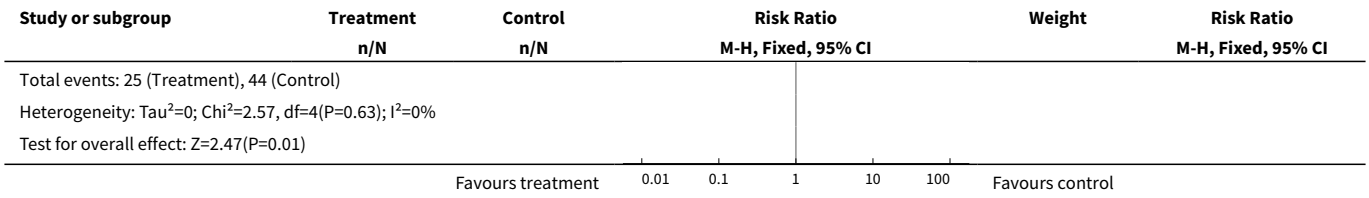
Analysis 7.12. Comparison 7 infections, Outcome 12 Abstracts excluded.



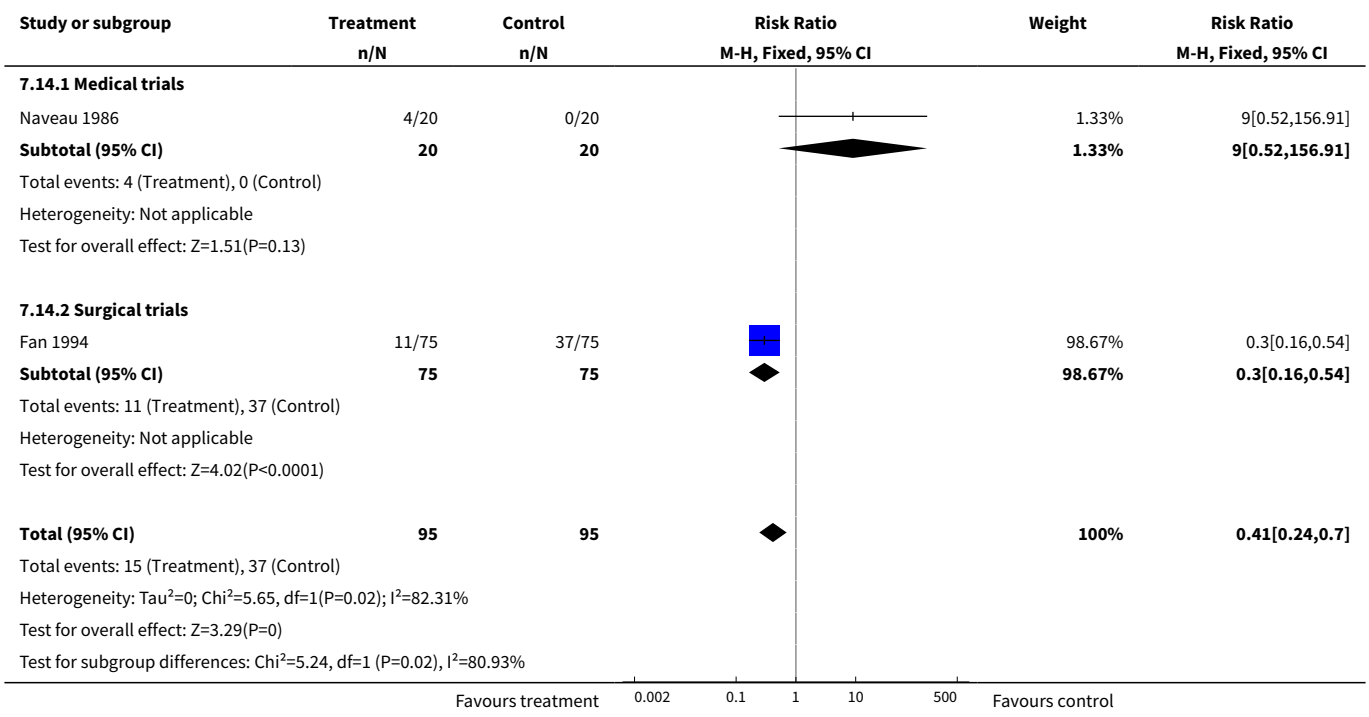


Analysis 7.13. Comparison 7 infections, Outcome 13 Surgical trials excluding transplants.

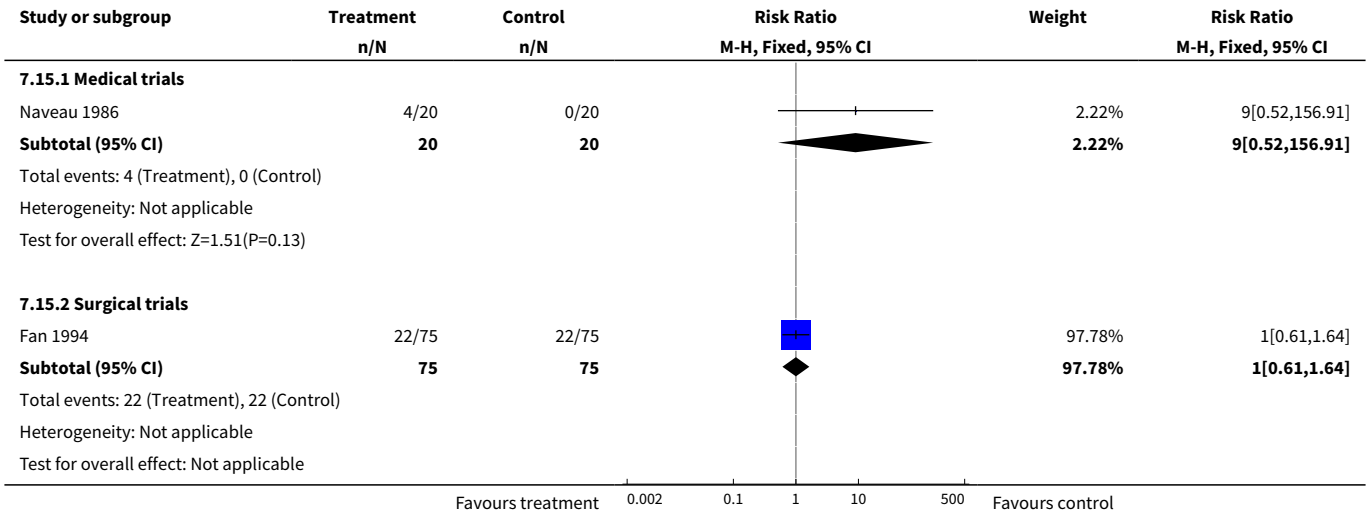




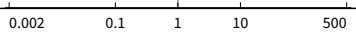
Analysis 7.14. Comparison 7 infections, Outcome 14 Parenteral nutrition - best-case scenario.



Analysis 7.15. Comparison 7 infections, Outcome 15 Parenteral nutrition - worst-case scenario.

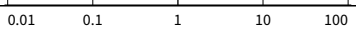


Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)	**95**	**95**		**100%**	**1.18[0.73,1.9]**
Total events: 26 (Treatment), 22 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.36, df=1(P=0.12); I^2=57.65%					
Test for overall effect: Z=0.67(P=0.5)					
Test for subgroup differences: Chi^2=2.2, df=1 (P=0.14), I^2=54.61%					



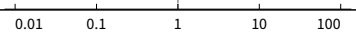
Analysis 7.16. Comparison 7 infections, Outcome 16 Enteral nutrition - best-case scenario.

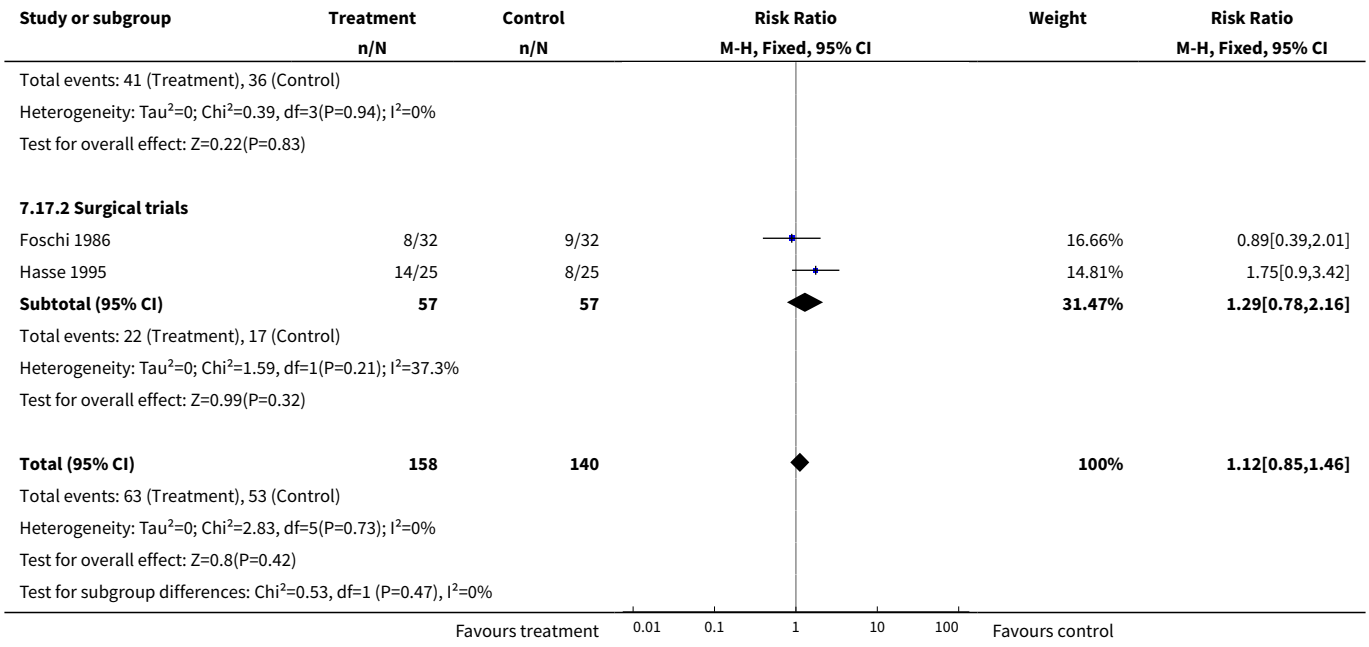
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.16.1 Medical trials					
Cabre 1990	7/16	7/19		9.85%	1.19[0.53,2.67]
Calvey 1985	11/42	6/22		12.12%	0.96[0.41,2.25]
DeLedinghen 1997	2/12	1/10		1.68%	1.67[0.18,15.8]
Norman 2008	16/31	25/32		37.87%	0.66[0.45,0.97]
Subtotal (95% CI)	**101**	**83**		**61.52%**	**0.83[0.6,1.16]**
Total events: 36 (Treatment), 39 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.58, df=3(P=0.46); I^2=0%					
Test for overall effect: Z=1.1(P=0.27)					
7.16.2 Surgical trials					
Foschi 1986	4/32	9/32		13.85%	0.44[0.15,1.3]
Hasse 1995	3/25	16/25		24.63%	0.19[0.06,0.56]
Subtotal (95% CI)	**57**	**57**		**38.48%**	**0.28[0.13,0.6]**
Total events: 7 (Treatment), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.22, df=1(P=0.27); I^2=18.3%					
Test for overall effect: Z=3.31(P=0)					
Total (95% CI)	**158**	**140**		**100%**	**0.62[0.46,0.84]**
Total events: 43 (Treatment), 64 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.25, df=5(P=0.1); I^2=45.93%					
Test for overall effect: Z=3.07(P=0)					
Test for subgroup differences: Chi^2=6.71, df=1 (P=0.01), I^2=85.11%					



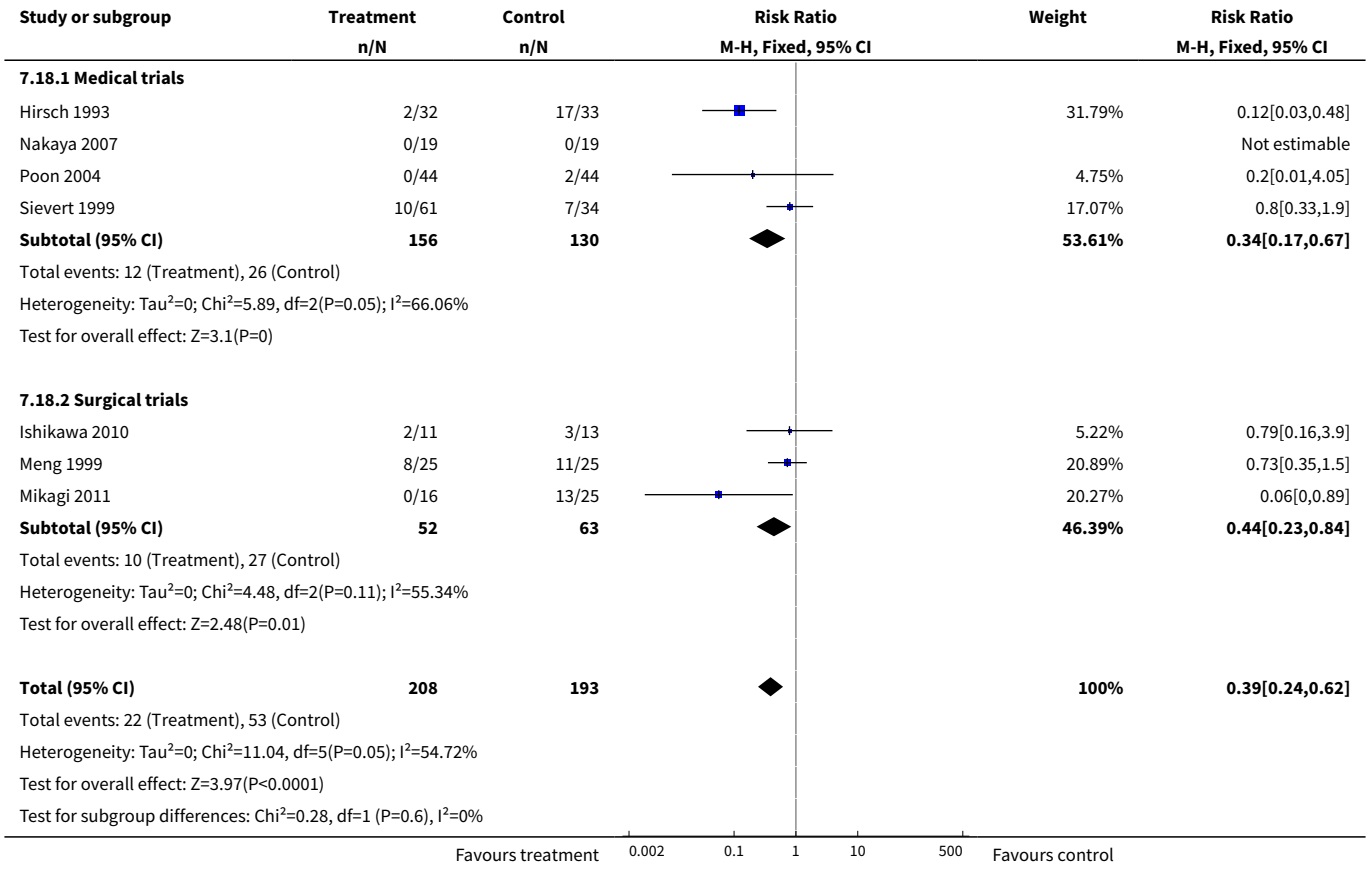
Analysis 7.17. Comparison 7 infections, Outcome 17 Enteral nutrition - worst-case scenario.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
7.17.1 Medical trials					
Cabre 1990	7/16	7/19		11.85%	1.19[0.53,2.67]
Calvey 1985	11/42	6/22		14.58%	0.96[0.41,2.25]
DeLedinghen 1997	2/12	1/10		2.02%	1.67[0.18,15.8]
Norman 2008	21/31	22/32		40.08%	0.99[0.7,1.38]
Subtotal (95% CI)	**101**	**83**		**68.53%**	**1.04[0.76,1.41]**

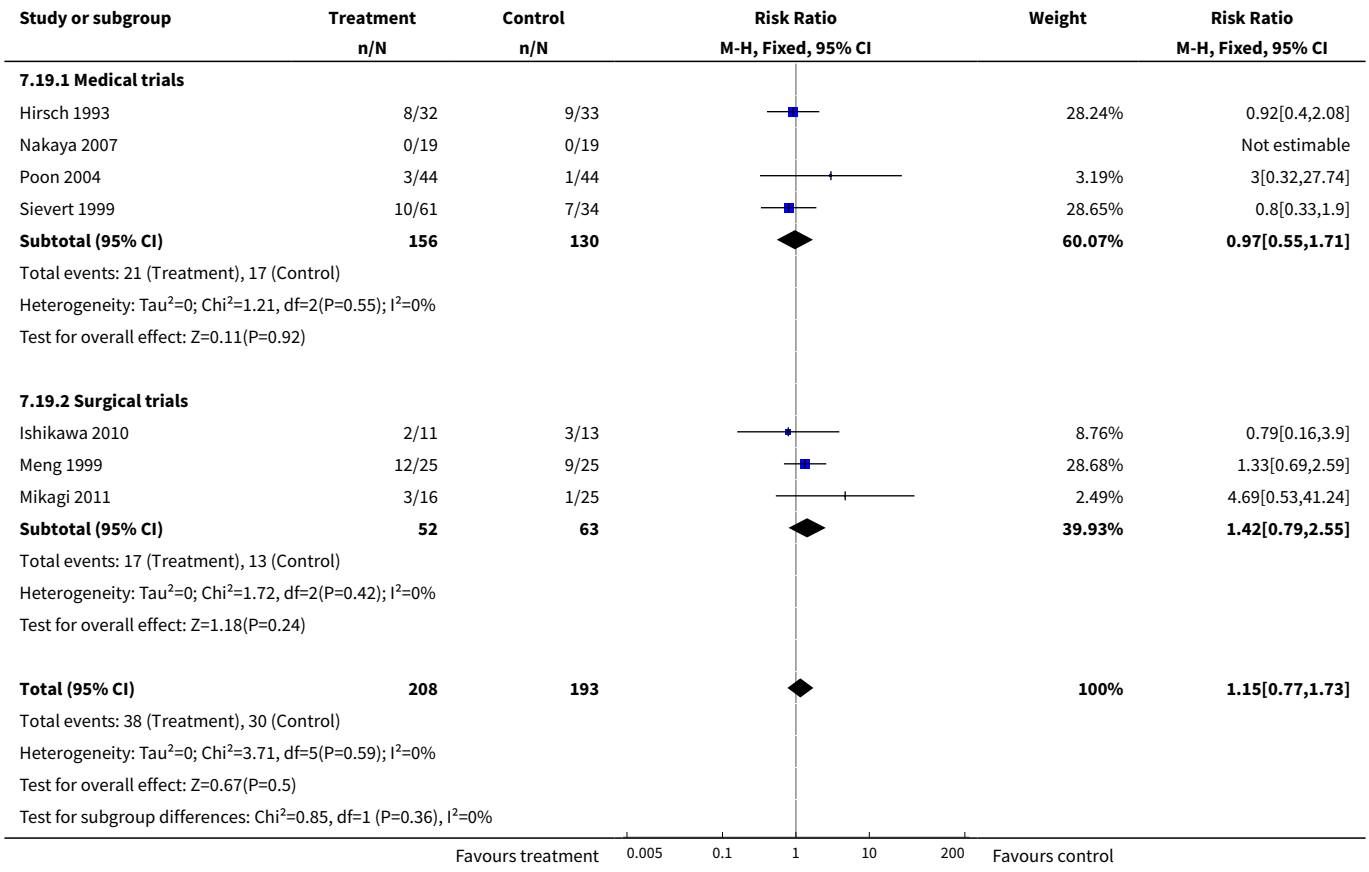




Analysis 7.18. Comparison 7 infections, Outcome 18 Supplements - best-case scenario.



Analysis 7.19. Comparison 7 infections, Outcome 19 Supplements - worst-case scenario.



Comparison 8. Serum bilirubin

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 All studies	10	450	Mean Difference (IV, Fixed, 95% CI)	-1.91 [-2.72, -1.11]
2 Parenteral nutrition	6	269	Mean Difference (IV, Fixed, 95% CI)	-2.52 [-3.45, -1.60]
2.1 Medical trials	3	106	Mean Difference (IV, Fixed, 95% CI)	-2.86 [-3.82, -1.89]
2.2 Surgical trials	3	163	Mean Difference (IV, Fixed, 95% CI)	1.32 [-1.95, 4.59]
3 Enteral nutrition (all medical trials)	2	94	Mean Difference (IV, Fixed, 95% CI)	-0.17 [-2.63, 2.29]
3.1 Medical trials	2	94	Mean Difference (IV, Fixed, 95% CI)	-0.17 [-2.63, 2.29]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.2 Surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	2	87	Mean Difference (IV, Fixed, 95% CI)	0.24 [-2.03, 2.51]
4.1 Medical trials	2	87	Mean Difference (IV, Fixed, 95% CI)	0.24 [-2.03, 2.51]
4.2 Surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Medical trials	7	287	Mean Difference (IV, Fixed, 95% CI)	-2.13 [-2.96, -1.30]
5.1 Parenteral nutrition	3	106	Mean Difference (IV, Fixed, 95% CI)	-2.86 [-3.82, -1.89]
5.2 Enteral nutrition	2	94	Mean Difference (IV, Fixed, 95% CI)	-0.17 [-2.63, 2.29]
5.3 Supplements	2	87	Mean Difference (IV, Fixed, 95% CI)	0.24 [-2.03, 2.51]
6 Surgical trials	3	163	Mean Difference (IV, Fixed, 95% CI)	1.32 [-1.95, 4.59]
6.1 Parenteral nutrition	3	163	Mean Difference (IV, Fixed, 95% CI)	1.32 [-1.95, 4.59]
6.2 Enteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Alcoholic hepatitis	5	184	Mean Difference (IV, Random, 95% CI)	-3.51 [-7.20, 0.18]
7.1 Parenteral nutrition	2	66	Mean Difference (IV, Random, 95% CI)	-6.41 [-9.41, -3.40]
7.2 Enteral nutrition	1	31	Mean Difference (IV, Random, 95% CI)	-5.90 [-17.54, 5.74]
7.3 Supplements	2	87	Mean Difference (IV, Random, 95% CI)	0.24 [-2.03, 2.51]
8 Cirrhosis	3	154	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-2.08, -0.12]
8.1 Parenteral nutrition	1	40	Mean Difference (IV, Fixed, 95% CI)	-1.60 [-2.74, -0.46]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.2 Enteral nutrition	1	63	Mean Difference (IV, Fixed, 95% CI)	0.10 [-2.42, 2.62]
8.3 Supplements	1	51	Mean Difference (IV, Fixed, 95% CI)	0.60 [-2.33, 3.53]
9 HCC	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Pareneral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Abstracts excluded	9	387	Mean Difference (IV, Fixed, 95% CI)	-2.15 [-3.01, -1.30]
10.1 Parenteral nutrition	6	269	Mean Difference (IV, Fixed, 95% CI)	-2.52 [-3.45, -1.60]
10.2 Enteral nutrition	1	31	Mean Difference (IV, Fixed, 95% CI)	-5.90 [-17.54, 5.74]
10.3 Supplements	2	87	Mean Difference (IV, Fixed, 95% CI)	0.24 [-2.03, 2.51]
11 Intent to treat - best-case scenario for intervention (cannot do analyses for continuous variables)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.1 Parenteral nutrition - medical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Parenteral nutrition - surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Enteral nutrition - medical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.4 Enteral nutrition - surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.5 Supplements - medical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.6 Supplements - surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12 Intent to treat - worst-case scenario for intervention (cannot do analyses for continuous variables)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.1 Parenteral nutrition - medical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 Parenteral nutrition - surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Enteral nutrition - medical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.4 Enteral nutrition - surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.6 Supplements - surgical trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Alcoholic liver disease	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.1 Parenteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Enteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Non-alcoholic liver disease	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.1 Parenteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 Enteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 8.1. Comparison 8 Serum bilirubin, Outcome 1 All studies.

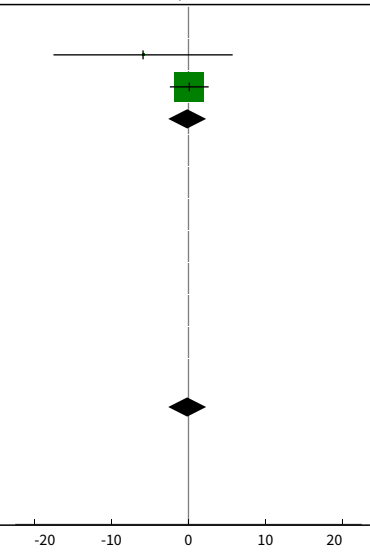
Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Achord 1987	14	3 (1)	14	8.5 (3.5)		17.95%	-5.5[-7.41,-3.59]
Bunout 1989	17	3.8 (4.9)	19	4.1 (6.1)		5.04%	-0.3[-3.9,3.3]
Hirsch 1993	26	2.1 (6.1)	25	1.5 (4.5)		7.58%	0.6[-2.33,3.53]
Kearns 1992	16	2.7 (9.2)	15	8.6 (21.2)		0.48%	-5.9[-17.54,5.74]
Naveau 1986	20	2.5 (1.4)	20	4.1 (2.2)		49.98%	-1.6[-2.74,-0.46]
Norman 2008	31	5.2 (4.9)	32	5.1 (5.3)		10.28%	0.1[-2.42,2.62]
Qiu 2009	44	3.8 (14)	21	3.1 (9.4)		1.96%	0.7[-5.07,6.47]
Reilly 1990	18	5.5 (5.7)	10	2.5 (7.9)		2.11%	3[-2.56,8.56]
Simon 1988	19	4.7 (3)	19	13.7 (11)		2.48%	-9[-14.13,-3.87]
Zheng 2003	40	2.7 (12)	30	2.4 (11.5)		2.12%	0.3[-5.25,5.85]
Total ***	**245**		**205**			**100%**	**-1.91[-2.72,-1.11]**
Heterogeneity: Tau²=0; Chi²=32.12, df=9(P=0); I²=71.98%							
Test for overall effect: Z=4.65(P<0.0001)							

Analysis 8.2. Comparison 8 Serum bilirubin, Outcome 2 Parenteral nutrition.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
8.2.1 Medical trials							
Achord 1987	14	3 (1)	14	8.5 (3.5)		23.47%	-5.5[-7.41,-3.59]
Naveau 1986	20	2.5 (1.4)	20	4.1 (2.2)		65.32%	-1.6[-2.74,-0.46]
Simon 1988	19	4.7 (3)	19	13.7 (11)		3.25%	-9[-14.13,-3.87]
Subtotal ***	**53**		**53**			**92.03%**	**-2.86[-3.82,-1.89]**
Heterogeneity: Tau²=0; Chi²=17.54, df=2(P=0); I²=88.6%							
Test for overall effect: Z=5.81(P<0.0001)							
8.2.2 Surgical trials							
Qiu 2009	44	3.8 (14)	21	3.1 (9.4)		2.56%	0.7[-5.07,6.47]
Reilly 1990	18	5.5 (6.3)	10	2.5 (7.9)		2.63%	3[-2.7,8.7]
Zheng 2003	40	2.7 (12)	30	2.4 (11.5)		2.77%	0.3[-5.25,5.85]
Subtotal ***	**102**		**61**			**7.97%**	**1.32[-1.95,4.59]**
Heterogeneity: Tau²=0; Chi²=0.51, df=2(P=0.78); I²=0%							
Test for overall effect: Z=0.79(P=0.43)							
Total ***	**155**		**114**			**100%**	**-2.52[-3.45,-1.6]**
Heterogeneity: Tau²=0; Chi²=23.81, df=5(P=0); I²=79%							
Test for overall effect: Z=5.35(P<0.0001)							
Test for subgroup differences: Chi²=5.76, df=1 (P=0.02), I²=82.62%							

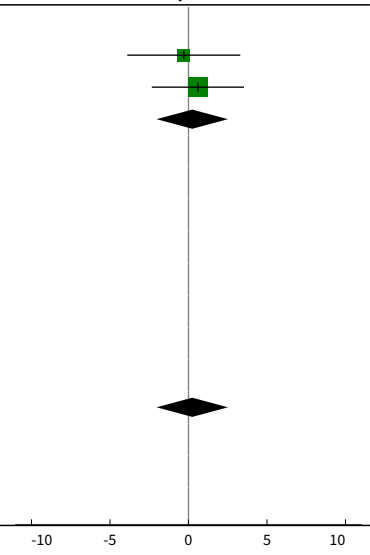
Analysis 8.3. Comparison 8 Serum bilirubin, Outcome 3 Enteral nutrition (all medical trials).

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
8.3.1 Medical trials							
Kearns 1992	16	2.7 (9.2)	15	8.6 (21.2)		4.48%	-5.9[-17.54,5.74]
Norman 2008	31	5.2 (4.9)	32	5.1 (5.3)		95.52%	0.1[-2.42,2.62]
Subtotal ***	**47**		**47**			**100%**	**-0.17[-2.63,2.29]**
Heterogeneity: Tau^2=0; Chi^2=0.98, df=1(P=0.32); I^2=0%							
Test for overall effect: Z=0.13(P=0.89)							
8.3.2 Surgical trials							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**47**		**47**			**100%**	**-0.17[-2.63,2.29]**
Heterogeneity: Tau^2=0; Chi^2=0.98, df=1(P=0.32); I^2=0%							
Test for overall effect: Z=0.13(P=0.89)							
Test for subgroup differences: Not applicable							



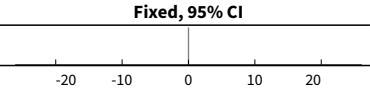
Analysis 8.4. Comparison 8 Serum bilirubin, Outcome 4 Supplements.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
8.4.1 Medical trials							
Bunout 1989	17	3.8 (4.9)	19	4.1 (6.1)		39.94%	-0.3[-3.9,3.3]
Hirsch 1993	26	2.1 (6.1)	25	1.5 (4.5)		60.06%	0.6[-2.33,3.53]
Subtotal ***	**43**		**44**			**100%**	**0.24[-2.03,2.51]**
Heterogeneity: Tau^2=0; Chi^2=0.14, df=1(P=0.7); I^2=0%							
Test for overall effect: Z=0.21(P=0.84)							
8.4.2 Surgical trials							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**43**		**44**			**100%**	**0.24[-2.03,2.51]**
Heterogeneity: Tau^2=0; Chi^2=0.14, df=1(P=0.7); I^2=0%							
Test for overall effect: Z=0.21(P=0.84)							
Test for subgroup differences: Not applicable							

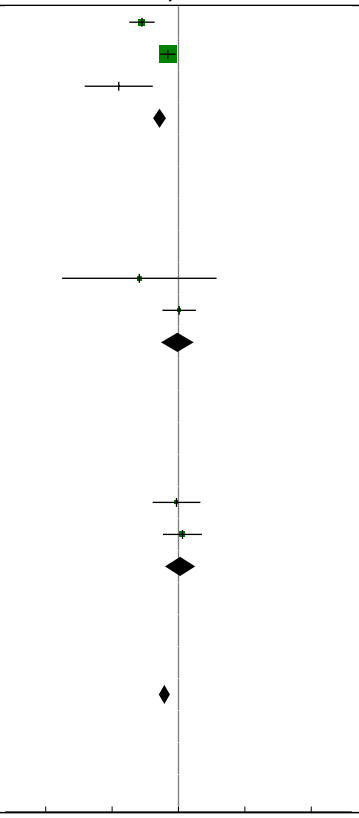


Analysis 8.5. Comparison 8 Serum bilirubin, Outcome 5 Medical trials.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
8.5.1 Parenteral nutrition							

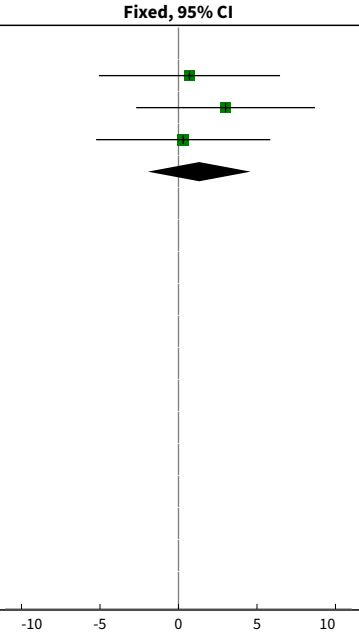


Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Achord 1987	14	3 (1)	14	8.5 (3.5)		19.14%	-5.5[-7.41,-3.59]
Naveau 1986	20	2.5 (1.4)	20	4.1 (2.2)		53.28%	-1.6[-2.74,-0.46]
Simon 1988	19	4.7 (3)	19	13.7 (11)		2.65%	-9[-14.13,-3.87]
Subtotal ***	**53**		**53**			**75.07%**	**-2.86[-3.82,-1.89]**
Heterogeneity: Tau²=0; Chi²=17.54, df=2(P=0); I²=88.6%							
Test for overall effect: Z=5.81(P<0.0001)							
8.5.2 Enteral nutrition							
Kearns 1992	16	2.7 (9.2)	15	8.6 (21.2)		0.51%	-5.9[-17.54,5.74]
Norman 2008	31	5.2 (4.9)	32	5.1 (5.3)		10.96%	0.1[-2.42,2.62]
Subtotal ***	**47**		**47**			**11.48%**	**-0.17[-2.63,2.29]**
Heterogeneity: Tau²=0; Chi²=0.98, df=1(P=0.32); I²=0%							
Test for overall effect: Z=0.13(P=0.89)							
8.5.3 Supplements							
Bunout 1989	17	3.8 (4.9)	19	4.1 (6.1)		5.37%	-0.3[-3.9,3.3]
Hirsch 1993	26	2.1 (6.1)	25	1.5 (4.5)		8.08%	0.6[-2.33,3.53]
Subtotal ***	**43**		**44**			**13.46%**	**0.24[-2.03,2.51]**
Heterogeneity: Tau²=0; Chi²=0.14, df=1(P=0.7); I²=0%							
Test for overall effect: Z=0.21(P=0.84)							
Total ***	**143**		**144**			**100%**	**-2.13[-2.96,-1.3]**
Heterogeneity: Tau²=0; Chi²=27.46, df=6(P=0); I²=78.15%							
Test for overall effect: Z=5.01(P<0.0001)							
Test for subgroup differences: Chi²=8.79, df=1 (P=0.01), I²=77.25%							

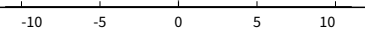


Analysis 8.6. Comparison 8 Serum bilirubin, Outcome 6 Surgical trials.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
8.6.1 Parenteral nutrition							
Qiu 2009	44	3.8 (14)	21	3.1 (9.4)		32.18%	0.7[-5.07,6.47]
Reilly 1990	18	5.5 (6.3)	10	2.5 (7.9)		33.01%	3[-2.7,8.7]
Zheng 2003	40	2.7 (12)	30	2.4 (11.5)		34.81%	0.3[-5.25,5.85]
Subtotal ***	**102**		**61**			**100%**	**1.32[-1.95,4.59]**
Heterogeneity: Tau²=0; Chi²=0.51, df=2(P=0.78); I²=0%							
Test for overall effect: Z=0.79(P=0.43)							
8.6.2 Enteral nutrition							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
8.6.3 Supplements							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



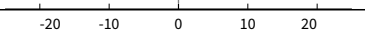
Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Total ***	**102**		**61**			**100%**	**1.32[-1.95,4.59]**
Heterogeneity: Tau²=0; Chi²=0.51, df=2(P=0.78); I²=0%							
Test for overall effect: Z=0.79(P=0.43)							
Test for subgroup differences: Not applicable							



Favours treatment Favours control

Analysis 8.7. Comparison 8 Serum bilirubin, Outcome 7 Alcoholic hepatitis.

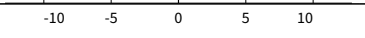
Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
8.7.1 Parenteral nutrition							
Achord 1987	14	3 (1)	14	8.5 (3.5)		26.85%	-5.5[-7.41,-3.59]
Simon 1988	19	4.7 (3)	19	13.7 (11)		18.56%	-9[-14.13,-3.87]
Subtotal ***	**33**		**33**			**45.41%**	**-6.41[-9.41,-3.4]**
Heterogeneity: Tau²=2.23; Chi²=1.57, df=1(P=0.21); I²=36.42%							
Test for overall effect: Z=4.18(P<0.0001)							
8.7.2 Enteral nutrition							
Kearns 1992	16	2.7 (9.2)	15	8.6 (21.2)		7.46%	-5.9[-17.54,5.74]
Subtotal ***	**16**		**15**			**7.46%**	**-5.9[-17.54,5.74]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.99(P=0.32)							
8.7.3 Supplements							
Bunout 1989	17	3.8 (4.9)	19	4.1 (6.1)		22.68%	-0.3[-3.9,3.3]
Hirsch 1993	26	2.1 (6.1)	25	1.5 (4.5)		24.45%	0.6[-2.33,3.53]
Subtotal ***	**43**		**44**			**47.13%**	**0.24[-2.03,2.51]**
Heterogeneity: Tau²=0; Chi²=0.14, df=1(P=0.7); I²=0%							
Test for overall effect: Z=0.21(P=0.84)							
Total ***	**92**		**92**			**100%**	**-3.51[-7.2,0.18]**
Heterogeneity: Tau²=12.25; Chi²=19.33, df=4(P=0); I²=79.3%							
Test for overall effect: Z=1.86(P=0.06)							
Test for subgroup differences: Chi²=12.33, df=1 (P=0), I²=83.78%							



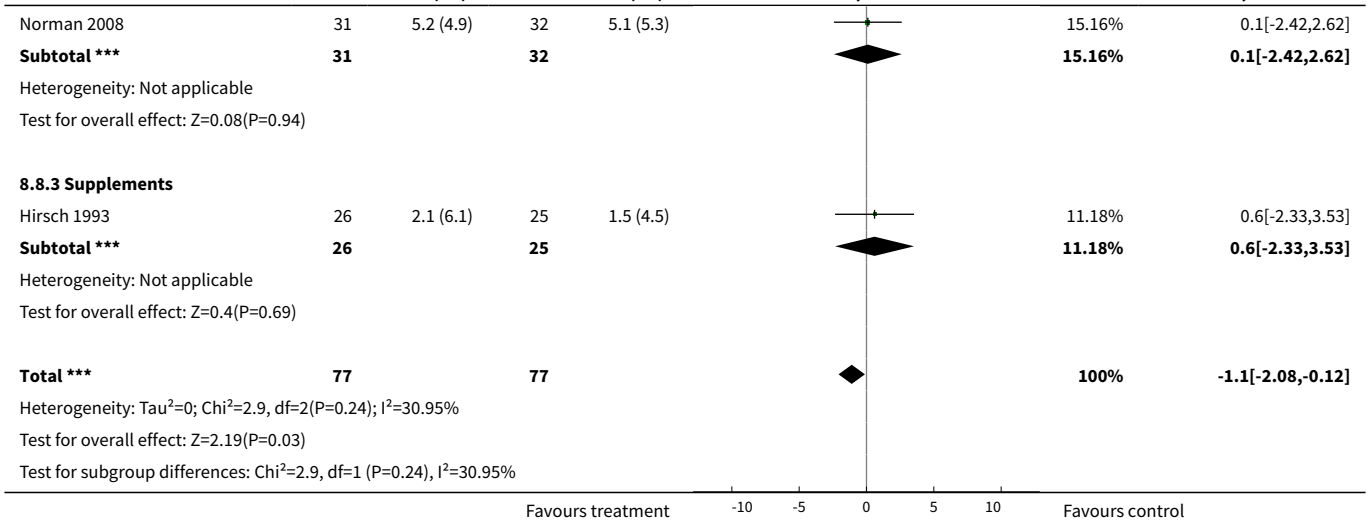
Favours treatment Favours control

Analysis 8.8. Comparison 8 Serum bilirubin, Outcome 8 Cirrhosis.

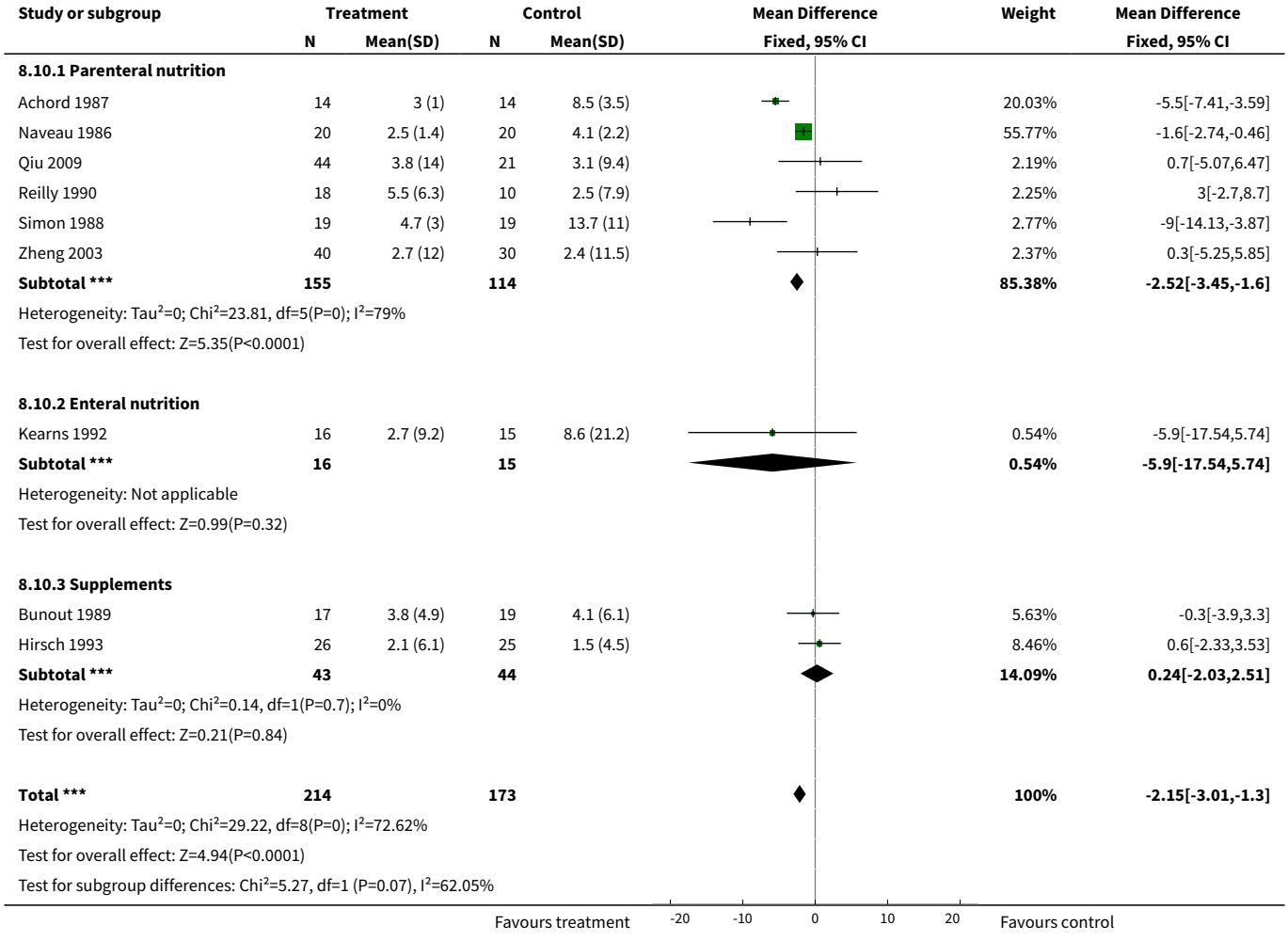
Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
8.8.1 Parenteral nutrition							
Naveau 1986	20	2.5 (1.4)	20	4.1 (2.2)		73.67%	-1.6[-2.74,-0.46]
Subtotal ***	**20**		**20**			**73.67%**	**-1.6[-2.74,-0.46]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.74(P=0.01)							
8.8.2 Enteral nutrition							



Favours treatment Favours control



Analysis 8.10. Comparison 8 Serum bilirubin, Outcome 10 Abstracts excluded.

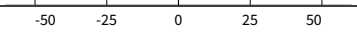


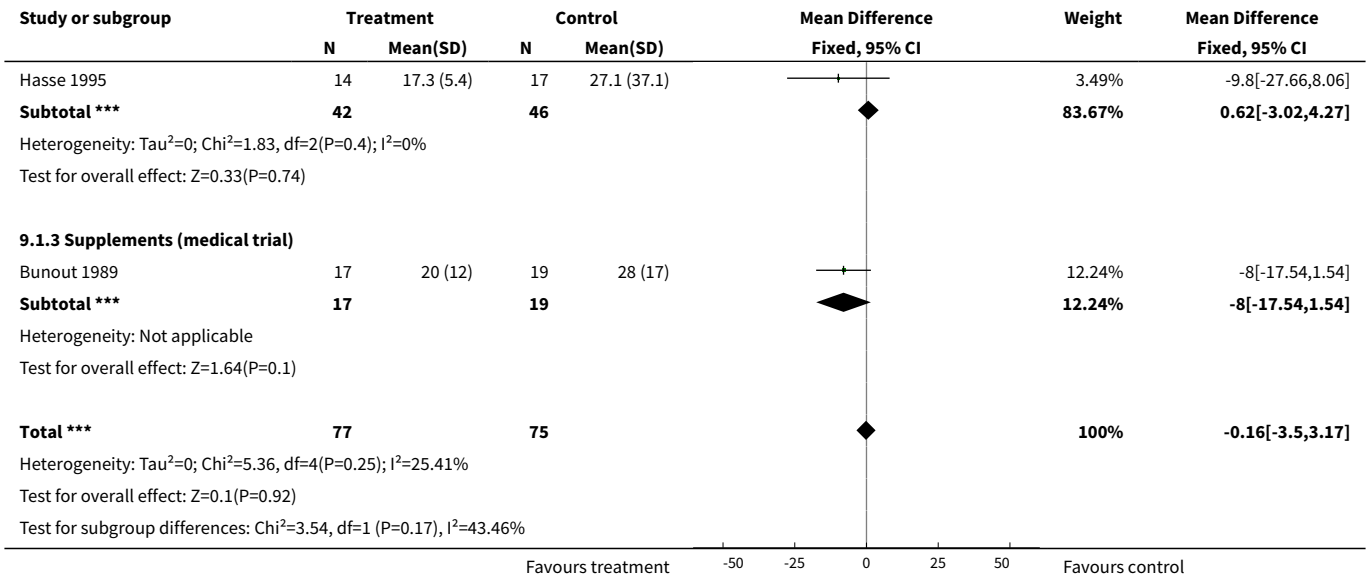
Comparison 9. Duration of hospitalisation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	5	152	Mean Difference (IV, Fixed, 95% CI)	-0.16 [-3.50, 3.17]
1.1 Parenteral nutrition (surgical trial)	1	28	Mean Difference (IV, Fixed, 95% CI)	7.20 [-9.29, 23.69]
1.2 Enteral nutrition	3	88	Mean Difference (IV, Fixed, 95% CI)	0.62 [-3.02, 4.27]
1.3 Supplements (medical trial)	1	36	Mean Difference (IV, Fixed, 95% CI)	-8.0 [-17.54, 1.54]
2 Enteral nutrition - medical versus surgical trials	3	88	Mean Difference (IV, Fixed, 95% CI)	0.62 [-3.02, 4.27]
2.1 Medical trials	2	57	Mean Difference (IV, Fixed, 95% CI)	1.08 [-2.65, 4.80]
2.2 Surgical trials	1	31	Mean Difference (IV, Fixed, 95% CI)	-9.8 [-27.66, 8.06]
3 Cirrhosis	2	57	Mean Difference (IV, Fixed, 95% CI)	1.08 [-2.65, 4.80]
3.1 Parenteral nutrition	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Enteral nutrition	2	57	Mean Difference (IV, Fixed, 95% CI)	1.08 [-2.65, 4.80]
3.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Surgery	2	59	Mean Difference (IV, Fixed, 95% CI)	-0.62 [-12.74, 11.49]
4.1 Parenteral nutrition	1	28	Mean Difference (IV, Fixed, 95% CI)	7.20 [-9.29, 23.69]
4.2 Enteral nutrition	1	31	Mean Difference (IV, Fixed, 95% CI)	-9.8 [-27.66, 8.06]
4.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

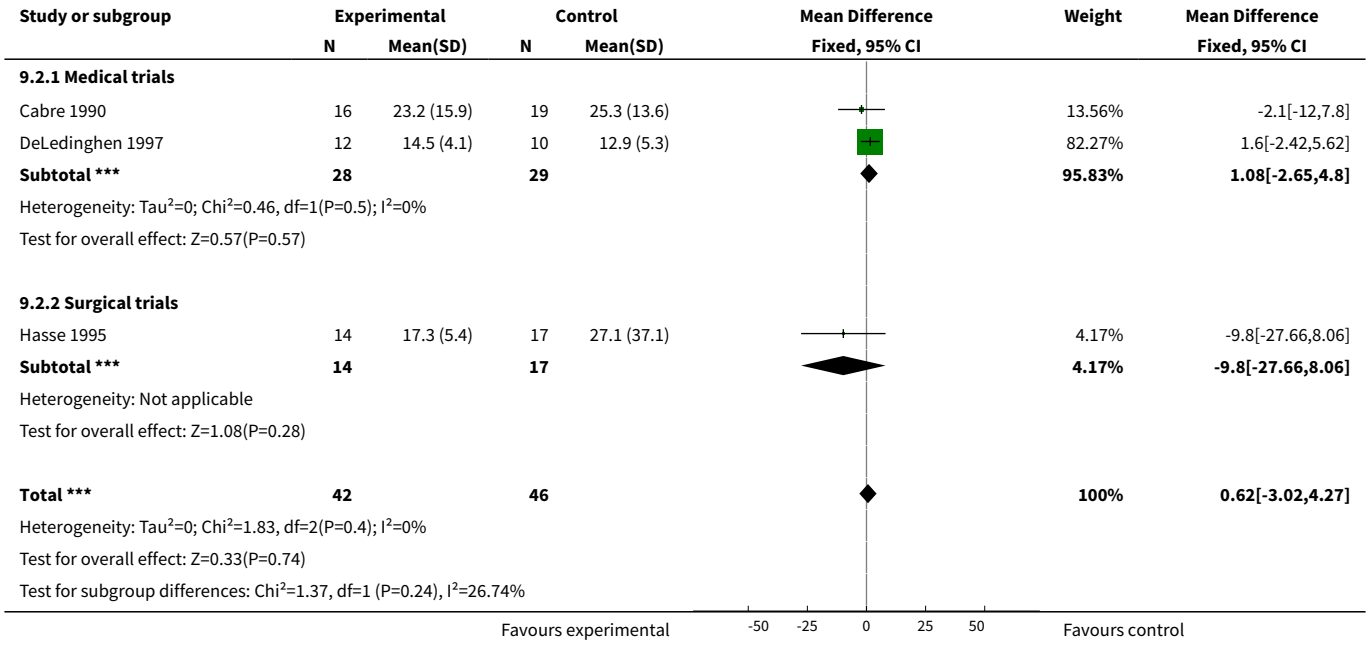
Analysis 9.1. Comparison 9 Duration of hospitalisation, Outcome 1 All studies.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
9.1.1 Parenteral nutrition (surgical trial)							
Reilly 1990	18	54.4 (25)	10	47.2 (19)		4.09%	7.2[-9.29,23.69]
Subtotal ***	**18**		**10**			**4.09%**	**7.2[-9.29,23.69]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.86(P=0.39)							
9.1.2 Enteral nutrition							
Cabre 1990	16	23.2 (15.9)	19	25.3 (13.6)		11.35%	-2.1[-12,7.8]
DeLedinghen 1997	12	14.5 (4.1)	10	12.9 (5.3)		68.83%	1.6[-2.42,5.62]

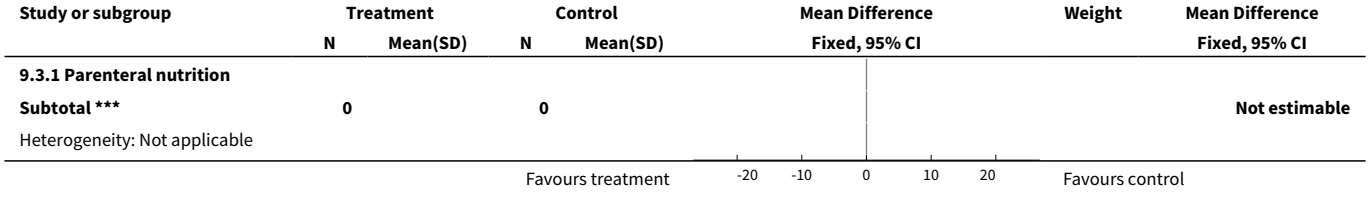


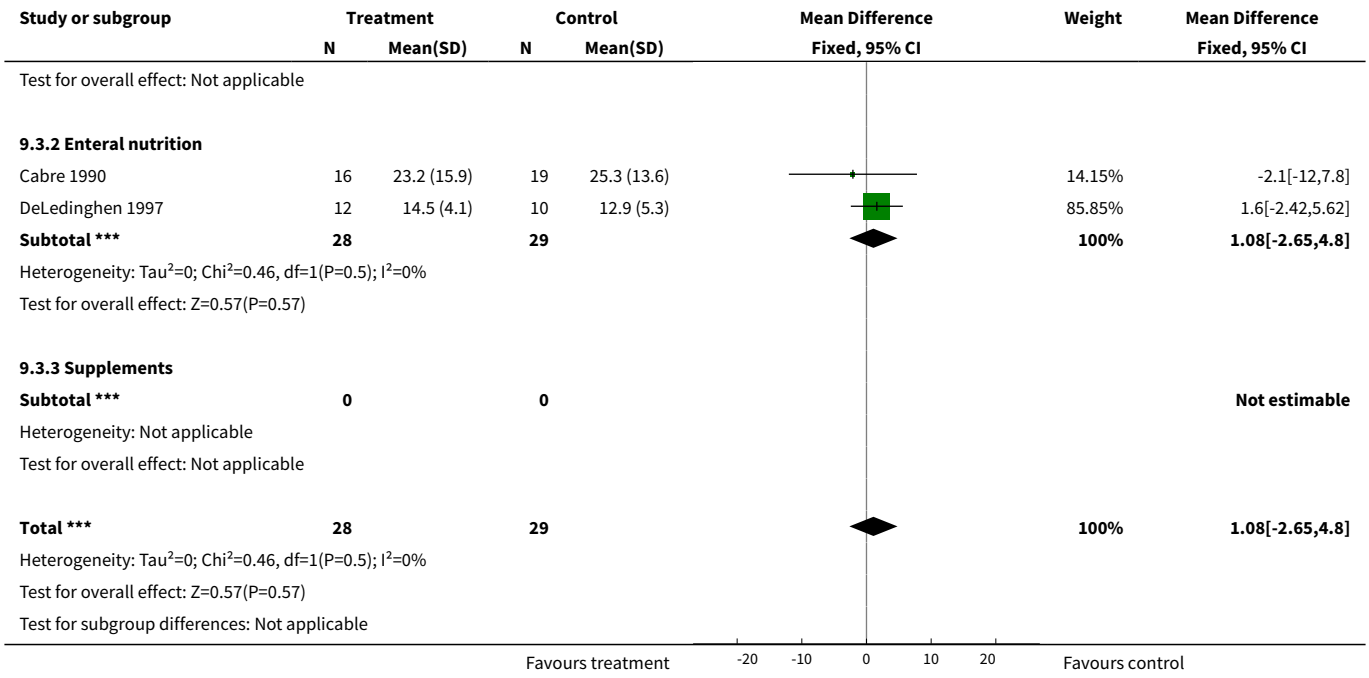


Analysis 9.2. Comparison 9 Duration of hospitalisation, Outcome 2 Enteral nutrition - medical versus surgical trials.

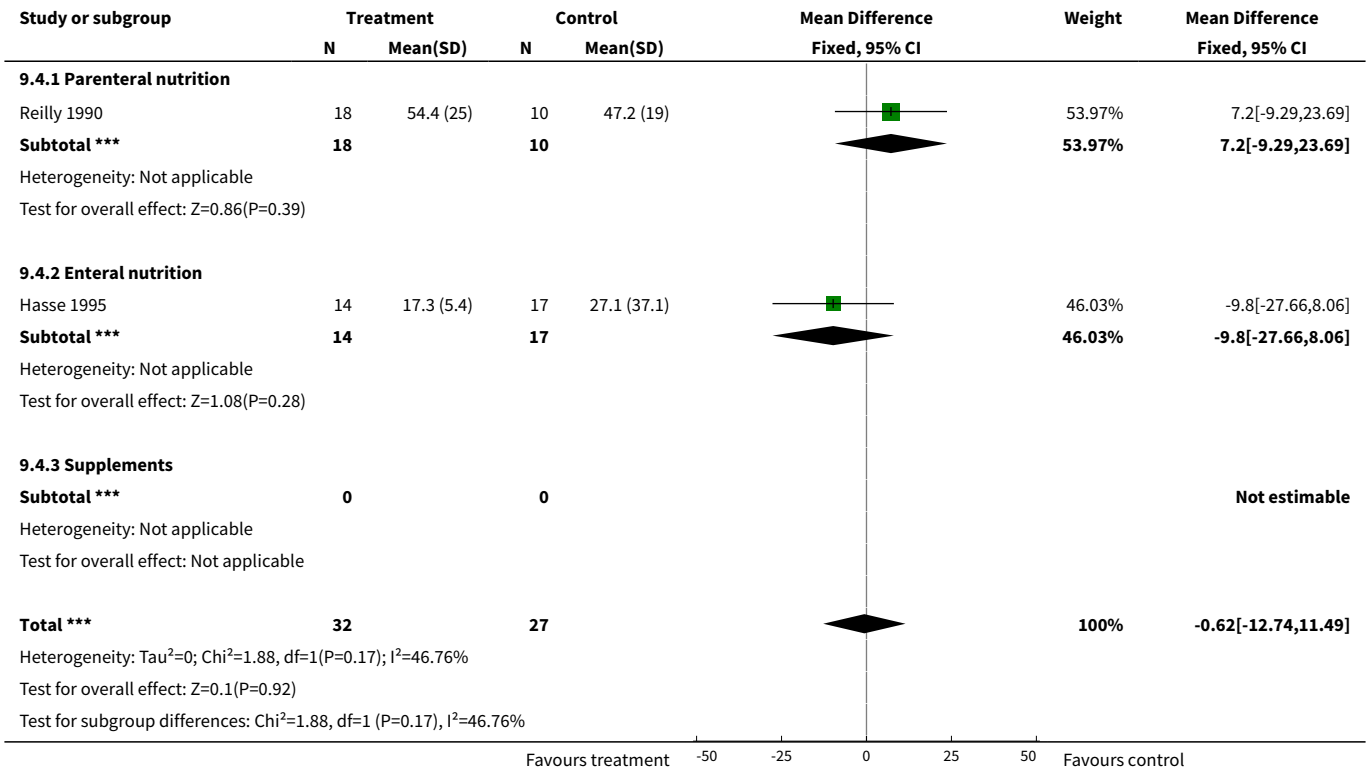


Analysis 9.3. Comparison 9 Duration of hospitalisation, Outcome 3 Cirrhosis.





Analysis 9.4. Comparison 9 Duration of hospitalisation, Outcome 4 Surgery.

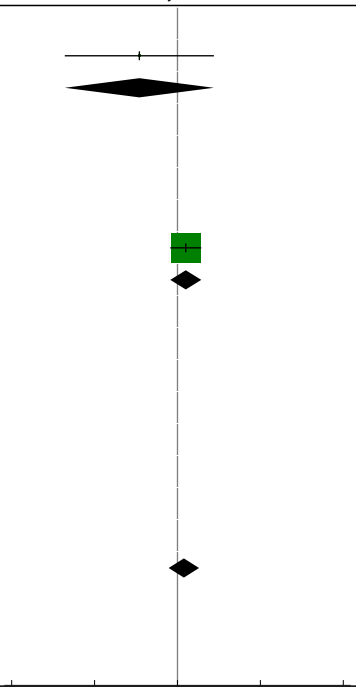


Comparison 10. Duration of stay in ICU

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies (all surgery [transplantation])	2	59	Mean Difference (IV, Fixed, 95% CI)	0.38 [-0.53, 1.30]
1.1 Parenteral nutrition	1	28	Mean Difference (IV, Fixed, 95% CI)	-2.3 [-6.80, 2.20]
1.2 Enteral nutrition	1	31	Mean Difference (IV, Fixed, 95% CI)	0.5 [-0.44, 1.44]
1.3 Supplements	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 10.1. Comparison 10 Duration of stay in ICU, Outcome 1 All studies (all surgery [transplantation]).

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
10.1.1 Parenteral nutrition							
Reilly 1990	18	3.7 (3)	10	6 (6.9)		4.15%	-2.3[-6.8,2.2]
Subtotal ***	**18**		**10**			**4.15%**	**-2.3[-6.8,2.2]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1(P=0.32)							
10.1.2 Enteral nutrition							
Hasse 1995	14	2.4 (1.7)	17	1.9 (0.6)		95.85%	0.5[-0.44,1.44]
Subtotal ***	**14**		**17**			**95.85%**	**0.5[-0.44,1.44]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.05(P=0.29)							
10.1.3 Supplements							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Total ***	**32**		**27**			**100%**	**0.38[-0.53,1.3]**
Heterogeneity: Tau^2=0; Chi^2=1.43, df=1(P=0.23); I^2=29.99%							
Test for overall effect: Z=0.82(P=0.41)							
Test for subgroup differences: Chi^2=1.43, df=1 (P=0.23), I^2=29.99%							



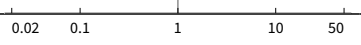
Comparison 11. Postoperative total complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	6	346	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.55, 0.86]
1.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.42, 0.94]

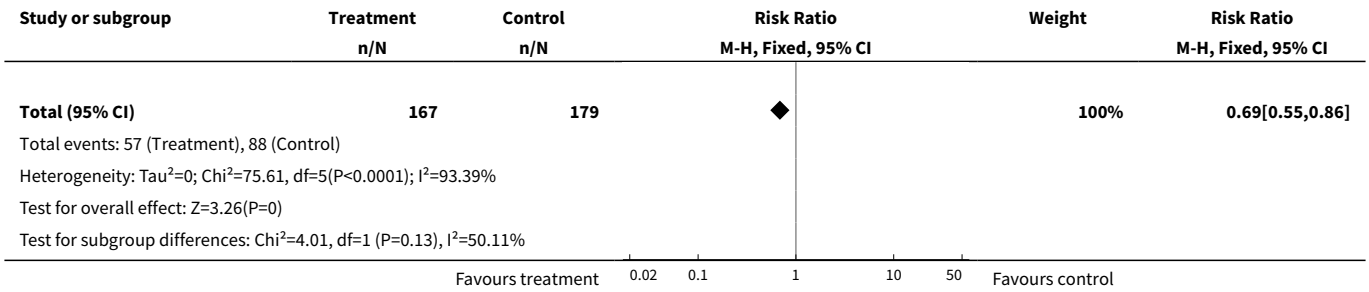
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.16, 0.91]
1.3 Supplements	4	162	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.66, 1.10]
2 All studies except those with total complications not patients	5	302	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.41, 0.80]
2.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.42, 0.94]
2.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.16, 0.91]
2.3 Supplements	3	118	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.31, 1.31]
3 HCC	2	168	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.62, 0.97]
3.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.42, 0.94]
3.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Supplements	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.92, 1.09]

Analysis 11.1. Comparison 11 Postoperative total complications, Outcome 1 All studies.

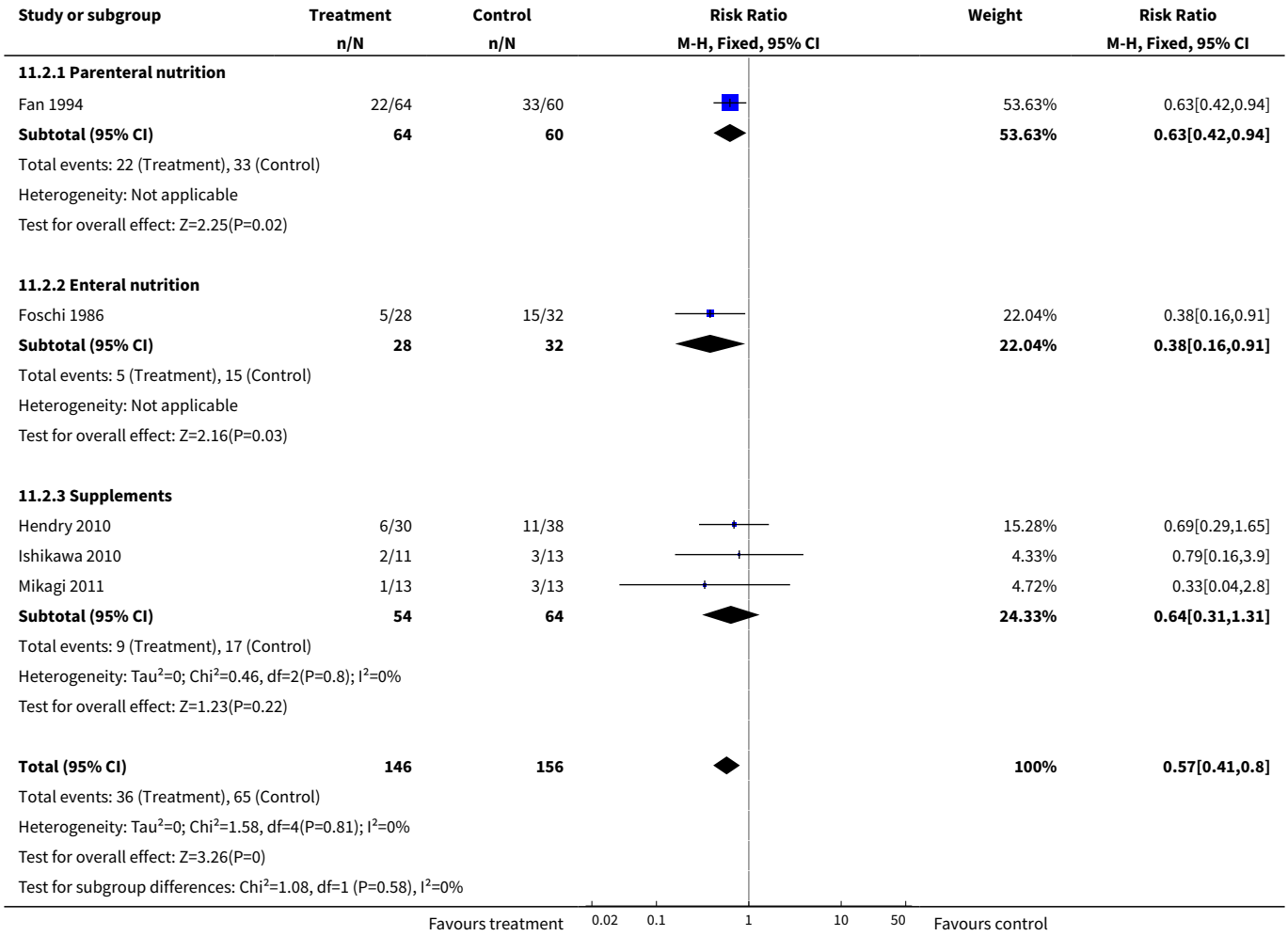
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
11.1.1 Parenteral nutrition					
Fan 1994	22/64	33/60		39.61%	0.63[0.42,0.94]
Subtotal (95% CI)	**64**	**60**		**39.61%**	**0.63[0.42,0.94]**
Total events: 22 (Treatment), 33 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.25(P=0.02)					
11.1.2 Enteral nutrition					
Foschi 1986	5/28	15/32		16.28%	0.38[0.16,0.91]
Subtotal (95% CI)	**28**	**32**		**16.28%**	**0.38[0.16,0.91]**
Total events: 5 (Treatment), 15 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.16(P=0.03)					
11.1.3 Supplements					
Hendry 2010	6/30	11/38		11.29%	0.69[0.29,1.65]
Ishikawa 2010	2/11	3/13		3.2%	0.79[0.16,3.9]
Meng 1999	21/21	23/23		26.14%	1[0.92,1.09]
Mikagi 2011	1/13	3/13		3.49%	0.33[0.04,2.8]
Subtotal (95% CI)	**75**	**87**		**44.11%**	**0.85[0.66,1.1]**
Total events: 30 (Treatment), 40 (Control)					
Heterogeneity: Tau^2=0; Chi^2=14.02, df=3(P=0); I^2=78.61%					
Test for overall effect: Z=1.21(P=0.23)					



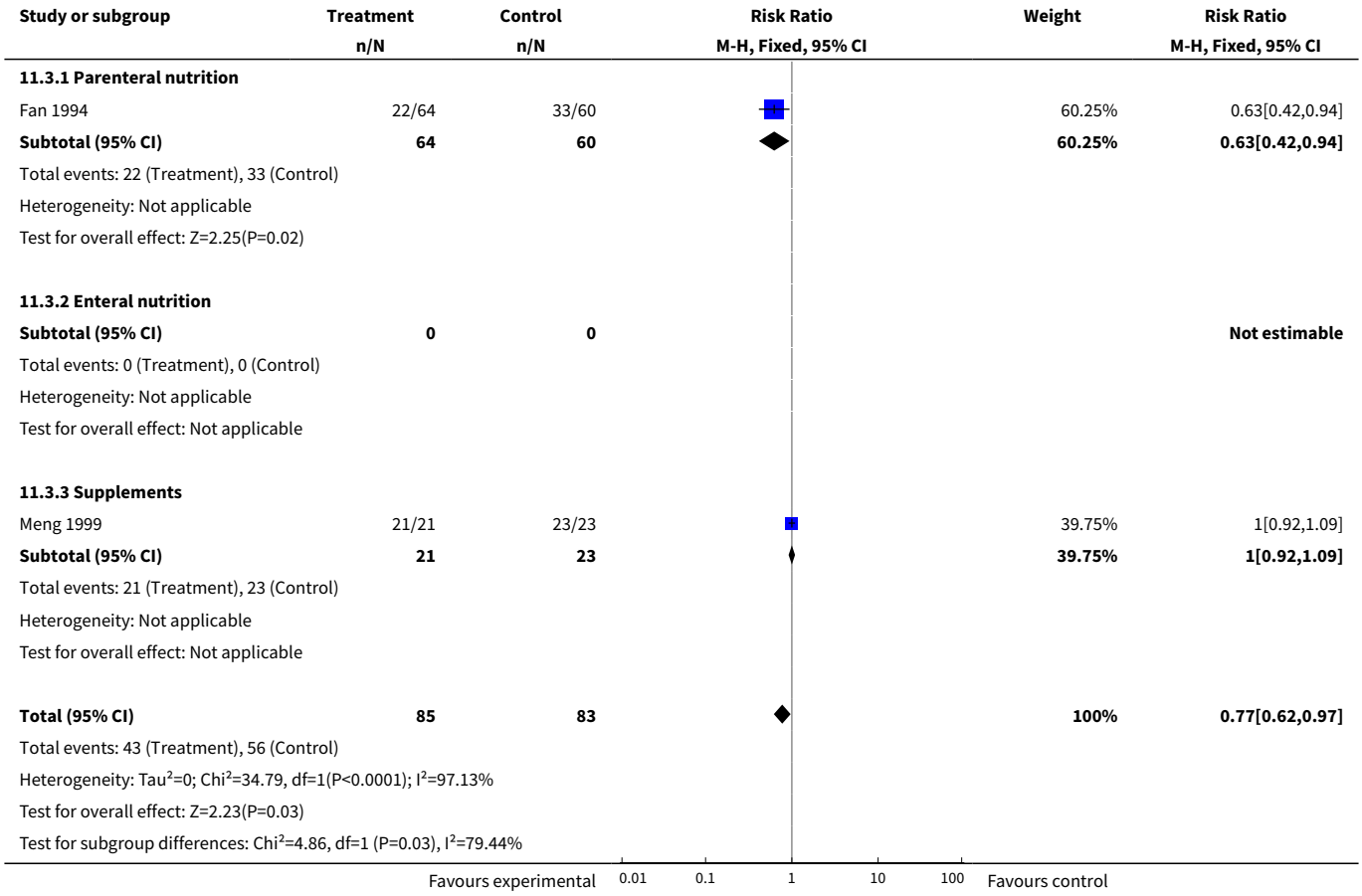
Favours treatment Favours control



Analysis 11.2. Comparison 11 Postoperative total complications, Outcome 2 All studies except those with total complications not patients.



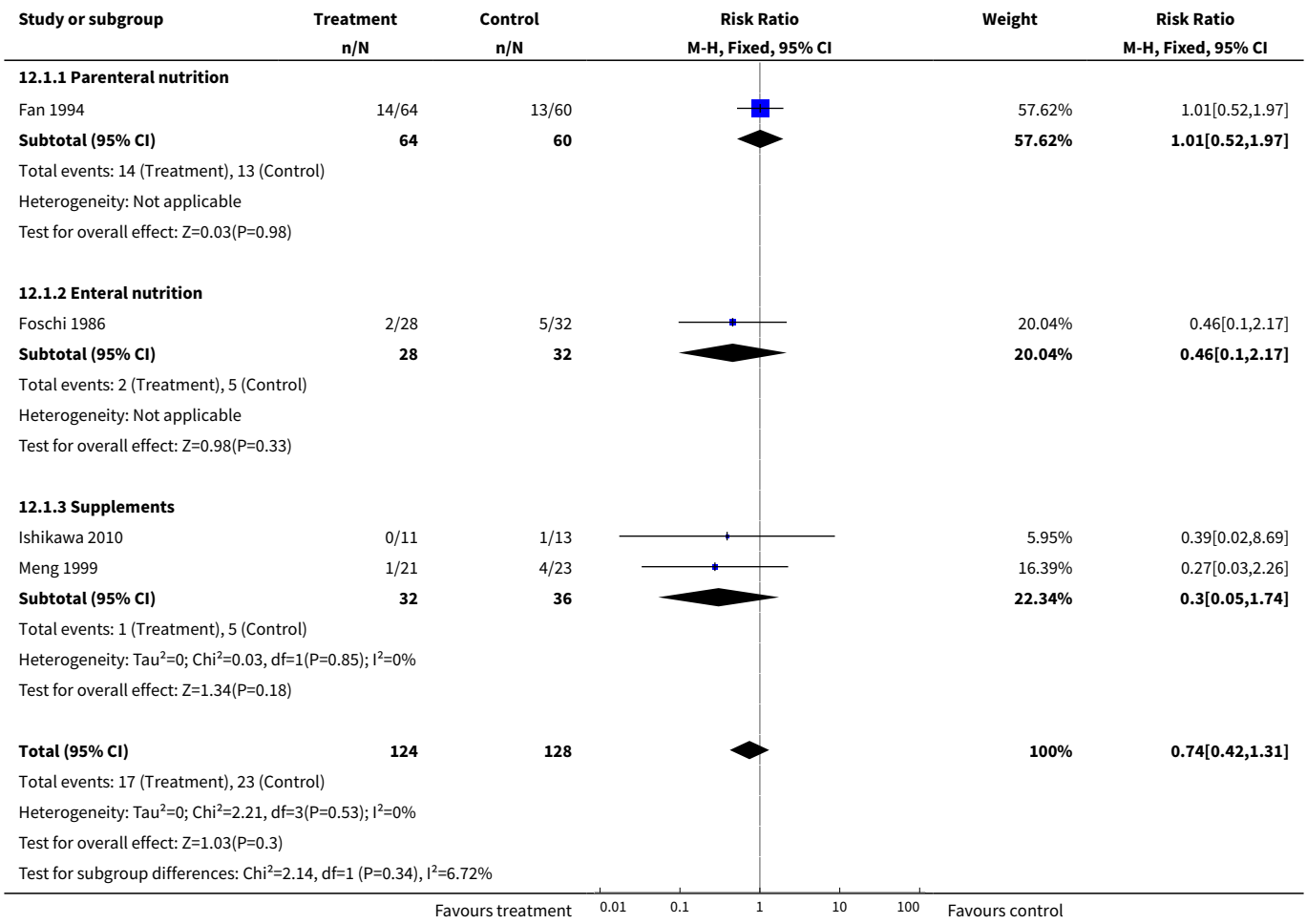
Analysis 11.3. Comparison 11 Postoperative total complications, Outcome 3 HCC.



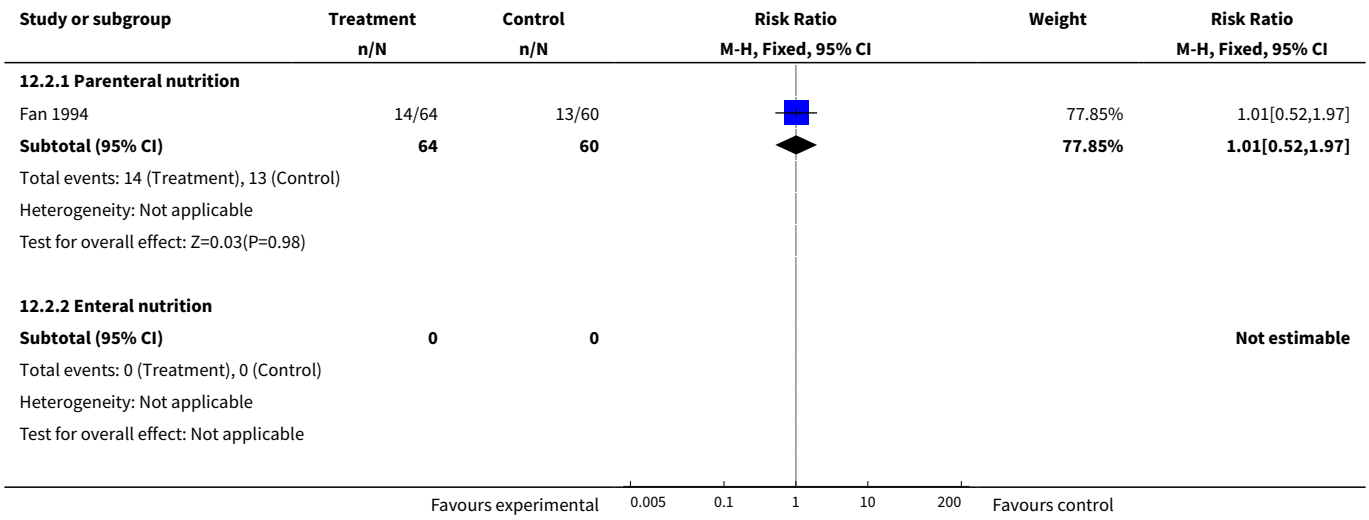
Comparison 12. Postoperative intra-abdominal complications

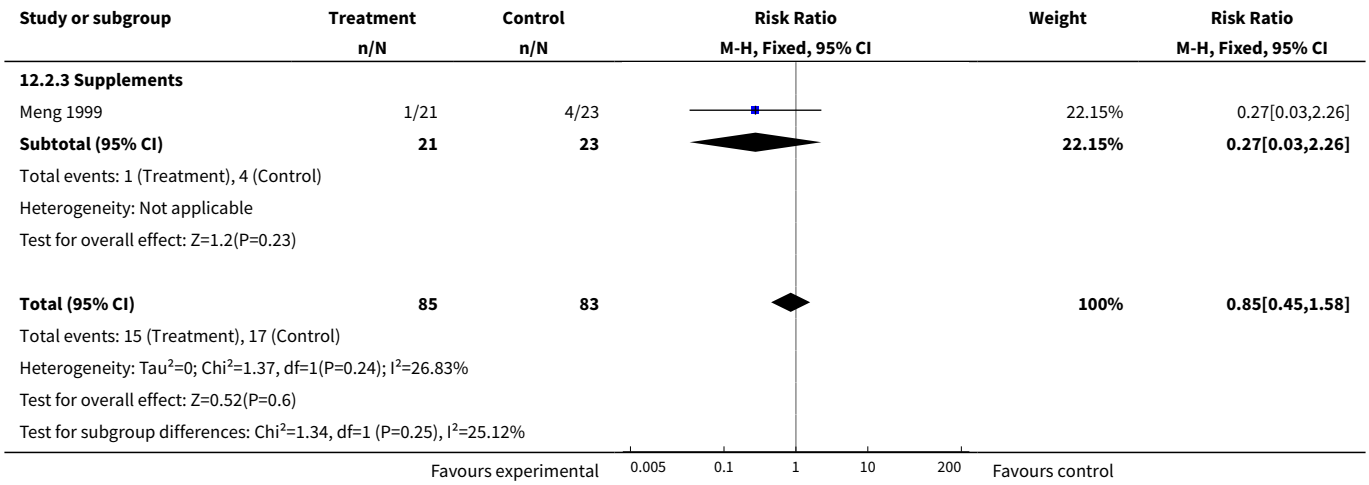
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	4	252	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.42, 1.31]
1.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.52, 1.97]
1.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.10, 2.17]
1.3 Supplements	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.05, 1.74]
2 HCC	2	168	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.45, 1.58]
2.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.52, 1.97]
2.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Supplements	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.03, 2.26]

Analysis 12.1. Comparison 12 Postoperative intra-abdominal complications, Outcome 1 All studies.



Analysis 12.2. Comparison 12 Postoperative intra-abdominal complications, Outcome 2 HCC.

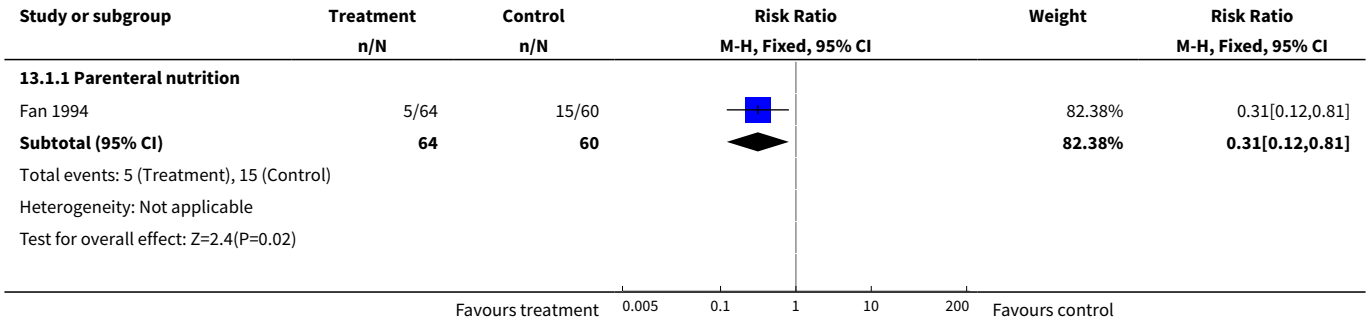


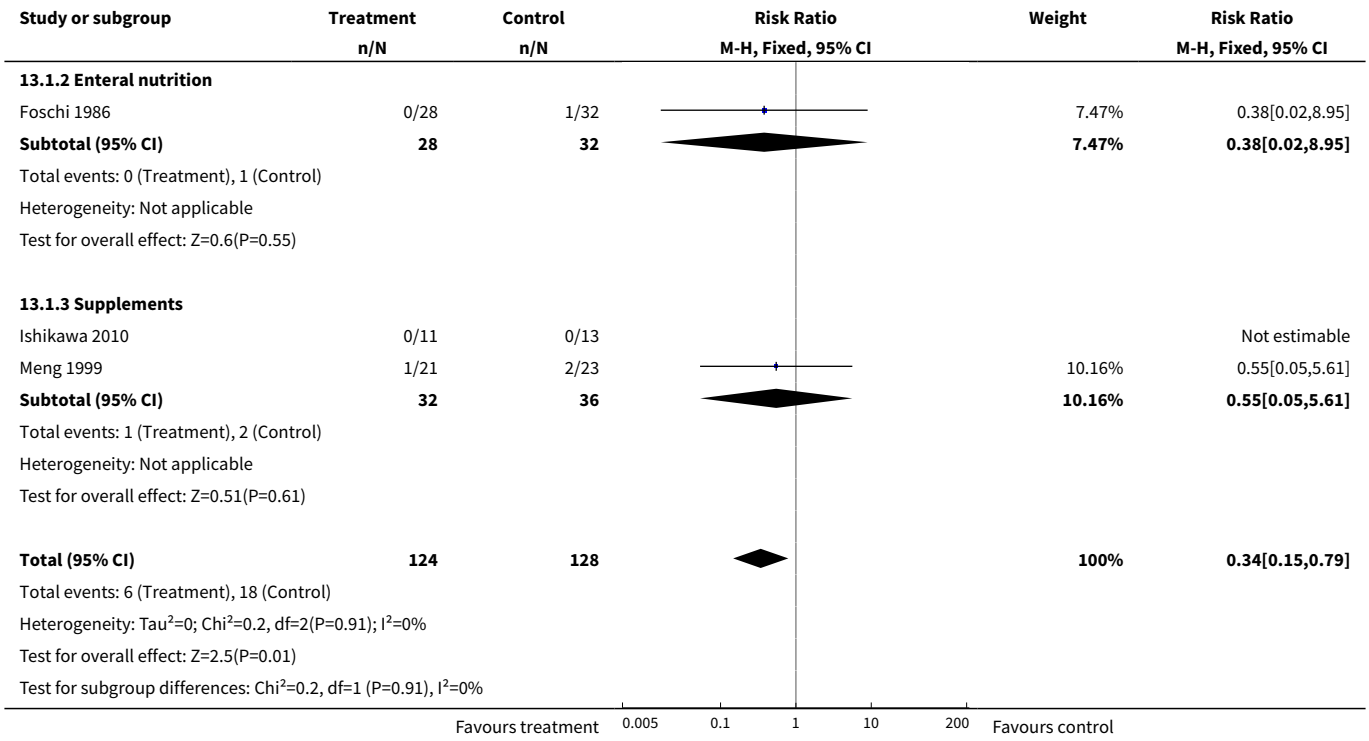


Comparison 13. Postoperative pneumonia

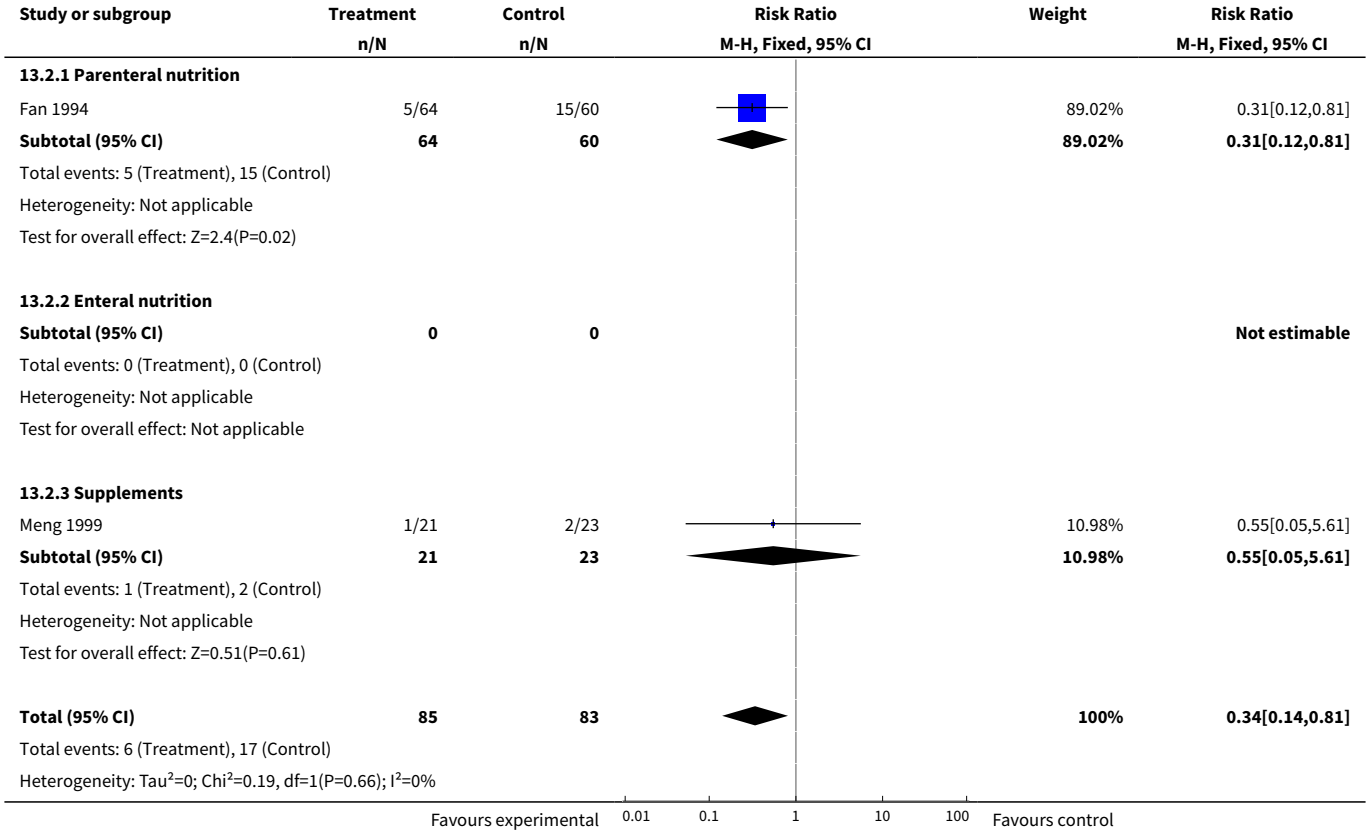
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	4	252	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.15, 0.79]
1.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.12, 0.81]
1.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.02, 8.95]
1.3 Supplements	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.05, 5.61]
2 HCC	2	168	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.14, 0.81]
2.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.12, 0.81]
2.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Supplements	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.05, 5.61]

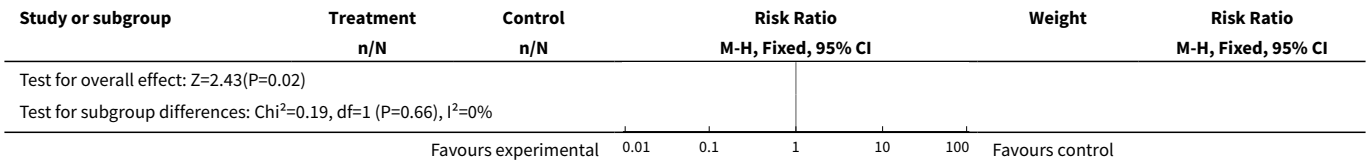
Analysis 13.1. Comparison 13 Postoperative pneumonia, Outcome 1 All studies.





Analysis 13.2. Comparison 13 Postoperative pneumonia, Outcome 2 HCC.

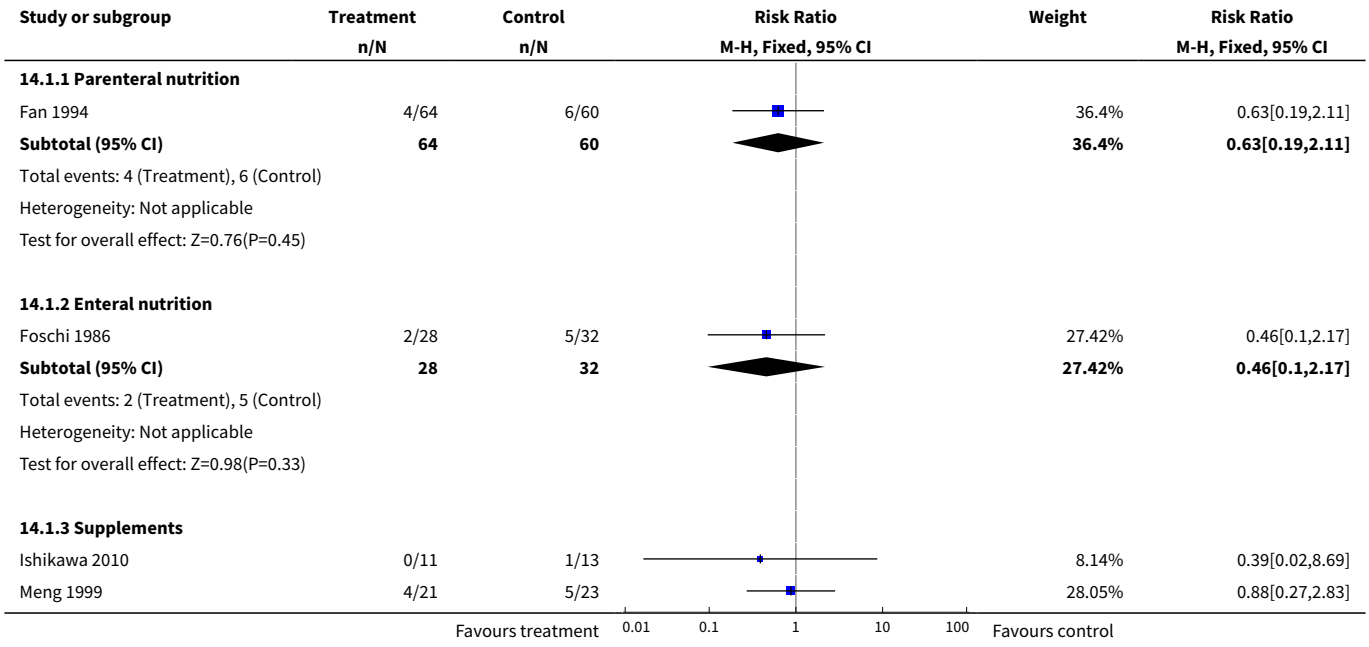


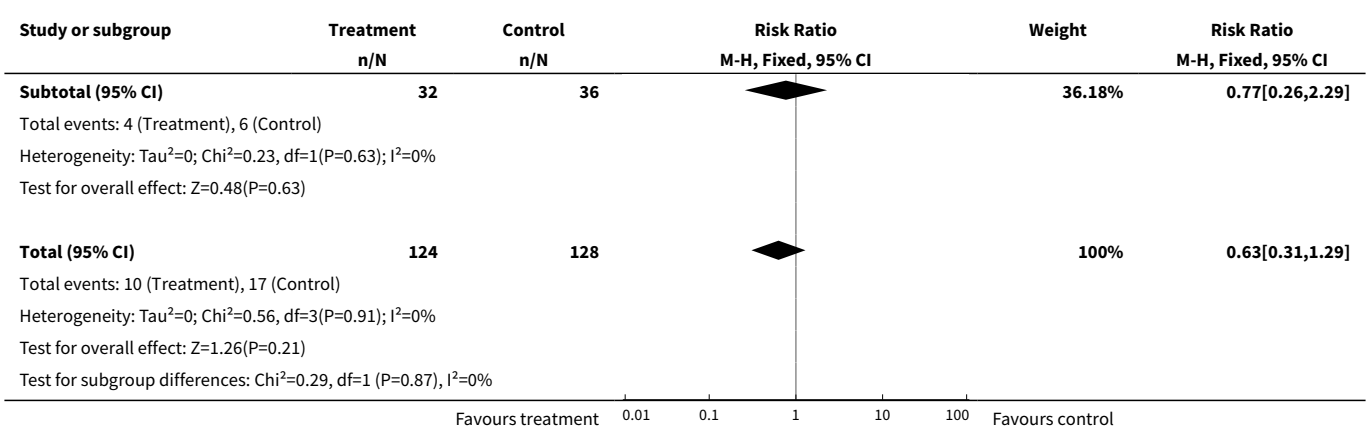


Comparison 14. Postoperative wound infections

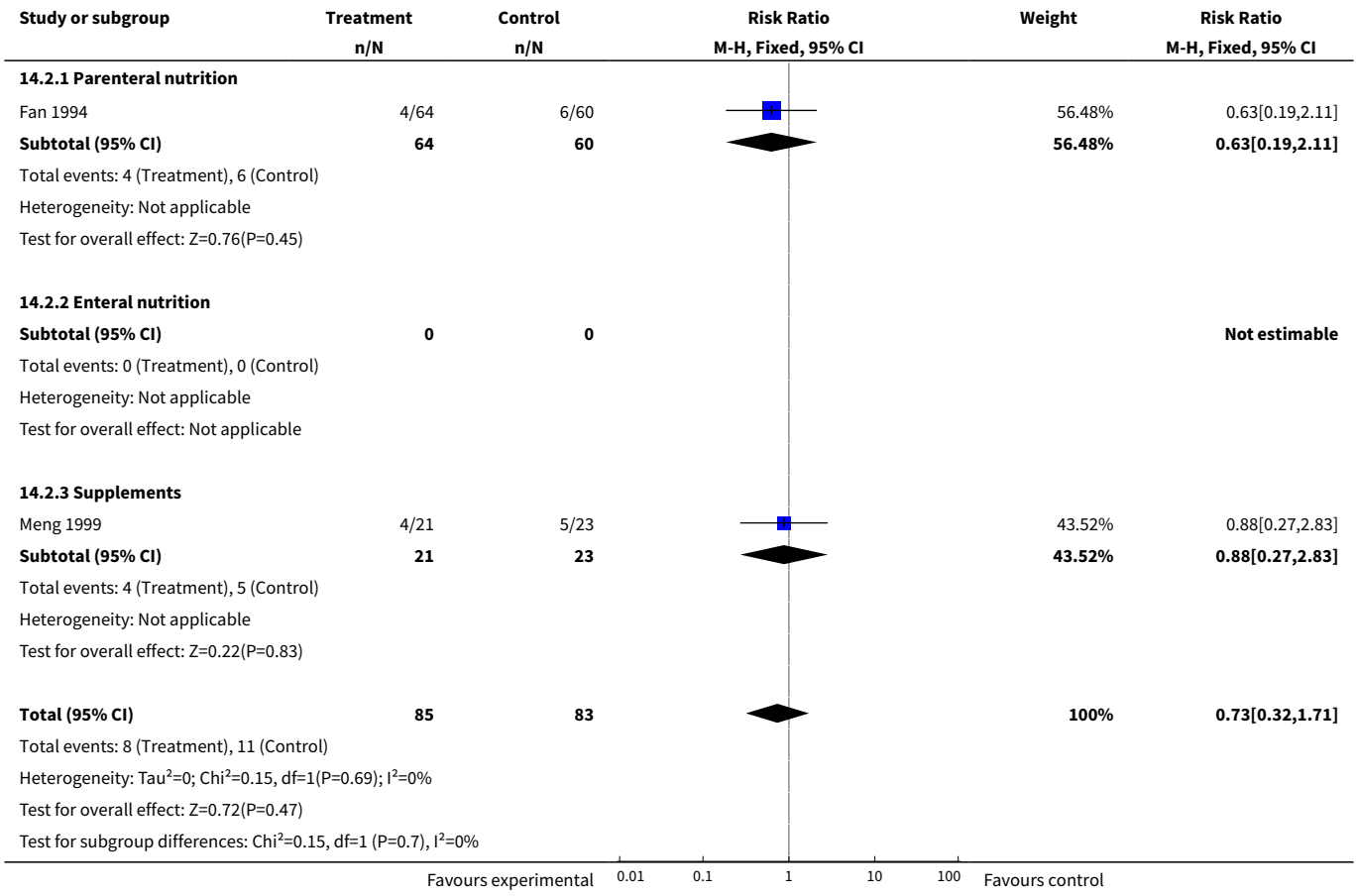
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	4	252	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.31, 1.29]
1.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.19, 2.11]
1.2 Enteral nutrition	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.10, 2.17]
1.3 Supplements	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.26, 2.29]
2 HCC	2	168	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.32, 1.71]
2.1 Parenteral nutrition	1	124	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.19, 2.11]
2.2 Enteral nutrition	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Supplements	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.27, 2.83]

Analysis 14.1. Comparison 14 Postoperative wound infections, Outcome 1 All studies.





Analysis 14.2. Comparison 14 Postoperative wound infections, Outcome 2 HCC.

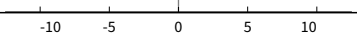


Comparison 15. Nitrogen balance

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies (all medical)	3	81	Mean Difference (IV, Fixed, 95% CI)	1.99 [0.69, 3.28]
1.1 Parenteral nutrition	1	21	Mean Difference (IV, Fixed, 95% CI)	3.60 [0.86, 6.34]
1.2 Enteral nutrition	1	22	Mean Difference (IV, Fixed, 95% CI)	1.40 [-3.16, 5.96]
1.3 Supplements	1	38	Mean Difference (IV, Fixed, 95% CI)	1.54 [-0.01, 3.09]
2 Cirrhosis	2	60	Mean Difference (IV, Random, 95% CI)	1.53 [0.06, 2.99]

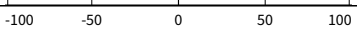
Analysis 15.1. Comparison 15 Nitrogen balance, Outcome 1 All studies (all medical).

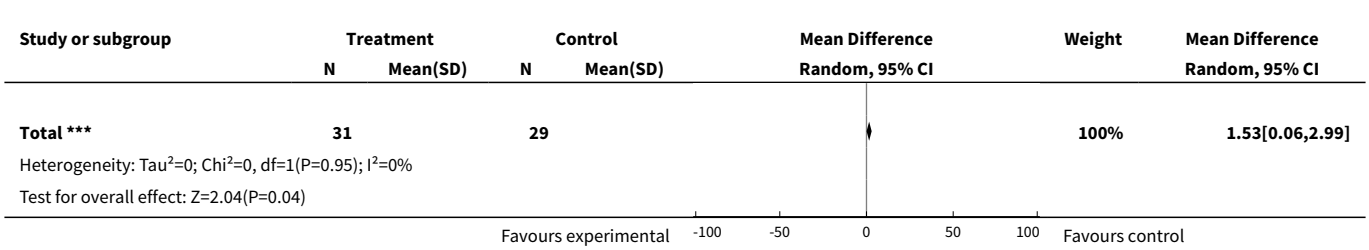
Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
15.1.1 Parenteral nutrition							
Bonkovsky 1991	9	6.8 (2.1)	12	3.2 (4.2)		22.22%	3.6[0.86,6.34]
Subtotal ***	**9**		**12**			**22.22%**	**3.6[0.86,6.34]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.57(P=0.01)							
15.1.2 Enteral nutrition							
DeLedinghen 1997	12	5.3 (5.8)	10	3.9 (5.1)		8.06%	1.4[-3.16,5.96]
Subtotal ***	**12**		**10**			**8.06%**	**1.4[-3.16,5.96]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=0.6(P=0.55)							
15.1.3 Supplements							
Nakaya 2007	19	1.5 (1.9)	19	0 (2.9)		69.73%	1.54[-0.01,3.09]
Subtotal ***	**19**		**19**			**69.73%**	**1.54[-0.01,3.09]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.95(P=0.05)							
Total ***	**40**		**41**			**100%**	**1.99[0.69,3.28]**
Heterogeneity: Tau^2=0; Chi^2=1.71, df=2(P=0.43); I^2=0%							
Test for overall effect: Z=3.01(P=0)							
Test for subgroup differences: Chi^2=1.71, df=1 (P=0.43), I^2=0%							



Analysis 15.2. Comparison 15 Nitrogen balance, Outcome 2 Cirrhosis.

Study or subgroup	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
DeLedinghen 1997	12	5.3 (5.8)	10	3.9 (5.1)		10.36%	1.4[-3.16,5.96]
Nakaya 2007	19	1.5 (1.9)	19	0 (2.9)		89.64%	1.54[-0.01,3.09]





Comparison 16. Mortality - absolute risk difference (ARD)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 All studies	28	1668	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.05, 0.01]
2 Parenteral nutrition	9	465	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.07, 0.01]
2.1 Medical trials	4	158	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.11, 0.06]
2.2 Surgical trials	5	307	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.08, 0.02]
3 Enteral nutrition	6	275	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.15, 0.03]
3.1 Medical trials	5	215	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.15, 0.06]
3.2 Surgical trials	1	60	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.22, 0.04]
4 Supplements	13	928	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.06, 0.03]
4.1 Medical trials	9	710	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.07, 0.05]
4.2 Surgical trials	4	218	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.12, 0.07]
5 Medical trials	18	1083	Risk Difference (M-H, Fixed, 95% CI)	-0.00 [-0.05, 0.04]
5.1 Parenteral nutrition	4	158	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.14, 0.06]
5.2 Enteral nutrition	5	215	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.15, 0.06]
5.3 Supplements	9	710	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.04, 0.08]

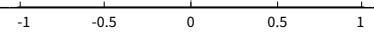
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Surgical trials	10	585	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.10, -0.01]
6.1 Parenteral nutrition	5	307	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.12, 0.00]
6.2 Enteral nutrition	1	60	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.22, 0.04]
6.3 Supplements	4	218	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.11, 0.04]
7 Alcoholic hepatitis	7	300	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.14, 0.04]
7.1 Parenteral nutrition	3	118	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.18, 0.07]
7.2 Enteral nutrition	2	95	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.16, 0.23]
7.3 Supplements	2	87	Risk Difference (M-H, Fixed, 95% CI)	-0.13 [-0.29, 0.03]
8 Cirrhosis	9	349	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.13, -0.01]
8.1 Parenteral nutrition	2	60	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.16, 0.09]
8.2 Enteral nutrition	3	120	Risk Difference (M-H, Fixed, 95% CI)	-0.11 [-0.22, 0.01]
8.3 Supplements	4	169	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.15, 0.03]
9 HCC	6	673	Risk Difference (M-H, Fixed, 95% CI)	0.04 [-0.02, 0.10]
9.1 Parenteral Nutrition	1	124	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.18, 0.04]
9.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	5	549	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.01, 0.14]
10 Abstracts excluded	25	1348	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.08, -0.01]
10.1 Medical trials - parenteral nutrition	4	158	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.14, 0.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.2 Surgical trials - parenteral nutrition	5	307	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.12, 0.00]
10.3 Medical trials - enteral nutrition	4	152	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.20, 0.09]
10.4 Surgical trials - enteral nutrition	1	60	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.22, 0.04]
10.5 Medical trials - supplements	8	477	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.10, 0.02]
10.6 Surgical trials - supplements	3	194	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.12, 0.04]
11 Surgical trials without transplant patients	7	410	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.09, 0.01]
11.1 Parenteral nutrition	3	214	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.14, 0.01]
11.2 Enteral nutrition	1	60	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.22, 0.04]
11.3 Supplements	3	136	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.06, 0.10]
12 Intent to treat - best-case scenario for intervention	24	1539	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.11, -0.03]
12.1 Medical trials - Parenteral nutrition	4	170	Risk Difference (M-H, Fixed, 95% CI)	-0.12 [-0.22, -0.02]
12.2 Surgical trials - Parenteral nutrition	4	268	Risk Difference (M-H, Fixed, 95% CI)	-0.17 [-0.25, -0.10]
12.3 Medical trials - Enteral nutrition	5	215	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.15, 0.06]
12.4 Surgical trials - enteral nutrition	1	64	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.22, 0.04]
12.5 Medical trials - Supplements	8	690	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.09, 0.03]
12.6 Surgical trials - Supplements	2	132	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.17, 0.05]
13 Intent to treat - worst-case scenario for intervention	24	1539	Risk Difference (M-H, Fixed, 95% CI)	0.04 [-0.00, 0.08]
13.1 Medical trials - Parenteral nutrition	4	170	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.08, 0.13]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.2 Surgical trials - Parenteral nutrition	4	268	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.06, 0.10]
13.3 Medical trials - Enteral nutrition	5	215	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.15, 0.06]
13.4 Surgical trials - Enteral nutrition	1	64	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.14, 0.20]
13.5 Medical trials - Supplements	8	690	Risk Difference (M-H, Fixed, 95% CI)	0.07 [0.01, 0.14]
13.6 Surgical trials - Supplements	2	132	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.09, 0.14]

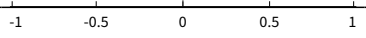
Analysis 16.1. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 1 All studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Achord 1987	1/14	3/14		1.7%	-0.14[-0.4,0.11]
Bonkovsky 1991	0/9	0/12		1.25%	0[-0.17,0.17]
Bunout 1989	2/17	5/19		2.18%	-0.15[-0.4,0.1]
Cabre 1990	2/16	9/19		2.11%	-0.35[-0.63,-0.07]
Calvey 1985	16/42	7/22		3.51%	0.06[-0.18,0.31]
DeLedinghen 1997	3/12	2/10		1.33%	0.05[-0.3,0.4]
Fan 1994	5/64	9/60		7.53%	-0.07[-0.18,0.04]
Foschi 1986	1/28	4/32		3.63%	-0.09[-0.22,0.04]
Hendry 2010	0/30	2/38		4.07%	-0.05[-0.14,0.04]
Hirsch 1993	3/26	6/25		3.1%	-0.12[-0.33,0.08]
Humbert 1988	2/27	4/22		2.95%	-0.11[-0.3,0.08]
Ichikawa 2010	0/12	0/9		1.25%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		1.45%	0[-0.15,0.15]
Kearns 1992	5/16	5/15		1.88%	-0.02[-0.35,0.31]
Kobashi 2006	63/119	44/114		14.15%	0.14[0.02,0.27]
LeCornu 2000	2/42	7/40		4.98%	-0.13[-0.26,0.01]
Meng 1999	4/21	1/23		2.67%	0.15[-0.04,0.33]
Nakaya 2007	1/25	0/23		2.91%	0.04[-0.07,0.15]
Naveau 1986	1/20	1/20		2.43%	0[-0.14,0.14]
Norman 2008	1/31	2/32		3.83%	-0.03[-0.13,0.07]
Poon 2004	0/41	3/43		5.1%	-0.07[-0.16,0.02]
Puglionisi 1985	0/10	1/10		1.22%	-0.1[-0.34,0.14]
Qiu 2009	0/44	0/21		3.45%	0[-0.07,0.07]
Reilly 1990	1/18	2/10		1.56%	-0.14[-0.41,0.13]
San-In Group 1997	34/67	32/65		8.02%	0.02[-0.16,0.19]
Simon 1988	5/33	7/36		4.18%	-0.04[-0.22,0.14]
Takeshita 2009	0/28	0/28		3.4%	0[-0.07,0.07]
Zheng 2003	0/40	1/30		4.17%	-0.03[-0.12,0.05]



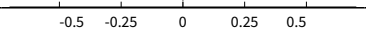
Favors treatment — Favors control

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Total (95% CI)	**863**	**805**		**100%**	**-0.02[-0.05,0.01]**
Total events: 152 (Treatment), 157 (Control)					
Heterogeneity: Tau^2=0; Chi^2=29.05, df=27(P=0.36); I^2=7.05%					
Test for overall effect: Z=1.12(P=0.26)					



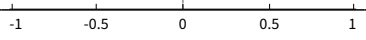
Analysis 16.2. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 2 Parenteral nutrition.

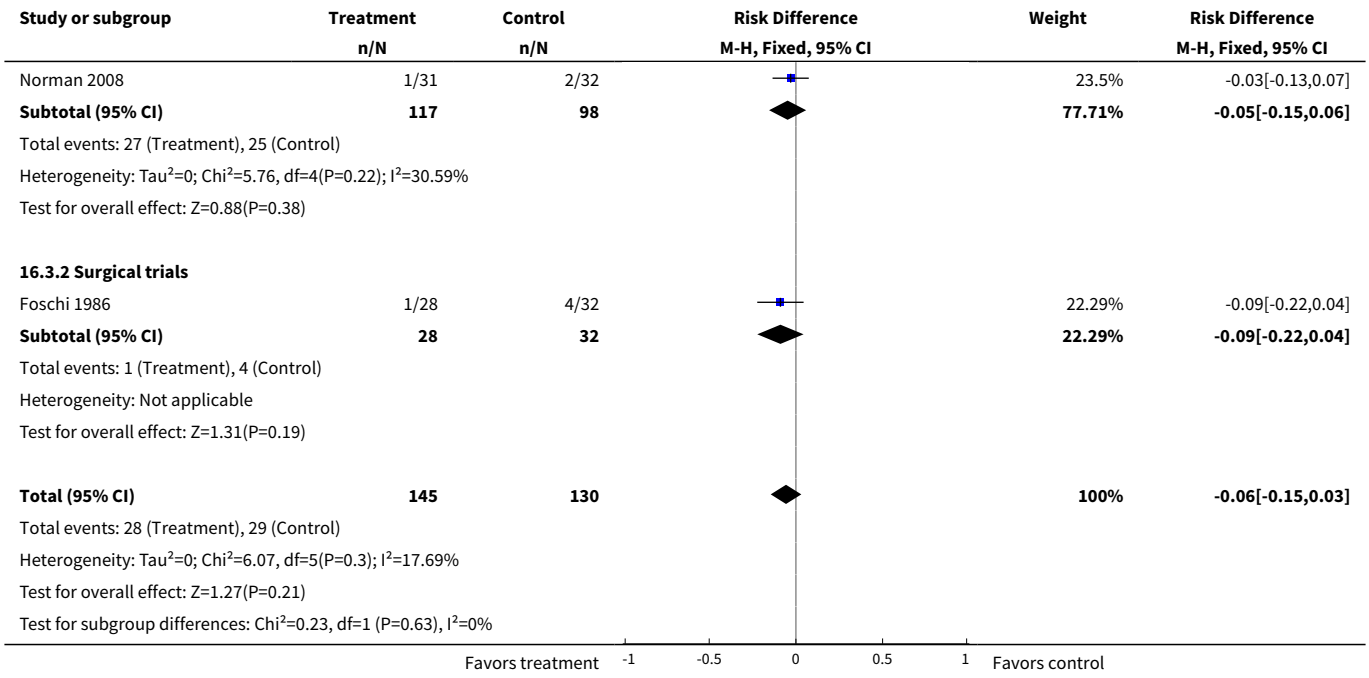
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
16.2.1 Medical trials					
Achord 1987	1/14	3/14		2.58%	-0.14[-0.4,0.11]
Bonkovsky 1991	0/9	0/12		5.7%	0[-0.17,0.17]
Naveau 1986	1/20	1/20		9.11%	0[-0.14,0.14]
Simon 1988	5/33	7/36		5.25%	-0.04[-0.22,0.14]
Subtotal (95% CI)	**76**	**82**		**22.63%**	**-0.03[-0.11,0.06]**
Total events: 7 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.25, df=3(P=0.74); I^2=0%					
Test for overall effect: Z=0.6(P=0.55)					
16.2.2 Surgical trials					
Fan 1994	5/64	9/60		13.31%	-0.07[-0.18,0.04]
Puglionisi 1985	0/10	1/10		2.95%	-0.1[-0.34,0.14]
Qiu 2009	0/44	0/21		34.51%	0[-0.07,0.07]
Reilly 1990	1/18	2/10		2.29%	-0.14[-0.41,0.13]
Zheng 2003	0/40	1/30		24.32%	-0.03[-0.12,0.05]
Subtotal (95% CI)	**176**	**131**		**77.37%**	**-0.03[-0.08,0.02]**
Total events: 6 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.53, df=4(P=0.47); I^2=0%					
Test for overall effect: Z=1.31(P=0.19)					
Total (95% CI)	**252**	**213**		**100%**	**-0.03[-0.07,0.01]**
Total events: 13 (Treatment), 24 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.59, df=8(P=0.8); I^2=0%					
Test for overall effect: Z=1.44(P=0.15)					
Test for subgroup differences: Chi^2=0.01, df=1 (P=0.92), I^2=0%					



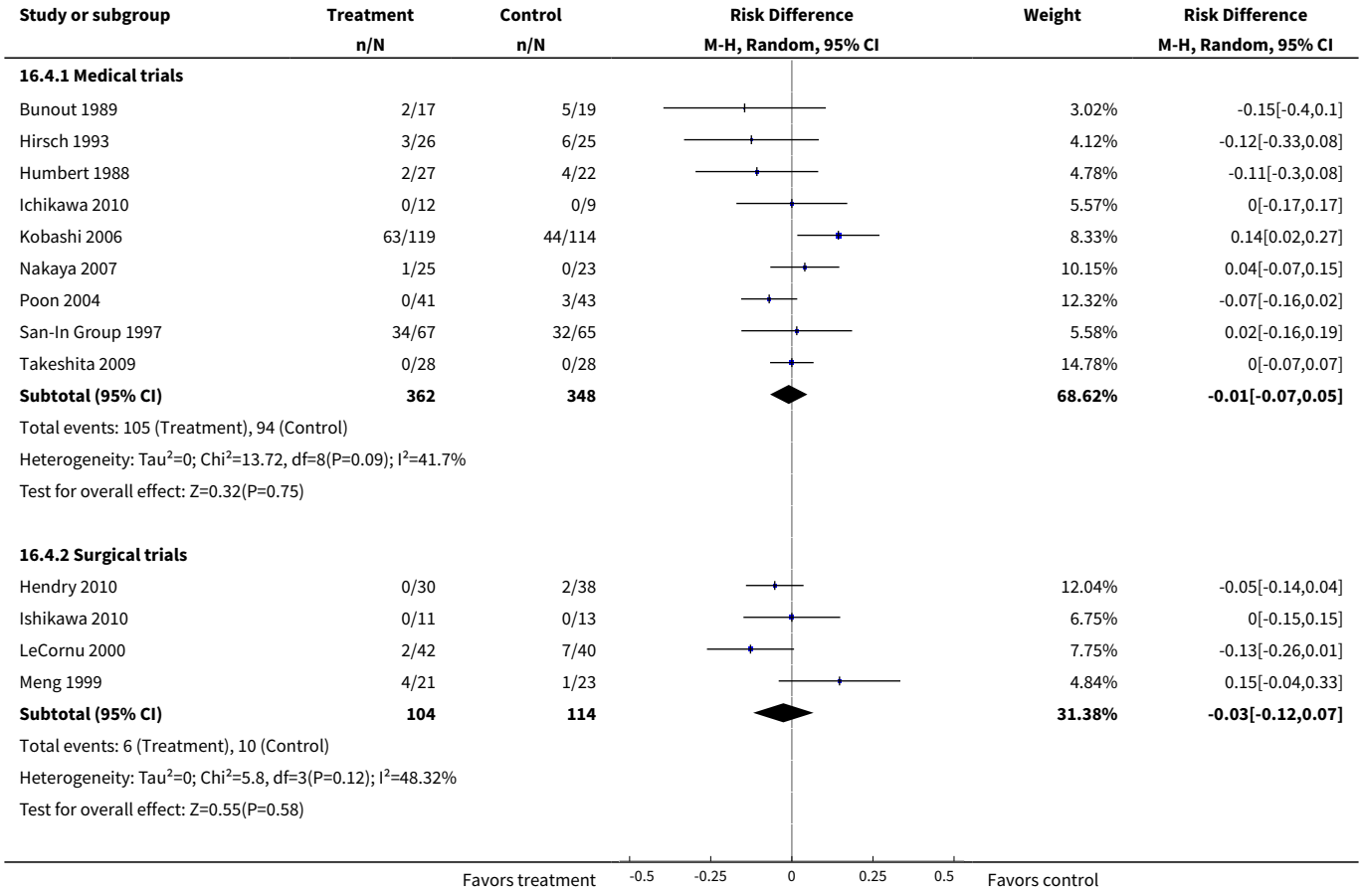
Analysis 16.3. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 3 Enteral nutrition.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.3.1 Medical trials					
Cabre 1990	2/16	9/19		12.96%	-0.35[-0.63,-0.07]
Calvey 1985	16/42	7/22		21.55%	0.06[-0.18,0.31]
DeLedinghen 1997	3/12	2/10		8.14%	0.05[-0.3,0.4]
Kearns 1992	5/16	5/15		11.56%	-0.02[-0.35,0.31]

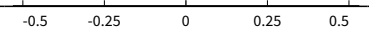




Analysis 16.4. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 4 Supplements.

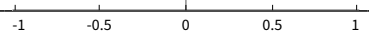


Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Total (95% CI)	**466**	**462**		**100%**	**-0.02[-0.06,0.03]**
Total events: 111 (Treatment), 104 (Control)					
Heterogeneity: Tau^2=0; Chi^2=20.16, df=12(P=0.06); I^2=40.47%					
Test for overall effect: Z=0.65(P=0.52)					
Test for subgroup differences: Chi^2=0.09, df=1 (P=0.77), I^2=0%					



Analysis 16.5. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 5 Medical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.5.1 Parenteral nutrition					
Achord 1987	1/14	3/14		2.61%	-0.14[-0.4,0.11]
Bonkovsky 1991	0/9	0/12		1.91%	0[-0.17,0.17]
Naveau 1986	1/20	1/20		3.72%	0[-0.14,0.14]
Simon 1988	5/33	7/36		6.41%	-0.04[-0.22,0.14]
Subtotal (95% CI)	**76**	**82**		**14.65%**	**-0.04[-0.14,0.06]**
Total events: 7 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.25, df=3(P=0.74); I^2=0%					
Test for overall effect: Z=0.87(P=0.38)					
16.5.2 Enteral nutrition					
Cabre 1990	2/16	9/19		3.23%	-0.35[-0.63,-0.07]
Calvey 1985	16/42	7/22		5.38%	0.06[-0.18,0.31]
DeLedinghen 1997	3/12	2/10		2.03%	0.05[-0.3,0.4]
Kearns 1992	5/16	5/15		2.88%	-0.02[-0.35,0.31]
Norman 2008	1/31	2/32		5.86%	-0.03[-0.13,0.07]
Subtotal (95% CI)	**117**	**98**		**19.38%**	**-0.05[-0.15,0.06]**
Total events: 27 (Treatment), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.76, df=4(P=0.22); I^2=30.59%					
Test for overall effect: Z=0.88(P=0.38)					
16.5.3 Supplements					
Bunout 1989	2/17	5/19		3.34%	-0.15[-0.4,0.1]
Hirsch 1993	3/26	6/25		4.75%	-0.12[-0.33,0.08]
Humbert 1988	2/27	4/22		4.51%	-0.11[-0.3,0.08]
Ichikawa 2010	0/12	0/9		1.91%	0[-0.17,0.17]
Kobashi 2006	63/119	44/114		21.68%	0.14[0.02,0.27]
Nakaya 2007	1/25	0/23		4.46%	0.04[-0.07,0.15]
Poon 2004	0/41	3/43		7.81%	-0.07[-0.16,0.02]
San-In Group 1997	34/67	32/65		12.28%	0.02[-0.16,0.19]
Takeshita 2009	0/28	0/28		5.21%	0[-0.07,0.07]
Subtotal (95% CI)	**362**	**348**		**65.96%**	**0.02[-0.04,0.08]**
Total events: 105 (Treatment), 94 (Control)					
Heterogeneity: Tau^2=0; Chi^2=13.72, df=8(P=0.09); I^2=41.7%					
Test for overall effect: Z=0.68(P=0.49)					
Total (95% CI)	**555**	**528**		**100%**	**-0[-0.05,0.04]**
Total events: 139 (Treatment), 130 (Control)					



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=19.93, df=17(P=0.28); I²=14.71%					
Test for overall effect: Z=0.09(P=0.93)					
Test for subgroup differences: Chi²=1.93, df=1 (P=0.38), I²=0%					

Favors treatment -1 -0.5 0 0.5 1 Favors control

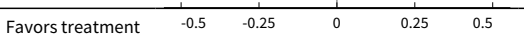
Analysis 16.6. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 6 Surgical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.6.1 Parenteral nutrition					
Fan 1994	5/64	9/60		21.67%	-0.07[-0.18,0.04]
Puglionisi 1985	0/10	1/10		3.5%	-0.1[-0.34,0.14]
Qiu 2009	0/44	0/21		9.95%	0[-0.07,0.07]
Reilly 1990	1/18	2/10		4.5%	-0.14[-0.41,0.13]
Zheng 2003	0/40	1/30		12%	-0.03[-0.12,0.05]
Subtotal (95% CI)	**176**	**131**		**51.62%**	**-0.06[-0.12,0]**
Total events: 6 (Treatment), 13 (Control)					
Heterogeneity: Tau²=0; Chi²=3.53, df=4(P=0.47); I²=0%					
Test for overall effect: Z=1.86(P=0.06)					
16.6.2 Enteral nutrition					
Foschi 1986	1/28	4/32		10.45%	-0.09[-0.22,0.04]
Subtotal (95% CI)	**28**	**32**		**10.45%**	**-0.09[-0.22,0.04]**
Total events: 1 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.31(P=0.19)					
16.6.3 Supplements					
Hendry 2010	0/30	2/38		11.73%	-0.05[-0.14,0.04]
Ishikawa 2010	0/11	0/13		4.17%	0[-0.15,0.15]
LeCornu 2000	2/42	7/40		14.34%	-0.13[-0.26,0.01]
Meng 1999	4/21	1/23		7.68%	0.15[-0.04,0.33]
Subtotal (95% CI)	**104**	**114**		**37.93%**	**-0.03[-0.11,0.04]**
Total events: 6 (Treatment), 10 (Control)					
Heterogeneity: Tau²=0; Chi²=5.8, df=3(P=0.12); I²=48.32%					
Test for overall effect: Z=0.95(P=0.34)					
Total (95% CI)	**308**	**277**		**100%**	**-0.05[-0.1,-0.01]**
Total events: 13 (Treatment), 27 (Control)					
Heterogeneity: Tau²=0; Chi²=9.39, df=9(P=0.4); I²=4.19%					
Test for overall effect: Z=2.34(P=0.02)					
Test for subgroup differences: Chi²=0.55, df=1 (P=0.76), I²=0%					

Favors treatment -0.5 -0.25 0 0.25 0.5 Favors control

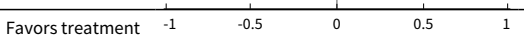
Analysis 16.7. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 7 Alcoholic hepatitis.

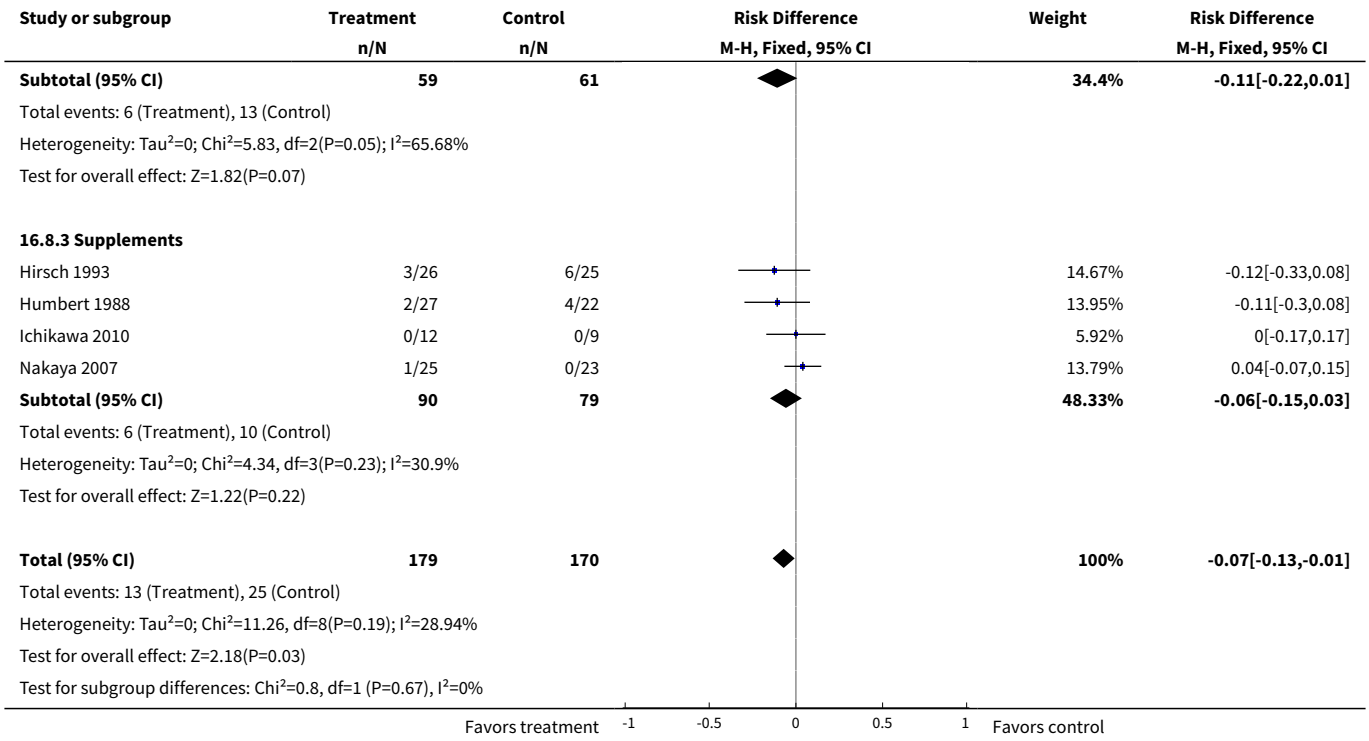
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.7.1 Parenteral nutrition					
Achord 1987	1/14	3/14		9.56%	-0.14[-0.4,0.11]
Bonkovsky 1991	0/9	0/12		7.02%	0[-0.17,0.17]
Simon 1988	5/33	7/36		23.5%	-0.04[-0.22,0.14]
Subtotal (95% CI)	**56**	**62**		**40.08%**	**-0.06[-0.18,0.07]**
Total events: 6 (Treatment), 10 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.91, df=2(P=0.63); I^2=0%					
Test for overall effect: Z=0.93(P=0.35)					
16.7.2 Enteral nutrition					
Calvey 1985	16/42	7/22		19.71%	0.06[-0.18,0.31]
Kearns 1992	5/16	5/15		10.57%	-0.02[-0.35,0.31]
Subtotal (95% CI)	**58**	**37**		**30.28%**	**0.03[-0.16,0.23]**
Total events: 21 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.16, df=1(P=0.69); I^2=0%					
Test for overall effect: Z=0.34(P=0.74)					
16.7.3 Supplements					
Bunout 1989	2/17	5/19		12.25%	-0.15[-0.4,0.1]
Hirsch 1993	3/26	6/25		17.4%	-0.12[-0.33,0.08]
Subtotal (95% CI)	**43**	**44**		**29.65%**	**-0.13[-0.29,0.03]**
Total events: 5 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.9); I^2=0%					
Test for overall effect: Z=1.63(P=0.1)					
Total (95% CI)	**157**	**143**		**100%**	**-0.05[-0.14,0.04]**
Total events: 32 (Treatment), 33 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.75, df=6(P=0.84); I^2=0%					
Test for overall effect: Z=1.14(P=0.25)					
Test for subgroup differences: Chi^2=1.68, df=1 (P=0.43), I^2=0%					



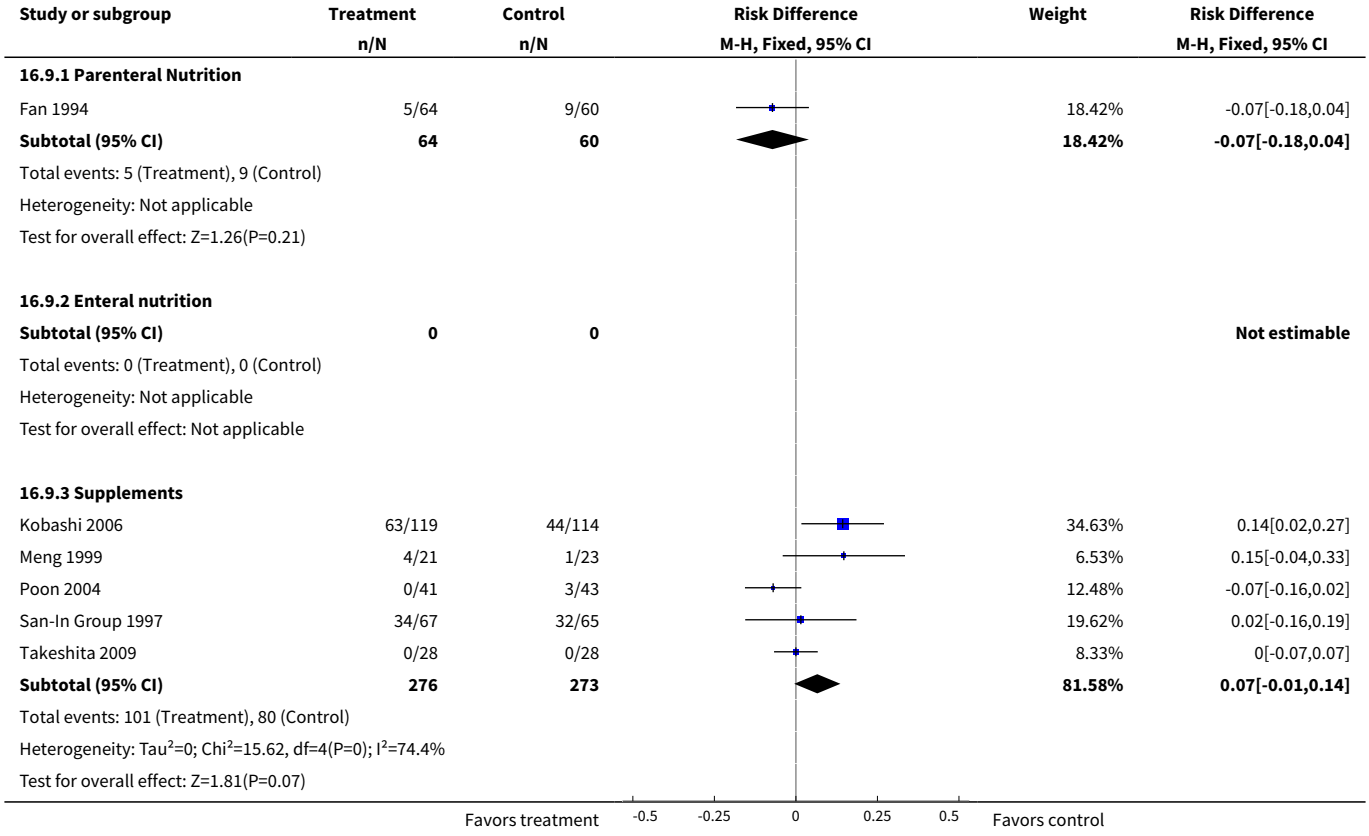
Analysis 16.8. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 8 Cirrhosis.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.8.1 Parenteral nutrition					
Naveau 1986	1/20	1/20		11.51%	0[-0.14,0.14]
Puglionisi 1985	0/10	1/10		5.76%	-0.1[-0.34,0.14]
Subtotal (95% CI)	**30**	**30**		**17.27%**	**-0.03[-0.16,0.09]**
Total events: 1 (Treatment), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.54, df=1(P=0.46); I^2=0%					
Test for overall effect: Z=0.52(P=0.6)					
16.8.2 Enteral nutrition					
Cabre 1990	2/16	9/19		10%	-0.35[-0.63,-0.07]
DeLedinghen 1997	3/12	2/10		6.28%	0.05[-0.3,0.4]
Norman 2008	1/31	2/32		18.12%	-0.03[-0.13,0.07]

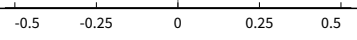




Analysis 16.9. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 9 HCC.



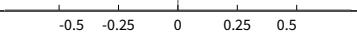
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Total (95% CI)	**340**	**333**		**100%**	**0.04[-0.02,0.1]**
Total events: 106 (Treatment), 89 (Control)					
Heterogeneity: Tau^2=0; Chi^2=15.37, df=5(P=0.01); I^2=67.47%					
Test for overall effect: Z=1.29(P=0.2)					
Test for subgroup differences: Chi^2=4.15, df=1 (P=0.04), I^2=75.88%					



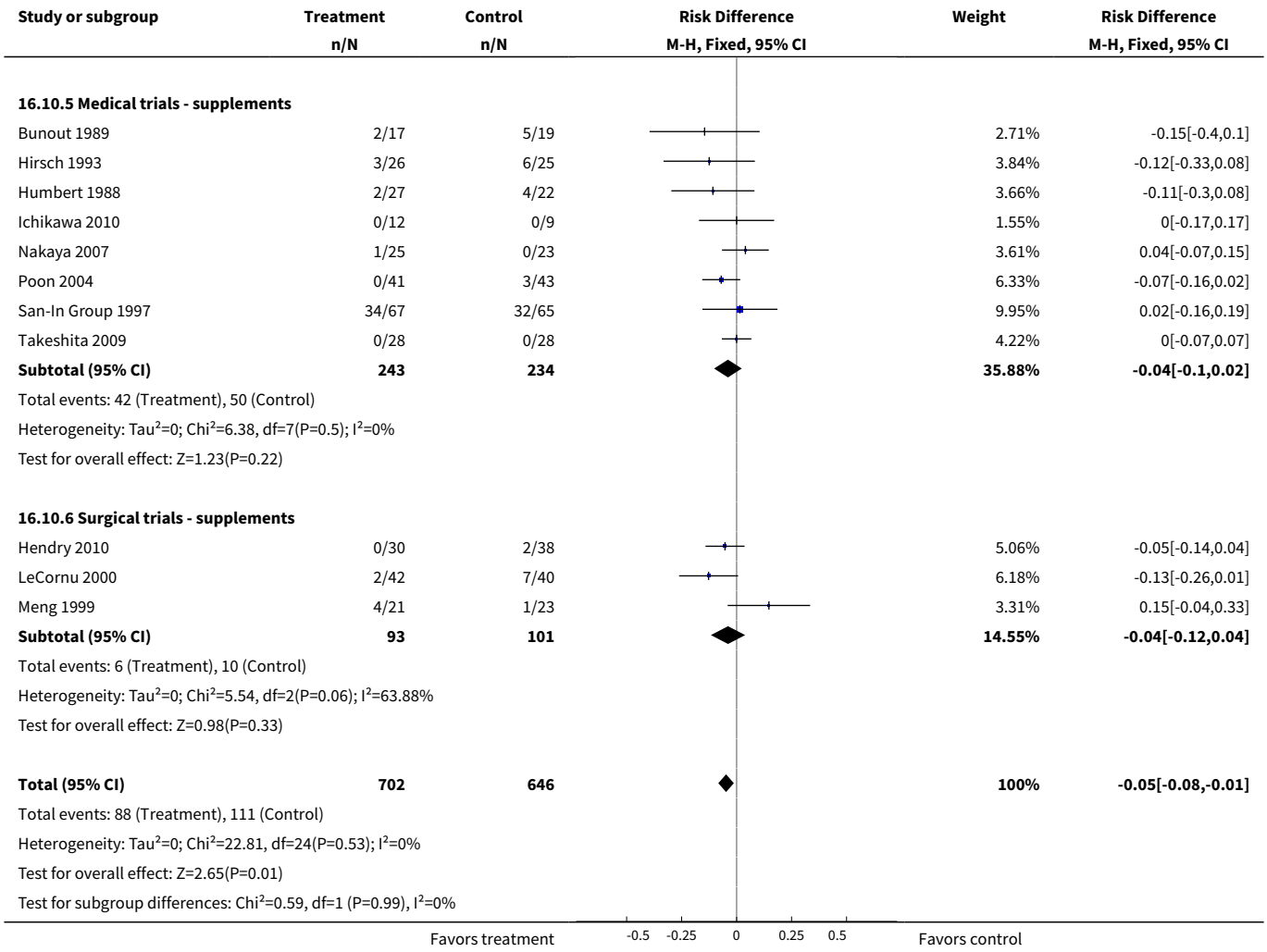
Favors treatment | Favors control

Analysis 16.10. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 10 Abstracts excluded.

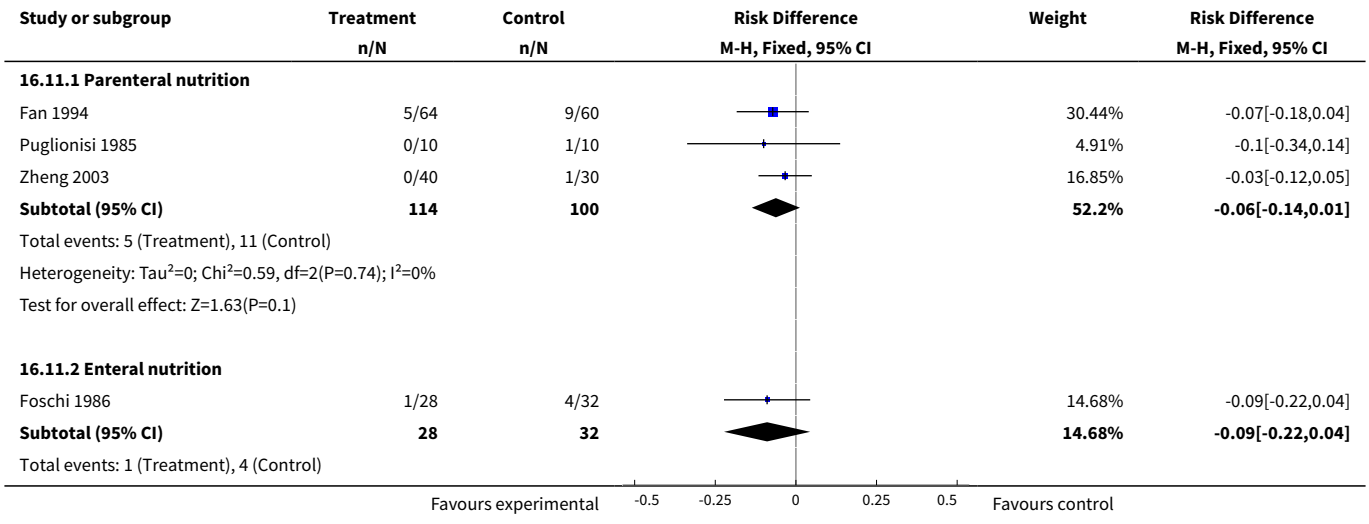
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.10.1 Medical trials - parenteral nutrition					
Achord 1987	1/14	3/14		2.11%	-0.14[-0.4,0.11]
Bonkovsky 1991	0/9	0/12		1.55%	0[-0.17,0.17]
Naveau 1986	1/20	1/20		3.02%	0[-0.14,0.14]
Simon 1988	5/33	7/36		5.19%	-0.04[-0.22,0.14]
Subtotal (95% CI)	**76**	**82**		**11.87%**	**-0.04[-0.14,0.06]**
Total events: 7 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.25, df=3(P=0.74); I^2=0%					
Test for overall effect: Z=0.87(P=0.38)					
16.10.2 Surgical trials - parenteral nutrition					
Fan 1994	5/64	9/60		9.34%	-0.07[-0.18,0.04]
Puglionisi 1985	0/10	1/10		1.51%	-0.1[-0.34,0.14]
Qiu 2009	0/44	0/21		4.29%	0[-0.07,0.07]
Reilly 1990	1/18	2/10		1.94%	-0.14[-0.41,0.13]
Zheng 2003	0/40	1/30		5.17%	-0.03[-0.12,0.05]
Subtotal (95% CI)	**176**	**131**		**22.25%**	**-0.06[-0.12,0]**
Total events: 6 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.53, df=4(P=0.47); I^2=0%					
Test for overall effect: Z=1.86(P=0.06)					
16.10.3 Medical trials - enteral nutrition					
Cabre 1990	2/16	9/19		2.62%	-0.35[-0.63,-0.07]
Calvey 1985	16/42	7/22		4.35%	0.06[-0.18,0.31]
DeLedinghen 1997	3/12	2/10		1.65%	0.05[-0.3,0.4]
Kearns 1992	5/16	5/15		2.34%	-0.02[-0.35,0.31]
Subtotal (95% CI)	**86**	**66**		**10.95%**	**-0.06[-0.2,0.09]**
Total events: 26 (Treatment), 23 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.61, df=3(P=0.13); I^2=46.49%					
Test for overall effect: Z=0.74(P=0.46)					
16.10.4 Surgical trials - enteral nutrition					
Foschi 1986	1/28	4/32		4.5%	-0.09[-0.22,0.04]
Subtotal (95% CI)	**28**	**32**		**4.5%**	**-0.09[-0.22,0.04]**
Total events: 1 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.31(P=0.19)					

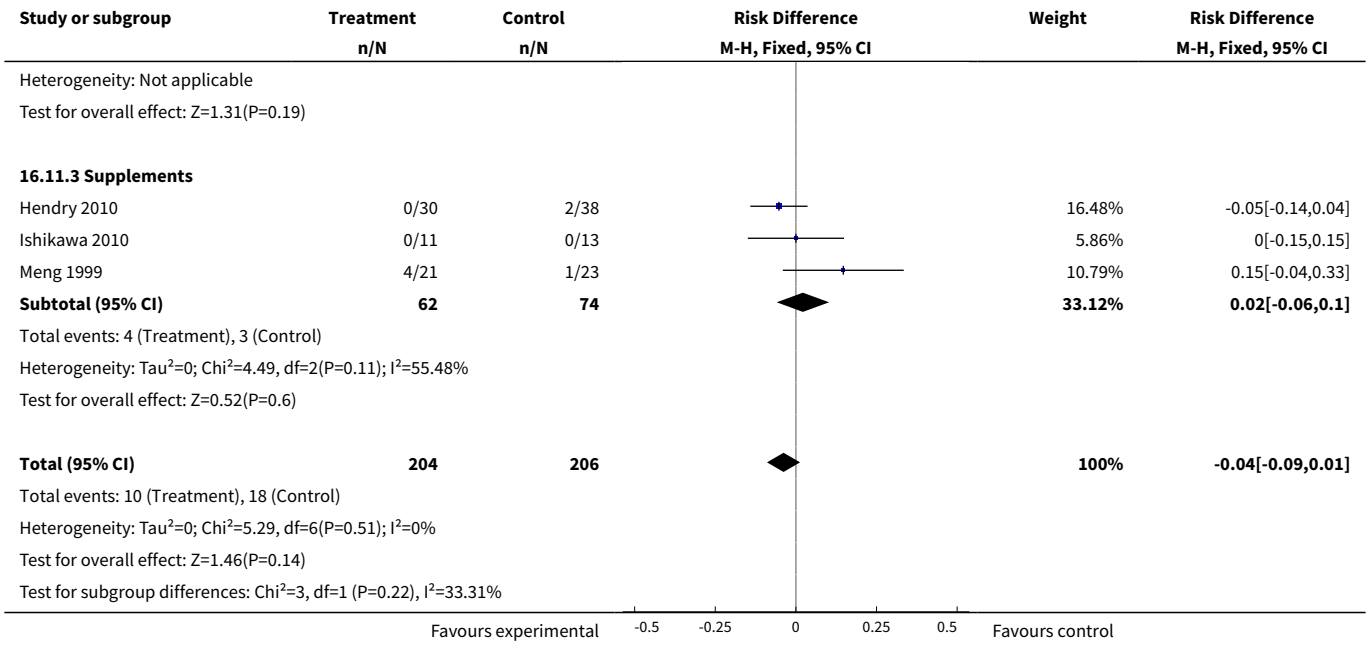


Favors treatment | Favors control

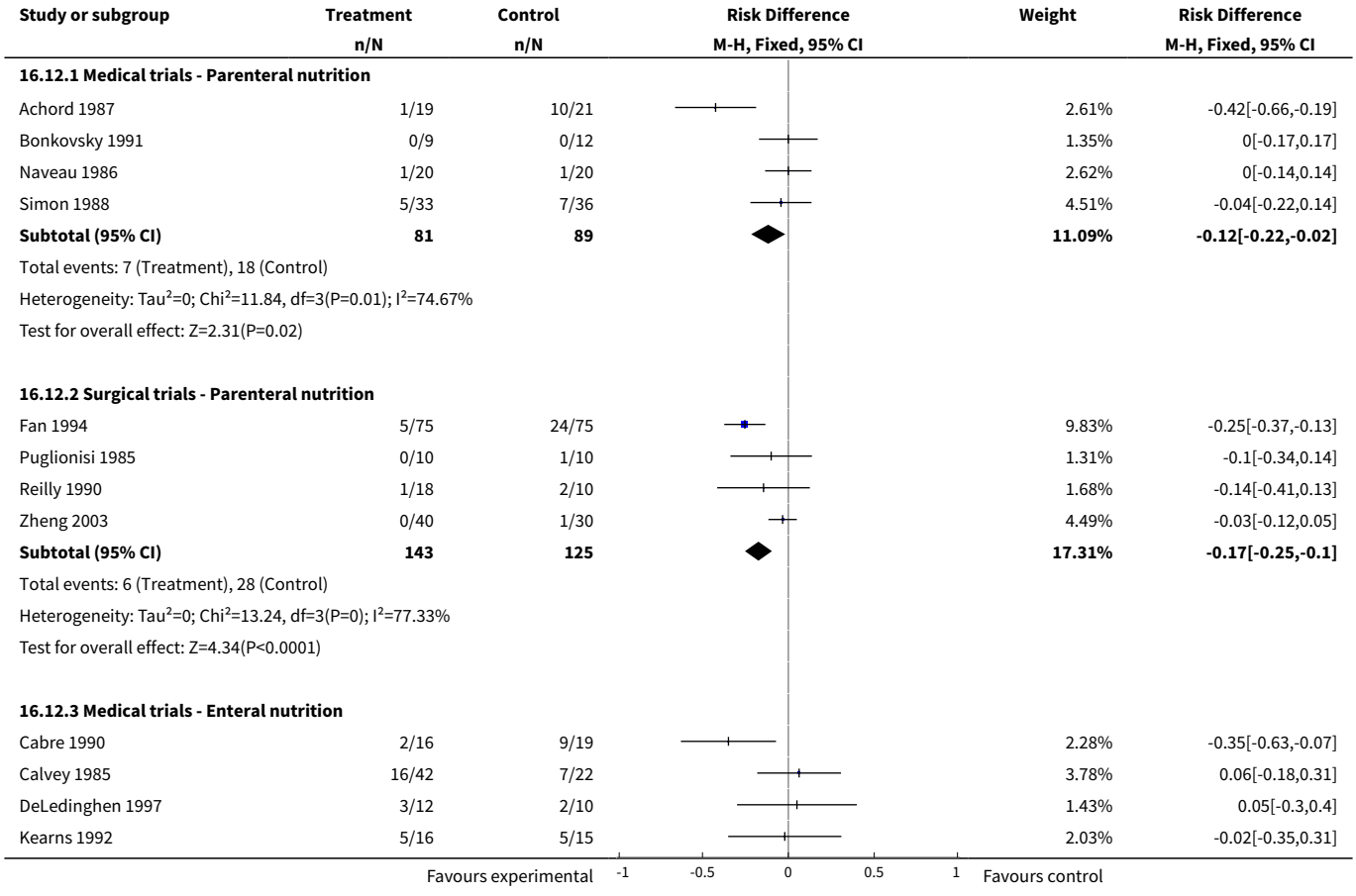


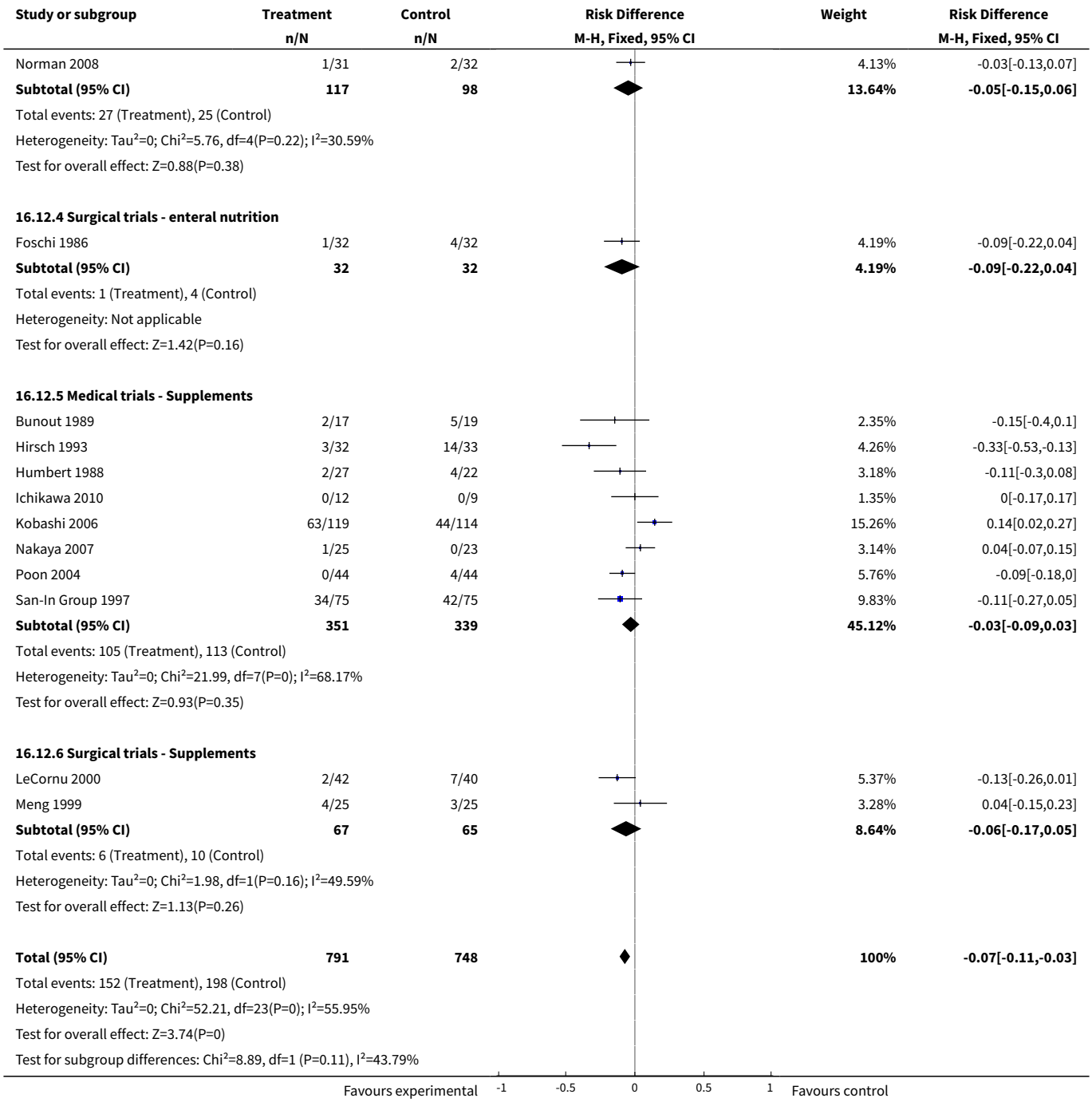
Analysis 16.11. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 11 Surgical trials without transplant patients.





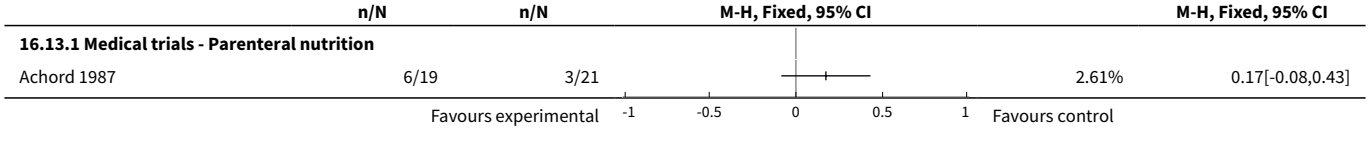
Analysis 16.12. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 12 Intent to treat - best-case scenario for intervention.



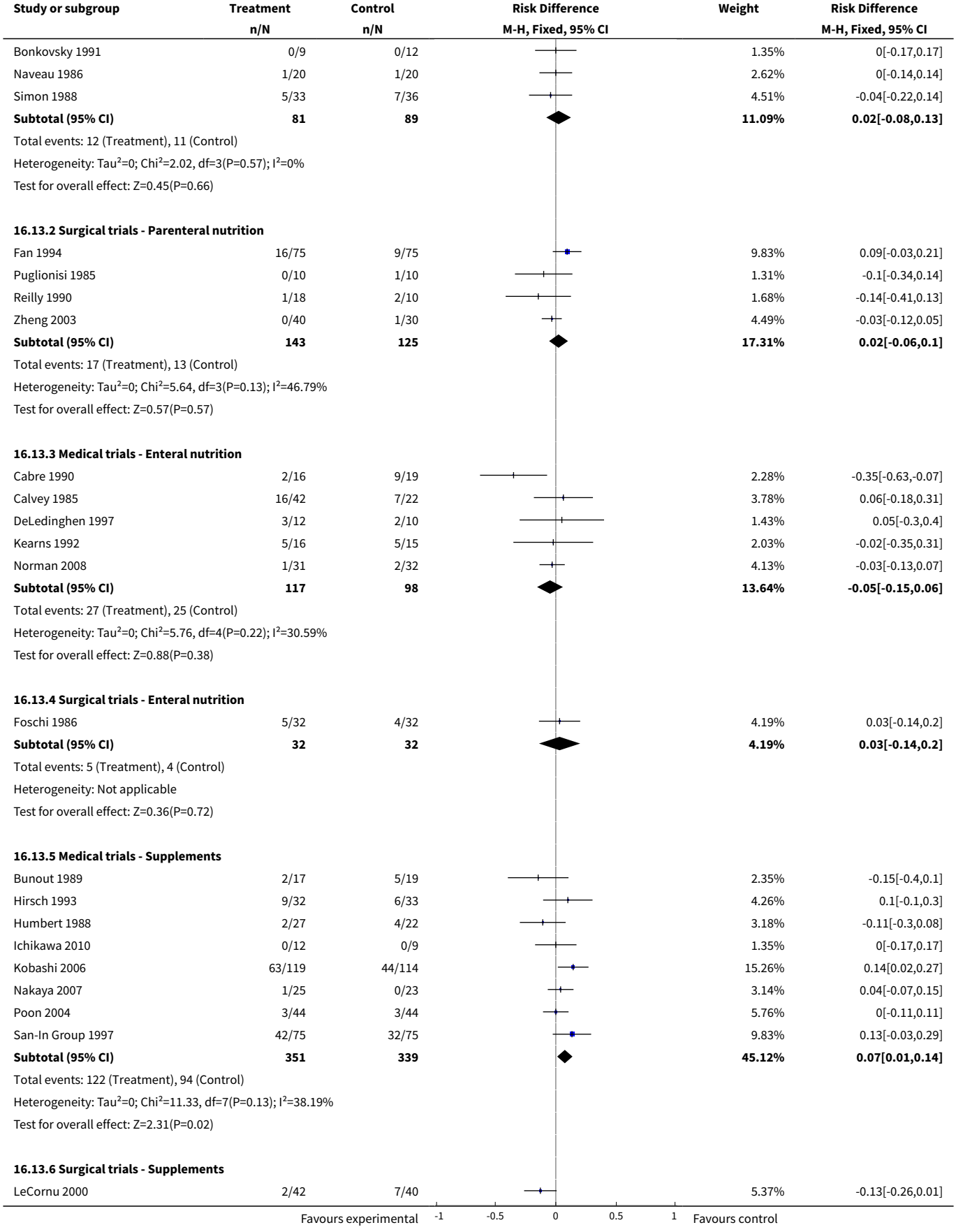


Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Norman 2008	1/31	2/32		4.13%	-0.03[-0.13,0.07]
Subtotal (95% CI)	**117**	**98**		**13.64%**	**-0.05[-0.15,0.06]**
Total events: 27 (Treatment), 25 (Control)					
Heterogeneity: Tau²=0; Chi²=5.76, df=4(P=0.22); I²=30.59%					
Test for overall effect: Z=0.88(P=0.38)					
16.12.4 Surgical trials - enteral nutrition					
Foschi 1986	1/32	4/32		4.19%	-0.09[-0.22,0.04]
Subtotal (95% CI)	**32**	**32**		**4.19%**	**-0.09[-0.22,0.04]**
Total events: 1 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.42(P=0.16)					
16.12.5 Medical trials - Supplements					
Bunout 1989	2/17	5/19		2.35%	-0.15[-0.4,0.1]
Hirsch 1993	3/32	14/33		4.26%	-0.33[-0.53,-0.13]
Humbert 1988	2/27	4/22		3.18%	-0.11[-0.3,0.08]
Ichikawa 2010	0/12	0/9		1.35%	0[-0.17,0.17]
Kobashi 2006	63/119	44/114		15.26%	0.14[0.02,0.27]
Nakaya 2007	1/25	0/23		3.14%	0.04[-0.07,0.15]
Poon 2004	0/44	4/44		5.76%	-0.09[-0.18,0]
San-In Group 1997	34/75	42/75		9.83%	-0.11[-0.27,0.05]
Subtotal (95% CI)	**351**	**339**		**45.12%**	**-0.03[-0.09,0.03]**
Total events: 105 (Treatment), 113 (Control)					
Heterogeneity: Tau²=0; Chi²=21.99, df=7(P=0); I²=68.17%					
Test for overall effect: Z=0.93(P=0.35)					
16.12.6 Surgical trials - Supplements					
LeCornu 2000	2/42	7/40		5.37%	-0.13[-0.26,0.01]
Meng 1999	4/25	3/25		3.28%	0.04[-0.15,0.23]
Subtotal (95% CI)	**67**	**65**		**8.64%**	**-0.06[-0.17,0.05]**
Total events: 6 (Treatment), 10 (Control)					
Heterogeneity: Tau²=0; Chi²=1.98, df=1(P=0.16); I²=49.59%					
Test for overall effect: Z=1.13(P=0.26)					
Total (95% CI)	**791**	**748**		**100%**	**-0.07[-0.11,-0.03]**
Total events: 152 (Treatment), 198 (Control)					
Heterogeneity: Tau²=0; Chi²=52.21, df=23(P=0); I²=55.95%					
Test for overall effect: Z=3.74(P=0)					
Test for subgroup differences: Chi²=8.89, df=1 (P=0.11), I²=43.79%					

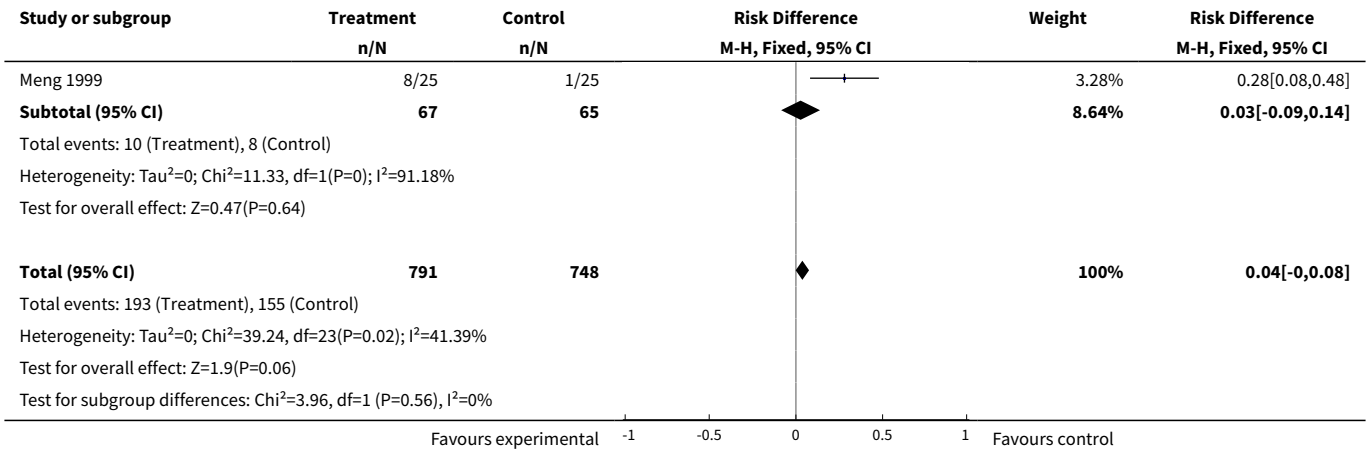
Analysis 16.13. Comparison 16 Mortality - absolute risk difference (ARD), Outcome 13 Intent to treat - worst-case scenario for intervention.



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
16.13.1 Medical trials - Parenteral nutrition					
Achord 1987	6/19	3/21		2.61%	0.17[-0.08,0.43]



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Bonkovsky 1991	0/9	0/12		1.35%	0[-0.17,0.17]
Naveau 1986	1/20	1/20		2.62%	0[-0.14,0.14]
Simon 1988	5/33	7/36		4.51%	-0.04[-0.22,0.14]
Subtotal (95% CI)	**81**	**89**		**11.09%**	**0.02[-0.08,0.13]**
Total events: 12 (Treatment), 11 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.02, df=3(P=0.57); I^2=0%					
Test for overall effect: Z=0.45(P=0.66)					
16.13.2 Surgical trials - Parenteral nutrition					
Fan 1994	16/75	9/75		9.83%	0.09[-0.03,0.21]
Puglionisi 1985	0/10	1/10		1.31%	-0.1[-0.34,0.14]
Reilly 1990	1/18	2/10		1.68%	-0.14[-0.41,0.13]
Zheng 2003	0/40	1/30		4.49%	-0.03[-0.12,0.05]
Subtotal (95% CI)	**143**	**125**		**17.31%**	**0.02[-0.06,0.1]**
Total events: 17 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.64, df=3(P=0.13); I^2=46.79%					
Test for overall effect: Z=0.57(P=0.57)					
16.13.3 Medical trials - Enteral nutrition					
Cabre 1990	2/16	9/19		2.28%	-0.35[-0.63,-0.07]
Calvey 1985	16/42	7/22		3.78%	0.06[-0.18,0.31]
DeLedinghen 1997	3/12	2/10		1.43%	0.05[-0.3,0.4]
Kearns 1992	5/16	5/15		2.03%	-0.02[-0.35,0.31]
Norman 2008	1/31	2/32		4.13%	-0.03[-0.13,0.07]
Subtotal (95% CI)	**117**	**98**		**13.64%**	**-0.05[-0.15,0.06]**
Total events: 27 (Treatment), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.76, df=4(P=0.22); I^2=30.59%					
Test for overall effect: Z=0.88(P=0.38)					
16.13.4 Surgical trials - Enteral nutrition					
Foschi 1986	5/32	4/32		4.19%	0.03[-0.14,0.2]
Subtotal (95% CI)	**32**	**32**		**4.19%**	**0.03[-0.14,0.2]**
Total events: 5 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.36(P=0.72)					
16.13.5 Medical trials - Supplements					
Bunout 1989	2/17	5/19		2.35%	-0.15[-0.4,0.1]
Hirsch 1993	9/32	6/33		4.26%	0.1[-0.1,0.3]
Humbert 1988	2/27	4/22		3.18%	-0.11[-0.3,0.08]
Ichikawa 2010	0/12	0/9		1.35%	0[-0.17,0.17]
Kobashi 2006	63/119	44/114		15.26%	0.14[0.02,0.27]
Nakaya 2007	1/25	0/23		3.14%	0.04[-0.07,0.15]
Poon 2004	3/44	3/44		5.76%	0[-0.11,0.11]
San-In Group 1997	42/75	32/75		9.83%	0.13[-0.03,0.29]
Subtotal (95% CI)	**351**	**339**		**45.12%**	**0.07[0.01,0.14]**
Total events: 122 (Treatment), 94 (Control)					
Heterogeneity: Tau^2=0; Chi^2=11.33, df=7(P=0.13); I^2=38.19%					
Test for overall effect: Z=2.31(P=0.02)					
16.13.6 Surgical trials - Supplements					
LeCornu 2000	2/42	7/40		5.37%	-0.13[-0.26,0.01]



Comparison 17. Appearance of ascites - absolute risk difference (ARD)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	8	582	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.21, -0.08]
2 Parenteral nutrition	4	214	Risk Difference (M-H, Random, 95% CI)	-0.16 [-0.30, -0.03]
2.1 Medical trials	2	26	Risk Difference (M-H, Random, 95% CI)	-0.13 [-0.48, 0.22]
2.2 Surgical trials	2	188	Risk Difference (M-H, Random, 95% CI)	-0.20 [-0.34, -0.07]
3 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	4	368	Risk Difference (M-H, Fixed, 95% CI)	-0.11 [-0.19, -0.03]
4.1 Medical trials	4	368	Risk Difference (M-H, Fixed, 95% CI)	-0.11 [-0.19, -0.03]
4.2 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Medical trials	6	394	Risk Difference (M-H, Fixed, 95% CI)	-0.11 [-0.19, -0.04]

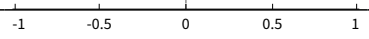
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
5.1 Parenteral nutrition	2	26	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.41, 0.12]
5.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.3 Supplements	4	368	Risk Difference (M-H, Fixed, 95% CI)	-0.11 [-0.19, -0.03]
6 Surgical trials	2	188	Risk Difference (M-H, Fixed, 95% CI)	-0.21 [-0.34, -0.07]
6.1 Parenteral nutrition	2	188	Risk Difference (M-H, Fixed, 95% CI)	-0.21 [-0.34, -0.07]
6.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Alcoholic hepatitis	3	77	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.33, 0.06]
7.1 Parenteral nutrition	2	26	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.41, 0.12]
7.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Supplements	1	51	Risk Difference (M-H, Fixed, 95% CI)	-0.13 [-0.40, 0.13]
8 Cirrhosis	2	82	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.26, 0.09]
8.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Supplements	2	82	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.26, 0.09]
9 HCC	2	286	Risk Difference (M-H, Fixed, 95% CI)	-0.12 [-0.21, -0.03]
9.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
9.3 Supplements	2	286	Risk Difference (M-H, Fixed, 95% CI)	-0.12 [-0.21, -0.03]
10 Abstracts excluded	7	380	Risk Difference (M-H, Fixed, 95% CI)	-0.17 [-0.25, -0.08]
10.1 Parenteral nutrition - medical trials	2	26	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.41, 0.12]
10.2 Parenteral nutrition - surgical trials	2	188	Risk Difference (M-H, Fixed, 95% CI)	-0.21 [-0.34, -0.07]
10.3 Enteral nutrition - medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.4 Enteral nutrition = surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.5 Supplements - medical trials	3	166	Risk Difference (M-H, Fixed, 95% CI)	-0.12 [-0.24, -0.01]
10.6 Supplements - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Surgical trials without transplant	2	188	Risk Difference (M-H, Fixed, 95% CI)	-0.21 [-0.34, -0.07]
11.1 Parenteral nutrition	2	188	Risk Difference (M-H, Fixed, 95% CI)	-0.21 [-0.34, -0.07]
11.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Intent to treat - best-case scenario for intervention	8	626	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.27, -0.14]
12.1 Parenteral nutrition - medical trials	2	26	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.41, 0.12]
12.2 Parenteral nutrition - surgical trials	2	214	Risk Difference (M-H, Fixed, 95% CI)	-0.31 [-0.43, -0.19]
12.3 Enteral nutrition - medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.4 Enteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	4	386	Risk Difference (M-H, Fixed, 95% CI)	-0.15 [-0.23, -0.07]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
12.6 Supplements - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Intent to treat - worst-case scenario for intervention	8	626	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.13, 0.00]
13.1 Parenteral nutrition - medical trials	2	26	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.41, 0.12]
13.2 Parenteral nutrition - surgical trials	2	214	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.19, 0.07]
13.3 Enteral nutrition - medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.4 Enteral nutrition = surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.5 Supplements - medical trials	4	386	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.14, 0.02]
13.6 Supplements - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 17.1. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 1 All studies.

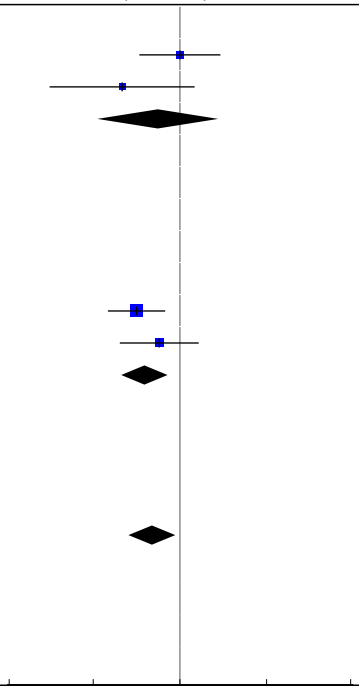
Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Achord 1987	0/9	0/6		2.48%	0[-0.23,0.23]
Fan 1994	16/64	30/60		21.38%	-0.25[-0.42,-0.08]
Hirsch 1993	8/26	11/25		8.8%	-0.13[-0.4,0.13]
Kobashi 2006	16/100	27/102		34.85%	-0.1[-0.22,0.01]
Nakaya 2007	1/16	1/15		5.34%	-0[-0.18,0.17]
Poon 2004	3/41	10/43		14.49%	-0.16[-0.31,-0.01]
Simon 1988	0/5	2/6		1.88%	-0.33[-0.75,0.08]
Zheng 2003	23/37	20/27		10.77%	-0.12[-0.35,0.11]
Total (95% CI)	**298**	**284**		**100%**	**-0.14[-0.21,-0.08]**
Total events: 67 (Experimental), 101 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.9, df=7(P=0.44); I^2=0%					
Test for overall effect: Z=4.17(P<0.0001)					



Favours experimental — Favours control

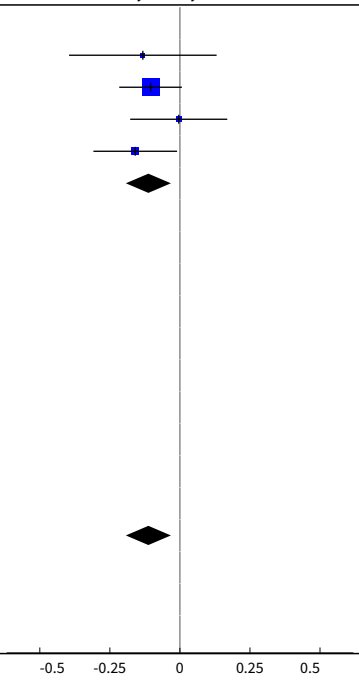
Analysis 17.2. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 2 Parenteral nutrition.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
17.2.1 Medical trials					
Achord 1987	0/9	0/6		24.91%	0[-0.23,0.23]
Simon 1988	0/5	2/6		9.44%	-0.33[-0.75,0.08]
Subtotal (95% CI)	**14**	**12**		**34.35%**	**-0.13[-0.48,0.22]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Tau^2=0.04; Chi^2=2.24, df=1(P=0.13); I^2=55.38%					
Test for overall effect: Z=0.72(P=0.47)					
17.2.2 Surgical trials					
Fan 1994	16/64	30/60		39.72%	-0.25[-0.42,-0.08]
Zheng 2003	23/37	20/27		25.93%	-0.12[-0.35,0.11]
Subtotal (95% CI)	**101**	**87**		**65.65%**	**-0.2[-0.34,-0.07]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.83, df=1(P=0.36); I^2=0%					
Test for overall effect: Z=3(P=0)					
Total (95% CI)	**115**	**99**		**100%**	**-0.16[-0.3,-0.03]**
Total events: 39 (Experimental), 52 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.01, df=3(P=0.26); I^2=25.26%					
Test for overall effect: Z=2.34(P=0.02)					
Test for subgroup differences: Chi^2=0.16, df=1 (P=0.69), I^2=0%					



Analysis 17.4. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 4 Supplements.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.4.1 Medical trials					
Hirsch 1993	8/26	11/25		13.86%	-0.13[-0.4,0.13]
Kobashi 2006	16/100	27/102		54.9%	-0.1[-0.22,0.01]
Nakaya 2007	1/16	1/15		8.42%	-0[-0.18,0.17]
Poon 2004	3/41	10/43		22.82%	-0.16[-0.31,-0.01]
Subtotal (95% CI)	**183**	**185**		**100%**	**-0.11[-0.19,-0.03]**
Total events: 28 (Experimental), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.92, df=3(P=0.59); I^2=0%					
Test for overall effect: Z=2.74(P=0.01)					
17.4.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**183**	**185**		**100%**	**-0.11[-0.19,-0.03]**
Total events: 28 (Experimental), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.92, df=3(P=0.59); I^2=0%					
Test for overall effect: Z=2.74(P=0.01)					

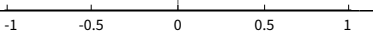


Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Test for subgroup differences: Not applicable					

Favours experimental | Favours control

Analysis 17.5. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 5 Medical trials.

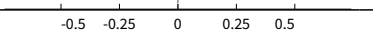
Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.5.1 Parenteral nutrition					
Achord 1987	0/9	0/6		3.66%	0[-0.23,0.23]
Simon 1988	0/5	2/6		2.77%	-0.33[-0.75,0.08]
Subtotal (95% CI)	**14**	**12**		**6.44%**	**-0.14[-0.41,0.12]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.24, df=1(P=0.13); I^2=55.38%					
Test for overall effect: Z=1.07(P=0.28)					
17.5.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.5.3 Supplements					
Hirsch 1993	8/26	11/25		12.97%	-0.13[-0.4,0.13]
Kobashi 2006	16/100	27/102		51.37%	-0.1[-0.22,0.01]
Nakaya 2007	1/16	1/15		7.88%	-0[-0.18,0.17]
Poon 2004	3/41	10/43		21.35%	-0.16[-0.31,-0.01]
Subtotal (95% CI)	**183**	**185**		**93.56%**	**-0.11[-0.19,-0.03]**
Total events: 28 (Experimental), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.92, df=3(P=0.59); I^2=0%					
Test for overall effect: Z=2.74(P=0.01)					
Total (95% CI)	**197**	**197**		**100%**	**-0.11[-0.19,-0.04]**
Total events: 28 (Experimental), 51 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.93, df=5(P=0.56); I^2=0%					
Test for overall effect: Z=2.91(P=0)					
Test for subgroup differences: Chi^2=0.05, df=1 (P=0.82), I^2=0%					



Favours experimental | Favours control

Analysis 17.6. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 6 Surgical trials.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.6.1 Parenteral nutrition					
Fan 1994	16/64	30/60		66.49%	-0.25[-0.42,-0.08]
Zheng 2003	23/37	20/27		33.51%	-0.12[-0.35,0.11]
Subtotal (95% CI)	**101**	**87**		**100%**	**-0.21[-0.34,-0.07]**
Total events: 39 (Experimental), 50 (Control)					



Favours experimental | Favours control

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=0.83, df=1(P=0.36); I²=0%					
Test for overall effect: Z=3.02(P=0)					
17.6.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.6.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**101**	**87**		**100%**	**-0.21[-0.34,-0.07]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau²=0; Chi²=0.83, df=1(P=0.36); I²=0%					
Test for overall effect: Z=3.02(P=0)					
Test for subgroup differences: Not applicable					

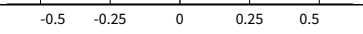
Analysis 17.7. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 7 Alcoholic hepatitis.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.7.1 Parenteral nutrition					
Achord 1987	0/9	0/6		18.88%	0[-0.23,0.23]
Simon 1988	0/5	2/6		14.3%	-0.33[-0.75,0.08]
Subtotal (95% CI)	**14**	**12**		**33.18%**	**-0.14[-0.41,0.12]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Tau²=0; Chi²=2.24, df=1(P=0.13); I²=55.38%					
Test for overall effect: Z=1.07(P=0.28)					
17.7.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.7.3 Supplements					
Hirsch 1993	8/26	11/25		66.82%	-0.13[-0.4,0.13]
Subtotal (95% CI)	**26**	**25**		**66.82%**	**-0.13[-0.4,0.13]**
Total events: 8 (Experimental), 11 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.98(P=0.32)					
Total (95% CI)	**40**	**37**		**100%**	**-0.14[-0.33,0.06]**
Total events: 8 (Experimental), 13 (Control)					

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=2.16, df=2(P=0.34); I²=7.28%					
Test for overall effect: Z=1.36(P=0.17)					
Test for subgroup differences: Chi²=0, df=1 (P=0.95), I²=0%					

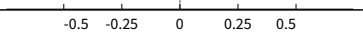
Analysis 17.8. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 8 Cirrhosis.

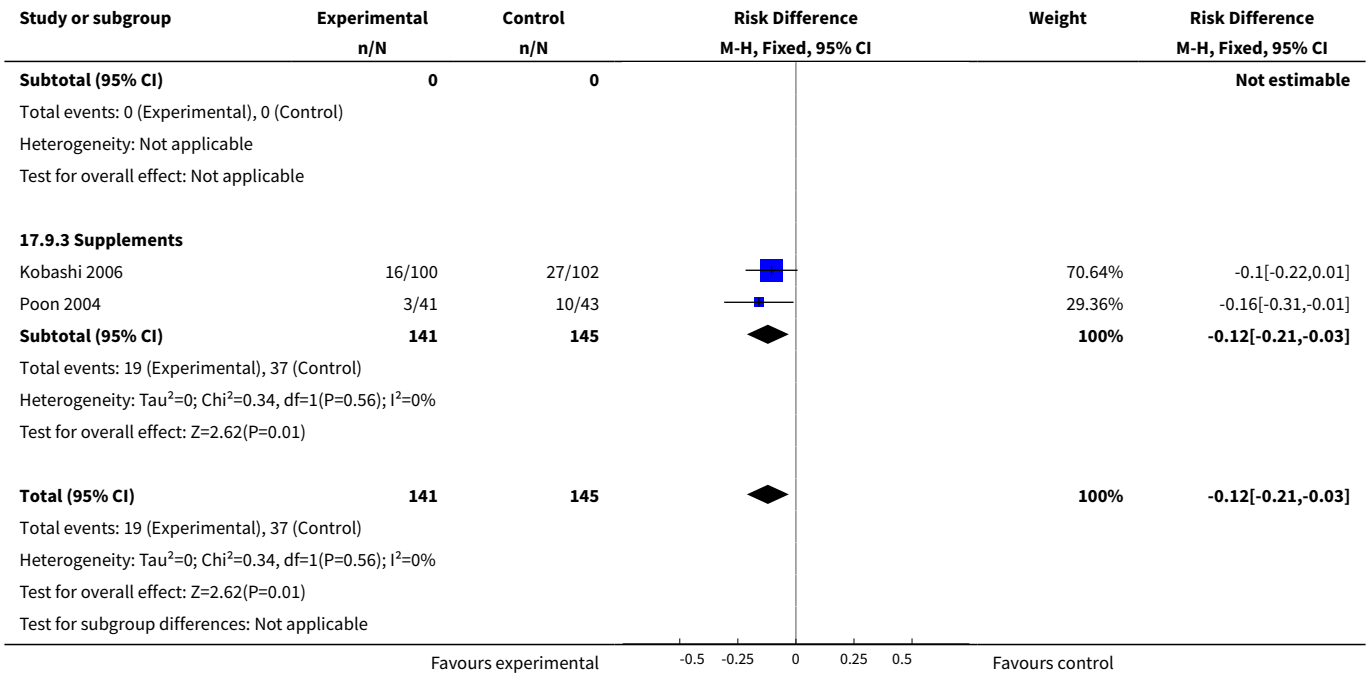
Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.8.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.8.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.8.3 Supplements					
Hirsch 1993	8/26	11/25		62.21%	-0.13[-0.4,0.13]
Nakaya 2007	1/16	1/15		37.79%	-0[-0.18,0.17]
Subtotal (95% CI)	**42**	**40**		**100%**	**-0.08[-0.26,0.09]**
Total events: 9 (Experimental), 12 (Control)					
Heterogeneity: Tau²=0; Chi²=0.94, df=1(P=0.33); I²=0%					
Test for overall effect: Z=0.93(P=0.35)					
Total (95% CI)	**42**	**40**		**100%**	**-0.08[-0.26,0.09]**
Total events: 9 (Experimental), 12 (Control)					
Heterogeneity: Tau²=0; Chi²=0.94, df=1(P=0.33); I²=0%					
Test for overall effect: Z=0.93(P=0.35)					
Test for subgroup differences: Not applicable					



Analysis 17.9. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 9 HCC.

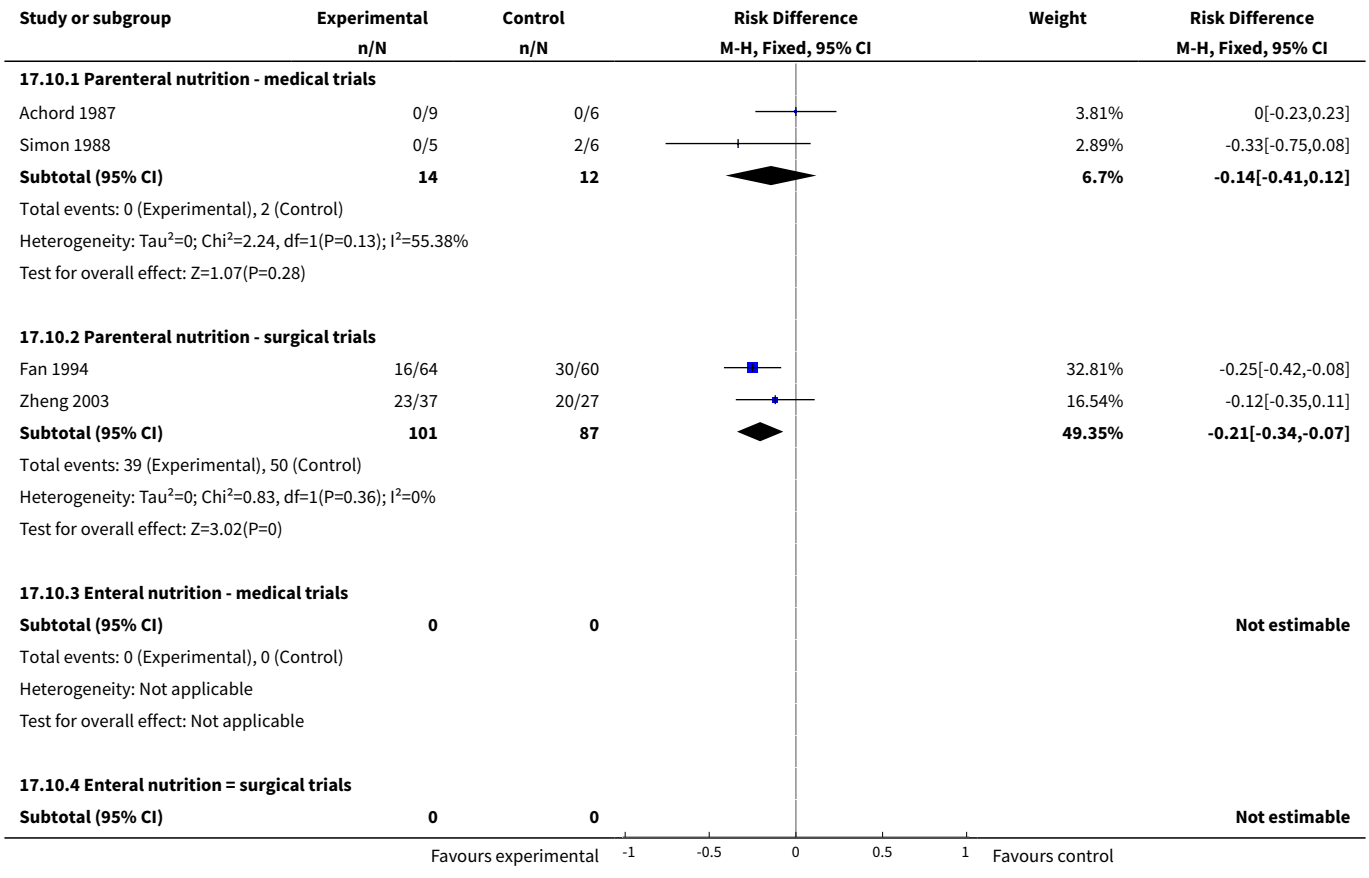
Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.9.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.9.2 Enteral nutrition					



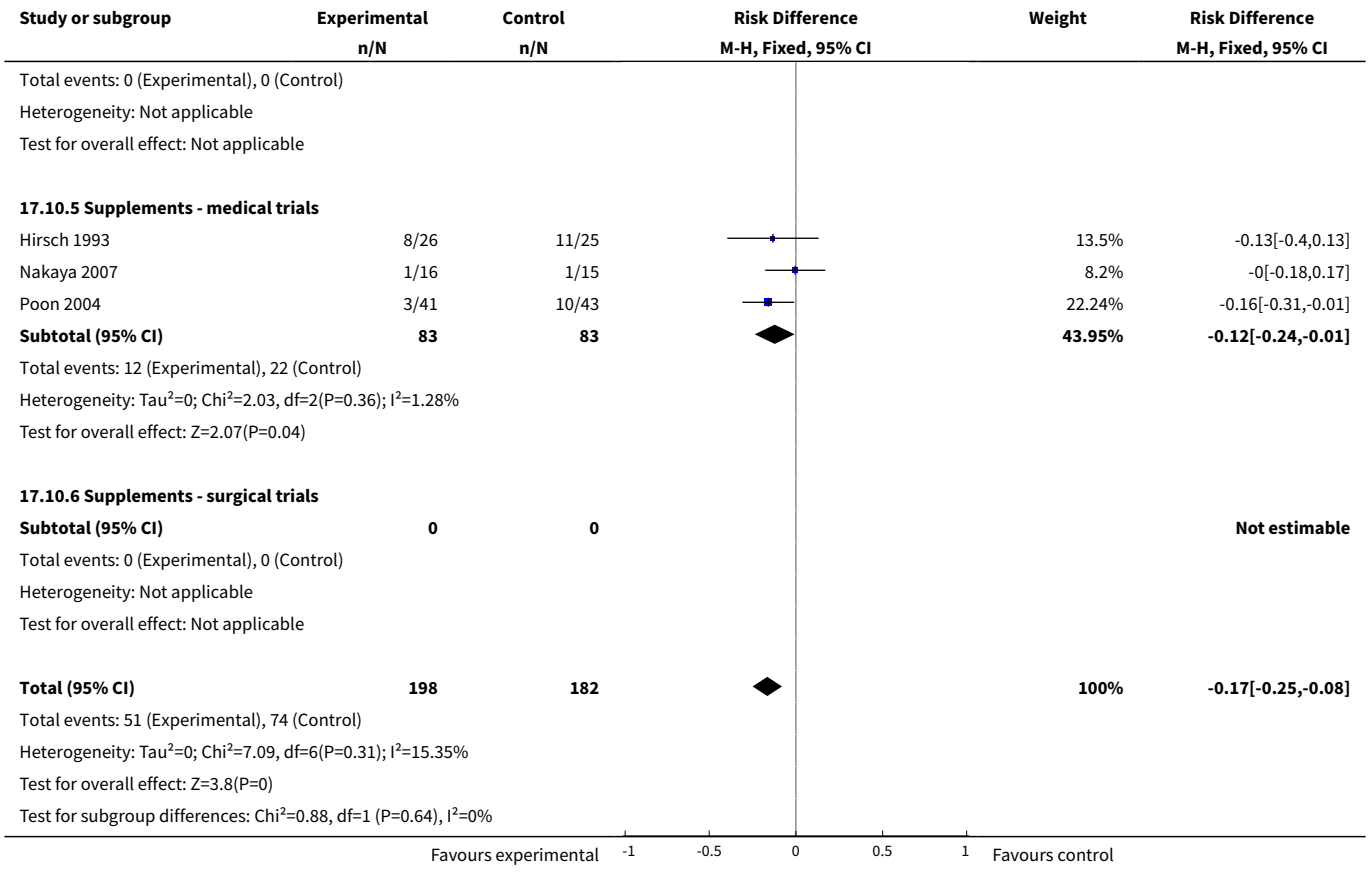


Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.9.3 Supplements					
Kobashi 2006	16/100	27/102		70.64%	-0.1[-0.22,0.01]
Poon 2004	3/41	10/43		29.36%	-0.16[-0.31,-0.01]
Subtotal (95% CI)	**141**	**145**		**100%**	**-0.12[-0.21,-0.03]**
Total events: 19 (Experimental), 37 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.34, df=1(P=0.56); I^2=0%					
Test for overall effect: Z=2.62(P=0.01)					
Total (95% CI)	**141**	**145**		**100%**	**-0.12[-0.21,-0.03]**
Total events: 19 (Experimental), 37 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.34, df=1(P=0.56); I^2=0%					
Test for overall effect: Z=2.62(P=0.01)					
Test for subgroup differences: Not applicable					

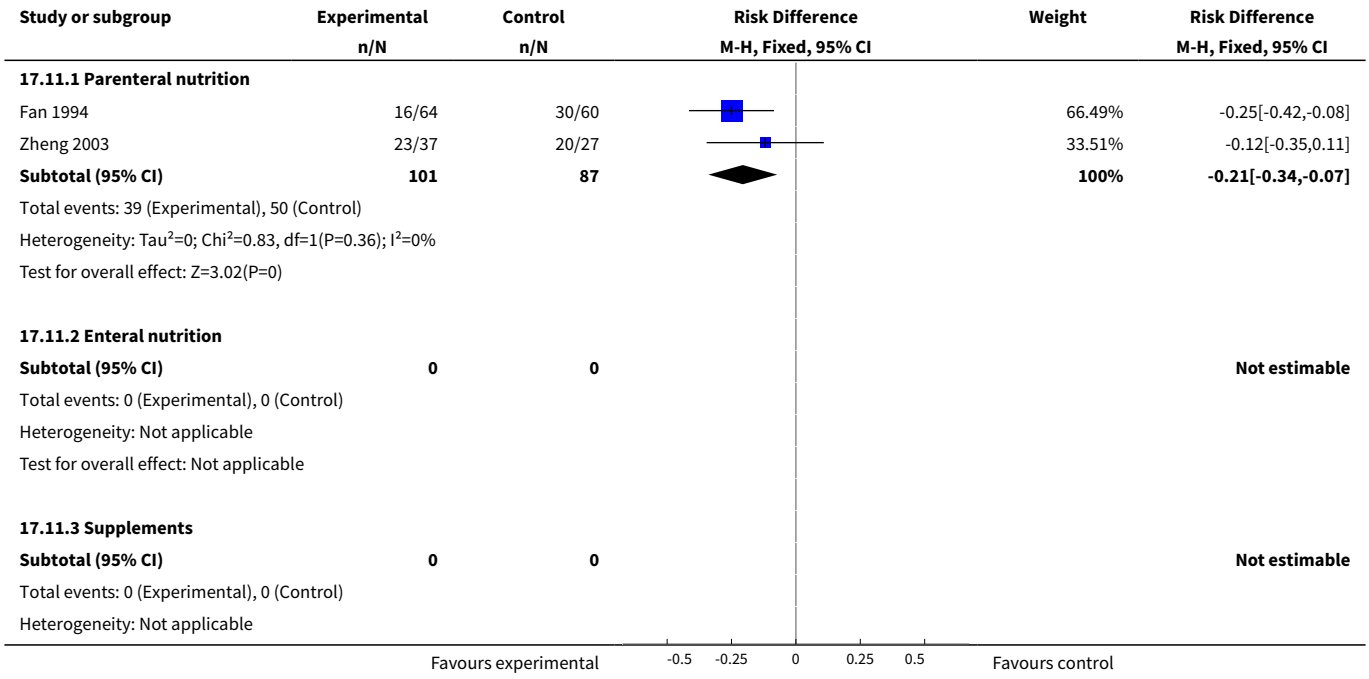
Analysis 17.10. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 10 Abstracts excluded.



Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.10.1 Parenteral nutrition - medical trials					
Achord 1987	0/9	0/6		3.81%	0[-0.23,0.23]
Simon 1988	0/5	2/6		2.89%	-0.33[-0.75,0.08]
Subtotal (95% CI)	**14**	**12**		**6.7%**	**-0.14[-0.41,0.12]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.24, df=1(P=0.13); I^2=55.38%					
Test for overall effect: Z=1.07(P=0.28)					
17.10.2 Parenteral nutrition - surgical trials					
Fan 1994	16/64	30/60		32.81%	-0.25[-0.42,-0.08]
Zheng 2003	23/37	20/27		16.54%	-0.12[-0.35,0.11]
Subtotal (95% CI)	**101**	**87**		**49.35%**	**-0.21[-0.34,-0.07]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.83, df=1(P=0.36); I^2=0%					
Test for overall effect: Z=3.02(P=0)					
17.10.3 Enteral nutrition - medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.10.4 Enteral nutrition = surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**



Analysis 17.11. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 11 Surgical trials without transplant.



Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Test for overall effect: Not applicable					
Total (95% CI)	**101**	**87**		**100%**	**-0.21[-0.34,-0.07]**
Total events: 39 (Experimental), 50 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.83, df=1(P=0.36); I^2=0%					
Test for overall effect: Z=3.02(P=0)					
Test for subgroup differences: Not applicable					

Favours experimental -0.5 -0.25 0 0.25 0.5 Favours control

Analysis 17.12. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 12 Intent to treat - best-case scenario for intervention.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.12.1 Parenteral nutrition - medical trials					
Achord 1987	0/9	0/6		2.31%	0[-0.23,0.23]
Simon 1988	0/5	2/6		1.75%	-0.33[-0.75,0.08]
Subtotal (95% CI)	**14**	**12**		**4.06%**	**-0.14[-0.41,0.12]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.24, df=1(P=0.13); I^2=55.38%					
Test for overall effect: Z=1.07(P=0.28)					
17.12.2 Parenteral nutrition - surgical trials					
Fan 1994	16/75	45/75		24.05%	-0.39[-0.53,-0.24]
Zheng 2003	23/37	20/27		10.01%	-0.12[-0.35,0.11]
Subtotal (95% CI)	**112**	**102**		**34.06%**	**-0.31[-0.43,-0.19]**
Total events: 39 (Experimental), 65 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.79, df=1(P=0.05); I^2=73.59%					
Test for overall effect: Z=4.95(P<0.0001)					
17.12.3 Enteral nutrition - medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.12.4 Enteral nutrition - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.12.5 Supplements - medical trials					
Hirsch 1993	8/32	19/33		10.42%	-0.33[-0.55,-0.1]
Kobashi 2006	16/100	27/102		32.39%	-0.1[-0.22,0.01]
Nakaya 2007	1/16	1/15		4.97%	-0[-0.18,0.17]
Poon 2004	3/44	11/44		14.11%	-0.18[-0.33,-0.03]
Subtotal (95% CI)	**192**	**194**		**61.88%**	**-0.15[-0.23,-0.07]**
Total events: 28 (Experimental), 58 (Control)					

Favours experimental -1 -0.5 0 0.5 1 Favours control

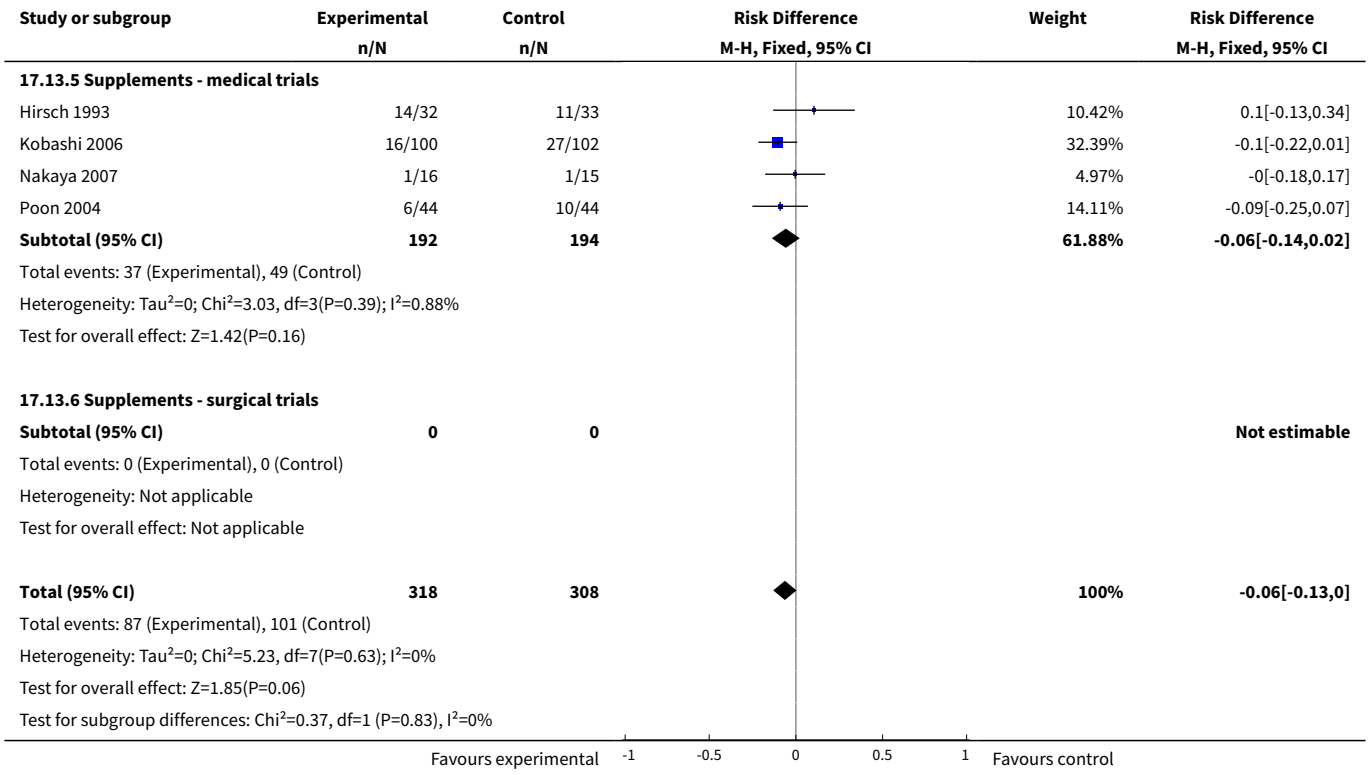
Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=5.9, df=3(P=0.12); I²=49.17%					
Test for overall effect: Z=3.77(P=0)					
17.12.6 Supplements - surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**318**	**308**		**100%**	**-0.2[-0.27,-0.14]**
Total events: 67 (Experimental), 125 (Control)					
Heterogeneity: Tau²=0; Chi²=19.35, df=7(P=0.01); I²=63.82%					
Test for overall effect: Z=6.17(P<0.0001)					
Test for subgroup differences: Chi²=4.62, df=1 (P=0.1), I²=56.71%					

Favours experimental -1 -0.5 0 0.5 1 Favours control

Analysis 17.13. Comparison 17 Appearance of ascites - absolute risk difference (ARD), Outcome 13 Intent to treat - worst-case scenario for intervention.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
17.13.1 Parenteral nutrition - medical trials					
Achord 1987	0/9	0/6		2.31%	0[-0.23,0.23]
Simon 1988	0/5	2/6		1.75%	-0.33[-0.75,0.08]
Subtotal (95% CI)	**14**	**12**		**4.06%**	**-0.14[-0.41,0.12]**
Total events: 0 (Experimental), 2 (Control)					
Heterogeneity: Tau²=0; Chi²=2.24, df=1(P=0.13); I²=55.38%					
Test for overall effect: Z=1.07(P=0.28)					
17.13.2 Parenteral nutrition - surgical trials					
Fan 1994	27/75	30/75		24.05%	-0.04[-0.2,0.12]
Zheng 2003	23/37	20/27		10.01%	-0.12[-0.35,0.11]
Subtotal (95% CI)	**112**	**102**		**34.06%**	**-0.06[-0.19,0.07]**
Total events: 50 (Experimental), 50 (Control)					
Heterogeneity: Tau²=0; Chi²=0.32, df=1(P=0.57); I²=0%					
Test for overall effect: Z=0.97(P=0.33)					
17.13.3 Enteral nutrition - medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
17.13.4 Enteral nutrition = surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours experimental -1 -0.5 0 0.5 1 Favours control



Comparison 18. Resolution of ascites - absolute risk difference (ARD)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 All studies	6	131	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.20, 0.11]
2 Parenteral nutrition	3	73	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.40, 0.00]
2.1 Medical trials	3	73	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.40, 0.00]
2.2 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Enteral nutrition	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
3.1 Medical trials	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
3.2 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]

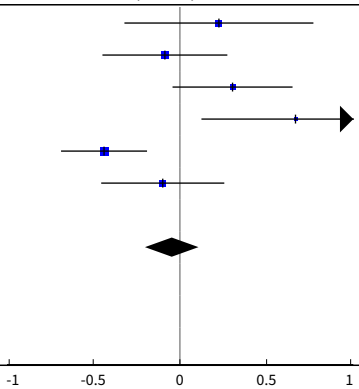
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
4.1 Medical trials	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]
4.2 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Medical trials	6	131	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.20, 0.11]
5.1 Parenteral nutrition	3	73	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.40, 0.00]
5.2 Enteral nutrition	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
5.3 Supplements	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]
6 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Alcoholic hepatitis	2	40	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.29, 0.30]
7.1 Parenteral nutrition	2	40	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.29, 0.30]
7.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Cirrhosis	4	91	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.25, 0.11]
8.1 Parenteral nutrition	1	33	Risk Difference (M-H, Fixed, 95% CI)	-0.44 [-0.69, -0.19]
8.2 Enteral nutrition	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
8.3 Supplements	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
9 HCC	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Abstracts excluded	6	131	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.20, 0.11]
10.1 Parenteral nutrition - medical trials	3	73	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.40, 0.00]
10.2 Parenteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Enteral nutrition - medical trials	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
10.4 Enteral nutrition = surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.5 Supplements - medical trials	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]
10.6 Supplements - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Surgical trials without transplant	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Intent to treat - best-case scenario for intervention - no changes made	6	131	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.20, 0.11]
12.1 Parenteral nutrition - medical trials	3	73	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.40, 0.00]
12.2 Parenteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
12.3 Enteral nutrition - medical trials	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
12.4 Enteral nutrition = surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]
12.6 Supplements - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Intent to treat - worst-case scenario for intervention - no changes made	6	131	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.20, 0.11]
13.1 Parenteral nutrition - medical trials	3	73	Risk Difference (M-H, Fixed, 95% CI)	-0.20 [-0.40, 0.00]
13.2 Parenteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 Enteral nutrition - medical trials	1	29	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.45, 0.27]
13.4 Enteral nutrition = surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.5 Supplements - medical trials	2	29	Risk Difference (M-H, Fixed, 95% CI)	0.40 [0.08, 0.71]
13.6 Supplements - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

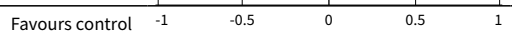
Analysis 18.1. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 1 All studies.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Achord 1987	3/5	3/8		9.6%	0.22[-0.32,0.77]
Cabre 1990	7/13	10/16		22.39%	-0.09[-0.45,0.27]
Hayashi 1991	6/14	1/8		15.89%	0.3[-0.04,0.65]
Nakaya 2007	2/3	0/4		5.35%	0.67[0.12,1.21]
Naveau 1986	9/16	17/17		25.73%	-0.44[-0.69,-0.19]
Simon 1988	4/14	5/13		21.04%	-0.1[-0.45,0.26]
Total (95% CI)	**65**	**66**		**100%**	**-0.05[-0.2,0.11]**
Total events: 31 (Experimental), 36 (Control)					
Heterogeneity: Tau^2=0; Chi^2=21.21, df=5(P=0); I^2=76.42%					
Test for overall effect: Z=0.6(P=0.55)					



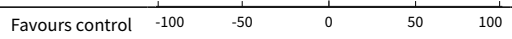
Analysis 18.2. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 2 Parenteral nutrition.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
18.2.1 Medical trials					
Achord 1987	3/5	3/8		17.04%	0.22[-0.32,0.77]
Naveau 1986	9/16	17/17		45.64%	-0.44[-0.69,-0.19]
Simon 1988	4/14	5/13		37.32%	-0.1[-0.45,0.26]
Subtotal (95% CI)	**35**	**38**		**100%**	**-0.2[-0.4,0]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.2, df=2(P=0.05); I^2=67.72%					
Test for overall effect: Z=1.93(P=0.05)					
18.2.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**35**	**38**		**100%**	**-0.2[-0.4,0]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.2, df=2(P=0.05); I^2=67.72%					
Test for overall effect: Z=1.93(P=0.05)					
Test for subgroup differences: Not applicable					



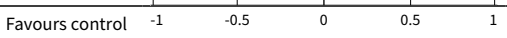
Analysis 18.3. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 3 Enteral nutrition.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
18.3.1 Medical trials					
Cabre 1990	7/13	10/16		100%	-0.09[-0.45,0.27]
Subtotal (95% CI)	**13**	**16**		**100%**	**-0.09[-0.45,0.27]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.47(P=0.64)					
18.3.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**13**	**16**		**100%**	**-0.09[-0.45,0.27]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.47(P=0.64)					
Test for subgroup differences: Not applicable					



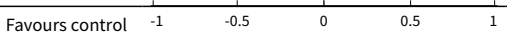
Analysis 18.4. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 4 Supplements.

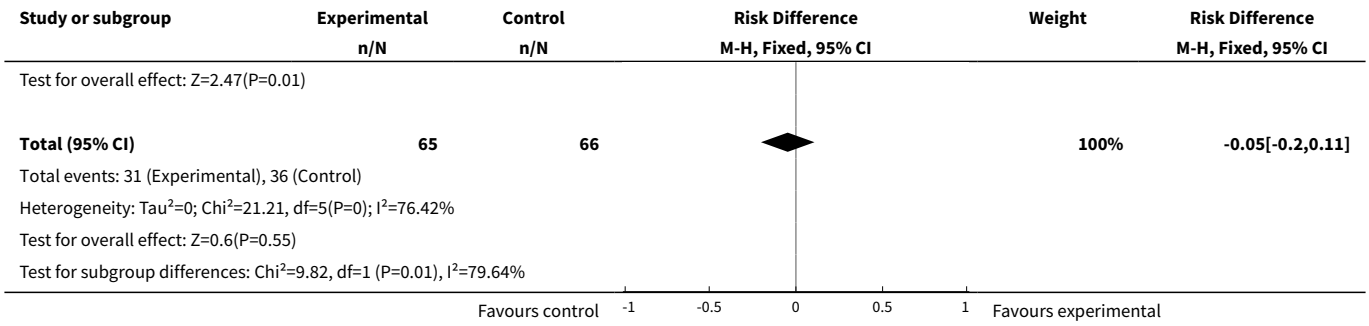
Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
18.4.1 Medical trials					
Hayashi 1991	6/14	1/8		74.81%	0.3[-0.04,0.65]
Nakaya 2007	2/3	0/4		25.19%	0.67[0.12,1.21]
Subtotal (95% CI)	**17**	**12**		**100%**	**0.4[0.08,0.71]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.23, df=1(P=0.27); I^2=18.81%					
Test for overall effect: Z=2.47(P=0.01)					
18.4.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Experimental), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**17**	**12**		**100%**	**0.4[0.08,0.71]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.23, df=1(P=0.27); I^2=18.81%					
Test for overall effect: Z=2.47(P=0.01)					
Test for subgroup differences: Not applicable					



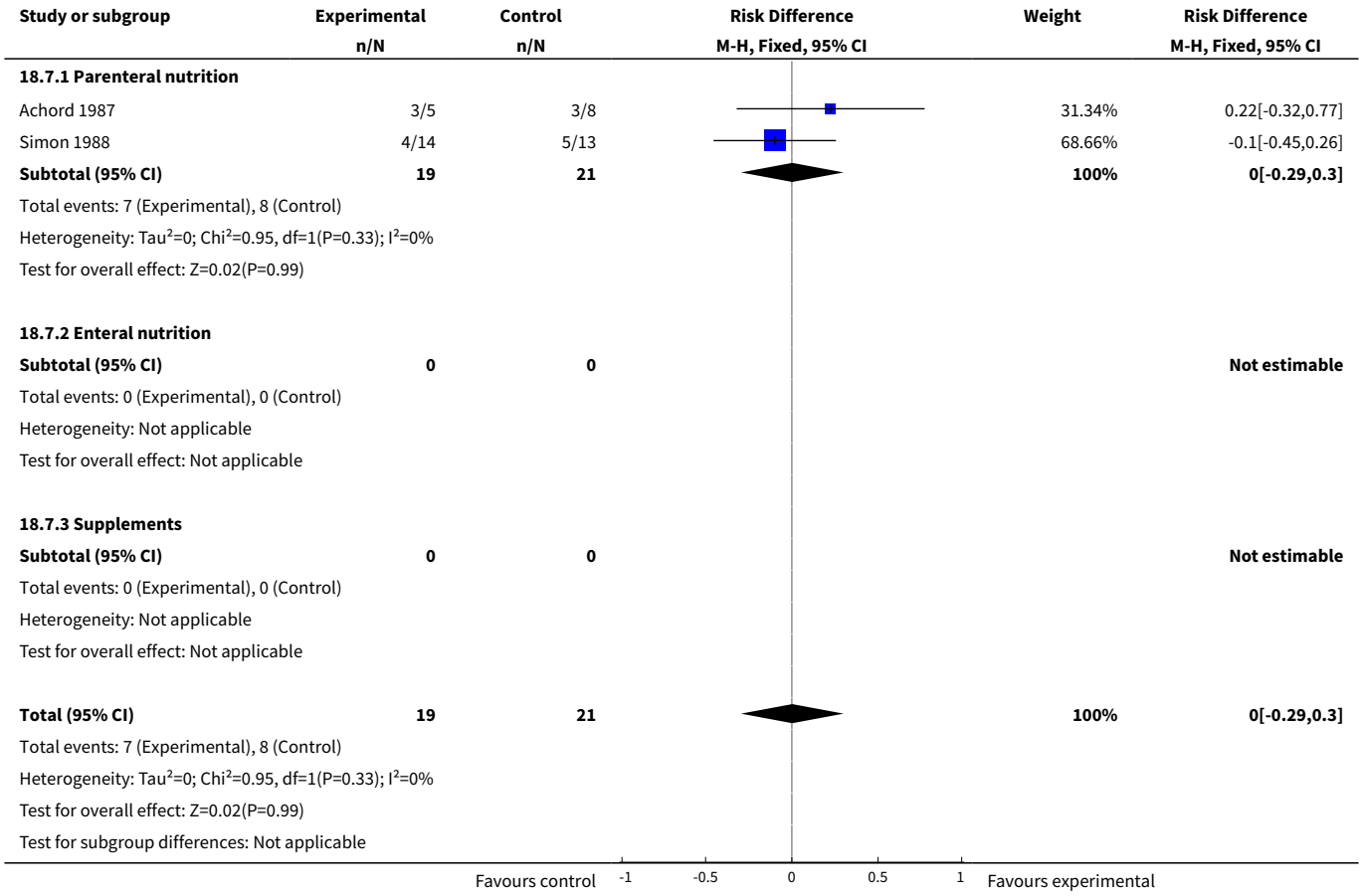
Analysis 18.5. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 5 Medical trials.

Study or subgroup	Experimental n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
18.5.1 Parenteral nutrition					
Achord 1987	3/5	3/8		9.6%	0.22[-0.32,0.77]
Naveau 1986	9/16	17/17		25.73%	-0.44[-0.69,-0.19]
Simon 1988	4/14	5/13		21.04%	-0.1[-0.45,0.26]
Subtotal (95% CI)	**35**	**38**		**56.37%**	**-0.2[-0.4,0]**
Total events: 16 (Experimental), 25 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.2, df=2(P=0.05); I^2=67.72%					
Test for overall effect: Z=1.93(P=0.05)					
18.5.2 Enteral nutrition					
Cabre 1990	7/13	10/16		22.39%	-0.09[-0.45,0.27]
Subtotal (95% CI)	**13**	**16**		**22.39%**	**-0.09[-0.45,0.27]**
Total events: 7 (Experimental), 10 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.47(P=0.64)					
18.5.3 Supplements					
Hayashi 1991	6/14	1/8		15.89%	0.3[-0.04,0.65]
Nakaya 2007	2/3	0/4		5.35%	0.67[0.12,1.21]
Subtotal (95% CI)	**17**	**12**		**21.24%**	**0.4[0.08,0.71]**
Total events: 8 (Experimental), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.23, df=1(P=0.27); I^2=18.81%					

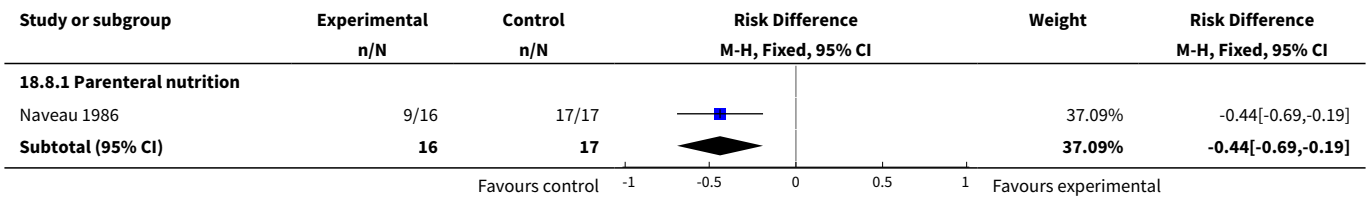


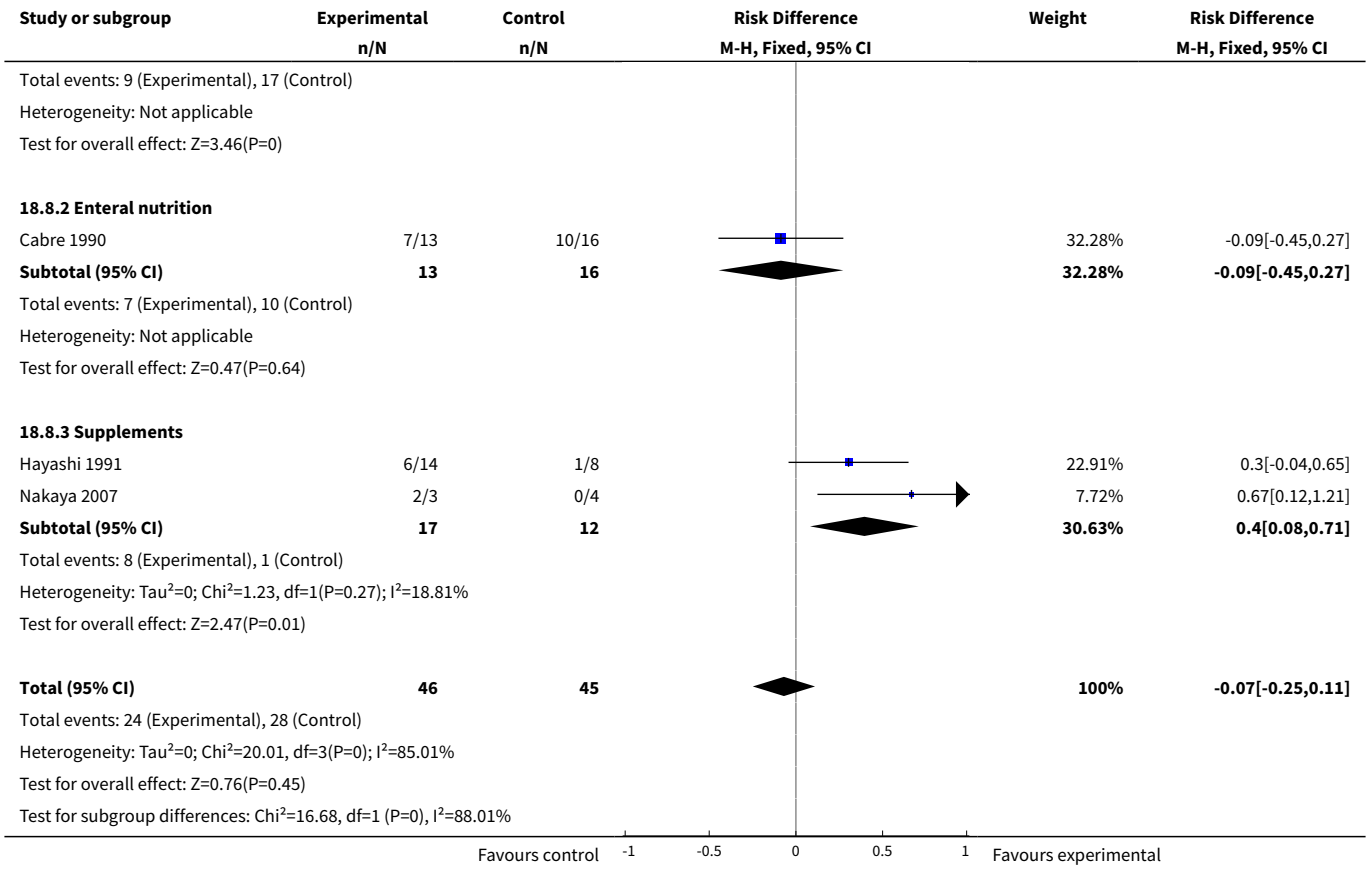


Analysis 18.7. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 7 Alcoholic hepatitis.

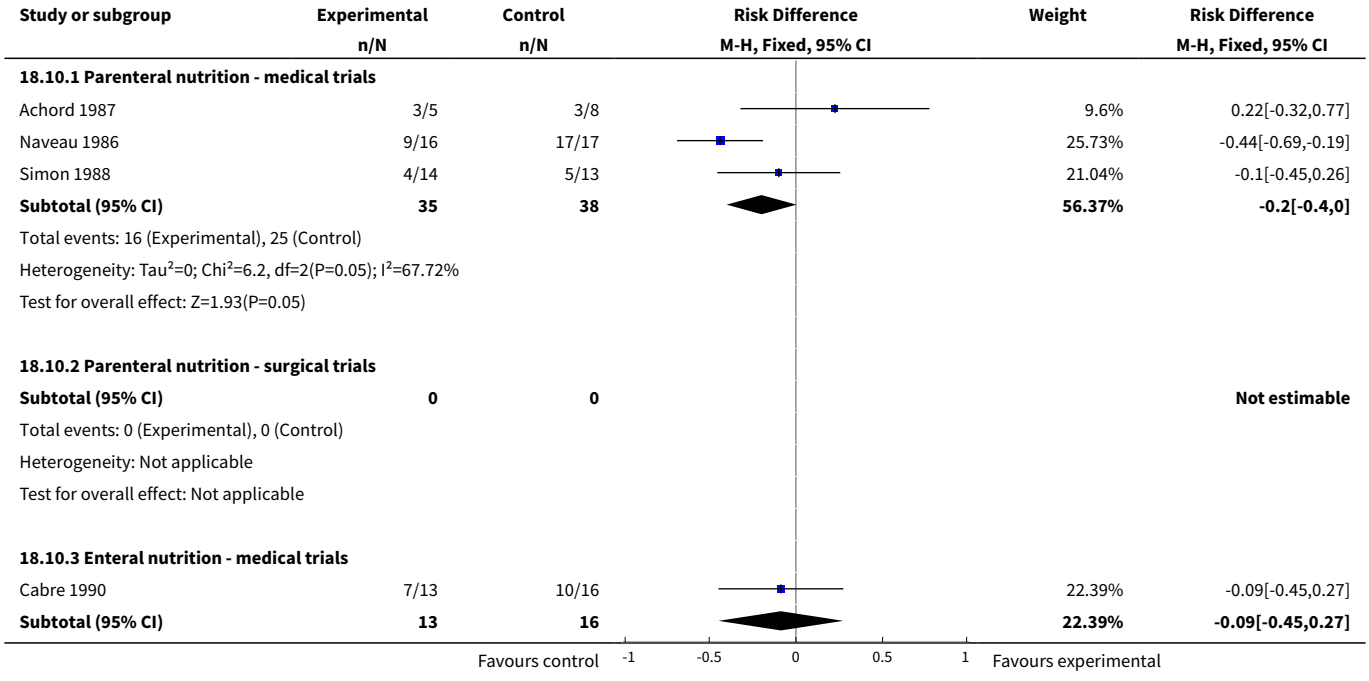


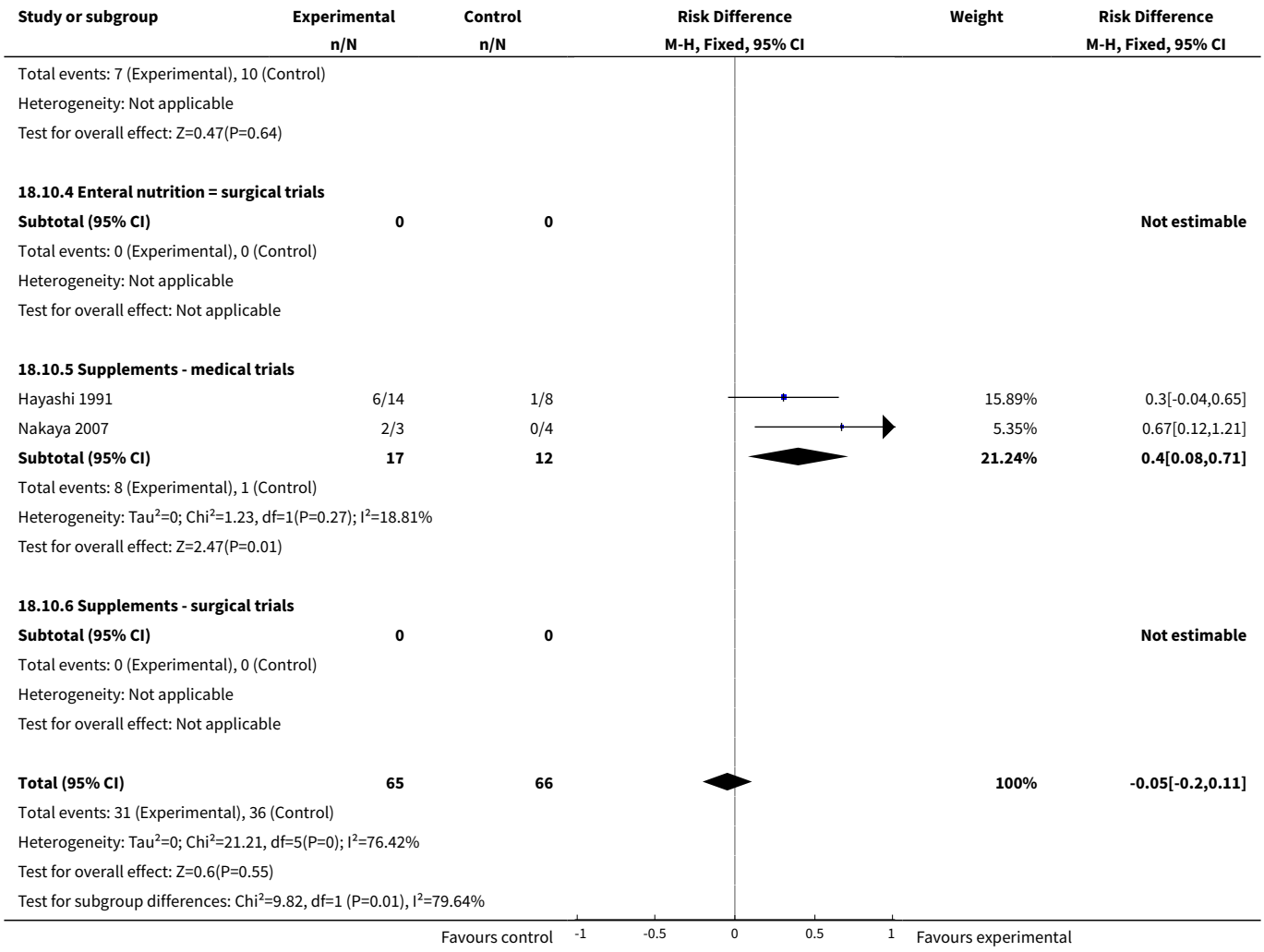
Analysis 18.8. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 8 Cirrhosis.



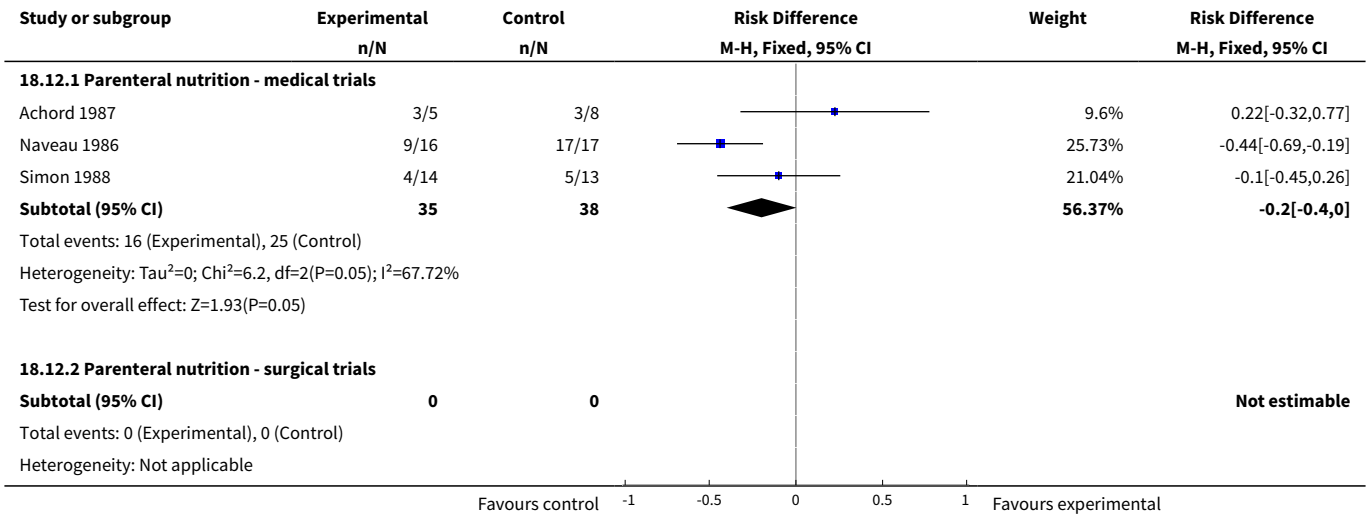


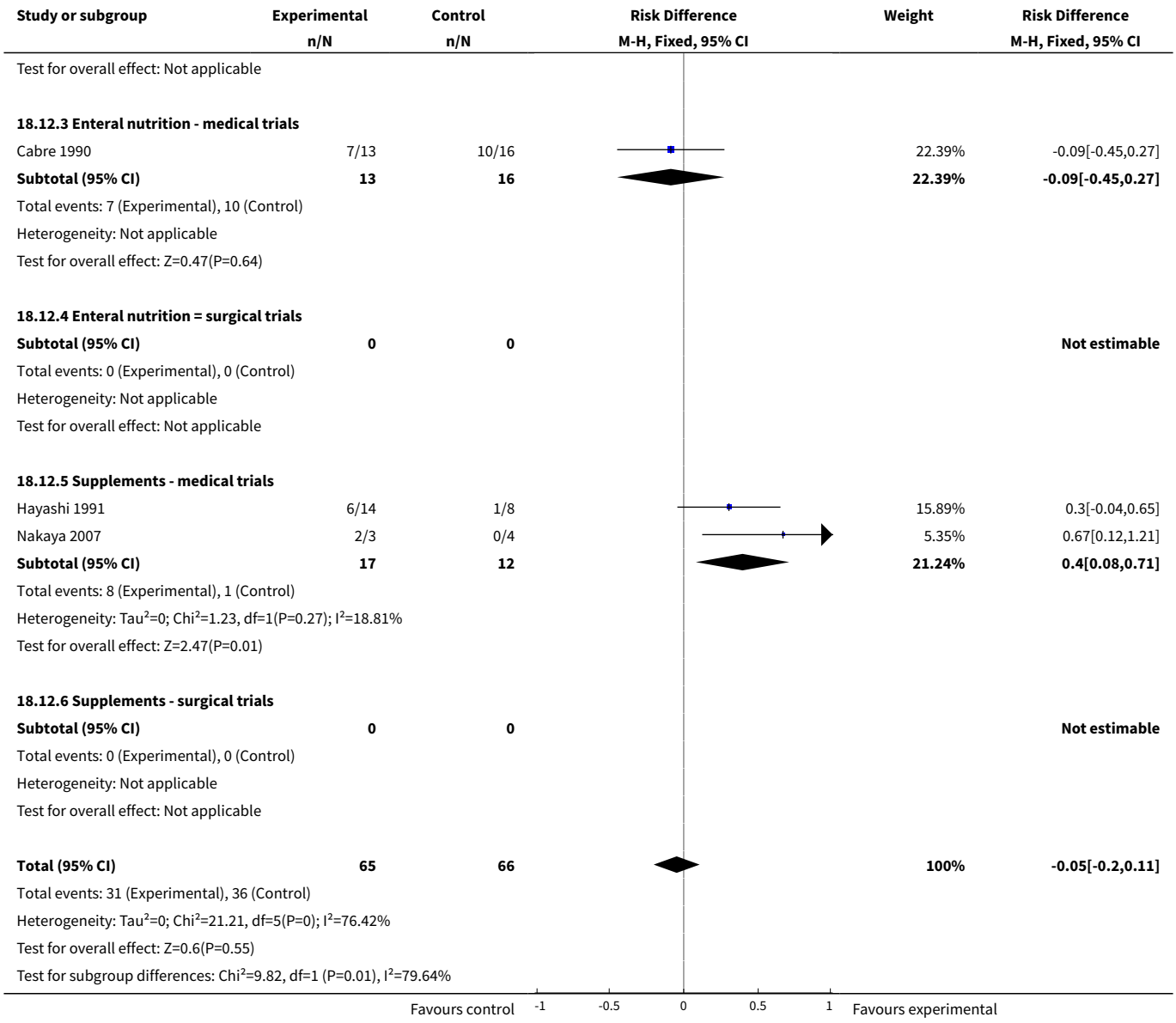
Analysis 18.10. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 10 Abstracts excluded.



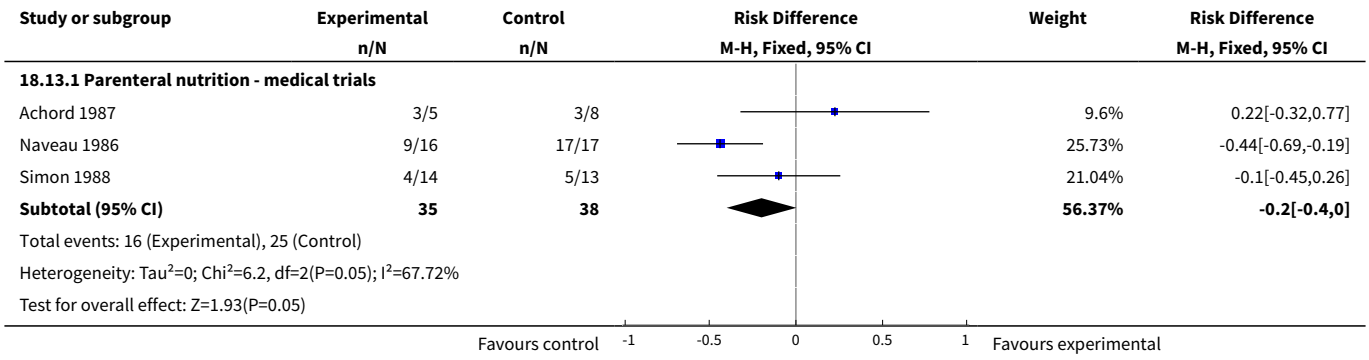


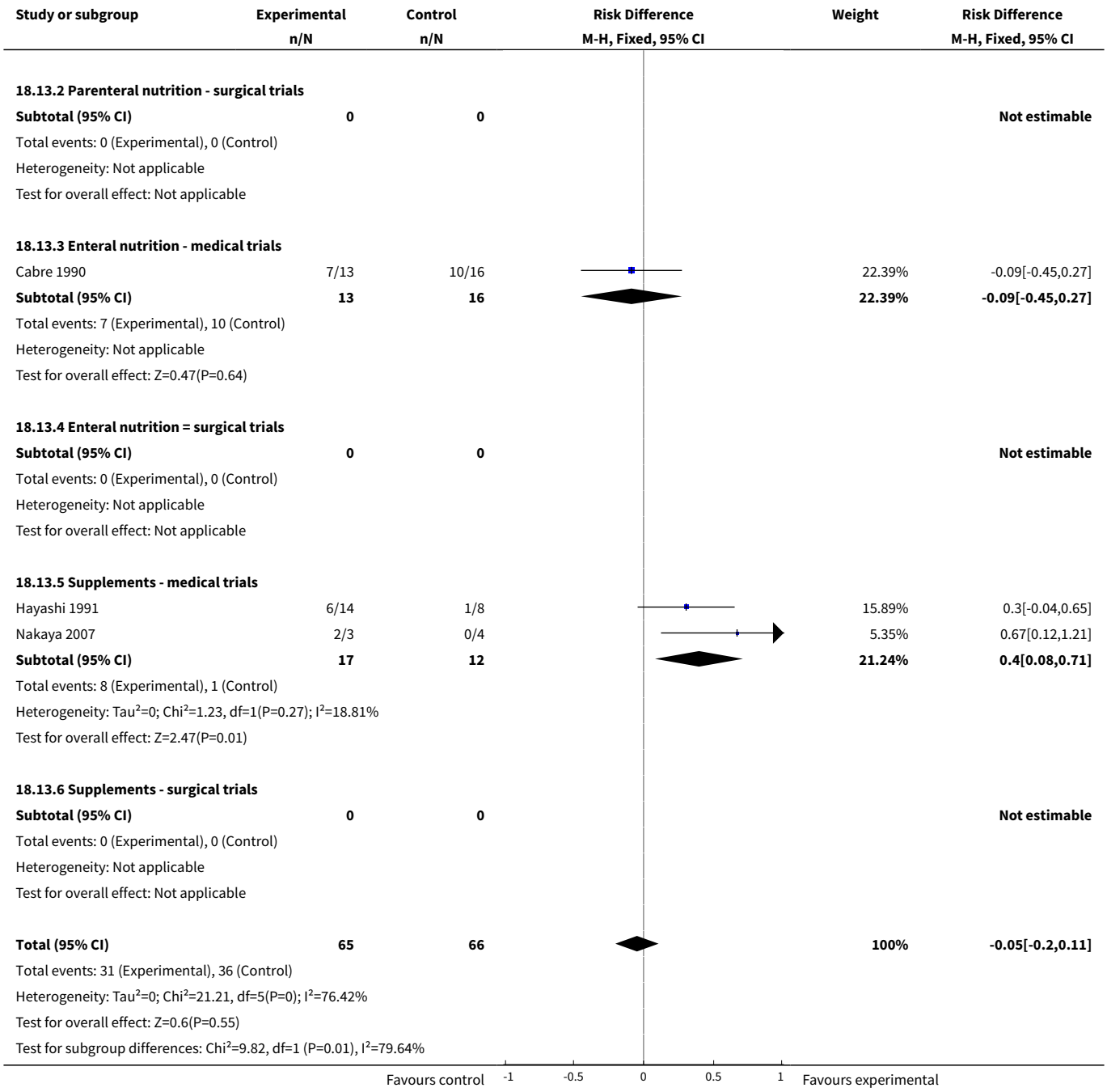
Analysis 18.12. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 12 Intent to treat - best-case scenario for intervention - no changes made.





Analysis 18.13. Comparison 18 Resolution of ascites - absolute risk difference (ARD), Outcome 13 Intent to treat - worst-case scenario for intervention - no changes made.





Comparison 19. Appearance gastrointestinal bleeding - absolute risk difference (ARD)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	11	783	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.01, 0.06]

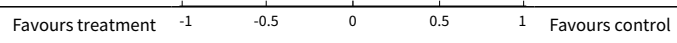
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2 Parenteral nutrition	1	124	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
2.1 Medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Surgical trials	1	124	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
3 Enteral nutrition (all medical)	4	180	Risk Difference (M-H, Fixed, 95% CI)	0.08 [-0.04, 0.19]
3.1 Medical trials	4	180	Risk Difference (M-H, Fixed, 95% CI)	0.08 [-0.04, 0.19]
3.2 Surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Supplements	6	479	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.04, 0.05]
4.1 Medical trials	5	435	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.04, 0.05]
4.2 Surgical trials	1	44	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.12, 0.13]
5 Medical trials	9	615	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.02, 0.07]
5.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 Enteral nutrition	4	180	Risk Difference (M-H, Fixed, 95% CI)	0.08 [-0.04, 0.19]
5.3 Supplements	5	435	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.04, 0.05]
6 Surgical trials	2	168	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.03, 0.06]
6.1 Parenteral nutrition	1	124	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
6.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Supplements	1	44	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.12, 0.13]
7 Alcoholic hepatitis	1	64	Risk Difference (M-H, Fixed, 95% CI)	0.17 [-0.01, 0.35]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7.1 Parenteral Nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Enteral nutrition	1	64	Risk Difference (M-H, Fixed, 95% CI)	0.17 [-0.01, 0.35]
7.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Cirrhosis	6	234	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.09, 0.10]
8.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Enteral nutrition	3	116	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.11, 0.17]
8.3 Supplements	3	118	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.15, 0.10]
9 HCC	2	317	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
9.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Eneral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	2	317	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
10 Abstracts excluded	9	491	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.02, 0.07]
10.1 Parenteral nutrition - medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 Parenteral nutrition - surgical trials	1	124	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
10.3 Enteral nutrition - medical trials	3	121	Risk Difference (M-H, Fixed, 95% CI)	0.09 [-0.04, 0.21]
10.4 Enteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.5 Supplements - medical trials	4	202	Risk Difference (M-H, Fixed, 95% CI)	-0.00 [-0.08, 0.07]
10.6 Supplements - surgical trials	1	44	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.12, 0.13]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11 Surgical trials without transplant patients (no trials with transplant patients)	2	168	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.03, 0.06]
11.1 Parenteral nutrition	1	124	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.06]
11.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Supplements	1	44	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.12, 0.13]
12 Intent to treat - best-case scenario for intervention	11	838	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.09, -0.01]
12.1 Parenteral nutrition - medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 Parenteral nutrition - surgical trials	1	150	Risk Difference (M-H, Fixed, 95% CI)	-0.19 [-0.28, -0.09]
12.3 Enteral nutrition - medical trials	4	184	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.07, 0.16]
12.4 Enteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.5 Supplements - medical trials	5	454	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.08, 0.01]
12.6 Supplements - surgical trials	1	50	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.23, 0.07]
13 Intent-to-treat - worst-case scenario for intervention	11	838	Risk Difference (M-H, Fixed, 95% CI)	0.09 [0.05, 0.13]
13.1 Parenteral nutrition - medical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Parenteral nutrition - surgical trials	1	150	Risk Difference (M-H, Fixed, 95% CI)	0.16 [0.07, 0.25]
13.3 Enteral nutrition - medical trials	4	184	Risk Difference (M-H, Fixed, 95% CI)	0.09 [-0.02, 0.20]
13.4 Enteral nutrition - surgical trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.5 Supplements - medical trials	5	454	Risk Difference (M-H, Fixed, 95% CI)	0.05 [0.00, 0.10]
13.6 Supplements - surgical trials	1	50	Risk Difference (M-H, Fixed, 95% CI)	0.16 [-0.01, 0.33]

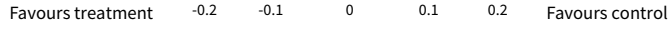
Analysis 19.1. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 1 All studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Cabre 1990	1/16	4/19		4.48%	-0.15[-0.37,0.07]
Calvey 1985	11/42	2/22		7.44%	0.17[-0.01,0.35]
DeLedinghen 1997	4/12	1/10		2.81%	0.23[-0.09,0.56]
Fan 1994	1/64	0/60		15.97%	0.02[-0.03,0.06]
Hirsch 1993	10/26	11/25		6.57%	-0.06[-0.33,0.21]
Kobashi 2006	7/119	5/114		30.02%	0.01[-0.04,0.07]
Meng 1999	1/21	1/23		5.66%	0[-0.12,0.13]
Nakaya 2007	0/19	0/19		4.9%	0[-0.1,0.1]
Norman 2008	8/30	6/29		7.6%	0.06[-0.16,0.28]
Poon 2004	1/41	0/43		10.82%	0.02[-0.04,0.09]
Tangkijvanich 2000	0/14	0/15		3.73%	0[-0.12,0.12]
Total (95% CI)	**404**	**379**		**100%**	**0.02[-0.01,0.06]**
Total events: 44 (Treatment), 30 (Control)					
Heterogeneity: Tau²=0; Chi²=7.68, df=10(P=0.66); I²=0%					
Test for overall effect: Z=1.22(P=0.22)					



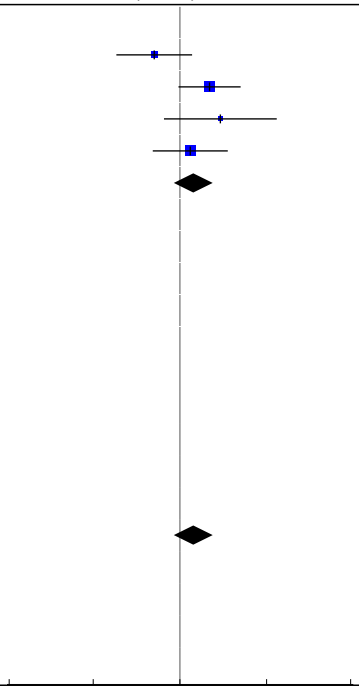
Analysis 19.2. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 2 Parenteral nutrition.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.2.1 Medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.2.2 Surgical trials					
Fan 1994	1/64	0/60		100%	0.02[-0.03,0.06]
Subtotal (95% CI)	**64**	**60**		**100%**	**0.02[-0.03,0.06]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.71(P=0.48)					
Total (95% CI)	**64**	**60**		**100%**	**0.02[-0.03,0.06]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.71(P=0.48)					
Test for subgroup differences: Not applicable					



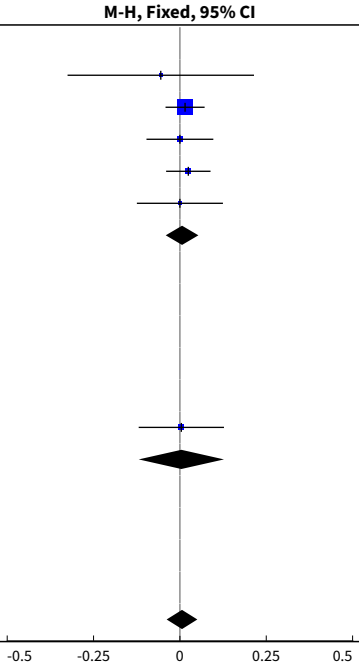
Analysis 19.3. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 3 Enteral nutrition (all medical).

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.3.1 Medical trials					
Cabre 1990	1/16	4/19		20.05%	-0.15[-0.37,0.07]
Calvey 1985	11/42	2/22		33.32%	0.17[-0.01,0.35]
DeLedinghen 1997	4/12	1/10		12.59%	0.23[-0.09,0.56]
Norman 2008	8/30	6/29		34.04%	0.06[-0.16,0.28]
Subtotal (95% CI)	**100**	**80**		**100%**	**0.08[-0.04,0.19]**
Total events: 24 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.05, df=3(P=0.11); I^2=50.41%					
Test for overall effect: Z=1.35(P=0.18)					
19.3.2 Surgical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**100**	**80**		**100%**	**0.08[-0.04,0.19]**
Total events: 24 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=6.05, df=3(P=0.11); I^2=50.41%					
Test for overall effect: Z=1.35(P=0.18)					
Test for subgroup differences: Not applicable					

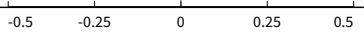


Analysis 19.4. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 4 Supplements.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.4.1 Medical trials					
Hirsch 1993	10/26	11/25		10.65%	-0.06[-0.33,0.21]
Kobashi 2006	7/119	5/114		48.65%	0.01[-0.04,0.07]
Nakaya 2007	0/19	0/19		7.94%	0[-0.1,0.1]
Poon 2004	1/41	0/43		17.54%	0.02[-0.04,0.09]
Tangkijvanich 2000	0/14	0/15		6.05%	0[-0.12,0.12]
Subtotal (95% CI)	**219**	**216**		**90.83%**	**0.01[-0.04,0.05]**
Total events: 18 (Treatment), 16 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.62, df=4(P=0.96); I^2=0%					
Test for overall effect: Z=0.26(P=0.8)					
19.4.2 Surgical trials					
Meng 1999	1/21	1/23		9.17%	0[-0.12,0.13]
Subtotal (95% CI)	**21**	**23**		**9.17%**	**0[-0.12,0.13]**
Total events: 1 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.07(P=0.95)					
Total (95% CI)	**240**	**239**		**100%**	**0.01[-0.04,0.05]**



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Total events: 19 (Treatment), 17 (Control)					
Heterogeneity: Tau²=0; Chi²=0.63, df=5(P=0.99); I²=0%					
Test for overall effect: Z=0.27(P=0.79)					
Test for subgroup differences: Chi²=0, df=1 (P=0.98), I²=0%					

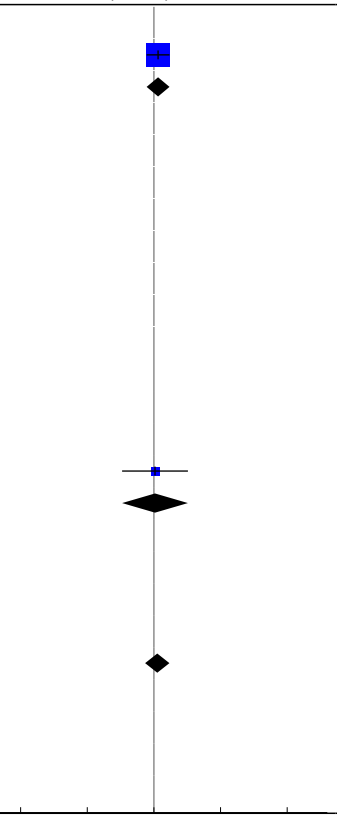


Analysis 19.5. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 5 Medical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.5.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.5.2 Enteral nutrition					
Cabre 1990	1/16	4/19		5.71%	-0.15[-0.37,0.07]
Calvey 1985	11/42	2/22		9.5%	0.17[-0.01,0.35]
DeLedinghen 1997	4/12	1/10		3.59%	0.23[-0.09,0.56]
Norman 2008	8/30	6/29		9.7%	0.06[-0.16,0.28]
Subtotal (95% CI)	**100**	**80**		**28.5%**	**0.08[-0.04,0.19]**
Total events: 24 (Treatment), 13 (Control)					
Heterogeneity: Tau²=0; Chi²=6.05, df=3(P=0.11); I²=50.41%					
Test for overall effect: Z=1.35(P=0.18)					
19.5.3 Supplements					
Hirsch 1993	10/26	11/25		8.38%	-0.06[-0.33,0.21]
Kobashi 2006	7/119	5/114		38.3%	0.01[-0.04,0.07]
Nakaya 2007	0/19	0/19		6.25%	0[-0.1,0.1]
Poon 2004	1/41	0/43		13.81%	0.02[-0.04,0.09]
Tangkijvanich 2000	0/14	0/15		4.76%	0[-0.12,0.12]
Subtotal (95% CI)	**219**	**216**		**71.5%**	**0.01[-0.04,0.05]**
Total events: 18 (Treatment), 16 (Control)					
Heterogeneity: Tau²=0; Chi²=0.62, df=4(P=0.96); I²=0%					
Test for overall effect: Z=0.26(P=0.8)					
Total (95% CI)	**319**	**296**		**100%**	**0.03[-0.02,0.07]**
Total events: 42 (Treatment), 29 (Control)					
Heterogeneity: Tau²=0; Chi²=7.57, df=8(P=0.48); I²=0%					
Test for overall effect: Z=1.11(P=0.27)					
Test for subgroup differences: Chi²=1.3, df=1 (P=0.25), I²=23.05%					

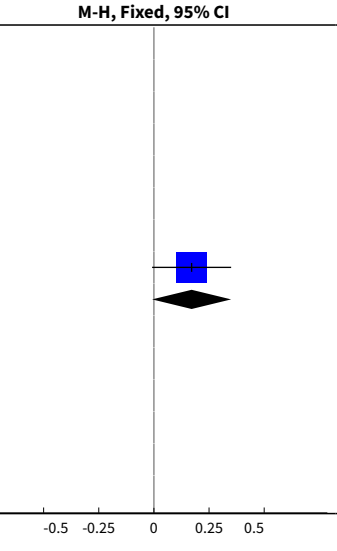
Analysis 19.6. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 6 Surgical trials.

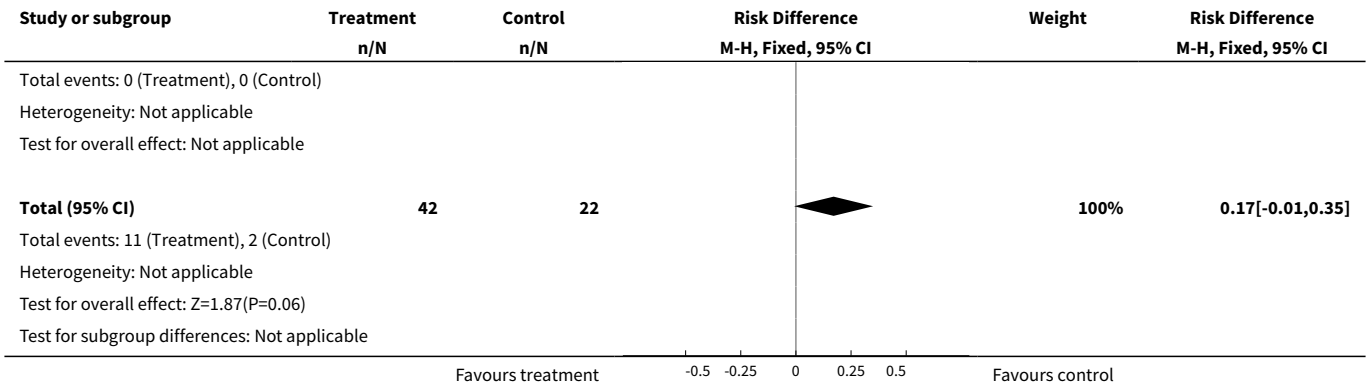
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.6.1 Parenteral nutrition					
Fan 1994	1/64	0/60		73.83%	0.02[-0.03,0.06]
Subtotal (95% CI)	**64**	**60**		**73.83%**	**0.02[-0.03,0.06]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.71(P=0.48)					
19.6.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.6.3 Supplements					
Meng 1999	1/21	1/23		26.17%	0[-0.12,0.13]
Subtotal (95% CI)	**21**	**23**		**26.17%**	**0[-0.12,0.13]**
Total events: 1 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.07(P=0.95)					
Total (95% CI)	**85**	**83**		**100%**	**0.01[-0.03,0.06]**
Total events: 2 (Treatment), 1 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.04, df=1(P=0.85); I^2=0%					
Test for overall effect: Z=0.54(P=0.59)					
Test for subgroup differences: Chi^2=0.03, df=1 (P=0.86), I^2=0%					



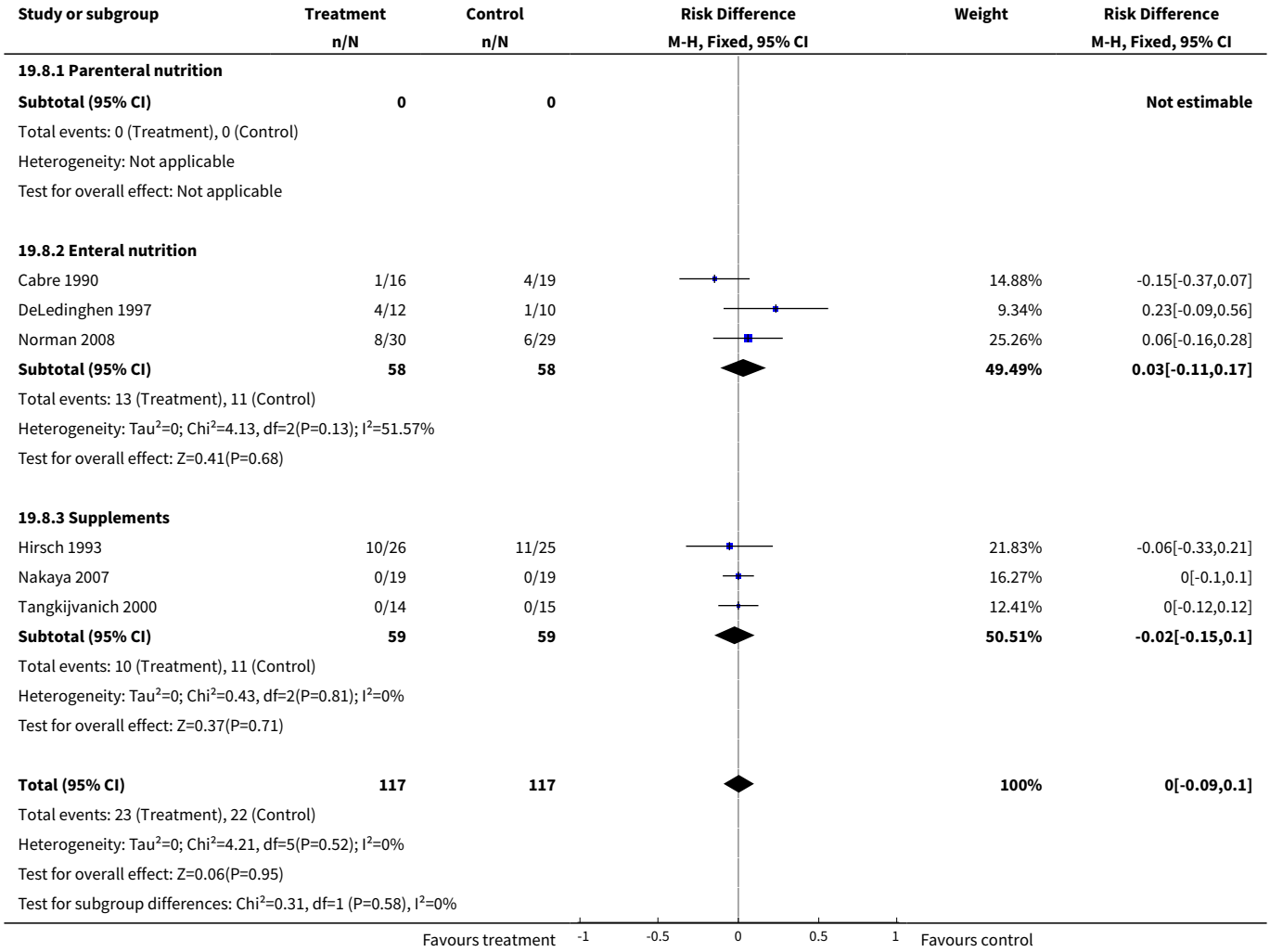
Analysis 19.7. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 7 Alcoholic hepatitis.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.7.1 Parenteral Nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.7.2 Enteral nutrition					
Calvey 1985	11/42	2/22		100%	0.17[-0.01,0.35]
Subtotal (95% CI)	**42**	**22**		**100%**	**0.17[-0.01,0.35]**
Total events: 11 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.87(P=0.06)					
19.7.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**



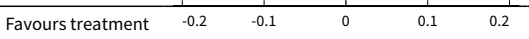


Analysis 19.8. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 8 Cirrhosis.



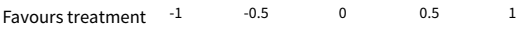
Analysis 19.9. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 9 HCC.

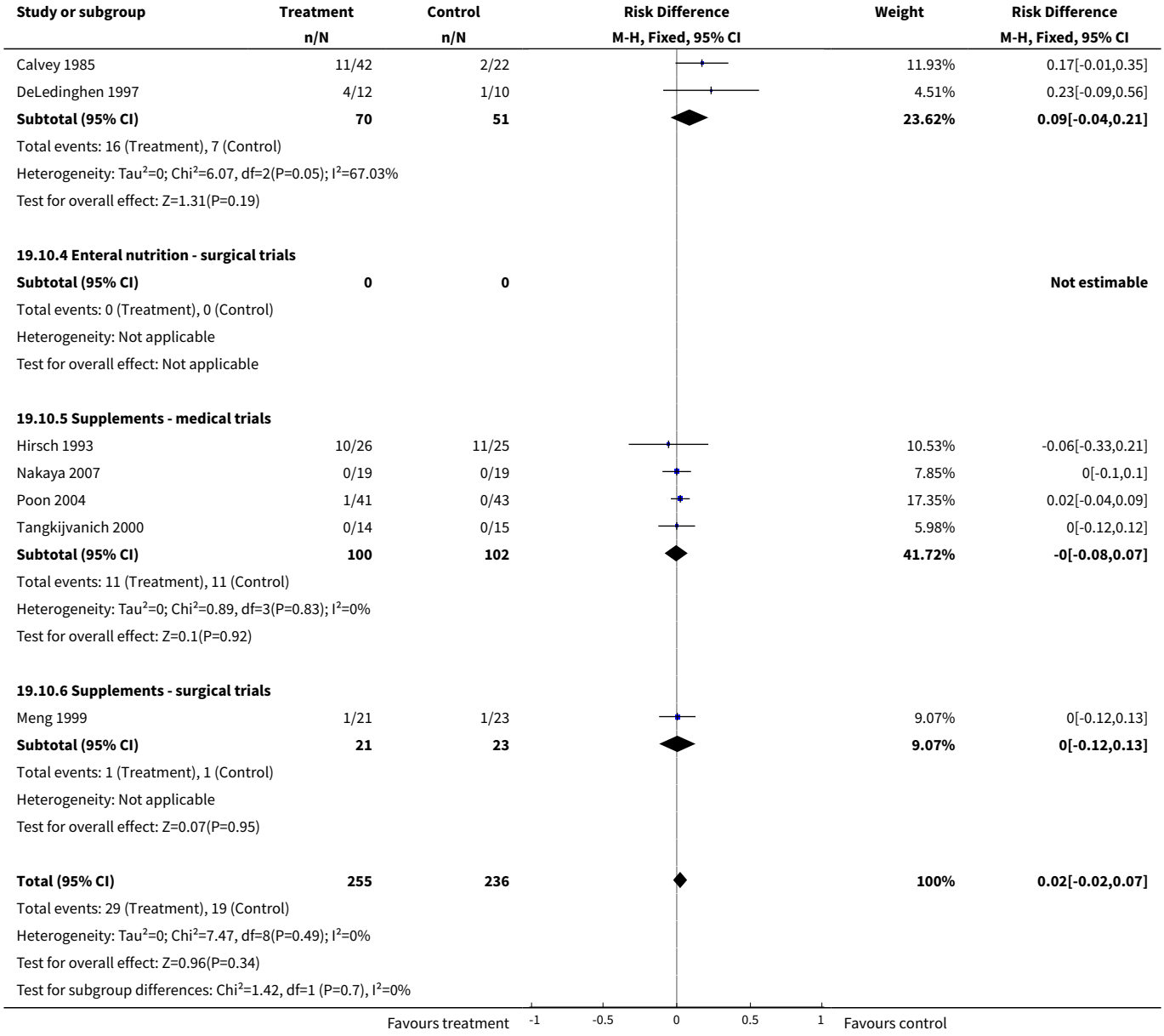
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.9.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.9.2 Eneral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.9.3 Supplements					
Kobashi 2006	7/119	5/114		73.5%	0.01[-0.04,0.07]
Poon 2004	1/41	0/43		26.5%	0.02[-0.04,0.09]
Subtotal (95% CI)	**160**	**157**		**100%**	**0.02[-0.03,0.06]**
Total events: 8 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.05, df=1(P=0.82); I^2=0%					
Test for overall effect: Z=0.76(P=0.45)					
Total (95% CI)	**160**	**157**		**100%**	**0.02[-0.03,0.06]**
Total events: 8 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.05, df=1(P=0.82); I^2=0%					
Test for overall effect: Z=0.76(P=0.45)					
Test for subgroup differences: Not applicable					



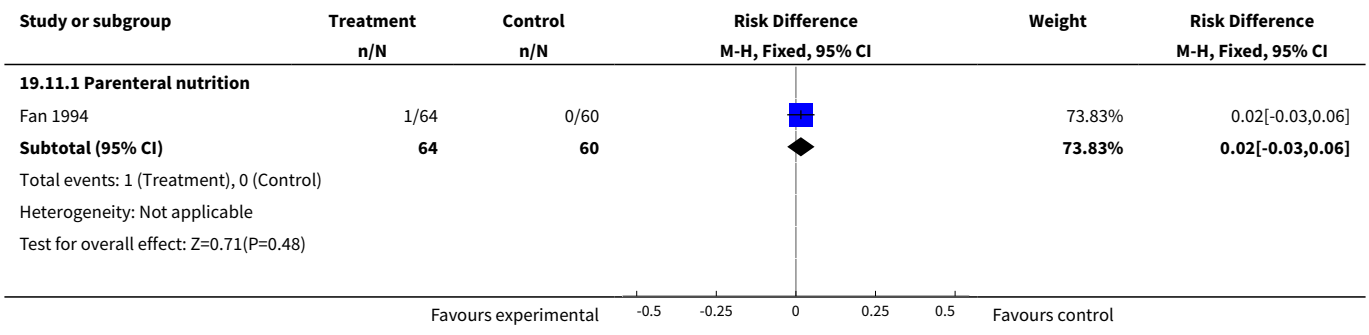
Analysis 19.10. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 10 Abstracts excluded.

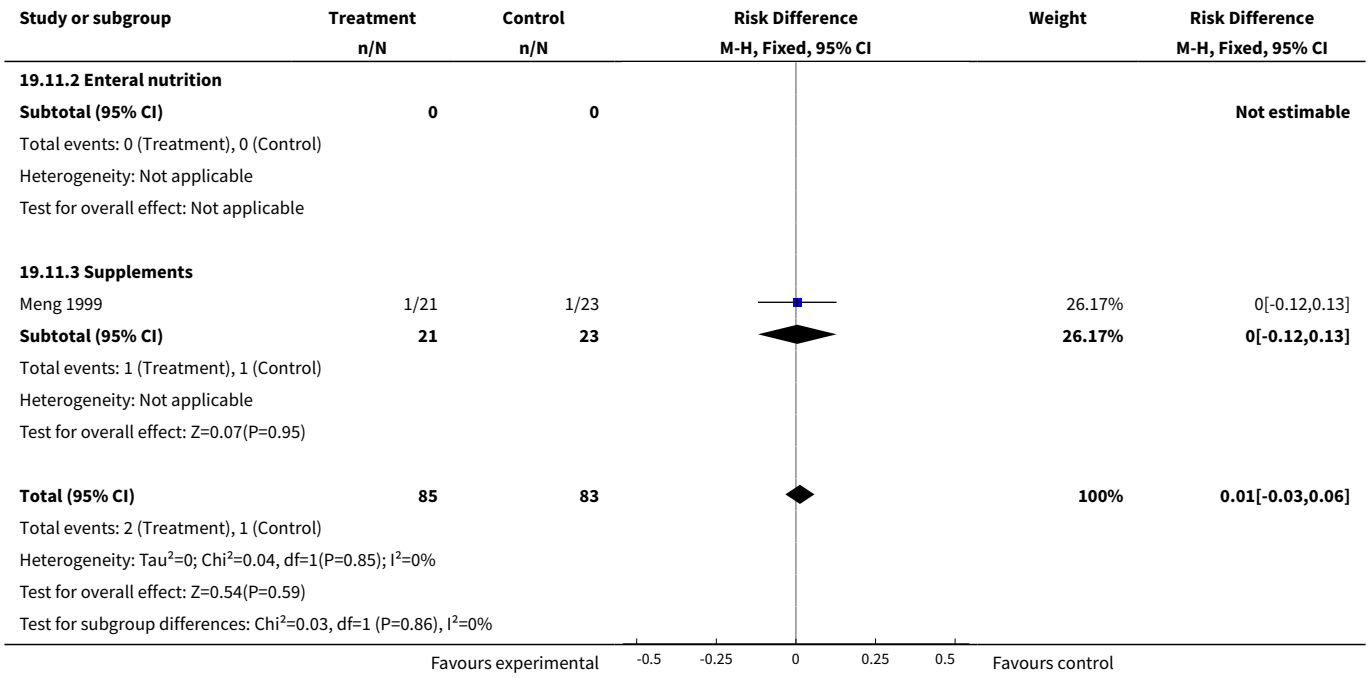
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
19.10.1 Parenteral nutrition - medical trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
19.10.2 Parenteral nutrition - surgical trials					
Fan 1994	1/64	0/60		25.59%	0.02[-0.03,0.06]
Subtotal (95% CI)	**64**	**60**		**25.59%**	**0.02[-0.03,0.06]**
Total events: 1 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.71(P=0.48)					
19.10.3 Enteral nutrition - medical trials					
Cabre 1990	1/16	4/19		7.18%	-0.15[-0.37,0.07]



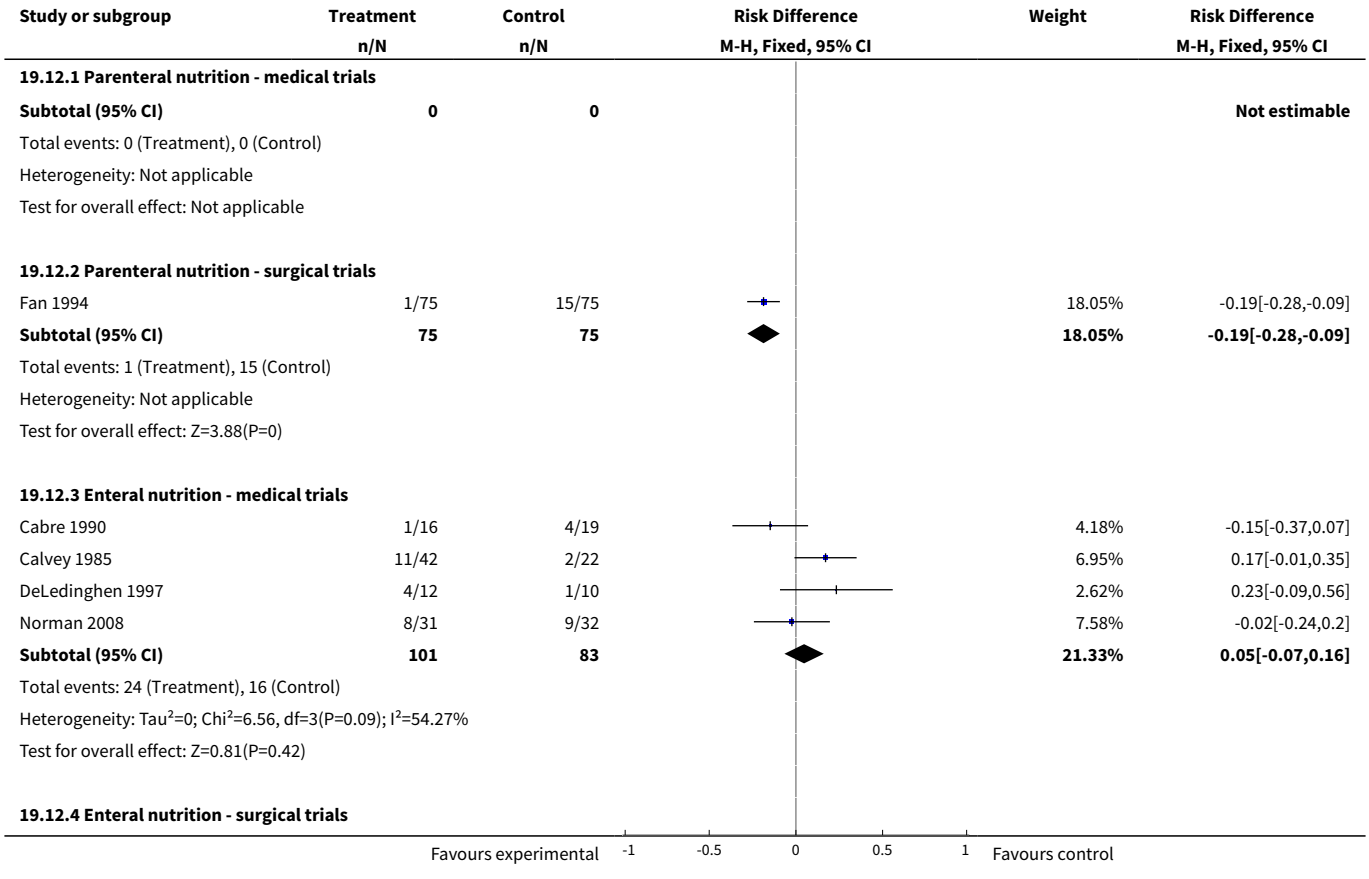


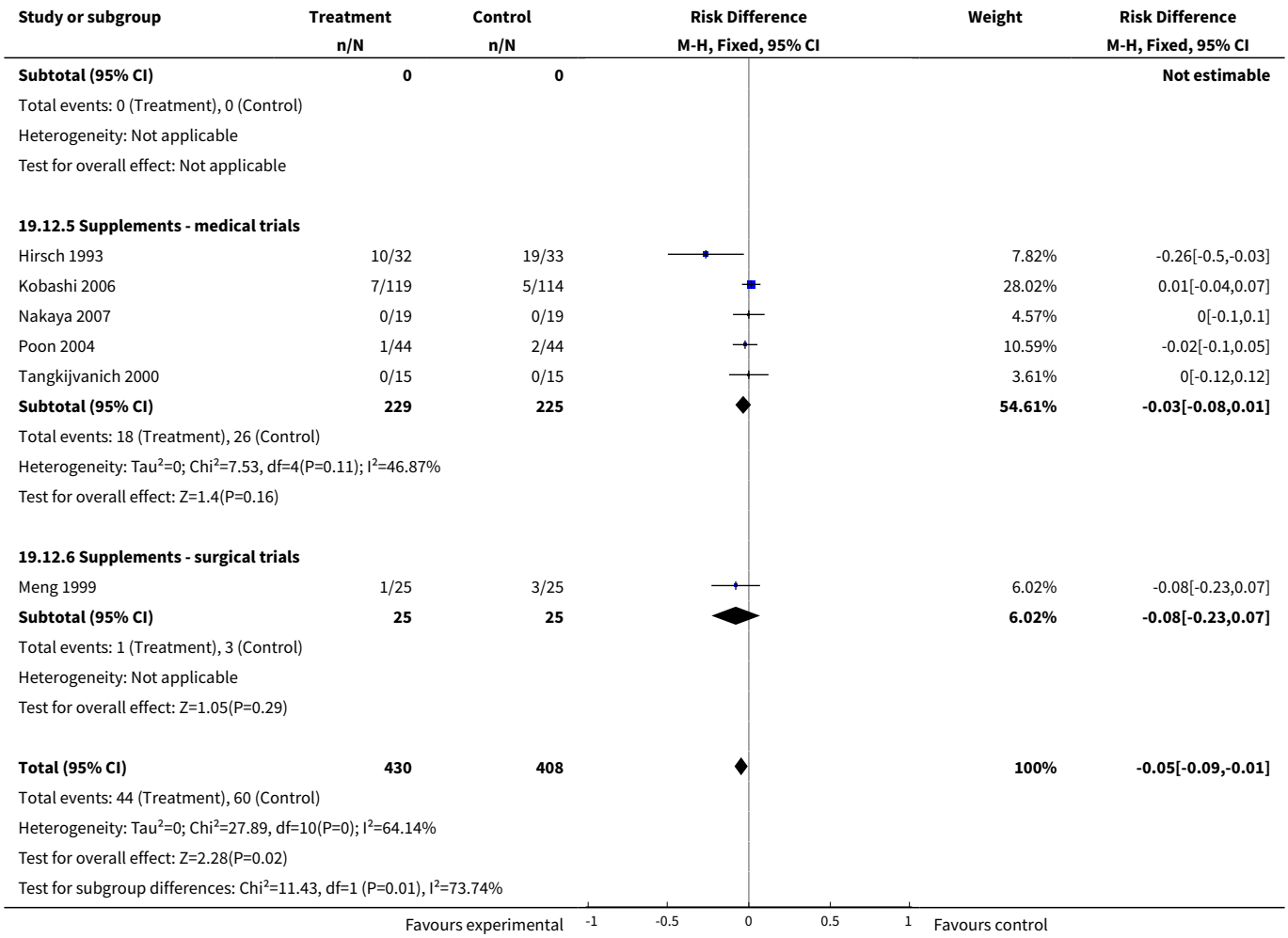
Analysis 19.11. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 11 Surgical trials without transplant patients (no trials with transplant patients).



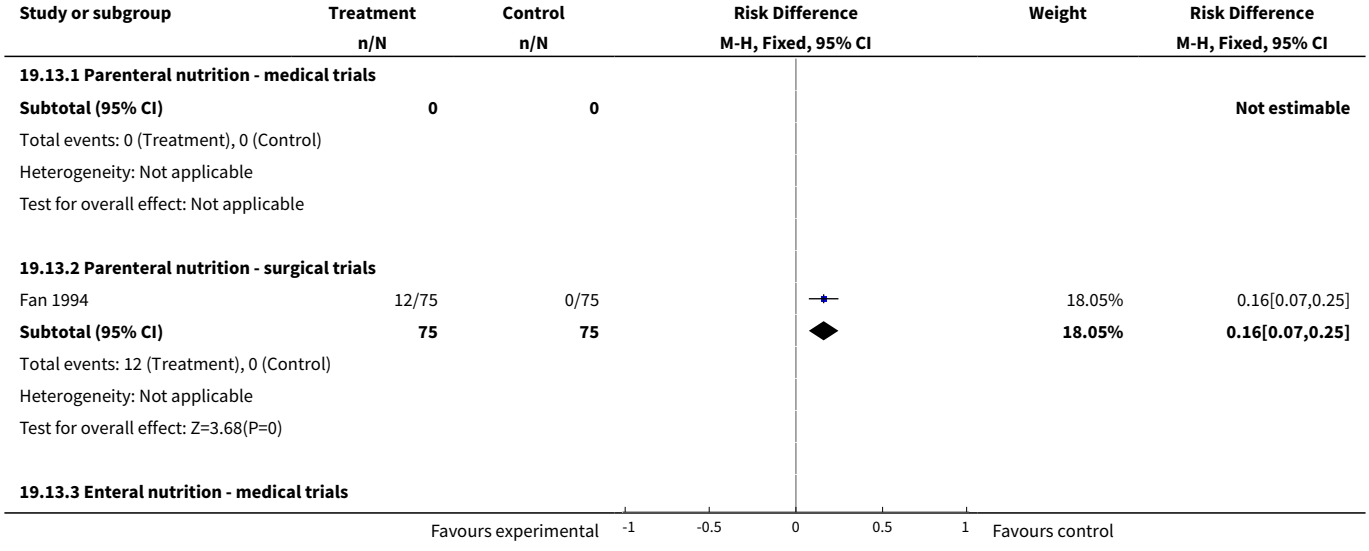


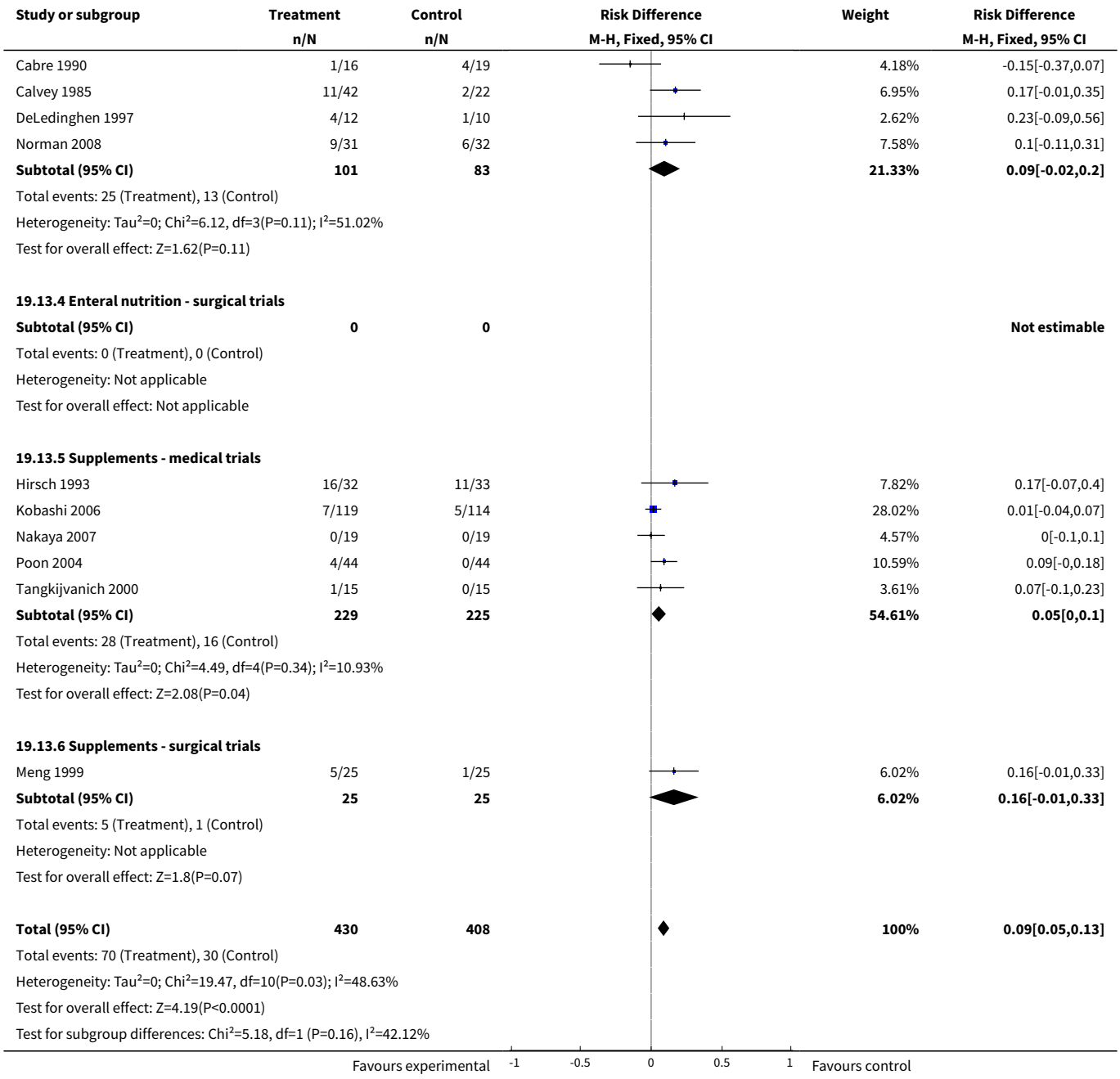
Analysis 19.12. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 12 Intent to treat - best-case scenario for intervention.





Analysis 19.13. Comparison 19 Appearance gastrointestinal bleeding - absolute risk difference (ARD), Outcome 13 Intent-to-treat - worst-case scenario for intervention.





Comparison 20. Appearance of encephalopathy - absolute risk difference (ARD)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	23		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
1.1 All trials	23	1062	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.06, 0.01]
1.2 Standard amino acids	11	339	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.09, 0.05]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.3 BCAAs	15	772	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.07, 0.01]
2 Parenteral nutrition - all trials	5		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
2.1 All trials	5	231	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.13, 0.02]
2.2 Standard amino acids	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
2.3 BCAAs	2	144	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.12, 0.05]
3 Parenteral nutrition - medical trials	3		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
3.1 All trials	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
3.2 Standard amino acids	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
3.3 BCAAs	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Parenteral nutrition - surgical trials	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
4.1 A;ll trials	2	144	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.12, 0.05]
4.2 Standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 BCAAs	2	144	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.12, 0.05]
5 Enteral nutrition - all studies	4		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
5.1 All trials	4	102	Risk Difference (M-H, Fixed, 95% CI)	0.10 [-0.04, 0.25]
5.2 Standard amino acids	4	91	Risk Difference (M-H, Fixed, 95% CI)	0.08 [-0.07, 0.24]
5.3 BCAAs	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
6 Enteral nutrition - medical trials	4		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
6.1 All studies	4	102	Risk Difference (M-H, Fixed, 95% CI)	0.04 [-0.10, 0.18]
6.2 Standard amino acids	4	91	Risk Difference (M-H, Fixed, 95% CI)	0.08 [-0.07, 0.24]
6.3 BCAAs	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
7 Enteral nutrition - surgical trials	0		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
7.1 All trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 BCAAs	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Supplements	14		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
8.1 All trials	14	734	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.07, 0.01]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
8.2 Standard amino acids -medical trials	4	170	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.13, 0.05]
8.3 BCAAs - medical trials	10	536	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.09, 0.01]
8.4 All supplements - medical	12	666	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.08, 0.01]
8.5 All surgical	2	68	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.08, 0.08]
9 Medical trials all trials	19	846	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.07, 0.02]
9.1 Parenteral nutrition	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
9.2 Enteral nutrition	4	102	Risk Difference (M-H, Fixed, 95% CI)	0.10 [-0.04, 0.25]
9.3 Supplements	12	657	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.08, 0.01]
10 Medical trials - standard amino acids	11	339	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.09, 0.05]
10.1 Parenteral nutrition	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
10.2 Enteral nutrition	4	91	Risk Difference (M-H, Fixed, 95% CI)	0.08 [-0.07, 0.24]
10.3 Supplements	4	161	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.13, 0.06]
11 Medical trials - BCAAs	11	560	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.08, 0.02]
11.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Enteral nutrition	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
11.3 Supplements	10	536	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.09, 0.01]
12 Surgical trials - all studies	4	212	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.09, 0.04]
12.1 Parenteral nutrition	2	144	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.12, 0.05]
12.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Supplements	2	68	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.08, 0.08]
13 Surgical trials - standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Surgical trials - BCAAs	4	212	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.09, 0.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Parenteral nutrition	2	144	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.12, 0.05]
14.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 Supplements	2	68	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.08, 0.08]
15 Alcoholic hepatitis - all studies	6	172	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.07, 0.12]
15.1 Parenteral nutrition	2	47	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.25, 0.07]
15.2 Enteral nutrition	2	48	Risk Difference (M-H, Fixed, 95% CI)	0.14 [-0.09, 0.37]
15.3 Supplements	2	77	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.11, 0.16]
16 Alcoholic hepatitis - standard amino acids	6	161	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.09, 0.11]
16.1 Parenteral nutrition	2	47	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.25, 0.07]
16.2 Enteral nutrition	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.11 [-0.15, 0.36]
16.3 Supplements	2	77	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.11, 0.16]
17 Alcoholic hepatitis - BCAA	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
17.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 Enteral nutrition	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
17.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Cirrhosis - all studies	12	420	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.10, 0.02]
18.1 Parenteral nutrition	1	40	Risk Difference (M-H, Fixed, 95% CI)	-0.1 [-0.32, 0.12]
18.2 Enteral nutrition	2	54	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.12, 0.26]
18.3 Supplements	9	326	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.11, 0.01]
19 Cirrhosis - standard amino acids	6	229	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.09, 0.08]
19.1 Parenteral nutrition	1	40	Risk Difference (M-H, Fixed, 95% CI)	-0.1 [-0.32, 0.12]
19.2 Enteral nutrition	2	54	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.12, 0.26]
19.3 Supplements	3	135	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.12, 0.10]
20 Cirrhosis - BCAAs	8	231	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.13, 0.02]
20.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

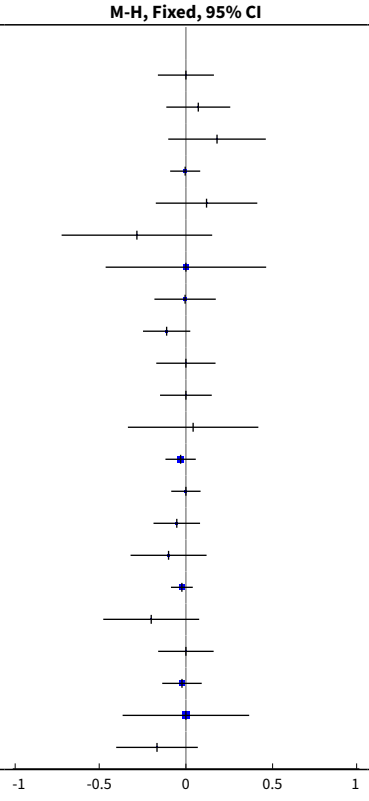
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
20.3 Supplementss	8	231	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.13, 0.02]
21 HCC - all studies	2	305	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.09, 0.04]
21.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.3 Supplements	2	305	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.09, 0.04]
22 HCC - standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 HCC - BCAAs	2	305	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.09, 0.04]
23.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 Supplements	2	305	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.09, 0.04]
24 Abstracts excluded	18		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
24.1 All trials	18	659	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.06, 0.02]
24.2 Standard amino acids	7	201	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.10, 0.08]
24.3 BCAAs	12	471	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.06, 0.02]
24.4 Parenteral nutrition all	5	231	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.13, 0.02]
24.5 Parenteral nutrition SAAs	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
24.6 Parenteral nutrition BCAAs	2	144	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.12, 0.05]
24.7 Enteral nutrition all	2	48	Risk Difference (M-H, Fixed, 95% CI)	0.14 [-0.09, 0.37]
24.8 Enteral nutrition SAAs	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.11 [-0.15, 0.36]
24.9 Enteral nutrition BCAAs	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
24.10 Supplements all	11	380	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.07, 0.03]
24.11 Supplements - SAAs	2	77	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.11, 0.16]
24.12 Supplements - BCAAs	9	303	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.08, 0.02]

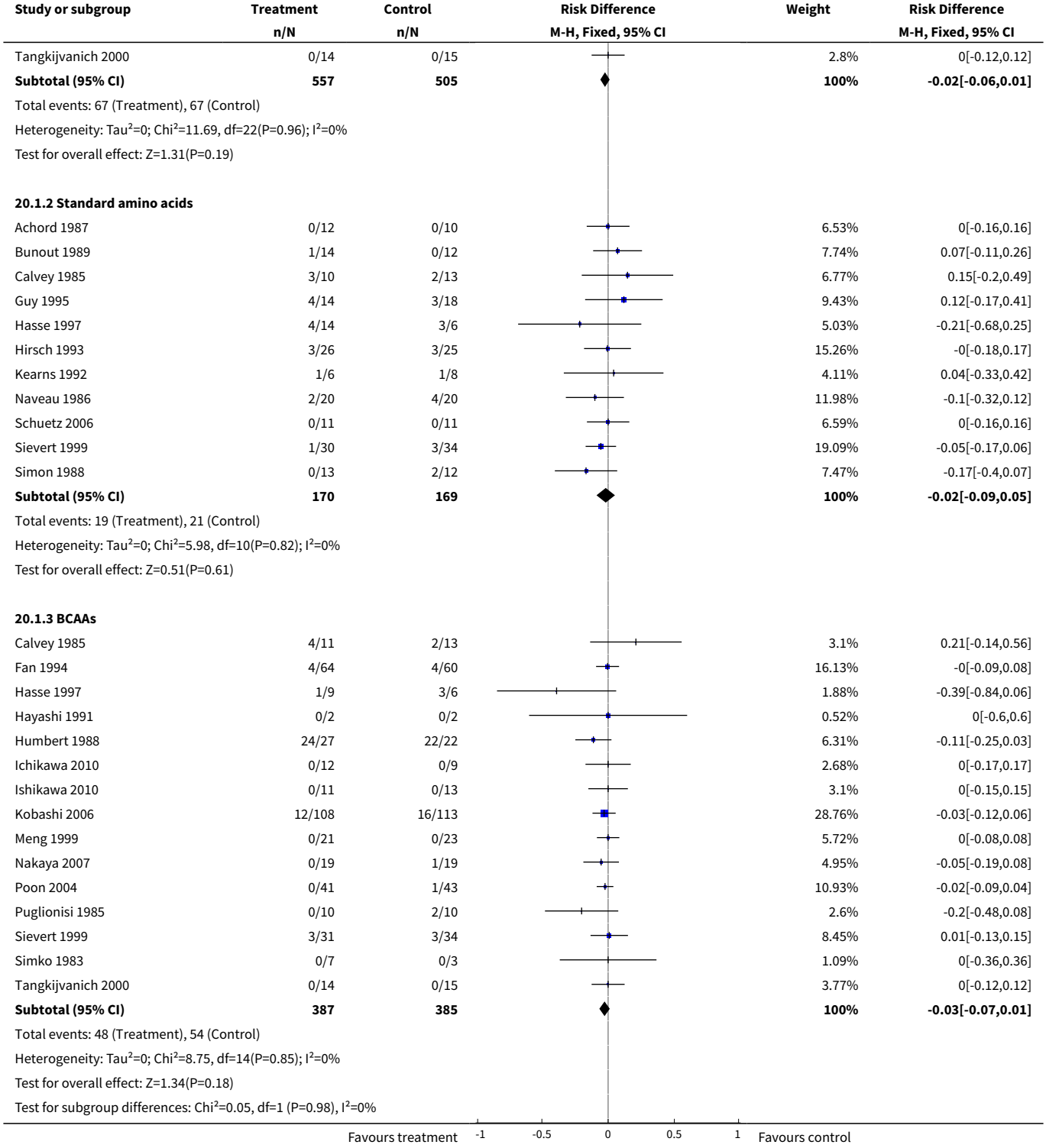
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
25 Surgical trials - transplant trials eliminated	3		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
25.1 All trials	3	192	Risk Difference (M-H, Fixed, 95% CI)	-0.00 [-0.07, 0.06]
25.2 Standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 BCAAs	3	192	Risk Difference (M-H, Fixed, 95% CI)	-0.00 [-0.07, 0.06]
26 ITT - Parenteral nutrition - best-case scenario for intervention	5		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
26.1 All trials	5	257	Risk Difference (M-H, Fixed, 95% CI)	-0.16 [-0.25, -0.08]
26.2 Standard amino acids	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
26.3 BCAAs	2	170	Risk Difference (M-H, Fixed, 95% CI)	-0.2 [-0.30, -0.10]
27 ITT - Parenteral nutrition - worst-case scenario for intervention	5		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
27.1 All trials	5	257	Risk Difference (M-H, Fixed, 95% CI)	0.04 [-0.04, 0.12]
27.2 Standard amino acids	3	87	Risk Difference (M-H, Fixed, 95% CI)	-0.09 [-0.23, 0.04]
27.3 BCAAs	2	170	Risk Difference (M-H, Fixed, 95% CI)	0.11 [0.01, 0.20]
28 ITT - Enteral nutrition - best-case scenario for intervention	4		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
28.1 All trials	4	112	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.11, 0.17]
28.2 Standard amino acids	4	101	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.13, 0.16]
28.3 BCAAs	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
29 ITT - Enteral nutrition - worst-case scenario for intervention	4		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
29.1 Standard amino acids	4	112	Risk Difference (M-H, Fixed, 95% CI)	0.21 [0.07, 0.35]
29.2 BCAAs	1	24	Risk Difference (M-H, Fixed, 95% CI)	0.21 [-0.14, 0.56]
29.3 All trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
30 ITT- Supplements - best-case scenario for intervention	14		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
30.1 All trials	14	782	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.12, -0.03]
30.2 Standard amino acids -medical trials	4	191	Risk Difference (M-H, Fixed, 95% CI)	-0.15 [-0.25, -0.06]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
30.3 BCAAs - medical trials	10	559	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.11, -0.02]
30.4 All supplements - medical	12	707	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.12, -0.03]
30.5 All surgical	2	74	Risk Difference (M-H, Fixed, 95% CI)	-0.05 [-0.16, 0.05]
31 ITT - Supplements - worst-case scenario for intervention	14		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
31.1 All trials	14	781	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.02, 0.07]
31.2 Standard amino acids -medical trials	4	191	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.03, 0.16]
31.3 BCAAs - medical trials	10	559	Risk Difference (M-H, Fixed, 95% CI)	0.00 [-0.05, 0.05]
31.4 All supplements - medical	12	707	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.07]
31.5 All surgical	2	74	Risk Difference (M-H, Fixed, 95% CI)	0.11 [-0.01, 0.23]

Analysis 20.1. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 1 All studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.1.1 All trials					
Achord 1987	0/12	0/10		2.11%	0[-0.16,0.16]
Bunout 1989	1/14	0/12		2.49%	0.07[-0.11,0.26]
Calvey 1985	7/21	2/13		3.1%	0.18[-0.1,0.46]
Fan 1994	4/64	4/60		11.95%	-0[-0.09,0.08]
Guy 1995	4/14	3/18		3.04%	0.12[-0.17,0.41]
Hasse 1997	5/23	3/6		1.84%	-0.28[-0.72,0.15]
Hayashi 1991	0/2	0/6		0.58%	0[-0.46,0.46]
Hirsch 1993	3/26	3/25		4.92%	-0[-0.18,0.17]
Humbert 1988	24/27	22/22		4.68%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		1.99%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		2.3%	0[-0.15,0.15]
Kearns 1992	1/6	1/8		1.32%	0.04[-0.33,0.42]
Kobashi 2006	12/108	16/113		21.32%	-0.03[-0.12,0.06]
Meng 1999	0/21	0/23		4.24%	0[-0.08,0.08]
Nakaya 2007	0/19	1/19		3.67%	-0.05[-0.19,0.08]
Naveau 1986	2/20	4/20		3.86%	-0.1[-0.32,0.12]
Poon 2004	0/41	1/43		8.1%	-0.02[-0.09,0.04]
Puglionisi 1985	0/10	2/10		1.93%	-0.2[-0.48,0.08]
Schuetz 2006	0/11	0/11		2.12%	0[-0.16,0.16]
Sievert 1999	4/61	3/34		8.43%	-0.02[-0.14,0.09]
Simko 1983	0/7	0/3		0.81%	0[-0.36,0.36]
Simon 1988	0/13	2/12		2.41%	-0.17[-0.4,0.07]

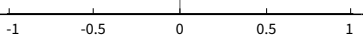




Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Tangkijvanich 2000	0/14	0/15		2.8%	0[-0.12,0.12]
Subtotal (95% CI)	**557**	**505**		**100%**	**-0.02[-0.06,0.01]**
Total events: 67 (Treatment), 67 (Control)					
Heterogeneity: Tau^2=0; Chi^2=11.69, df=22(P=0.96); I^2=0%					
Test for overall effect: Z=1.31(P=0.19)					
20.1.2 Standard amino acids					
Achord 1987	0/12	0/10		6.53%	0[-0.16,0.16]
Bunout 1989	1/14	0/12		7.74%	0.07[-0.11,0.26]
Calvey 1985	3/10	2/13		6.77%	0.15[-0.2,0.49]
Guy 1995	4/14	3/18		9.43%	0.12[-0.17,0.41]
Hasse 1997	4/14	3/6		5.03%	-0.21[-0.68,0.25]
Hirsch 1993	3/26	3/25		15.26%	-0[-0.18,0.17]
Kearns 1992	1/6	1/8		4.11%	0.04[-0.33,0.42]
Naveau 1986	2/20	4/20		11.98%	-0.1[-0.32,0.12]
Schuetz 2006	0/11	0/11		6.59%	0[-0.16,0.16]
Sievert 1999	1/30	3/34		19.09%	-0.05[-0.17,0.06]
Simon 1988	0/13	2/12		7.47%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**170**	**169**		**100%**	**-0.02[-0.09,0.05]**
Total events: 19 (Treatment), 21 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.98, df=10(P=0.82); I^2=0%					
Test for overall effect: Z=0.51(P=0.61)					
20.1.3 BCAAs					
Calvey 1985	4/11	2/13		3.1%	0.21[-0.14,0.56]
Fan 1994	4/64	4/60		16.13%	-0[-0.09,0.08]
Hasse 1997	1/9	3/6		1.88%	-0.39[-0.84,0.06]
Hayashi 1991	0/2	0/2		0.52%	0[-0.6,0.6]
Humbert 1988	24/27	22/22		6.31%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		2.68%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		3.1%	0[-0.15,0.15]
Kobashi 2006	12/108	16/113		28.76%	-0.03[-0.12,0.06]
Meng 1999	0/21	0/23		5.72%	0[-0.08,0.08]
Nakaya 2007	0/19	1/19		4.95%	-0.05[-0.19,0.08]
Poon 2004	0/41	1/43		10.93%	-0.02[-0.09,0.04]
Puglionisi 1985	0/10	2/10		2.6%	-0.2[-0.48,0.08]
Sievert 1999	3/31	3/34		8.45%	0.01[-0.13,0.15]
Simko 1983	0/7	0/3		1.09%	0[-0.36,0.36]
Tangkijvanich 2000	0/14	0/15		3.77%	0[-0.12,0.12]
Subtotal (95% CI)	**387**	**385**		**100%**	**-0.03[-0.07,0.01]**
Total events: 48 (Treatment), 54 (Control)					
Heterogeneity: Tau^2=0; Chi^2=8.75, df=14(P=0.85); I^2=0%					
Test for overall effect: Z=1.34(P=0.18)					
Test for subgroup differences: Chi^2=0.05, df=1 (P=0.98), I^2=0%					

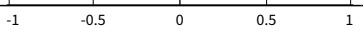
Analysis 20.2. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 2 Parenteral nutrition - all trials.

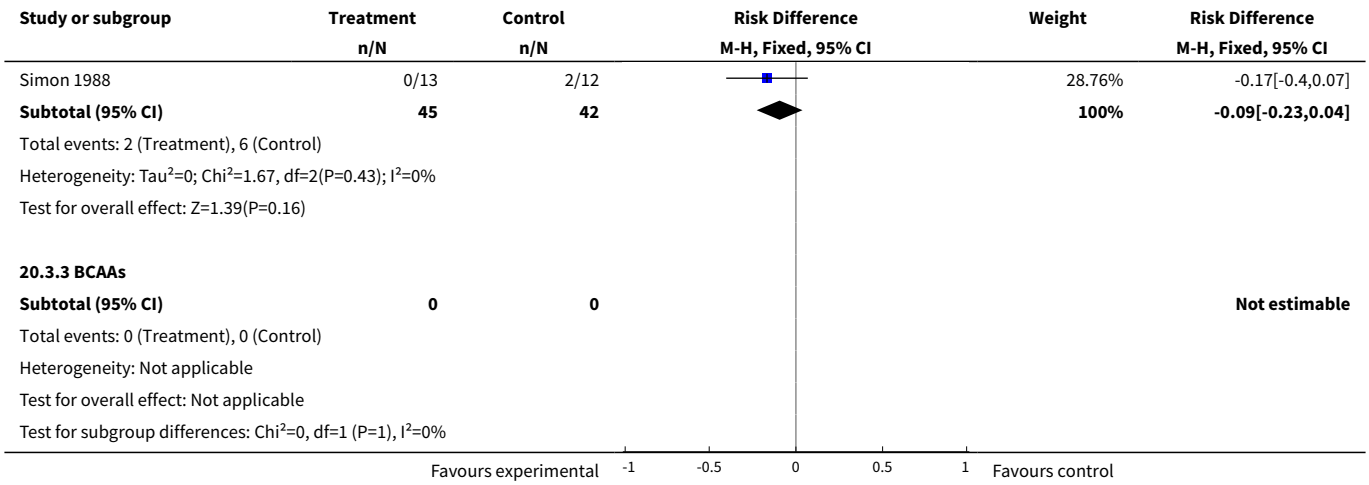
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.2.1 All trials					
Achord 1987	0/12	0/10		9.46%	0[-0.16,0.16]
Fan 1994	4/64	4/60		53.71%	-0[-0.09,0.08]
Naveau 1986	2/20	4/20		17.34%	-0.1[-0.32,0.12]
Puglionisi 1985	0/10	2/10		8.67%	-0.2[-0.48,0.08]
Simon 1988	0/13	2/12		10.82%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**119**	**112**		**100%**	**-0.05[-0.13,0.02]**
Total events: 6 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.85, df=4(P=0.43); I^2=0%					
Test for overall effect: Z=1.47(P=0.14)					
20.2.2 Standard amino acids					
Achord 1987	0/12	0/10		25.14%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		46.09%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		28.76%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**45**	**42**		**100%**	**-0.09[-0.23,0.04]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.67, df=2(P=0.43); I^2=0%					
Test for overall effect: Z=1.39(P=0.16)					
20.2.3 BCAAs					
Fan 1994	4/64	4/60		86.1%	-0[-0.09,0.08]
Puglionisi 1985	0/10	2/10		13.9%	-0.2[-0.48,0.08]
Subtotal (95% CI)	**74**	**70**		**100%**	**-0.03[-0.12,0.05]**
Total events: 4 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.81, df=1(P=0.18); I^2=44.67%					
Test for overall effect: Z=0.72(P=0.47)					
Test for subgroup differences: Chi^2=0.62, df=1 (P=0.74), I^2=0%					



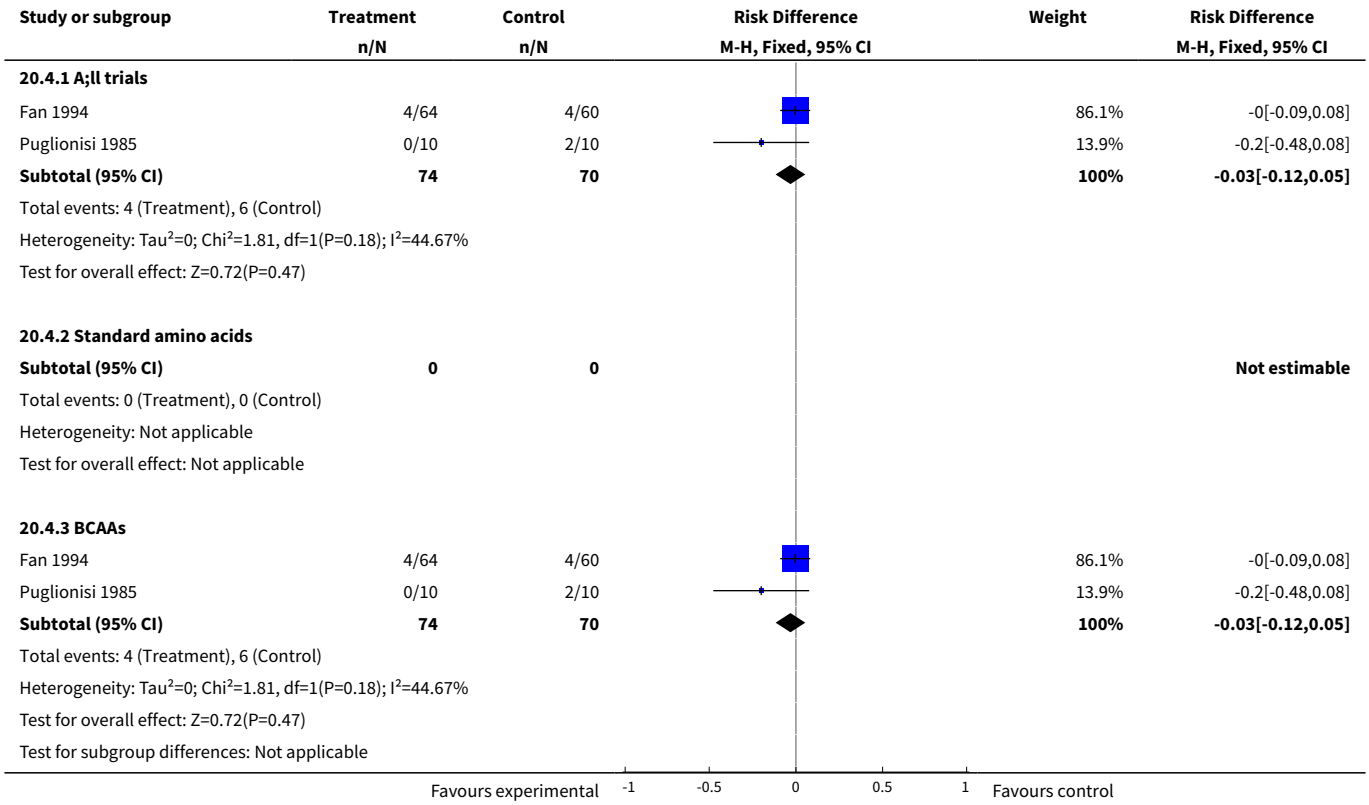
Analysis 20.3. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 3 Parenteral nutrition - medical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.3.1 All trials					
Achord 1987	0/12	0/10		25.14%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		46.09%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		28.76%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**45**	**42**		**100%**	**-0.09[-0.23,0.04]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.67, df=2(P=0.43); I^2=0%					
Test for overall effect: Z=1.39(P=0.16)					
20.3.2 Standard amino acids					
Achord 1987	0/12	0/10		25.14%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		46.09%	-0.1[-0.32,0.12]



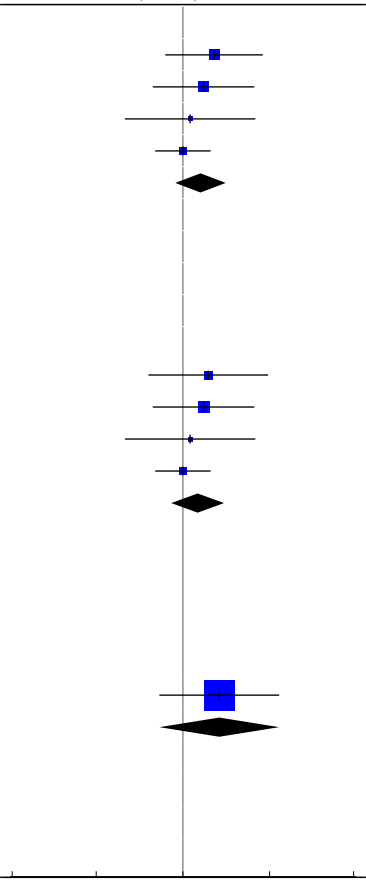


Analysis 20.4. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 4 Parenteral nutrition - surgical trials.



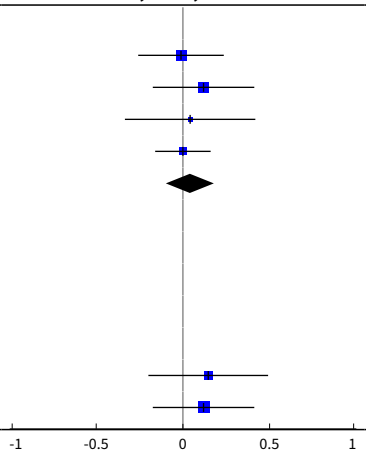
Analysis 20.5. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 5 Enteral nutrition - all studies.

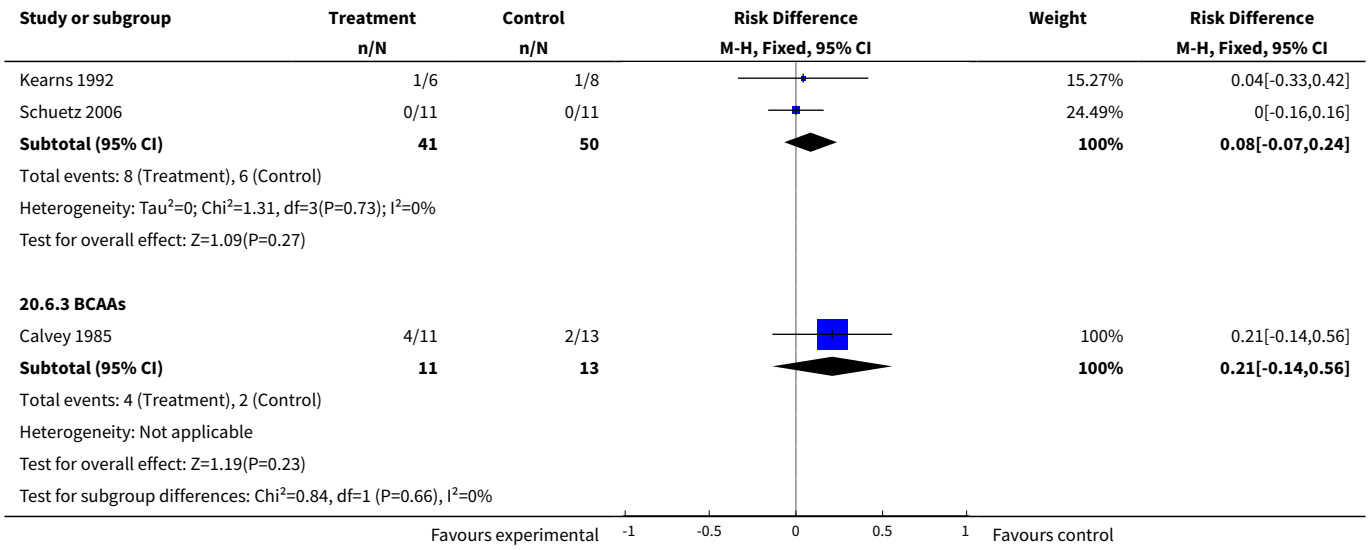
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.5.1 All trials					
Calvey 1985	7/21	2/13		32.33%	0.18[-0.1,0.46]
Guy 1995	4/14	3/18		31.71%	0.12[-0.17,0.41]
Kearns 1992	1/6	1/8		13.81%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		22.15%	0[-0.16,0.16]
Subtotal (95% CI)	**52**	**50**		**100%**	**0.1[-0.04,0.25]**
Total events: 12 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.96, df=3(P=0.58); I^2=0%					
Test for overall effect: Z=1.37(P=0.17)					
20.5.2 Standard amino acids					
Calvey 1985	3/10	2/13		25.17%	0.15[-0.2,0.49]
Guy 1995	4/14	3/18		35.07%	0.12[-0.17,0.41]
Kearns 1992	1/6	1/8		15.27%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		24.49%	0[-0.16,0.16]
Subtotal (95% CI)	**41**	**50**		**100%**	**0.08[-0.07,0.24]**
Total events: 8 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.31, df=3(P=0.73); I^2=0%					
Test for overall effect: Z=1.09(P=0.27)					
20.5.3 BCAAs					
Calvey 1985	4/11	2/13		100%	0.21[-0.14,0.56]
Subtotal (95% CI)	**11**	**13**		**100%**	**0.21[-0.14,0.56]**
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.23)					
Test for subgroup differences: Chi^2=0.42, df=1 (P=0.81), I^2=0%					



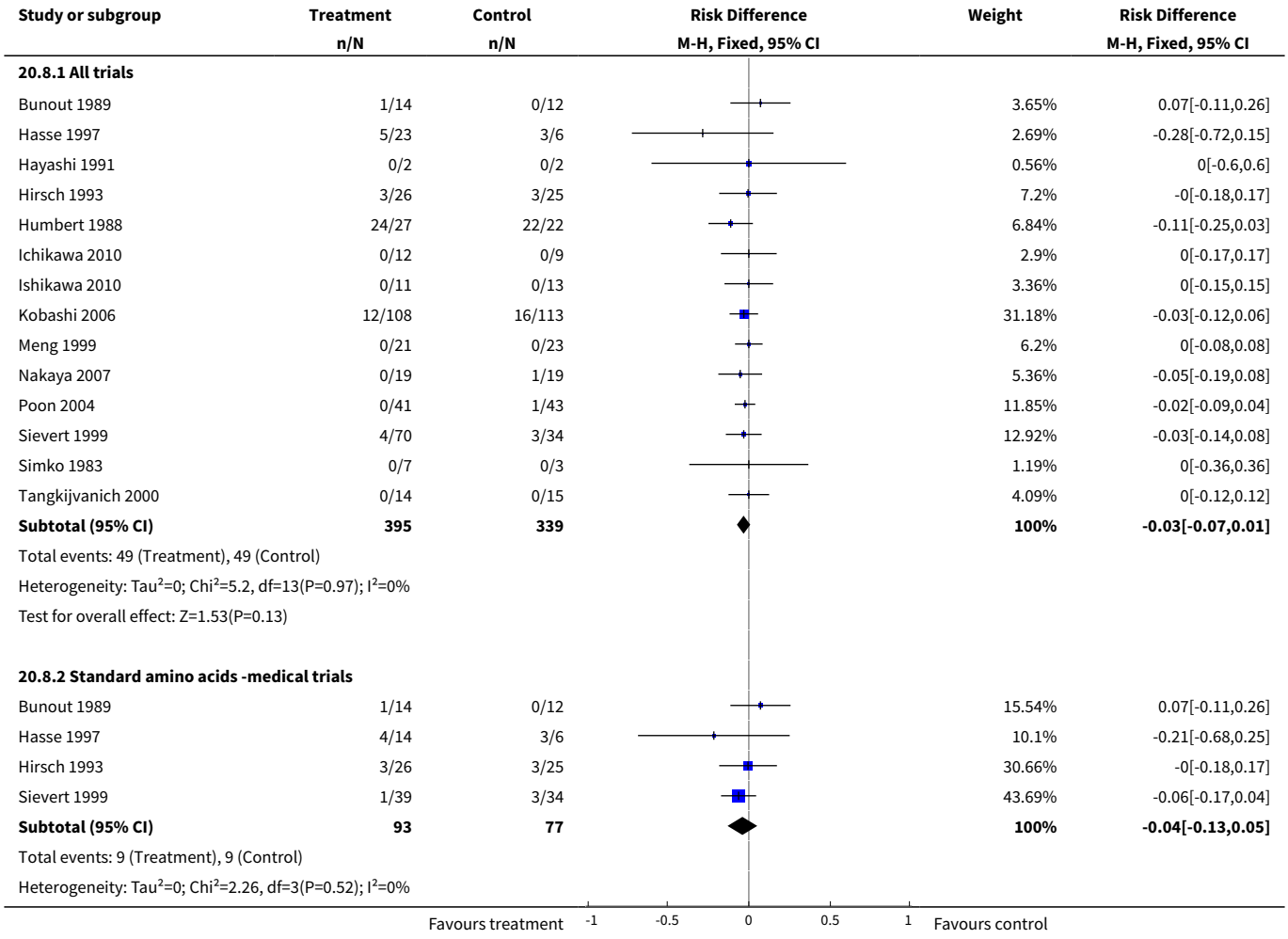
Analysis 20.6. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 6 Enteral nutrition - medical trials.

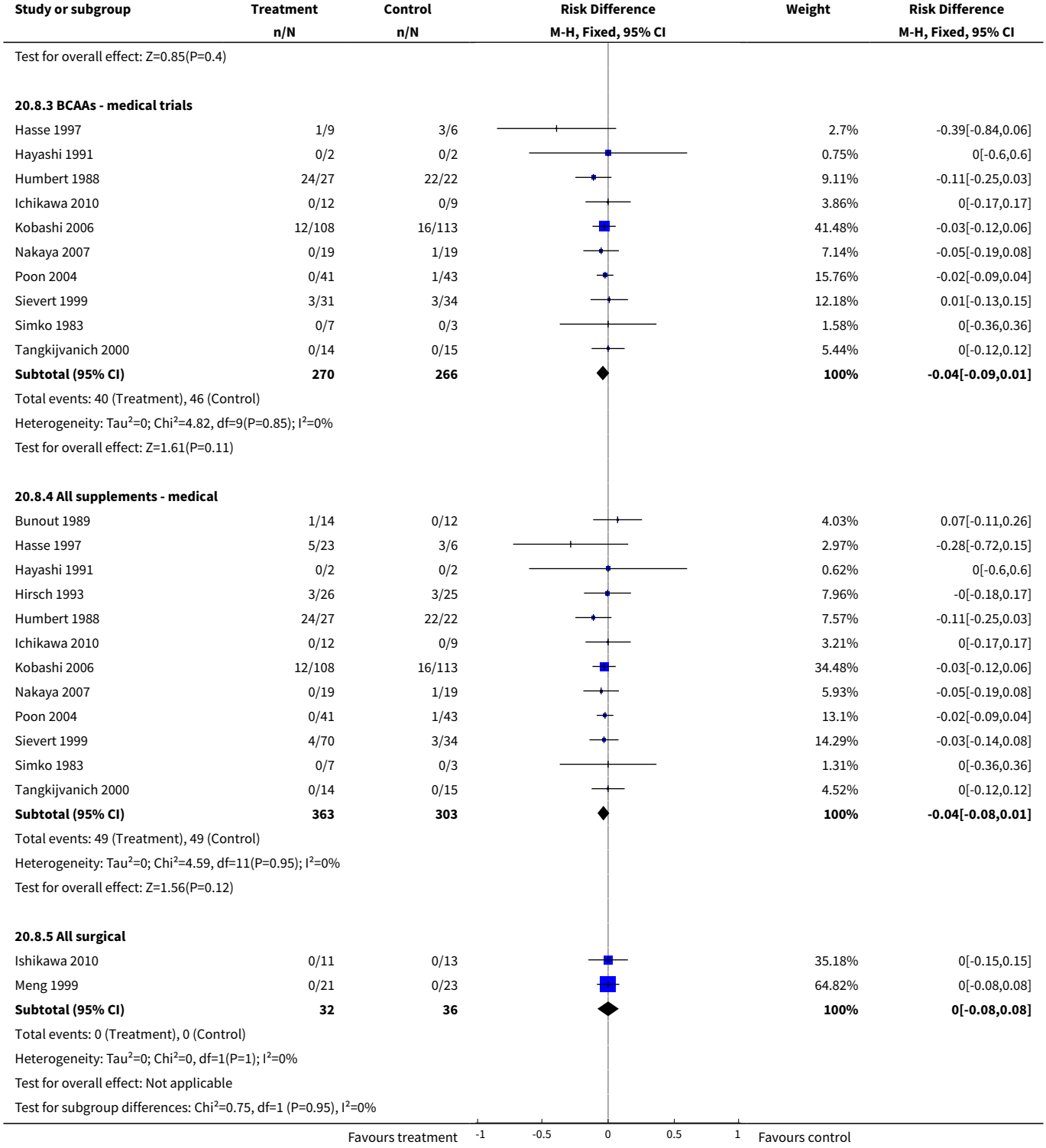
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.6.1 All studies					
Calvey 1985	3/21	2/13		32.33%	-0.01[-0.26,0.24]
Guy 1995	4/14	3/18		31.71%	0.12[-0.17,0.41]
Kearns 1992	1/6	1/8		13.81%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		22.15%	0[-0.16,0.16]
Subtotal (95% CI)	**52**	**50**		**100%**	**0.04[-0.1,0.18]**
Total events: 8 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.68, df=3(P=0.88); I^2=0%					
Test for overall effect: Z=0.57(P=0.57)					
20.6.2 Standard amino acids					
Calvey 1985	3/10	2/13		25.17%	0.15[-0.2,0.49]
Guy 1995	4/14	3/18		35.07%	0.12[-0.17,0.41]





Analysis 20.8. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 8 Supplements.





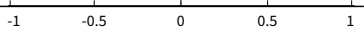
Analysis 20.9. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 9 Medical trials all trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.9.1 Parenteral nutrition					
Achord 1987	0/12	0/10		2.65%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		4.86%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		3.03%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**45**	**42**		**10.55%**	**-0.09[-0.23,0.04]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.67, df=2(P=0.43); I^2=0%					
Test for overall effect: Z=1.39(P=0.16)					
20.9.2 Enteral nutrition					
Calvey 1985	7/21	2/13		3.9%	0.18[-0.1,0.46]
Guy 1995	4/14	3/18		3.83%	0.12[-0.17,0.41]
Kearns 1992	1/6	1/8		1.67%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		2.67%	0[-0.16,0.16]
Subtotal (95% CI)	**52**	**50**		**12.08%**	**0.1[-0.04,0.25]**
Total events: 12 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.96, df=3(P=0.58); I^2=0%					
Test for overall effect: Z=1.37(P=0.17)					
20.9.3 Supplements					
Bunout 1989	1/14	0/12		3.14%	0.07[-0.11,0.26]
Hasse 1997	5/23	3/6		2.31%	-0.28[-0.72,0.15]
Hayashi 1991	0/2	0/2		0.49%	0[-0.6,0.6]
Hirsch 1993	3/26	3/25		6.2%	-0[-0.18,0.17]
Humbert 1988	24/27	22/22		5.89%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		2.5%	0[-0.17,0.17]
Kobashi 2006	12/108	16/113		26.85%	-0.03[-0.12,0.06]
Nakaya 2007	0/19	1/19		4.62%	-0.05[-0.19,0.08]
Poon 2004	0/41	1/43		10.21%	-0.02[-0.09,0.04]
Sievert 1999	4/61	3/34		10.62%	-0.02[-0.14,0.09]
Simko 1983	0/7	0/3		1.02%	0[-0.36,0.36]
Tangkijvanich 2000	0/14	0/15		3.52%	0[-0.12,0.12]
Subtotal (95% CI)	**354**	**303**		**77.37%**	**-0.03[-0.08,0.01]**
Total events: 49 (Treatment), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.58, df=11(P=0.95); I^2=0%					
Test for overall effect: Z=1.5(P=0.13)					
Total (95% CI)	**451**	**395**		**100%**	**-0.02[-0.07,0.02]**
Total events: 63 (Treatment), 61 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.54, df=18(P=0.95); I^2=0%					
Test for overall effect: Z=1.15(P=0.25)					
Test for subgroup differences: Chi^2=4.09, df=1 (P=0.13), I^2=51.07%					

Favours treatment — Favours control

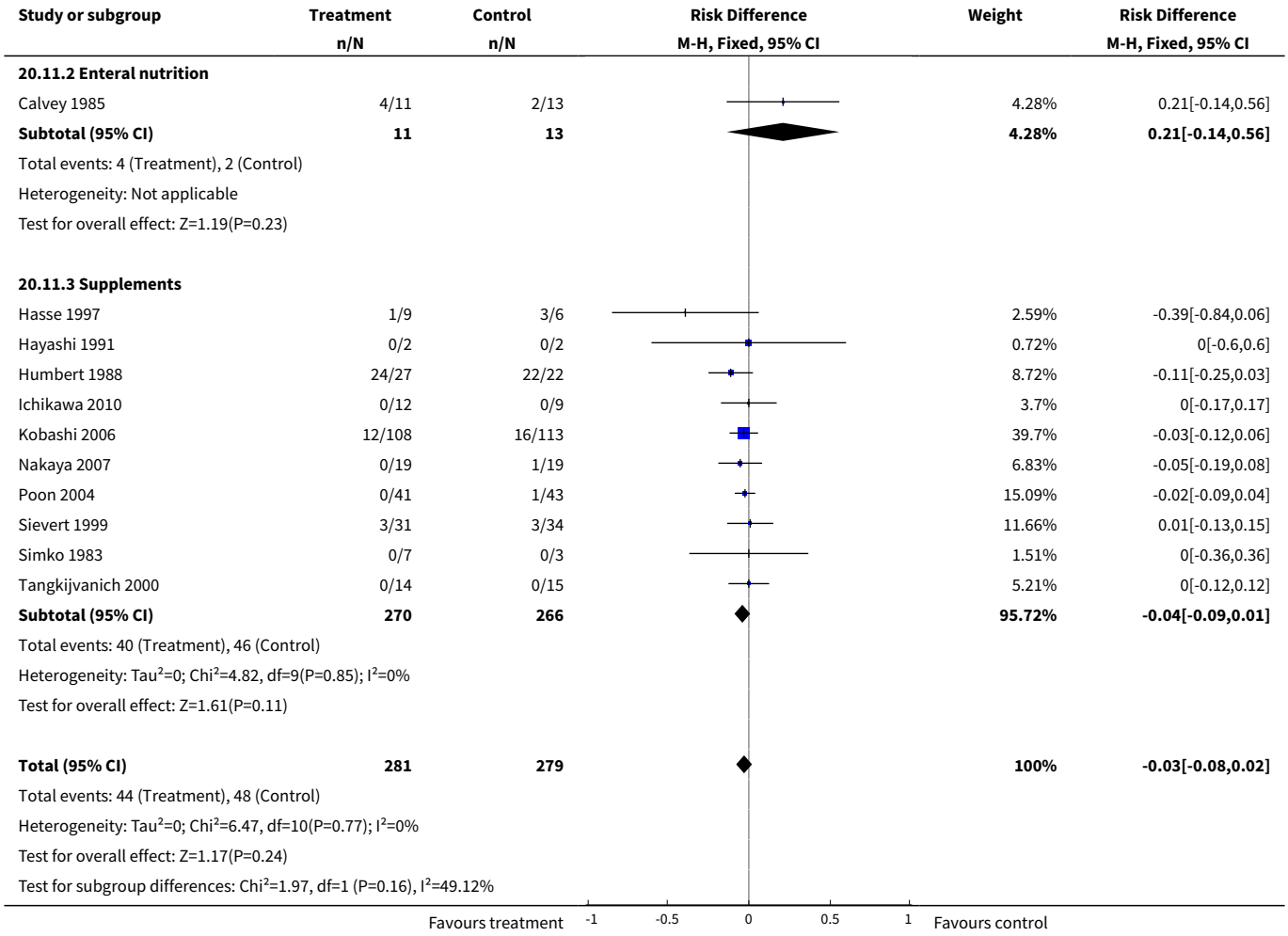
Analysis 20.10. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 10 Medical trials - standard amino acids.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.10.1 Parenteral nutrition					
Achord 1987	0/12	0/10		6.53%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		11.98%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		7.47%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**45**	**42**		**25.98%**	**-0.09[-0.23,0.04]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.67, df=2(P=0.43); I^2=0%					
Test for overall effect: Z=1.39(P=0.16)					
20.10.2 Enteral nutrition					
Calvey 1985	3/10	2/13		6.77%	0.15[-0.2,0.49]
Guy 1995	4/14	3/18		9.43%	0.12[-0.17,0.41]
Kearns 1992	1/6	1/8		4.11%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		6.59%	0[-0.16,0.16]
Subtotal (95% CI)	**41**	**50**		**26.89%**	**0.08[-0.07,0.24]**
Total events: 8 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.31, df=3(P=0.73); I^2=0%					
Test for overall effect: Z=1.09(P=0.27)					
20.10.3 Supplements					
Bunout 1989	1/14	0/12		7.74%	0.07[-0.11,0.26]
Hasse 1997	4/14	3/6		5.03%	-0.21[-0.68,0.25]
Hirsch 1993	3/26	3/25		15.26%	-0[-0.18,0.17]
Sievert 1999	1/30	3/34		19.09%	-0.05[-0.17,0.06]
Subtotal (95% CI)	**84**	**77**		**47.12%**	**-0.03[-0.13,0.06]**
Total events: 9 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.08, df=3(P=0.56); I^2=0%					
Test for overall effect: Z=0.72(P=0.47)					
Total (95% CI)	**170**	**169**		**100%**	**-0.02[-0.09,0.05]**
Total events: 19 (Treatment), 21 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.98, df=10(P=0.82); I^2=0%					
Test for overall effect: Z=0.51(P=0.61)					
Test for subgroup differences: Chi^2=3.08, df=1 (P=0.21), I^2=35.17%					

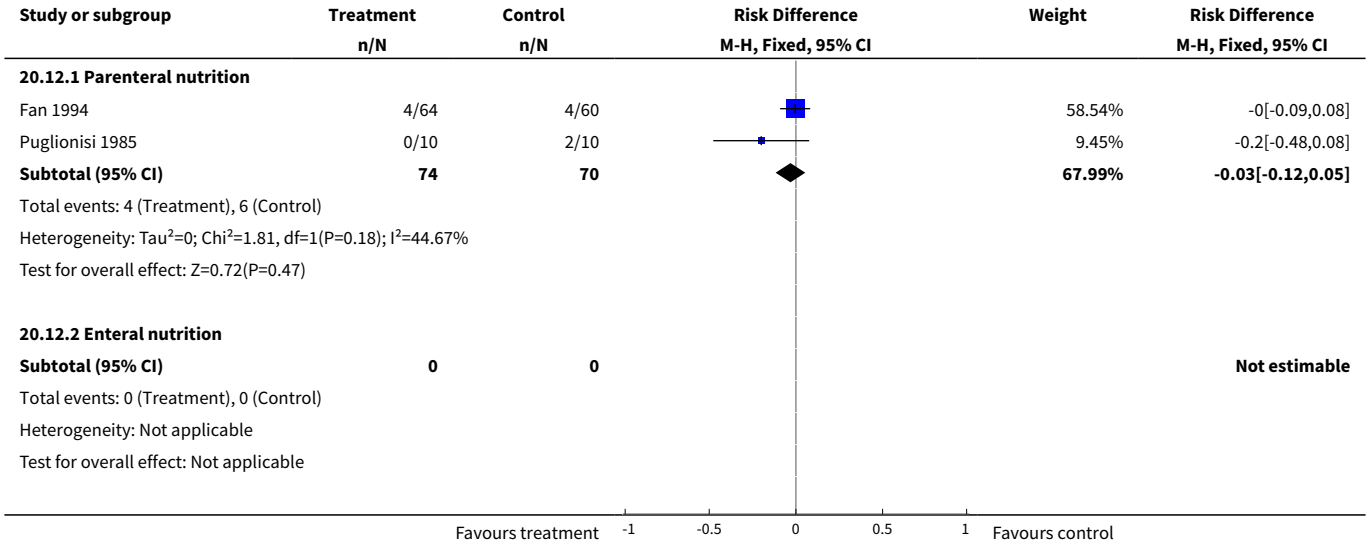


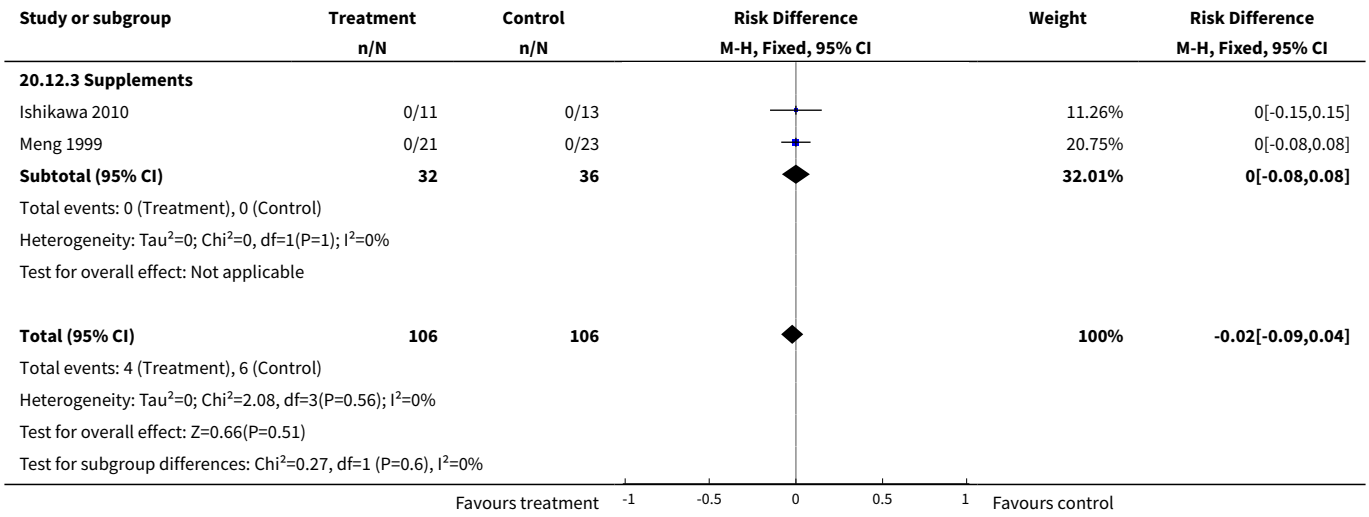
Analysis 20.11. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 11 Medical trials - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.11.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

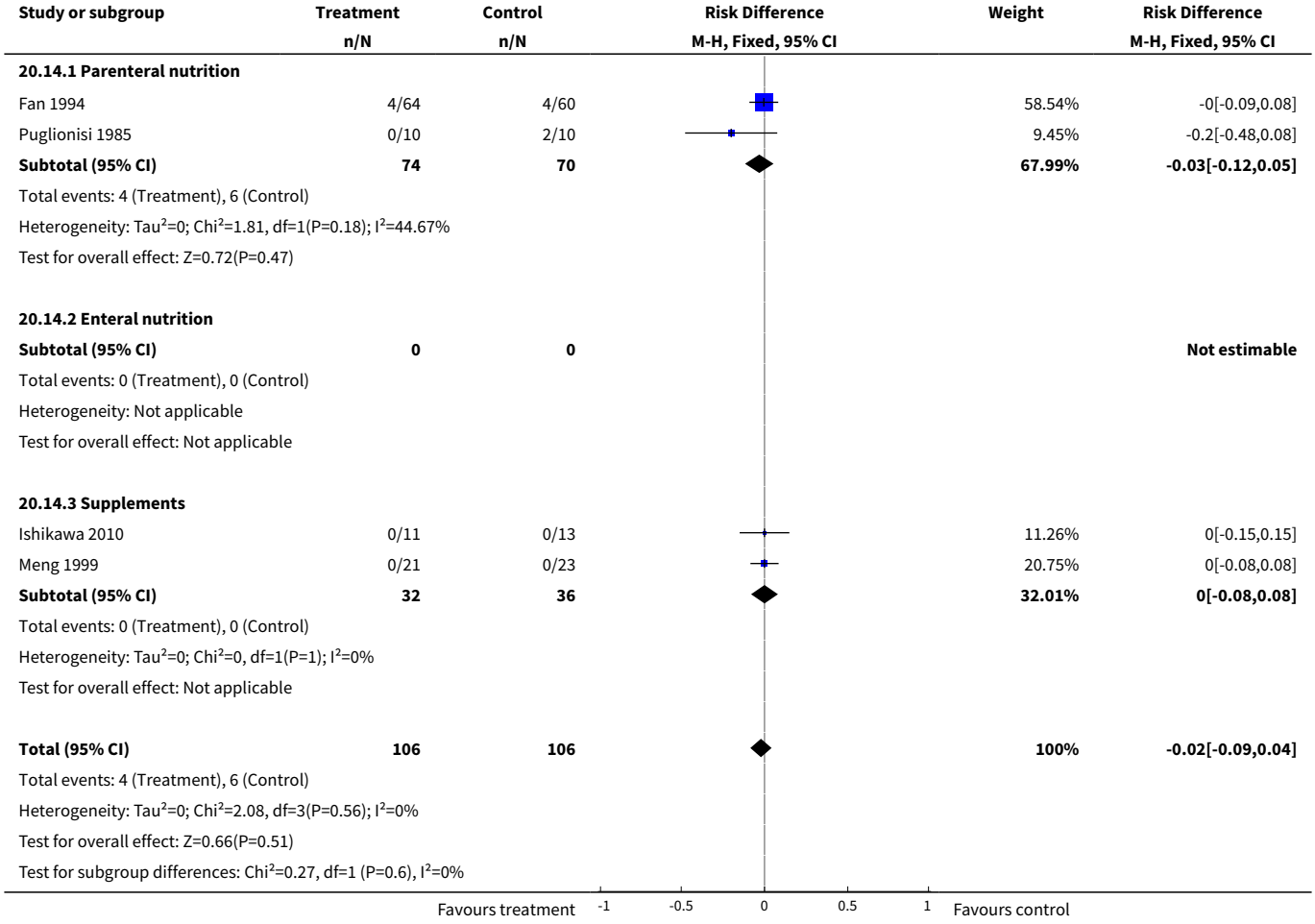


Analysis 20.12. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 12 Surgical trials - all studies.



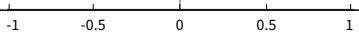


Analysis 20.14. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 14 Surgical trials - BCAAs.



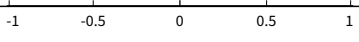
Analysis 20.15. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 15 Alcoholic hepatitis - all studies.

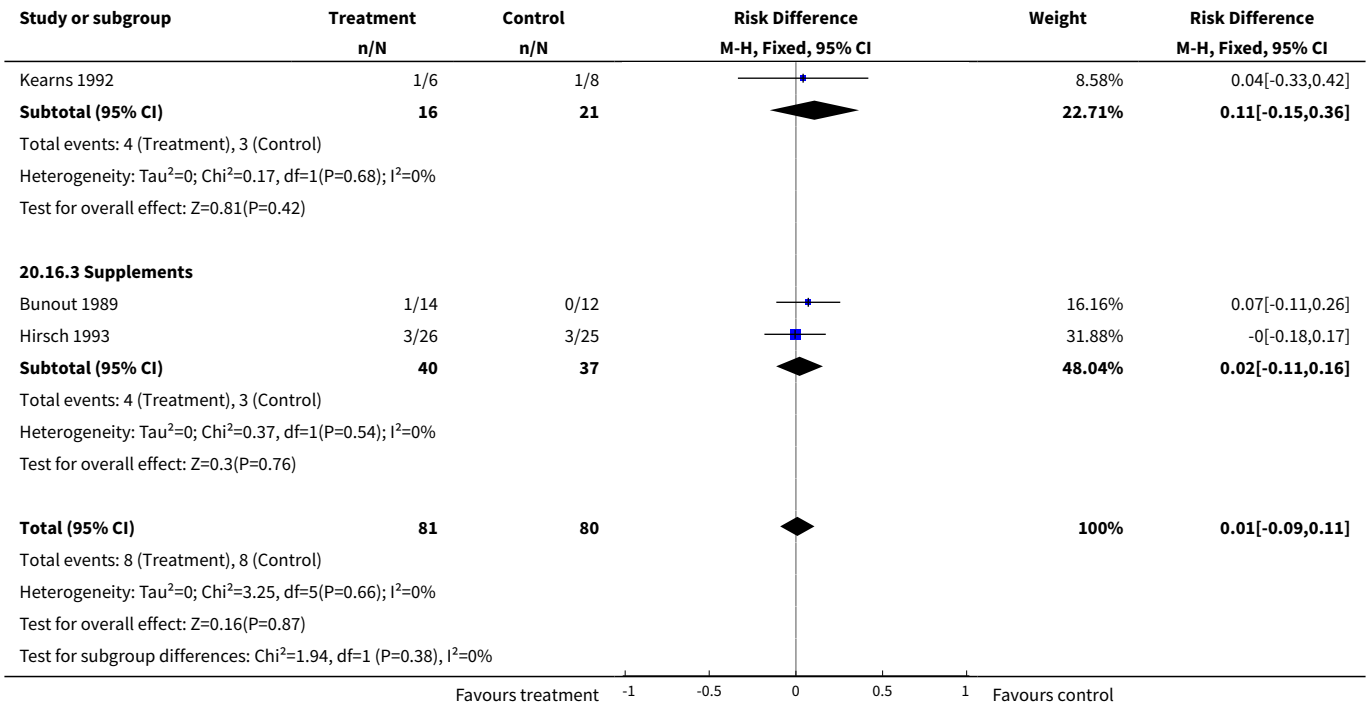
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.15.1 Parenteral nutrition					
Achord 1987	0/12	0/10		12.88%	0[-0.16,0.16]
Simon 1988	0/13	2/12		14.73%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**25**	**22**		**27.61%**	**-0.09[-0.25,0.07]**
Total events: 0 (Treatment), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.58, df=1(P=0.21); I^2=36.88%					
Test for overall effect: Z=1.1(P=0.27)					
20.15.2 Enteral nutrition					
Calvey 1985	7/21	2/13		18.96%	0.18[-0.1,0.46]
Kearns 1992	1/6	1/8		8.09%	0.04[-0.33,0.42]
Subtotal (95% CI)	**27**	**21**		**27.05%**	**0.14[-0.09,0.37]**
Total events: 8 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.34, df=1(P=0.56); I^2=0%					
Test for overall effect: Z=1.19(P=0.23)					
20.15.3 Supplements					
Bunout 1989	1/14	0/12		15.25%	0.07[-0.11,0.26]
Hirsch 1993	3/26	3/25		30.09%	-0[-0.18,0.17]
Subtotal (95% CI)	**40**	**37**		**45.34%**	**0.02[-0.11,0.16]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.37, df=1(P=0.54); I^2=0%					
Test for overall effect: Z=0.3(P=0.76)					
Total (95% CI)	**92**	**80**		**100%**	**0.02[-0.07,0.12]**
Total events: 12 (Treatment), 8 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.12, df=5(P=0.53); I^2=0%					
Test for overall effect: Z=0.45(P=0.65)					
Test for subgroup differences: Chi^2=2.72, df=1 (P=0.26), I^2=26.53%					



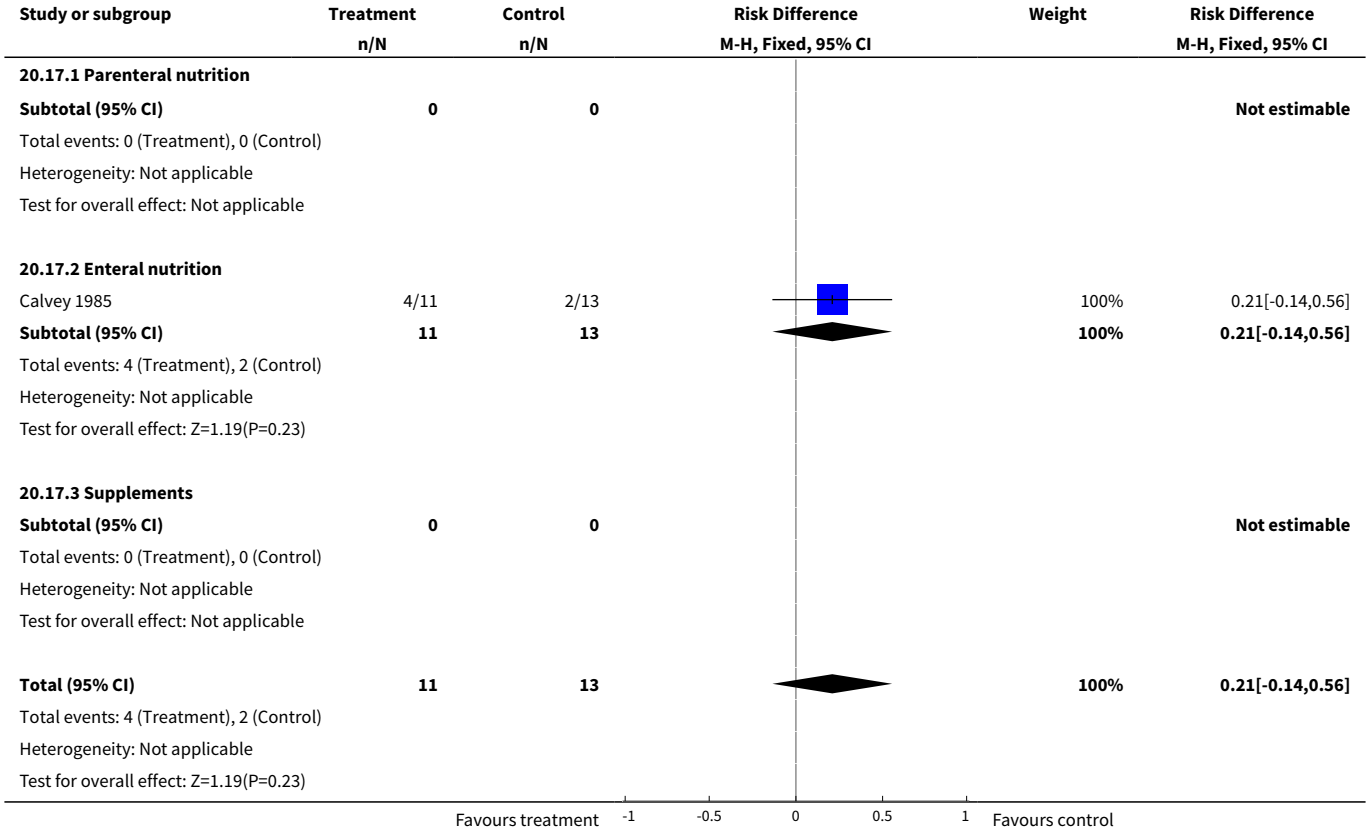
Analysis 20.16. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 16 Alcoholic hepatitis - standard amino acids.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.16.1 Parenteral nutrition					
Achord 1987	0/12	0/10		13.64%	0[-0.16,0.16]
Simon 1988	0/13	2/12		15.61%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**25**	**22**		**29.25%**	**-0.09[-0.25,0.07]**
Total events: 0 (Treatment), 2 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.58, df=1(P=0.21); I^2=36.88%					
Test for overall effect: Z=1.1(P=0.27)					
20.16.2 Enteral nutrition					
Calvey 1985	3/10	2/13		14.14%	0.15[-0.2,0.49]





Analysis 20.17. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 17 Alcoholic hepatitis - BCAA.



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Test for subgroup differences: Not applicable					

Favours treatment -1 -0.5 0 0.5 1 Favours control

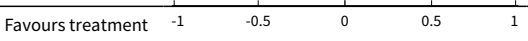
Analysis 20.18. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 18 Cirrhosis - all studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.18.1 Parenteral nutrition					
Naveau 1986	2/20	4/20		10.02%	-0.1[-0.32,0.12]
Subtotal (95% CI)	**20**	**20**		**10.02%**	**-0.1[-0.32,0.12]**
Total events: 2 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.89(P=0.37)					
20.18.2 Enteral nutrition					
Guy 1995	4/14	3/18		7.89%	0.12[-0.17,0.41]
Schuetz 2006	0/11	0/11		5.51%	0[-0.16,0.16]
Subtotal (95% CI)	**25**	**29**		**13.4%**	**0.07[-0.12,0.26]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.85, df=1(P=0.36); I^2=0%					
Test for overall effect: Z=0.74(P=0.46)					
20.18.3 Supplements					
Hasse 1997	5/23	3/6		4.77%	-0.28[-0.72,0.15]
Hayashi 1991	0/2	0/2		1%	0[-0.6,0.6]
Hirsch 1993	3/26	3/25		12.77%	-0[-0.18,0.17]
Humbert 1988	24/27	22/22		12.14%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		5.15%	0[-0.17,0.17]
Nakaya 2007	0/19	1/19		9.52%	-0.05[-0.19,0.08]
Sievert 1999	4/61	3/34		21.87%	-0.02[-0.14,0.09]
Simko 1983	0/7	0/3		2.1%	0[-0.36,0.36]
Tangkijvanich 2000	0/14	0/15		7.25%	0[-0.12,0.12]
Subtotal (95% CI)	**191**	**135**		**76.58%**	**-0.05[-0.11,0.01]**
Total events: 36 (Treatment), 32 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.37, df=8(P=0.91); I^2=0%					
Test for overall effect: Z=1.5(P=0.13)					
Total (95% CI)	**236**	**184**		**100%**	**-0.04[-0.1,0.02]**
Total events: 42 (Treatment), 39 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.82, df=11(P=0.94); I^2=0%					
Test for overall effect: Z=1.26(P=0.21)					
Test for subgroup differences: Chi^2=1.7, df=1 (P=0.43), I^2=0%					

Favours treatment -1 -0.5 0 0.5 1 Favours control

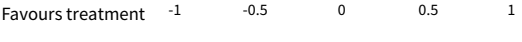
Analysis 20.19. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 19 Cirrhosis - standard amino acids.

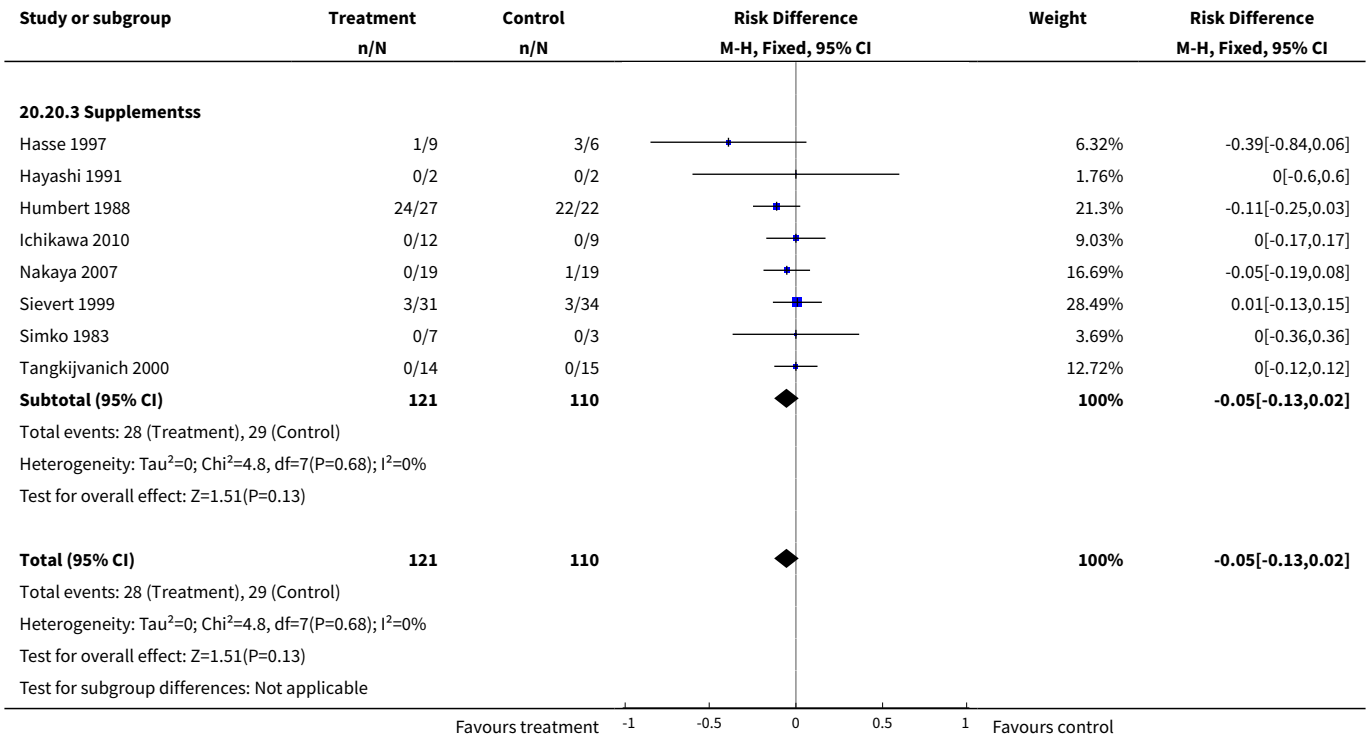
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.19.1 Parenteral nutrition					
Naveau 1986	2/20	4/20		17.78%	-0.1[-0.32,0.12]
Subtotal (95% CI)	**20**	**20**		**17.78%**	**-0.1[-0.32,0.12]**
Total events: 2 (Treatment), 4 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.89(P=0.37)					
20.19.2 Enteral nutrition					
Guy 1995	4/14	3/18		14%	0.12[-0.17,0.41]
Schuetz 2006	0/11	0/11		9.78%	0[-0.16,0.16]
Subtotal (95% CI)	**25**	**29**		**23.77%**	**0.07[-0.12,0.26]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.85, df=1(P=0.36); I^2=0%					
Test for overall effect: Z=0.74(P=0.46)					
20.19.3 Supplements					
Hasse 1997	9/14	3/6		7.47%	0.14[-0.33,0.62]
Hirsch 1993	3/26	3/25		22.65%	-0[-0.18,0.17]
Sievert 1999	1/30	3/34		28.33%	-0.05[-0.17,0.06]
Subtotal (95% CI)	**70**	**65**		**58.45%**	**-0.01[-0.12,0.1]**
Total events: 13 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.99, df=2(P=0.61); I^2=0%					
Test for overall effect: Z=0.19(P=0.85)					
Total (95% CI)	**115**	**114**		**100%**	**-0.01[-0.09,0.08]**
Total events: 19 (Treatment), 16 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.47, df=5(P=0.78); I^2=0%					
Test for overall effect: Z=0.16(P=0.87)					
Test for subgroup differences: Chi^2=1.35, df=1 (P=0.51), I^2=0%					



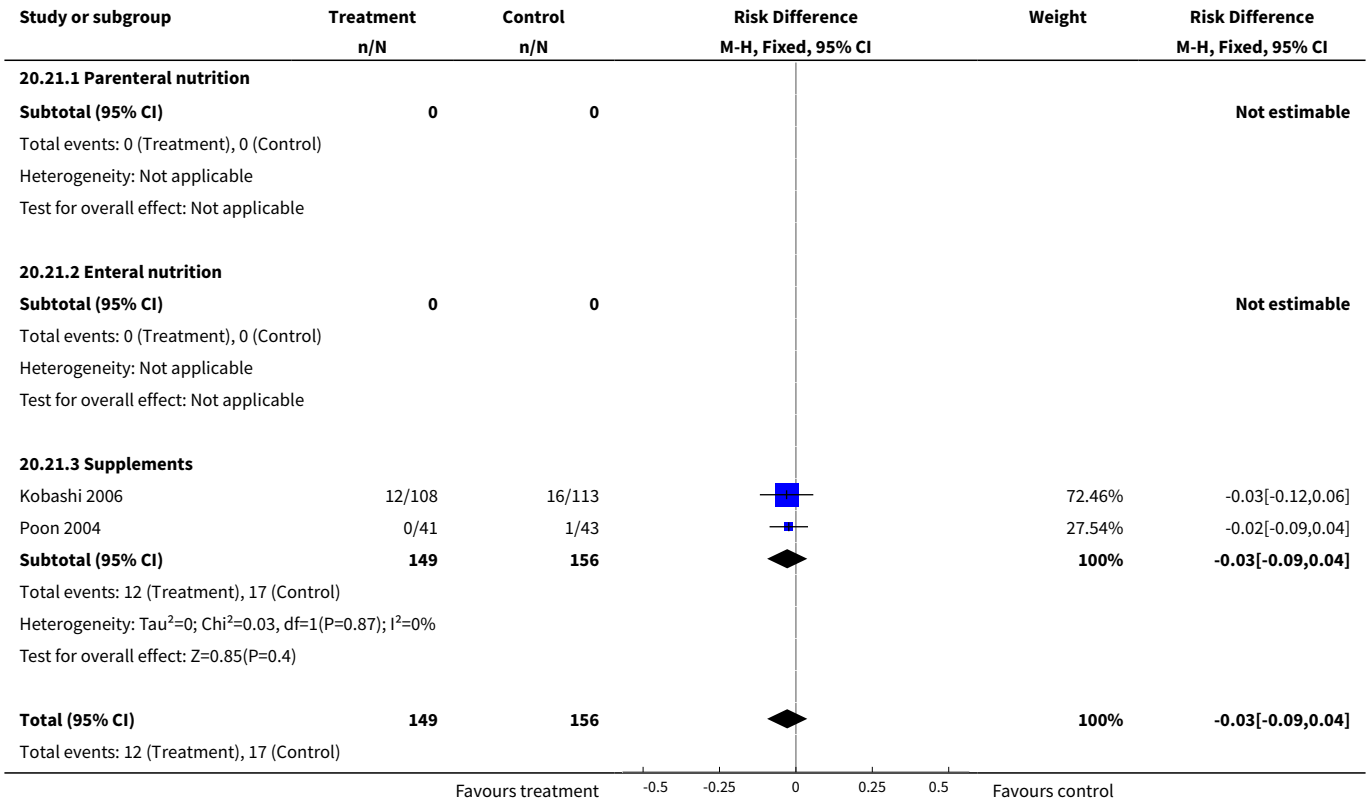
Analysis 20.20. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 20 Cirrhosis - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.20.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
20.20.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

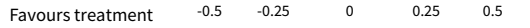




Analysis 20.21. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 21 HCC - all studies.

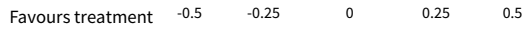


Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Heterogeneity: Tau²=0; Chi²=0.03, df=1(P=0.87); I²=0%					
Test for overall effect: Z=0.85(P=0.4)					
Test for subgroup differences: Not applicable					



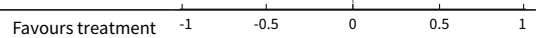
Analysis 20.23. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 23 HCC - BCAAs.

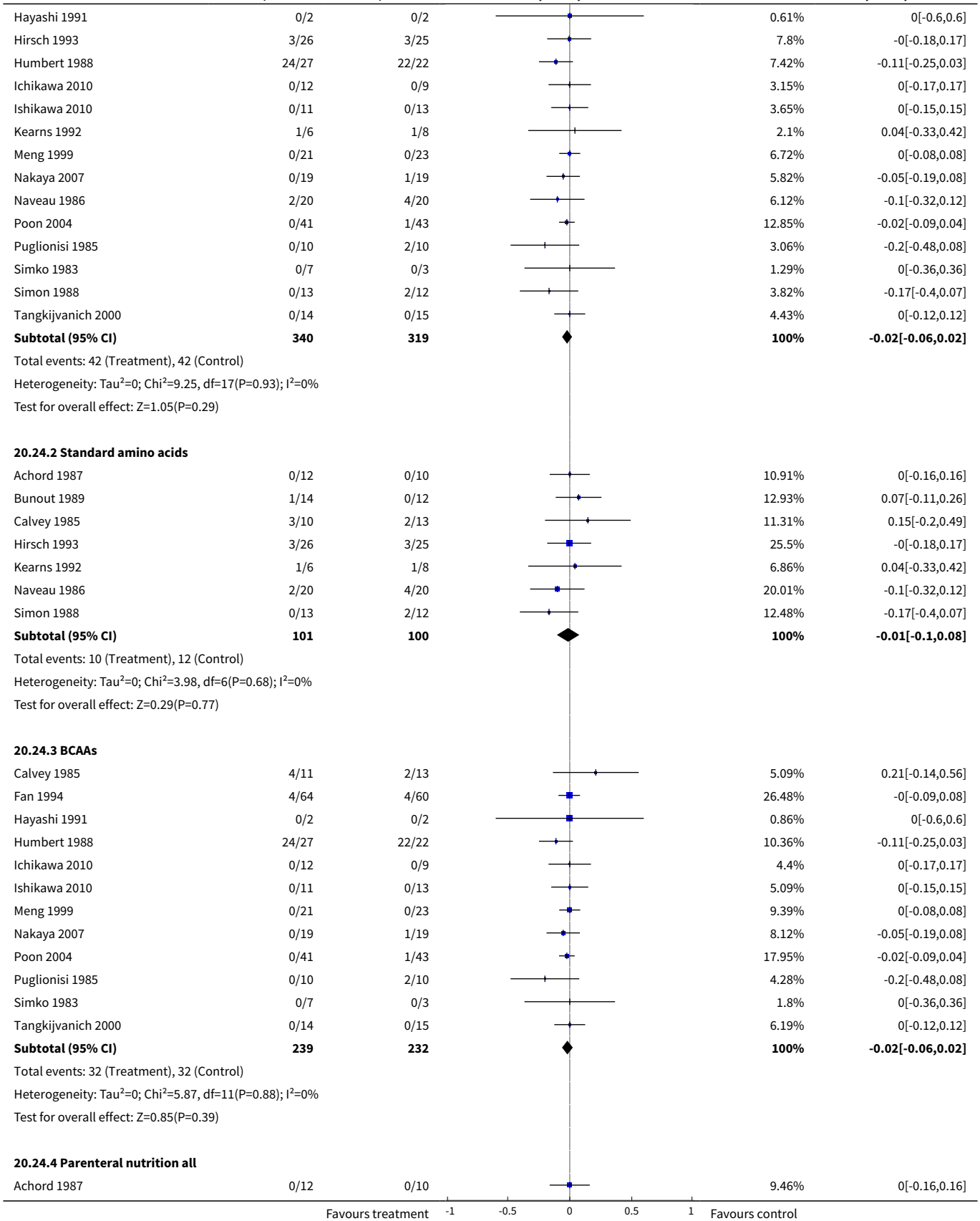
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.23.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
20.23.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
20.23.3 Supplements					
Kobashi 2006	12/108	16/113		72.46%	-0.03[-0.12,0.06]
Poon 2004	0/41	1/43		27.54%	-0.02[-0.09,0.04]
Subtotal (95% CI)	**149**	**156**		**100%**	**-0.03[-0.09,0.04]**
Total events: 12 (Treatment), 17 (Control)					
Heterogeneity: Tau²=0; Chi²=0.03, df=1(P=0.87); I²=0%					
Test for overall effect: Z=0.85(P=0.4)					
Total (95% CI)	**149**	**156**		**100%**	**-0.03[-0.09,0.04]**
Total events: 12 (Treatment), 17 (Control)					
Heterogeneity: Tau²=0; Chi²=0.03, df=1(P=0.87); I²=0%					
Test for overall effect: Z=0.85(P=0.4)					
Test for subgroup differences: Not applicable					



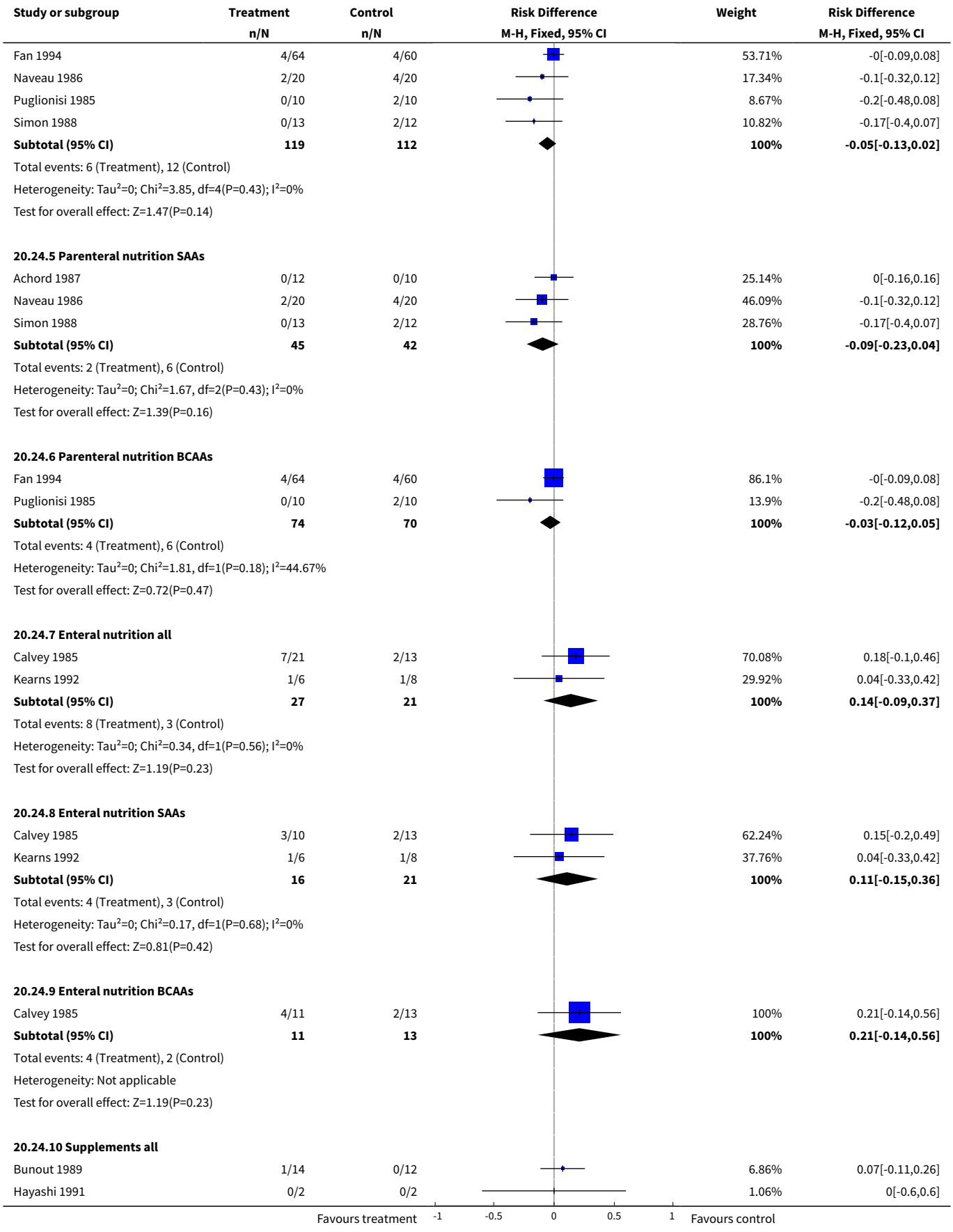
Analysis 20.24. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 24 Abstracts excluded.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.24.1 All trials					
Achord 1987	0/12	0/10		3.34%	0[-0.16,0.16]
Bunout 1989	1/14	0/12		3.96%	0.07[-0.11,0.26]
Calvey 1985	7/21	2/13		4.92%	0.18[-0.1,0.46]
Fan 1994	4/64	4/60		18.96%	-0[-0.09,0.08]



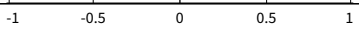


Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Hayashi 1991	0/2	0/2		0.61%	0[-0.6,0.6]
Hirsch 1993	3/26	3/25		7.8%	-0[-0.18,0.17]
Humbert 1988	24/27	22/22		7.42%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		3.15%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		3.65%	0[-0.15,0.15]
Kearns 1992	1/6	1/8		2.1%	0.04[-0.33,0.42]
Meng 1999	0/21	0/23		6.72%	0[-0.08,0.08]
Nakaya 2007	0/19	1/19		5.82%	-0.05[-0.19,0.08]
Naveau 1986	2/20	4/20		6.12%	-0.1[-0.32,0.12]
Poon 2004	0/41	1/43		12.85%	-0.02[-0.09,0.04]
Puglionisi 1985	0/10	2/10		3.06%	-0.2[-0.48,0.08]
Simko 1983	0/7	0/3		1.29%	0[-0.36,0.36]
Simon 1988	0/13	2/12		3.82%	-0.17[-0.4,0.07]
Tangkijvanich 2000	0/14	0/15		4.43%	0[-0.12,0.12]
Subtotal (95% CI)	**340**	**319**		**100%**	**-0.02[-0.06,0.02]**
Total events: 42 (Treatment), 42 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.25, df=17(P=0.93); I^2=0%					
Test for overall effect: Z=1.05(P=0.29)					
20.24.2 Standard amino acids					
Achord 1987	0/12	0/10		10.91%	0[-0.16,0.16]
Bunout 1989	1/14	0/12		12.93%	0.07[-0.11,0.26]
Calvey 1985	3/10	2/13		11.31%	0.15[-0.2,0.49]
Hirsch 1993	3/26	3/25		25.5%	-0[-0.18,0.17]
Kearns 1992	1/6	1/8		6.86%	0.04[-0.33,0.42]
Naveau 1986	2/20	4/20		20.01%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		12.48%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**101**	**100**		**100%**	**-0.01[-0.1,0.08]**
Total events: 10 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.98, df=6(P=0.68); I^2=0%					
Test for overall effect: Z=0.29(P=0.77)					
20.24.3 BCAAs					
Calvey 1985	4/11	2/13		5.09%	0.21[-0.14,0.56]
Fan 1994	4/64	4/60		26.48%	-0[-0.09,0.08]
Hayashi 1991	0/2	0/2		0.86%	0[-0.6,0.6]
Humbert 1988	24/27	22/22		10.36%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		4.4%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		5.09%	0[-0.15,0.15]
Meng 1999	0/21	0/23		9.39%	0[-0.08,0.08]
Nakaya 2007	0/19	1/19		8.12%	-0.05[-0.19,0.08]
Poon 2004	0/41	1/43		17.95%	-0.02[-0.09,0.04]
Puglionisi 1985	0/10	2/10		4.28%	-0.2[-0.48,0.08]
Simko 1983	0/7	0/3		1.8%	0[-0.36,0.36]
Tangkijvanich 2000	0/14	0/15		6.19%	0[-0.12,0.12]
Subtotal (95% CI)	**239**	**232**		**100%**	**-0.02[-0.06,0.02]**
Total events: 32 (Treatment), 32 (Control)					
Heterogeneity: Tau^2=0; Chi^2=5.87, df=11(P=0.88); I^2=0%					
Test for overall effect: Z=0.85(P=0.39)					
20.24.4 Parenteral nutrition all					
Achord 1987	0/12	0/10		9.46%	0[-0.16,0.16]



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Fan 1994	4/64	4/60		53.71%	-0[-0.09,0.08]
Naveau 1986	2/20	4/20		17.34%	-0.1[-0.32,0.12]
Puglionisi 1985	0/10	2/10		8.67%	-0.2[-0.48,0.08]
Simon 1988	0/13	2/12		10.82%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**119**	**112**		**100%**	**-0.05[-0.13,0.02]**
Total events: 6 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.85, df=4(P=0.43); I^2=0%					
Test for overall effect: Z=1.47(P=0.14)					
20.24.5 Parenteral nutrition SAAs					
Achord 1987	0/12	0/10		25.14%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		46.09%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		28.76%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**45**	**42**		**100%**	**-0.09[-0.23,0.04]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.67, df=2(P=0.43); I^2=0%					
Test for overall effect: Z=1.39(P=0.16)					
20.24.6 Parenteral nutrition BCAAs					
Fan 1994	4/64	4/60		86.1%	-0[-0.09,0.08]
Puglionisi 1985	0/10	2/10		13.9%	-0.2[-0.48,0.08]
Subtotal (95% CI)	**74**	**70**		**100%**	**-0.03[-0.12,0.05]**
Total events: 4 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.81, df=1(P=0.18); I^2=44.67%					
Test for overall effect: Z=0.72(P=0.47)					
20.24.7 Enteral nutrition all					
Calvey 1985	7/21	2/13		70.08%	0.18[-0.1,0.46]
Kearns 1992	1/6	1/8		29.92%	0.04[-0.33,0.42]
Subtotal (95% CI)	**27**	**21**		**100%**	**0.14[-0.09,0.37]**
Total events: 8 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.34, df=1(P=0.56); I^2=0%					
Test for overall effect: Z=1.19(P=0.23)					
20.24.8 Enteral nutrition SAAs					
Calvey 1985	3/10	2/13		62.24%	0.15[-0.2,0.49]
Kearns 1992	1/6	1/8		37.76%	0.04[-0.33,0.42]
Subtotal (95% CI)	**16**	**21**		**100%**	**0.11[-0.15,0.36]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.17, df=1(P=0.68); I^2=0%					
Test for overall effect: Z=0.81(P=0.42)					
20.24.9 Enteral nutrition BCAAs					
Calvey 1985	4/11	2/13		100%	0.21[-0.14,0.56]
Subtotal (95% CI)	**11**	**13**		**100%**	**0.21[-0.14,0.56]**
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.23)					
20.24.10 Supplements all					
Bunout 1989	1/14	0/12		6.86%	0.07[-0.11,0.26]
Hayashi 1991	0/2	0/2		1.06%	0[-0.6,0.6]

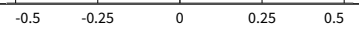
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Hirsch 1993	3/26	3/25		13.52%	-0[-0.18,0.17]
Humbert 1988	24/27	22/22		12.86%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		5.46%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		6.32%	0[-0.15,0.15]
Meng 1999	0/21	0/23		11.65%	0[-0.08,0.08]
Nakaya 2007	0/19	1/19		10.08%	-0.05[-0.19,0.08]
Poon 2004	0/41	1/43		22.27%	-0.02[-0.09,0.04]
Simko 1983	0/7	0/3		2.23%	0[-0.36,0.36]
Tangkijvanich 2000	0/14	0/15		7.68%	0[-0.12,0.12]
Subtotal (95% CI)	**194**	**186**		**100%**	**-0.02[-0.07,0.03]**
Total events: 28 (Treatment), 27 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.39, df=10(P=0.97); I^2=0%					
Test for overall effect: Z=0.87(P=0.38)					
20.24.11 Supplements - SAAs					
Bunout 1989	1/14	0/12		33.64%	0.07[-0.11,0.26]
Hirsch 1993	3/26	3/25		66.36%	-0[-0.18,0.17]
Subtotal (95% CI)	**40**	**37**		**100%**	**0.02[-0.11,0.16]**
Total events: 4 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.37, df=1(P=0.54); I^2=0%					
Test for overall effect: Z=0.3(P=0.76)					
20.24.12 Supplements - BCAAs					
Hayashi 1991	0/2	0/2		1.33%	0[-0.6,0.6]
Humbert 1988	24/27	22/22		16.16%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		6.85%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		7.94%	0[-0.15,0.15]
Meng 1999	0/21	0/23		14.63%	0[-0.08,0.08]
Nakaya 2007	0/19	1/19		12.66%	-0.05[-0.19,0.08]
Poon 2004	0/41	1/43		27.97%	-0.02[-0.09,0.04]
Simko 1983	0/7	0/3		2.8%	0[-0.36,0.36]
Tangkijvanich 2000	0/14	0/15		9.65%	0[-0.12,0.12]
Subtotal (95% CI)	**154**	**149**		**100%**	**-0.03[-0.08,0.02]**
Total events: 24 (Treatment), 24 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.58, df=8(P=0.96); I^2=0%					
Test for overall effect: Z=1.32(P=0.19)					
Test for subgroup differences: Chi^2=7.16, df=1 (P=0.79), I^2=0%					



Favours treatment Favours control

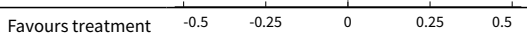
Analysis 20.25. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 25 Surgical trials - transplant trials eliminated.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.25.1 All trials					
Fan 1994	4/64	4/60		64.65%	-0[-0.09,0.08]
Ishikawa 2010	0/11	0/13		12.44%	0[-0.15,0.15]
Meng 1999	0/21	0/23		22.92%	0[-0.08,0.08]
Subtotal (95% CI)	**96**	**96**		**100%**	**-0[-0.07,0.06]**



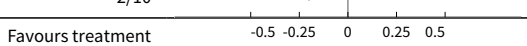
Favours treatment Favours control

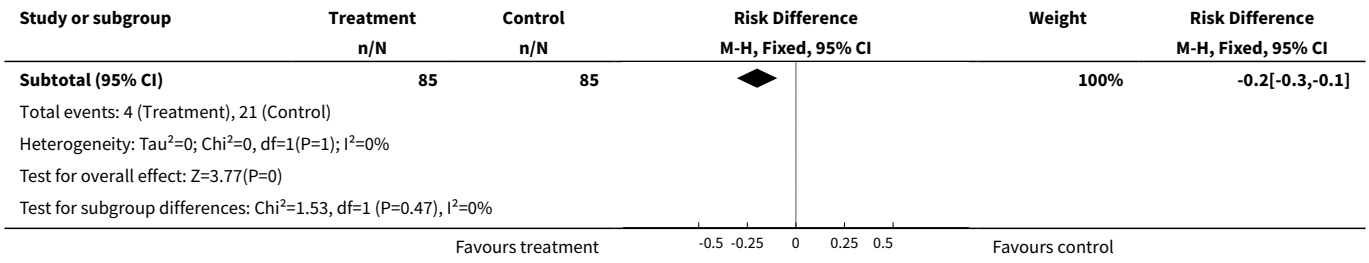
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Total events: 4 (Treatment), 4 (Control)					
Heterogeneity: Tau²=0; Chi²=0.01, df=2(P=1); I²=0%					
Test for overall effect: Z=0.08(P=0.93)					
20.25.2 Standard amino acids					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
20.25.3 BCAAs					
Fan 1994	4/64	4/60		64.65%	-0[-0.09,0.08]
Ishikawa 2010	0/11	0/13		12.44%	0[-0.15,0.15]
Meng 1999	0/21	0/23		22.92%	0[-0.08,0.08]
Subtotal (95% CI)	**96**	**96**		**100%**	**-0[-0.07,0.06]**
Total events: 4 (Treatment), 4 (Control)					
Heterogeneity: Tau²=0; Chi²=0.01, df=2(P=1); I²=0%					
Test for overall effect: Z=0.08(P=0.93)					
Test for subgroup differences: Not applicable					



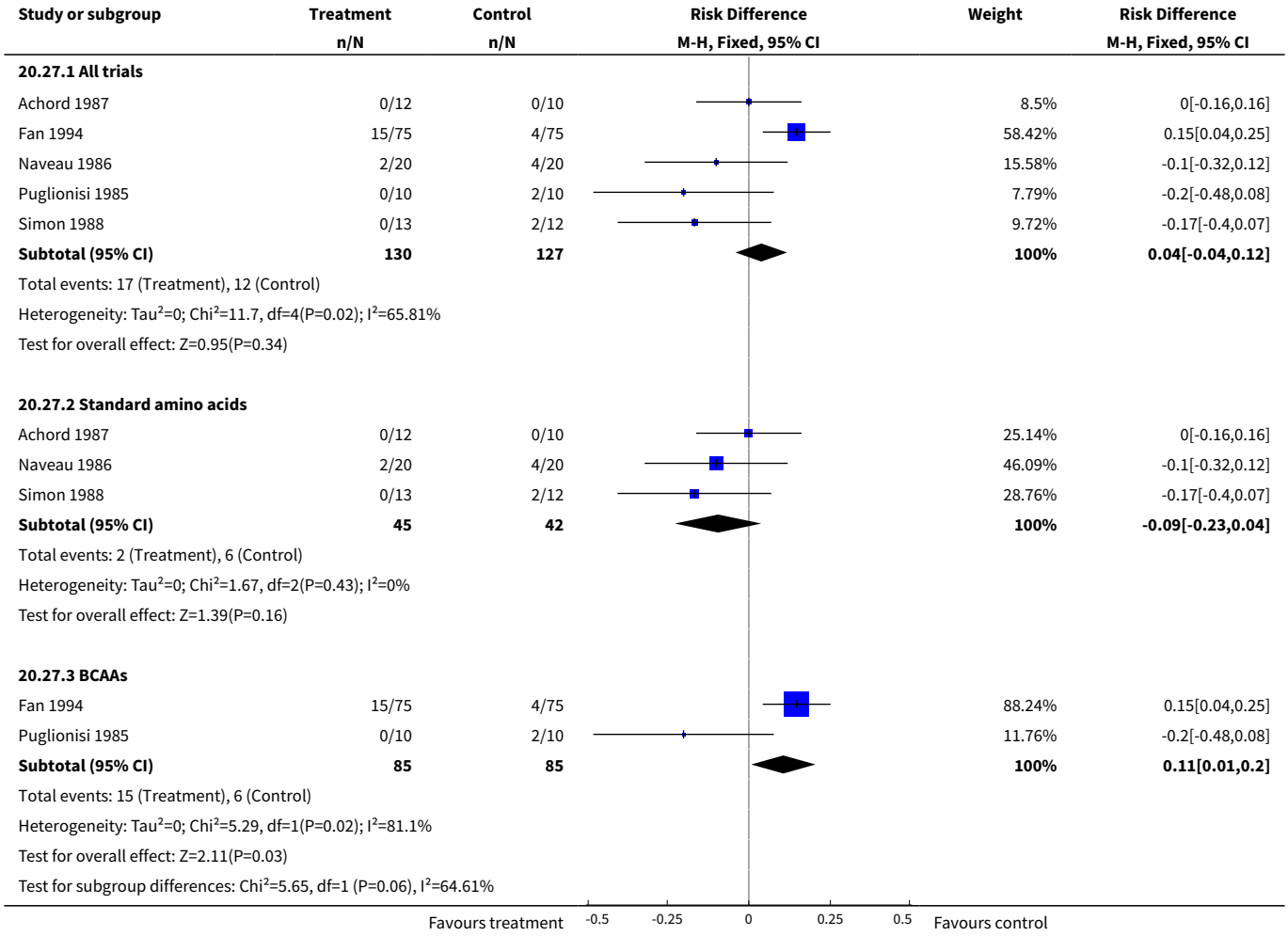
Analysis 20.26. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 26 ITT - Parenteral nutrition - best-case scenario for intervention.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.26.1 All trials					
Achord 1987	0/12	0/10		8.5%	0[-0.16,0.16]
Fan 1994	4/75	19/75		58.42%	-0.2[-0.31,-0.09]
Naveau 1986	2/20	4/20		15.58%	-0.1[-0.32,0.12]
Puglionisi 1985	0/10	2/10		7.79%	-0.2[-0.48,0.08]
Simon 1988	0/13	2/12		9.72%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**130**	**127**		**100%**	**-0.16[-0.25,-0.08]**
Total events: 6 (Treatment), 27 (Control)					
Heterogeneity: Tau²=0; Chi²=4.77, df=4(P=0.31); I²=16.08%					
Test for overall effect: Z=3.92(P<0.0001)					
20.26.2 Standard amino acids					
Achord 1987	0/12	0/10		25.14%	0[-0.16,0.16]
Naveau 1986	2/20	4/20		46.09%	-0.1[-0.32,0.12]
Simon 1988	0/13	2/12		28.76%	-0.17[-0.4,0.07]
Subtotal (95% CI)	**45**	**42**		**100%**	**-0.09[-0.23,0.04]**
Total events: 2 (Treatment), 6 (Control)					
Heterogeneity: Tau²=0; Chi²=1.67, df=2(P=0.43); I²=0%					
Test for overall effect: Z=1.39(P=0.16)					
20.26.3 BCAAs					
Fan 1994	4/75	19/75		88.24%	-0.2[-0.31,-0.09]
Puglionisi 1985	0/10	2/10		11.76%	-0.2[-0.48,0.08]



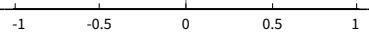


Analysis 20.27. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 27 ITT - Parenteral nutrition - worst-case scenario for intervention.



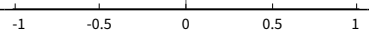
Analysis 20.28. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 28 ITT - Enteral nutrition - best-case scenario for intervention.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.28.1 All trials					
Calvey 1985	7/21	2/13		29.27%	0.18[-0.1,0.46]
Guy 1995	4/22	5/20		38.19%	-0.07[-0.32,0.18]
Kearns 1992	1/6	1/8		12.5%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		20.05%	0[-0.16,0.16]
Subtotal (95% CI)	**60**	**52**		**100%**	**0.03[-0.11,0.17]**
Total events: 12 (Treatment), 8 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.83, df=3(P=0.61); I^2=0%					
Test for overall effect: Z=0.45(P=0.65)					
20.28.2 Standard amino acids					
Calvey 1985	3/10	2/13		22.56%	0.15[-0.2,0.49]
Guy 1995	4/22	5/20		41.81%	-0.07[-0.32,0.18]
Kearns 1992	1/6	1/8		13.68%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		21.95%	0[-0.16,0.16]
Subtotal (95% CI)	**49**	**52**		**100%**	**0.01[-0.13,0.16]**
Total events: 8 (Treatment), 8 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.02, df=3(P=0.8); I^2=0%					
Test for overall effect: Z=0.14(P=0.89)					
20.28.3 BCAAs					
Calvey 1985	4/11	2/13		100%	0.21[-0.14,0.56]
Subtotal (95% CI)	**11**	**13**		**100%**	**0.21[-0.14,0.56]**
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.23)					
Test for subgroup differences: Chi^2=1.1, df=1 (P=0.58), I^2=0%					

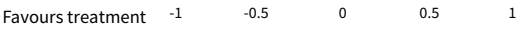


Analysis 20.29. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 29 ITT - Enteral nutrition - worst-case scenario for intervention.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.29.1 Standard amino acids					
Calvey 1985	7/21	2/13		29.27%	0.18[-0.1,0.46]
Guy 1995	12/22	3/20		38.19%	0.4[0.14,0.66]
Kearns 1992	1/6	1/8		12.5%	0.04[-0.33,0.42]
Schuetz 2006	0/11	0/11		20.05%	0[-0.16,0.16]
Subtotal (95% CI)	**60**	**52**		**100%**	**0.21[0.07,0.35]**
Total events: 20 (Treatment), 6 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9.32, df=3(P=0.03); I^2=67.82%					
Test for overall effect: Z=2.89(P=0)					
20.29.2 BCAAs					
Calvey 1985	4/11	2/13		100%	0.21[-0.14,0.56]
Subtotal (95% CI)	**11**	**13**		**100%**	**0.21[-0.14,0.56]**

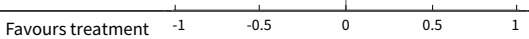


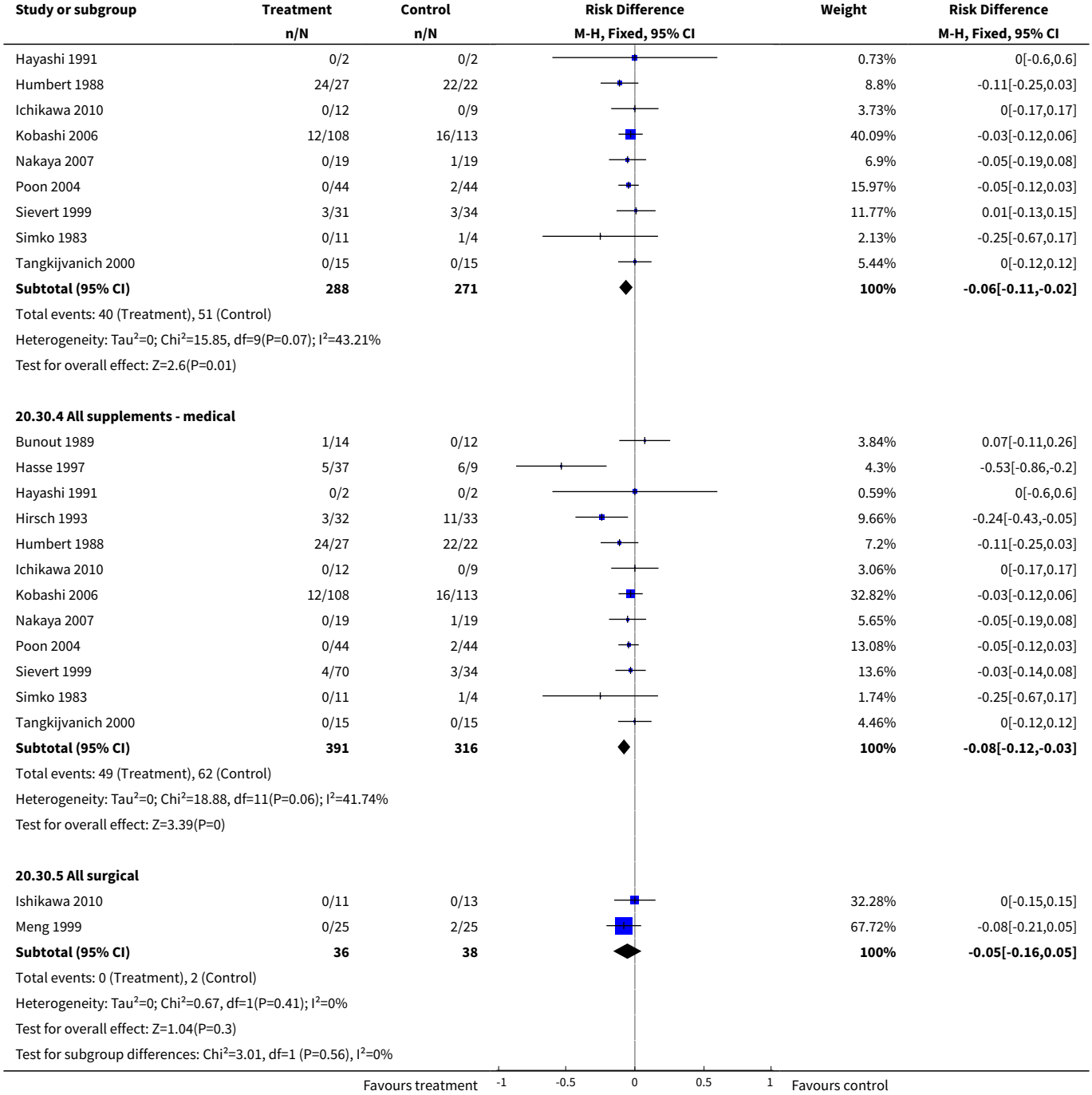
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Total events: 4 (Treatment), 2 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.23)					
20.29.3 All trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi²=0, df=1 (P=1), I²=0%					



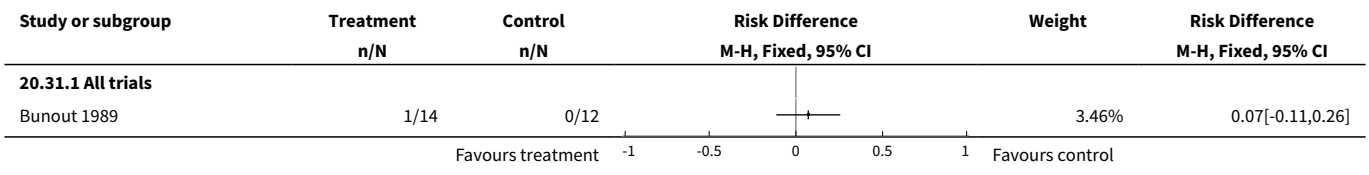
Analysis 20.30. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 30 ITT- Supplements - best-case scenario for intervention.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
20.30.1 All trials					
Bunout 1989	1/14	0/12		3.46%	0.07[-0.11,0.26]
Hasse 1997	5/37	6/9		3.88%	-0.53[-0.86,-0.2]
Hayashi 1991	0/2	0/2		0.54%	0[-0.6,0.6]
Hirsch 1993	3/32	11/33		8.7%	-0.24[-0.43,-0.05]
Humbert 1988	24/27	22/22		6.49%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		2.75%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		3.19%	0[-0.15,0.15]
Kobashi 2006	12/108	16/113		29.56%	-0.03[-0.12,0.06]
Meng 1999	0/25	2/25		6.69%	-0.08[-0.21,0.05]
Nakaya 2007	0/19	1/19		5.09%	-0.05[-0.19,0.08]
Poon 2004	0/44	2/44		11.78%	-0.05[-0.12,0.03]
Sievert 1999	4/71	3/34		12.31%	-0.03[-0.14,0.08]
Simko 1983	0/11	1/4		1.57%	-0.25[-0.67,0.17]
Tangkijvanich 2000	0/15	0/15		4.01%	0[-0.12,0.12]
Subtotal (95% CI)	**428**	**354**		**100%**	**-0.08[-0.12,-0.03]**
Total events: 49 (Treatment), 64 (Control)					
Heterogeneity: Tau²=0; Chi²=19.54, df=13(P=0.11); I²=33.48%					
Test for overall effect: Z=3.54(P=0)					
20.30.2 Standard amino acids -medical trials					
Bunout 1989	1/14	0/12		13.79%	0.07[-0.11,0.26]
Hasse 1997	4/18	6/9		12.8%	-0.44[-0.81,-0.08]
Hirsch 1993	3/32	11/33		34.66%	-0.24[-0.43,-0.05]
Sievert 1999	1/39	3/34		38.75%	-0.06[-0.17,0.04]
Subtotal (95% CI)	**103**	**88**		**100%**	**-0.15[-0.25,-0.06]**
Total events: 9 (Treatment), 20 (Control)					
Heterogeneity: Tau²=0; Chi²=11.79, df=3(P=0.01); I²=74.56%					
Test for overall effect: Z=3.19(P=0)					
20.30.3 BCAAs - medical trials					
Hasse 1997	1/19	6/9		4.43%	-0.61[-0.94,-0.29]

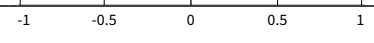




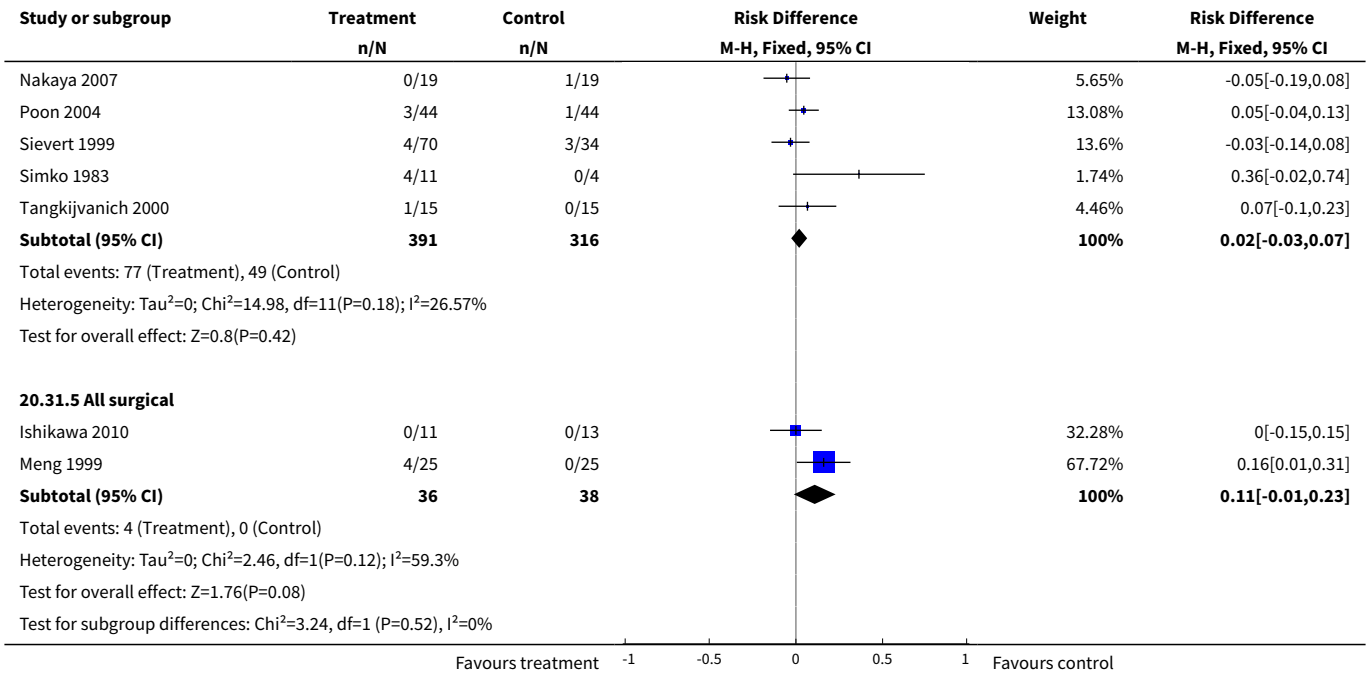
Analysis 20.31. Comparison 20 Appearance of encephalopathy - absolute risk difference (ARD), Outcome 31 ITT - Supplements - worst-case scenario for intervention.



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Hasse 1997	19/37	3/9		3.88%	0.18[-0.17,0.53]
Hayashi 1991	0/2	0/2		0.54%	0[-0.6,0.6]
Hirsch 1993	9/32	3/33		8.7%	0.19[0.01,0.37]
Humbert 1988	24/27	22/22		6.49%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		2.75%	0[-0.17,0.17]
Ishikawa 2010	0/11	0/13		3.19%	0[-0.15,0.15]
Kobashi 2006	12/108	16/113		29.58%	-0.03[-0.12,0.06]
Meng 1999	4/25	0/25		6.69%	0.16[0.01,0.31]
Nakaya 2007	0/19	1/19		5.09%	-0.05[-0.19,0.08]
Poon 2004	3/44	1/44		11.78%	0.05[-0.04,0.13]
Sievert 1999	4/70	3/34		12.26%	-0.03[-0.14,0.08]
Simko 1983	4/11	0/4		1.57%	0.36[-0.02,0.74]
Tangkijvanich 2000	1/15	0/15		4.02%	0.07[-0.1,0.23]
Subtotal (95% CI)	**427**	**354**		**100%**	**0.03[-0.02,0.07]**
Total events: 81 (Treatment), 49 (Control)					
Heterogeneity: Tau^2=0; Chi^2=18.56, df=13(P=0.14); I^2=29.95%					
Test for overall effect: Z=1.26(P=0.21)					
20.31.2 Standard amino acids -medical trials					
Bunout 1989	1/14	0/12		13.79%	0.07[-0.11,0.26]
Hasse 1997	8/18	3/9		12.8%	0.11[-0.27,0.5]
Hirsch 1993	9/32	3/33		34.66%	0.19[0.01,0.37]
Sievert 1999	1/39	3/34		38.75%	-0.06[-0.17,0.04]
Subtotal (95% CI)	**103**	**88**		**100%**	**0.07[-0.03,0.16]**
Total events: 19 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=0; Chi^2=7.3, df=3(P=0.06); I^2=58.89%					
Test for overall effect: Z=1.36(P=0.17)					
20.31.3 BCAAs - medical trials					
Hasse 1997	11/19	3/9		4.43%	0.25[-0.13,0.63]
Hayashi 1991	0/2	0/2		0.73%	0[-0.6,0.6]
Humbert 1988	24/27	22/22		8.8%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		3.73%	0[-0.17,0.17]
Kobashi 2006	12/108	16/113		40.09%	-0.03[-0.12,0.06]
Nakaya 2007	0/19	1/19		6.9%	-0.05[-0.19,0.08]
Poon 2004	3/44	1/44		15.97%	0.05[-0.04,0.13]
Sievert 1999	3/31	3/34		11.77%	0.01[-0.13,0.15]
Simko 1983	4/11	0/4		2.13%	0.36[-0.02,0.74]
Tangkijvanich 2000	1/15	0/15		5.44%	0.07[-0.1,0.23]
Subtotal (95% CI)	**288**	**271**		**100%**	**0[-0.05,0.05]**
Total events: 58 (Treatment), 46 (Control)					
Heterogeneity: Tau^2=0; Chi^2=10.47, df=9(P=0.31); I^2=14.07%					
Test for overall effect: Z=0.19(P=0.85)					
20.31.4 All supplements - medical					
Bunout 1989	1/14	0/12		3.84%	0.07[-0.11,0.26]
Hasse 1997	19/37	3/9		4.3%	0.18[-0.17,0.53]
Hayashi 1991	0/2	0/2		0.59%	0[-0.6,0.6]
Hirsch 1993	9/32	3/33		9.66%	0.19[0.01,0.37]
Humbert 1988	24/27	22/22		7.2%	-0.11[-0.25,0.03]
Ichikawa 2010	0/12	0/9		3.06%	0[-0.17,0.17]
Kobashi 2006	12/108	16/113		32.82%	-0.03[-0.12,0.06]



Favours treatment Favours control



Comparison 21. Resolution of encephalopathy - absolute risk difference (ARD)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 All trials	6		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
1.1 All studies	6	119	Risk Difference (M-H, Fixed, 95% CI)	0.25 [0.10, 0.41]
1.2 Standard amino acids	5	66	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.17, 0.27]
1.3 BCAA's	2	62	Risk Difference (M-H, Fixed, 95% CI)	0.45 [0.25, 0.64]
2 Parenteral nutrition (all medical trials)	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
2.1 All trials	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
2.2 Standard amino acids	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
2.3 BCAA's	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Enteral nutrition (all medical trials)	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.1 All trials	2	47	Risk Difference (M-H, Fixed, 95% CI)	0.13 [-0.12, 0.39]
3.2 Standard amino acids	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.20, 0.35]
3.3 BCAA's	1	19	Risk Difference (M-H, Fixed, 95% CI)	0.29 [-0.08, 0.66]
4 Supplements (all medical trials)	2		Risk Difference (M-H, Random, 95% CI)	Subtotals only
4.1 All trials	2	53	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.86, 0.99]
4.2 Standard amino acids	1	10	Risk Difference (M-H, Random, 95% CI)	-0.43 [-0.90, 0.04]
4.3 BCAA's	1	43	Risk Difference (M-H, Random, 95% CI)	0.52 [0.29, 0.74]
5 Medical trials - all trials	6	119	Risk Difference (M-H, Fixed, 95% CI)	0.25 [0.10, 0.41]
5.1 Parenteral nutrition	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
5.2 Enteral nutrition	2	47	Risk Difference (M-H, Fixed, 95% CI)	0.13 [-0.12, 0.39]
5.3 Supplements	2	53	Risk Difference (M-H, Fixed, 95% CI)	0.36 [0.15, 0.57]
6 Medical trials - standard amino acids	5	66	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.17, 0.27]
6.1 Parenteral nutrition	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
6.2 Enteral nutrition	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.20, 0.35]
6.3 Supplements	1	10	Risk Difference (M-H, Fixed, 95% CI)	-0.43 [-0.90, 0.04]
7 Medical trials - BCAAs	2	62	Risk Difference (M-H, Fixed, 95% CI)	0.45 [0.25, 0.64]
7.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Enteral nutrition	1	19	Risk Difference (M-H, Fixed, 95% CI)	0.29 [-0.08, 0.66]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
7.3 Supplements	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]
8 Surgical trials - all trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.1 Pareneral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Surgical trials - standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Pareneral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Surgical trials - BCAAs	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.1 Pareneral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Alcoholic hepatitis - all trials	5	76	Risk Difference (M-H, Fixed, 95% CI)	0.09 [-0.12, 0.30]
11.1 Parenteral nutrition	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
11.2 Enteral nutrition	2	47	Risk Difference (M-H, Fixed, 95% CI)	0.13 [-0.12, 0.39]
11.3 Supplements	1	10	Risk Difference (M-H, Fixed, 95% CI)	-0.43 [-0.90, 0.04]
12 Alcoholic hepatitis - standard amino acids	5	66	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.17, 0.27]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
12.1 Parenteral nutrition	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
12.2 Enteral nutrition	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.20, 0.35]
12.3 Supplements	1	10	Risk Difference (M-H, Fixed, 95% CI)	-0.43 [-0.90, 0.04]
13 Alcoholic hepatitis - BCAAs	1	19	Risk Difference (M-H, Fixed, 95% CI)	0.29 [-0.08, 0.66]
13.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Enteral nutrition	1	19	Risk Difference (M-H, Fixed, 95% CI)	0.29 [-0.08, 0.66]
13.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Cirrhosis - all	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]
14.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 Supplements	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]
15 Cirrhosis - standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Cirrhosis - BCAAs	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]
16.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
16.3 Supplements	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]
17 HCC - all studies	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 Enteral nutritionBCAA's	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 HCC - standard amino acids	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 Enteral nutritionBCAA's	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 HCC - BCAAs	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 Enteral nutrition BCAA's	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Abstracts excluded - all trials	6	119	Risk Difference (M-H, Fixed, 95% CI)	0.25 [0.10, 0.41]
20.1 Parenteral nutrition	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
20.2 Enteral nutrition	2	47	Risk Difference (M-H, Fixed, 95% CI)	0.13 [-0.12, 0.39]
20.3 Supplements	2	53	Risk Difference (M-H, Fixed, 95% CI)	0.36 [0.15, 0.57]
21 Abstracts excluded - standard amino acids	5	66	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.17, 0.27]

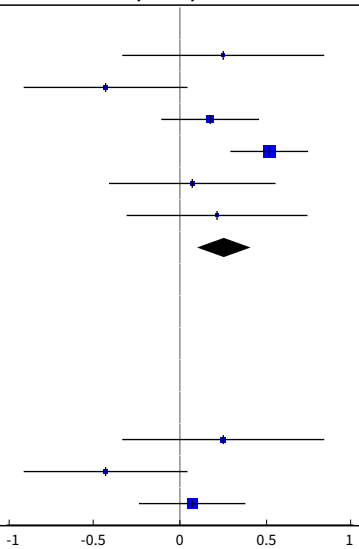
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
21.1 Parenteral nutrition	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
21.2 Enteral nutrition	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.20, 0.35]
21.3 Supplements	1	10	Risk Difference (M-H, Fixed, 95% CI)	-0.43 [-0.90, 0.04]
22 Abstracts excluded - BCAAs	3	72	Risk Difference (M-H, Random, 95% CI)	0.16 [-0.34, 0.66]
22.1 Parenteral nutrition	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
22.2 Enteral nutrition	1	19	Risk Difference (M-H, Random, 95% CI)	0.29 [-0.08, 0.66]
22.3 Supplements	2	53	Risk Difference (M-H, Random, 95% CI)	0.07 [-0.86, 0.99]
23 Surgical trials (transplant patients removed) - all trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.1 Parenteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 Supplements	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 ITT - All trials - best case scenario - no changes made because all patients reported	6		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
24.1 All studies	6	119	Risk Difference (M-H, Fixed, 95% CI)	0.25 [0.10, 0.41]
24.2 Standard amino acids	5	66	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.17, 0.27]
24.3 BCAA's	2	62	Risk Difference (M-H, Fixed, 95% CI)	0.45 [0.25, 0.64]
25 ITT - Parenteral nutrition trials - best-case scenario - no changes made because all patients reported	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
25.1 All studies	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]

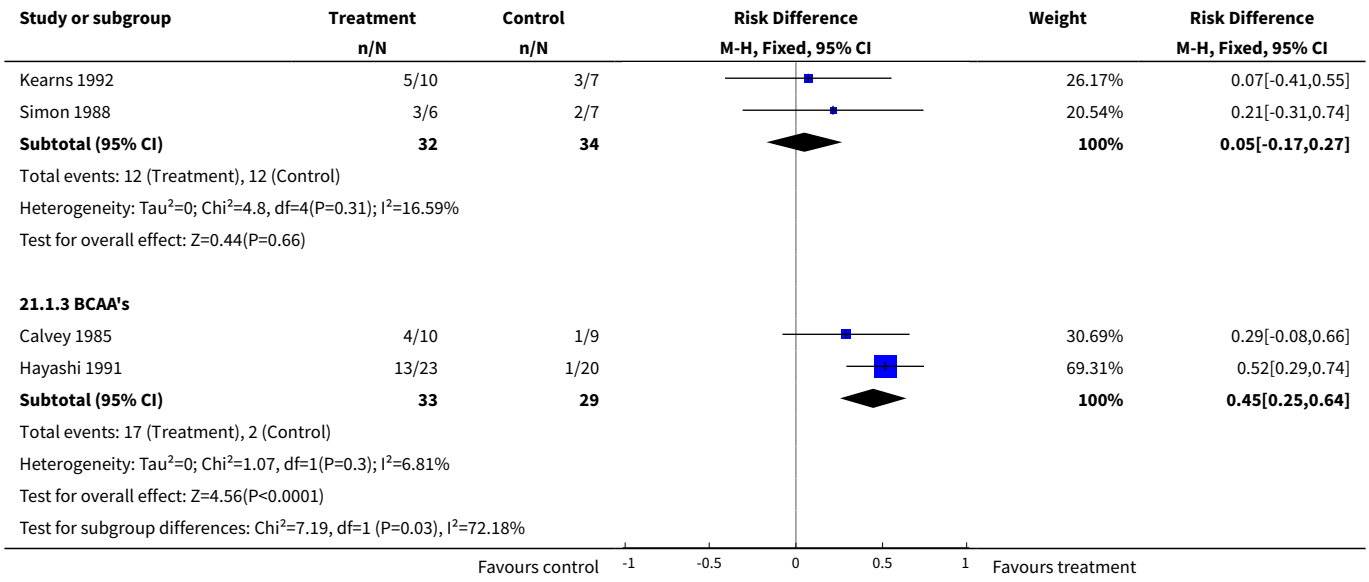
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
25.2 Standard amino acids	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
25.3 BCAA's	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 ITT - Enteral nutrition trials - best-case scenario - no changes made because all patients reported	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
26.1 All studies	2	47	Risk Difference (M-H, Fixed, 95% CI)	0.13 [-0.12, 0.39]
26.2 Standard amino acids	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.20, 0.35]
26.3 BCAA's	1	19	Risk Difference (M-H, Fixed, 95% CI)	0.29 [-0.08, 0.66]
27 ITT - Supplement trials - best-case scenario - no changes made because all patients reported	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
27.1 All studies	2	53	Risk Difference (M-H, Fixed, 95% CI)	0.36 [0.15, 0.57]
27.2 Standard amino acids	1	10	Risk Difference (M-H, Fixed, 95% CI)	-0.43 [-0.90, 0.04]
27.3 BCAA's	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]
28 ITT - All trials - worst-case scenario - no changes made because all patients reported	6		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
28.1 All studies	6	119	Risk Difference (M-H, Fixed, 95% CI)	0.25 [0.10, 0.41]
28.2 Standard amino acids	5	66	Risk Difference (M-H, Fixed, 95% CI)	0.05 [-0.17, 0.27]
28.3 BCAA's	2	62	Risk Difference (M-H, Fixed, 95% CI)	0.45 [0.25, 0.64]
29 ITT - Parenteral nutrition trials - worst-case scenario - no changes made because all patients reported	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
29.1 All studies	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]
29.2 Standard amino acids	2	19	Risk Difference (M-H, Fixed, 95% CI)	0.22 [-0.22, 0.66]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
29.3 BCAA's	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
30 ITT - Enteral nutrition trials - worst-case scenario - no changes made because all patients reported	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
30.1 All studies	2	47	Risk Difference (M-H, Fixed, 95% CI)	0.13 [-0.12, 0.39]
30.2 Standard amino acids	2	37	Risk Difference (M-H, Fixed, 95% CI)	0.07 [-0.20, 0.35]
30.3 BCAA's	1	19	Risk Difference (M-H, Fixed, 95% CI)	0.29 [-0.08, 0.66]
31 ITT - Supplement trials - worst-case scenario - no changes made because all patients reported	2		Risk Difference (M-H, Fixed, 95% CI)	Subtotals only
31.1 All studies	2	53	Risk Difference (M-H, Fixed, 95% CI)	0.36 [0.15, 0.57]
31.2 Standard amino acids	1	10	Risk Difference (M-H, Fixed, 95% CI)	-0.43 [-0.90, 0.04]
31.3 BCAA's	1	43	Risk Difference (M-H, Fixed, 95% CI)	0.52 [0.29, 0.74]

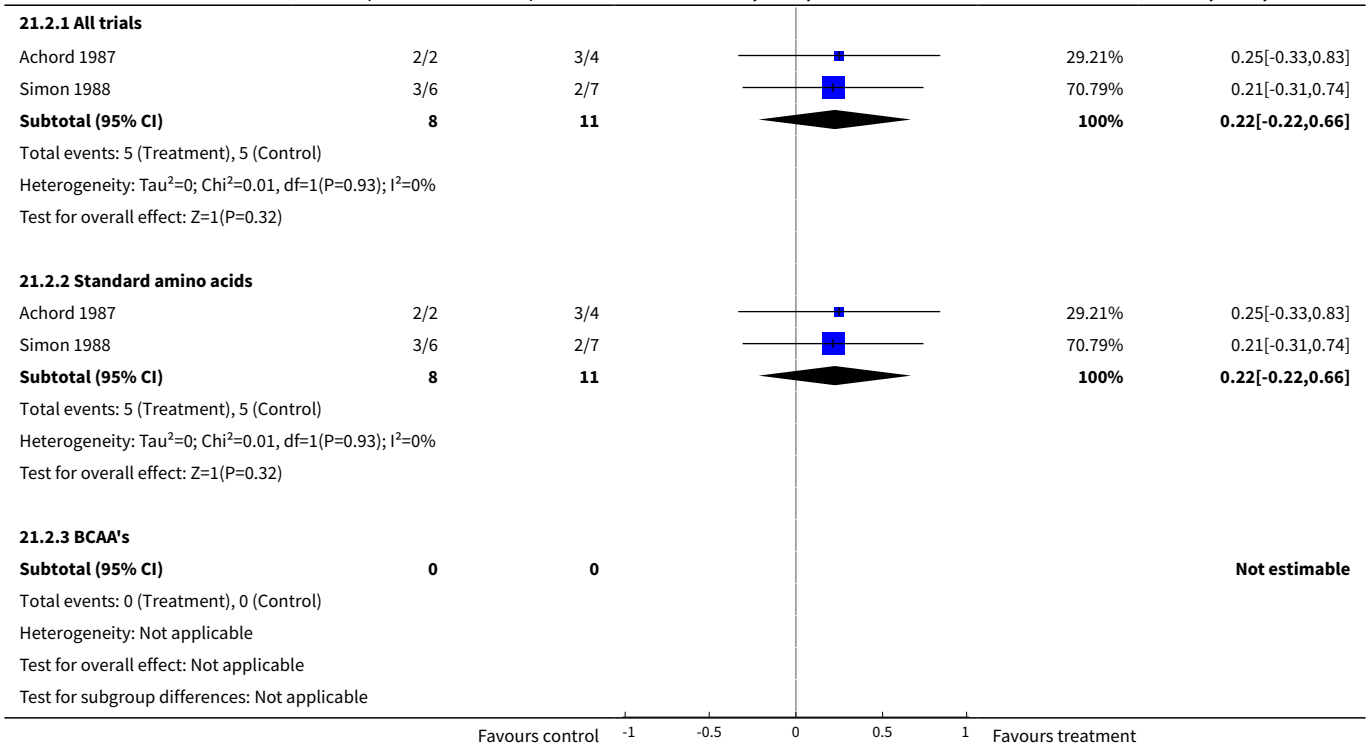
Analysis 21.1. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 1 All trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.1.1 All studies					
Achord 1987	2/2	3/4		4.8%	0.25[-0.33,0.83]
Bunout 1989	0/3	3/7		7.56%	-0.43[-0.9,0.04]
Calvey 1985	6/21	1/9		22.68%	0.17[-0.11,0.46]
Hayashi 1991	13/23	1/20		38.51%	0.52[0.29,0.74]
Kearns 1992	5/10	3/7		14.82%	0.07[-0.41,0.55]
Simon 1988	3/6	2/7		11.63%	0.21[-0.31,0.74]
Subtotal (95% CI)	**65**	**54**		**100%**	**0.25[0.1,0.41]**
Total events: 29 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=14.13, df=5(P=0.01); I^2=64.61%					
Test for overall effect: Z=3.21(P=0)					
21.1.2 Standard amino acids					
Achord 1987	2/2	3/4		8.48%	0.25[-0.33,0.83]
Bunout 1989	0/3	3/7		13.35%	-0.43[-0.9,0.04]
Calvey 1985	2/11	1/9		31.47%	0.07[-0.24,0.38]



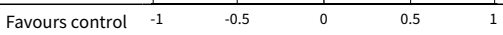


Analysis 21.2. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 2 Parenteral nutrition (all medical trials).



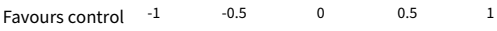
Analysis 21.3. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 3 Enteral nutrition (all medical trials).

Study or subgroup	Tretment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.3.1 All trials					
Calvey 1985	6/21	1/9		60.47%	0.17[-0.11,0.46]
Kearns 1992	5/10	3/7		39.53%	0.07[-0.41,0.55]
Subtotal (95% CI)	**31**	**16**		**100%**	**0.13[-0.12,0.39]**
Total events: 11 (Tretment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.15, df=1(P=0.7); I^2=0%					
Test for overall effect: Z=1.03(P=0.3)					
21.3.2 Standard amino acids					
Calvey 1985	2/11	1/9		54.59%	0.07[-0.24,0.38]
Kearns 1992	5/10	3/7		45.41%	0.07[-0.41,0.55]
Subtotal (95% CI)	**21**	**16**		**100%**	**0.07[-0.2,0.35]**
Total events: 7 (Tretment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%					
Test for overall effect: Z=0.51(P=0.61)					
21.3.3 BCAA's					
Calvey 1985	4/10	1/9		100%	0.29[-0.08,0.66]
Subtotal (95% CI)	**10**	**9**		**100%**	**0.29[-0.08,0.66]**
Total events: 4 (Tretment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					
Test for subgroup differences: Chi^2=0.88, df=1 (P=0.65), I^2=0%					

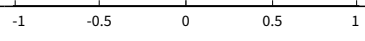


Analysis 21.4. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 4 Supplements (all medical trials).

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
21.4.1 All trials					
Bunout 1989	0/3	3/7		47.48%	-0.43[-0.9,0.04]
Hayashi 1991	13/23	1/20		52.52%	0.52[0.29,0.74]
Subtotal (95% CI)	**26**	**27**		**100%**	**0.07[-0.86,0.99]**
Total events: 13 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0.41; Chi^2=12.55, df=1(P=0); I^2=92.03%					
Test for overall effect: Z=0.14(P=0.89)					
21.4.2 Standard amino acids					
Bunout 1989	0/3	3/7		100%	-0.43[-0.9,0.04]
Subtotal (95% CI)	**3**	**7**		**100%**	**-0.43[-0.9,0.04]**
Total events: 0 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.78(P=0.08)					
21.4.3 BCAA's					
Hayashi 1991	13/23	1/20		100%	0.52[0.29,0.74]

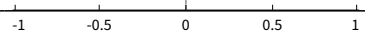


Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
Subtotal (95% CI)	**23**	**20**		**100%**	**0.52[0.29,0.74]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.51(P<0.0001)					
Test for subgroup differences: Chi²=12.84, df=1 (P=0), I²=84.42%					



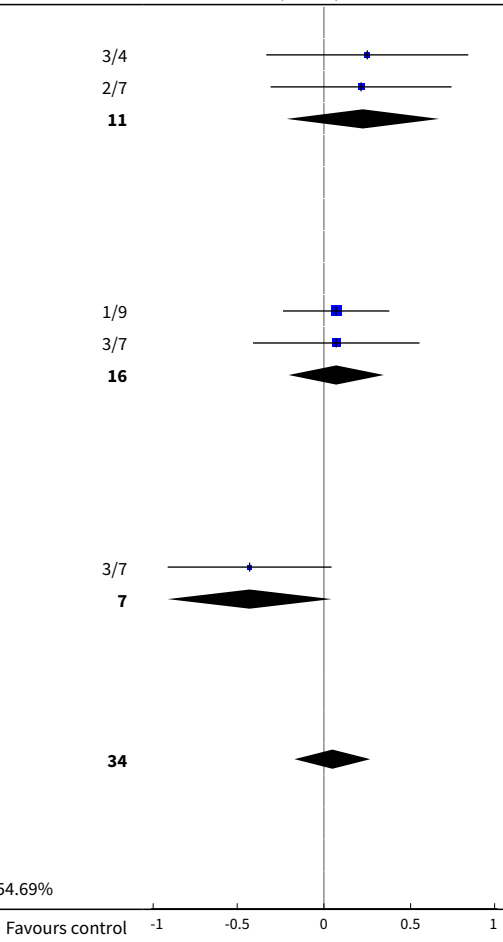
Analysis 21.5. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 5 Medical trials - all trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.5.1 Parenteral nutrition					
Achord 1987	2/2	3/4		4.8%	0.25[-0.33,0.83]
Simon 1988	3/6	2/7		11.63%	0.21[-0.31,0.74]
Subtotal (95% CI)	**8**	**11**		**16.43%**	**0.22[-0.22,0.66]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau²=0; Chi²=0.01, df=1(P=0.93); I²=0%					
Test for overall effect: Z=1(P=0.32)					
21.5.2 Enteral nutrition					
Calvey 1985	6/21	1/9		22.68%	0.17[-0.11,0.46]
Kearns 1992	5/10	3/7		14.82%	0.07[-0.41,0.55]
Subtotal (95% CI)	**31**	**16**		**37.5%**	**0.13[-0.12,0.39]**
Total events: 11 (Treatment), 4 (Control)					
Heterogeneity: Tau²=0; Chi²=0.15, df=1(P=0.7); I²=0%					
Test for overall effect: Z=1.03(P=0.3)					
21.5.3 Supplements					
Bunout 1989	0/3	3/7		7.56%	-0.43[-0.9,0.04]
Hayashi 1991	13/23	1/20		38.51%	0.52[0.29,0.74]
Subtotal (95% CI)	**26**	**27**		**46.07%**	**0.36[0.15,0.57]**
Total events: 13 (Treatment), 4 (Control)					
Heterogeneity: Tau²=0; Chi²=12.55, df=1(P=0); I²=92.03%					
Test for overall effect: Z=3.34(P=0)					
Total (95% CI)	**65**	**54**		**100%**	**0.25[0.1,0.41]**
Total events: 29 (Treatment), 13 (Control)					
Heterogeneity: Tau²=0; Chi²=14.13, df=5(P=0.01); I²=64.61%					
Test for overall effect: Z=3.21(P=0)					
Test for subgroup differences: Chi²=1.83, df=1 (P=0.4), I²=0%					



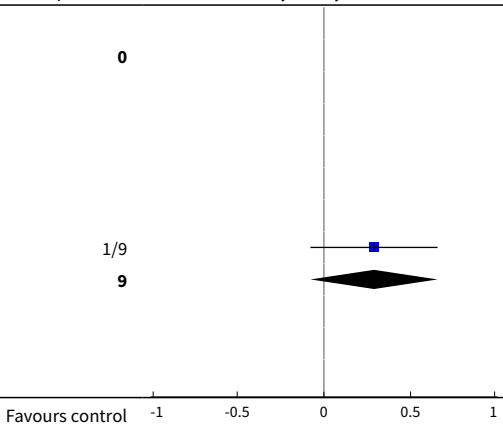
Analysis 21.6. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 6 Medical trials - standard amino acids.

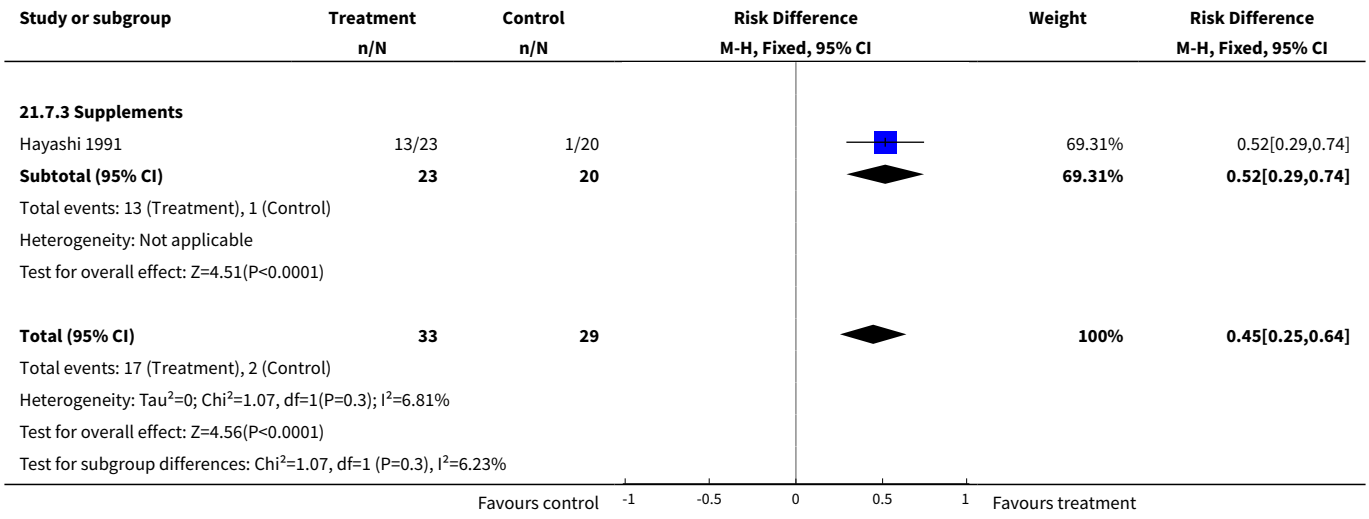
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.6.1 Parenteral nutrition					
Achord 1987	2/2	3/4		8.48%	0.25[-0.33,0.83]
Simon 1988	3/6	2/7		20.54%	0.21[-0.31,0.74]
Subtotal (95% CI)	**8**	**11**		**29.01%**	**0.22[-0.22,0.66]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.93); I^2=0%					
Test for overall effect: Z=1(P=0.32)					
21.6.2 Enteral nutrition					
Calvey 1985	2/11	1/9		31.47%	0.07[-0.24,0.38]
Kearns 1992	5/10	3/7		26.17%	0.07[-0.41,0.55]
Subtotal (95% CI)	**21**	**16**		**57.64%**	**0.07[-0.2,0.35]**
Total events: 7 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%					
Test for overall effect: Z=0.51(P=0.61)					
21.6.3 Supplements					
Bunout 1989	0/3	3/7		13.35%	-0.43[-0.9,0.04]
Subtotal (95% CI)	**3**	**7**		**13.35%**	**-0.43[-0.9,0.04]**
Total events: 0 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.78(P=0.08)					
Total (95% CI)	**32**	**34**		**100%**	**0.05[-0.17,0.27]**
Total events: 12 (Treatment), 12 (Control)					
Heterogeneity: Tau^2=0; Chi^2=4.8, df=4(P=0.31); I^2=16.59%					
Test for overall effect: Z=0.44(P=0.66)					
Test for subgroup differences: Chi^2=4.41, df=1 (P=0.11), I^2=54.69%					



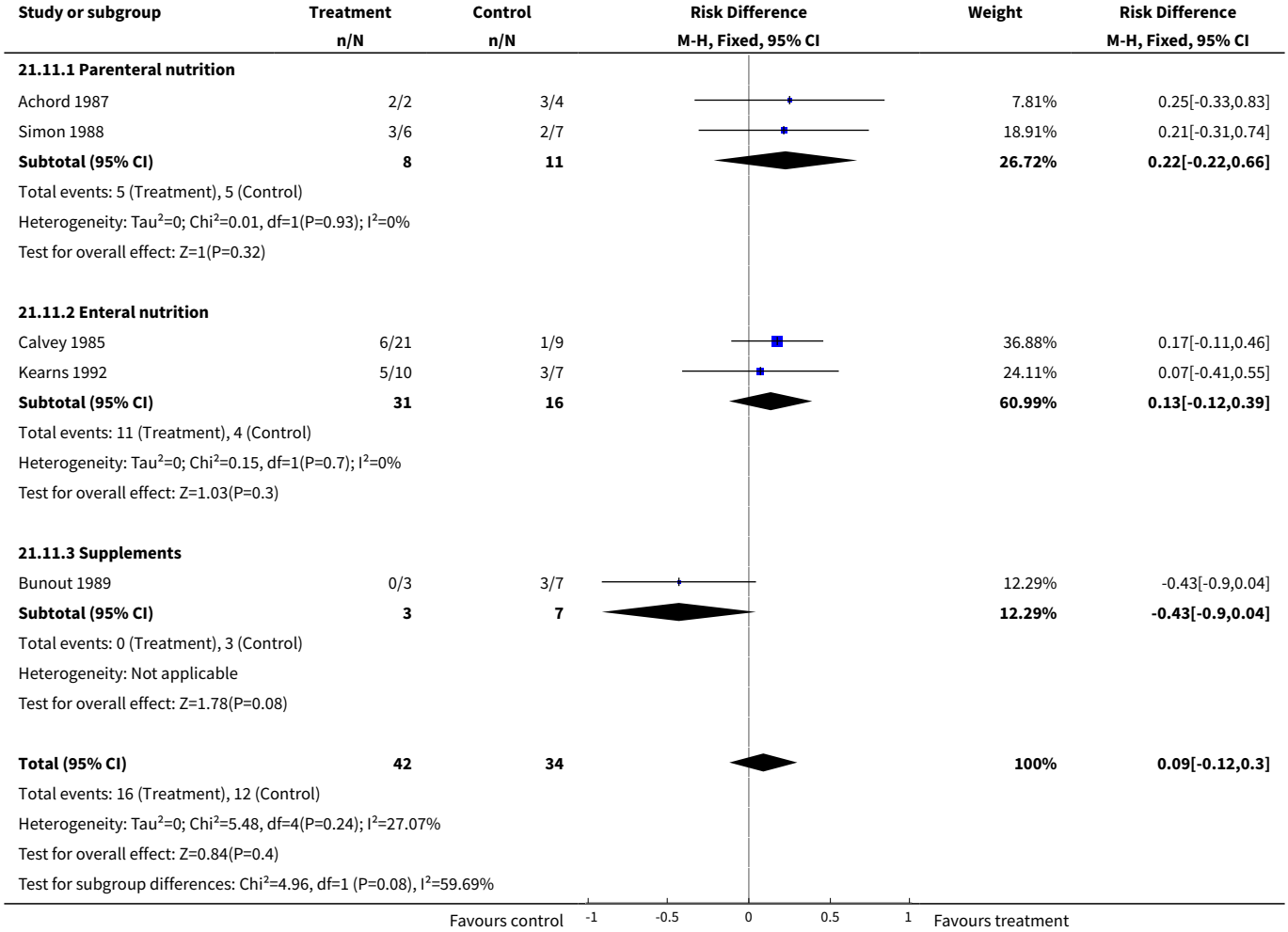
Analysis 21.7. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 7 Medical trials - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.7.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
21.7.2 Enteral nutrition					
Calvey 1985	4/10	1/9		30.69%	0.29[-0.08,0.66]
Subtotal (95% CI)	**10**	**9**		**30.69%**	**0.29[-0.08,0.66]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					

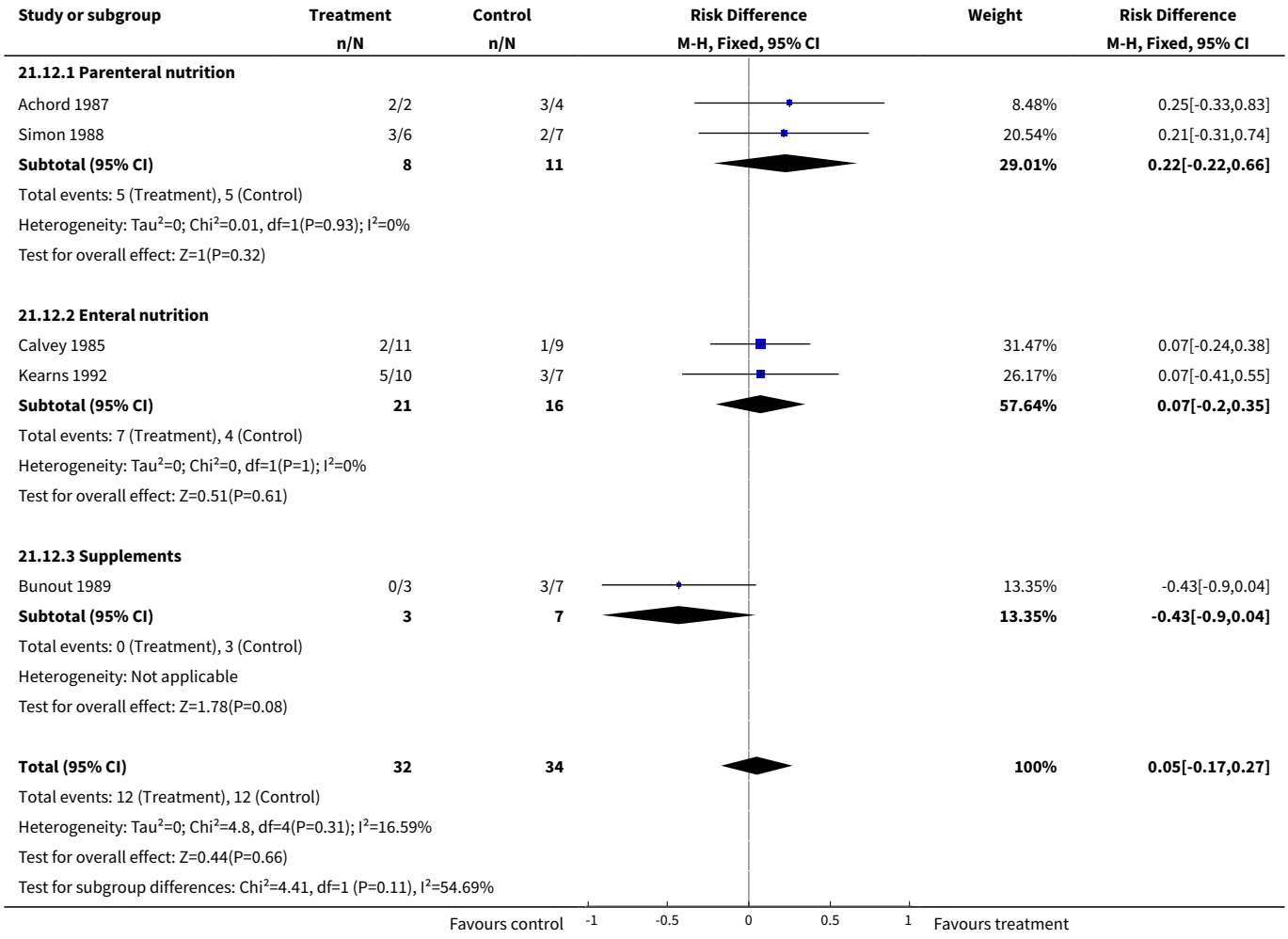




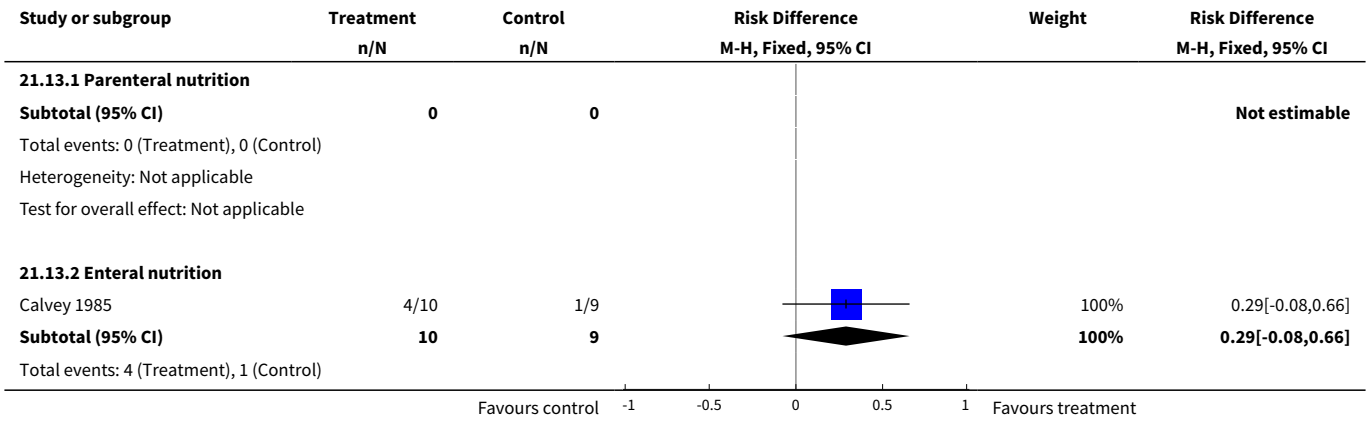
Analysis 21.11. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 11 Alcoholic hepatitis - all trials.



Analysis 21.12. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 12 Alcoholic hepatitis - standard amino acids.



Analysis 21.13. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 13 Alcoholic hepatitis - BCAAs.



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					
21.13.3 Supplements					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**10**	**9**		**100%**	**0.29[-0.08,0.66]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					
Test for subgroup differences: Not applicable					

Analysis 21.14. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 14 Cirrhosis - all.

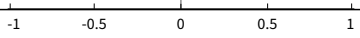
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.14.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
21.14.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
21.14.3 Supplements					
Hayashi 1991	13/23	1/20		100%	0.52[0.29,0.74]
Subtotal (95% CI)	**23**	**20**		**100%**	**0.52[0.29,0.74]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.51(P<0.0001)					
Total (95% CI)	**23**	**20**		**100%**	**0.52[0.29,0.74]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.51(P<0.0001)					
Test for subgroup differences: Not applicable					

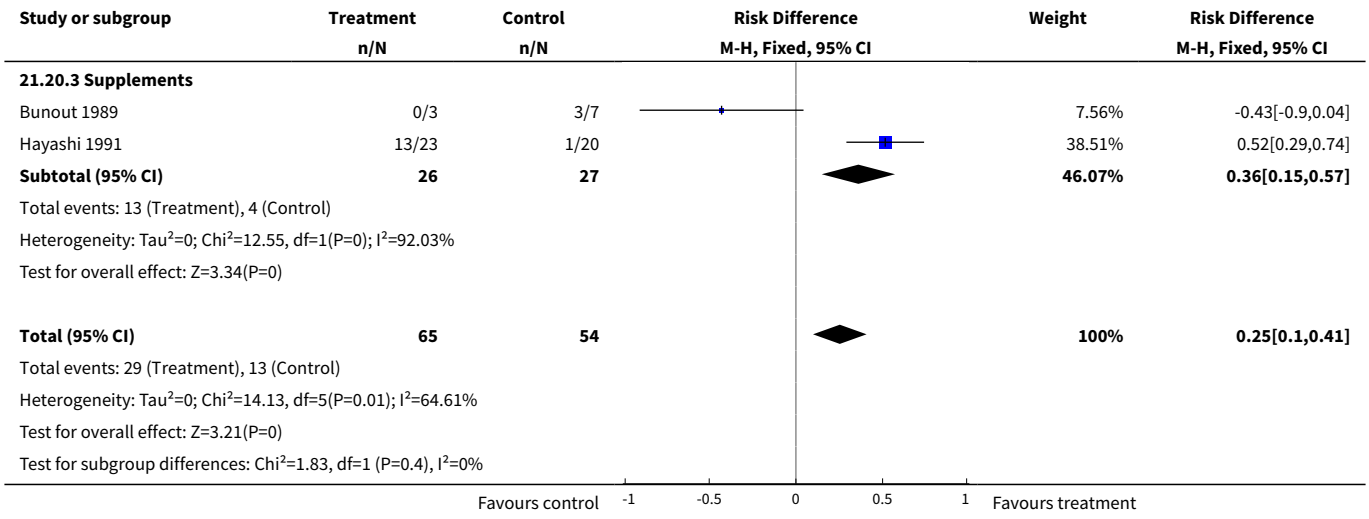
Analysis 21.16. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 16 Cirrhosis - BCAAs.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.16.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
21.16.2 Enteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
21.16.3 Supplements					
Hayashi 1991	13/23	1/20		100%	0.52[0.29,0.74]
Subtotal (95% CI)	**23**	**20**		**100%**	**0.52[0.29,0.74]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.51(P<0.0001)					
Total (95% CI)	**23**	**20**		**100%**	**0.52[0.29,0.74]**
Total events: 13 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=4.51(P<0.0001)					
Test for subgroup differences: Not applicable					

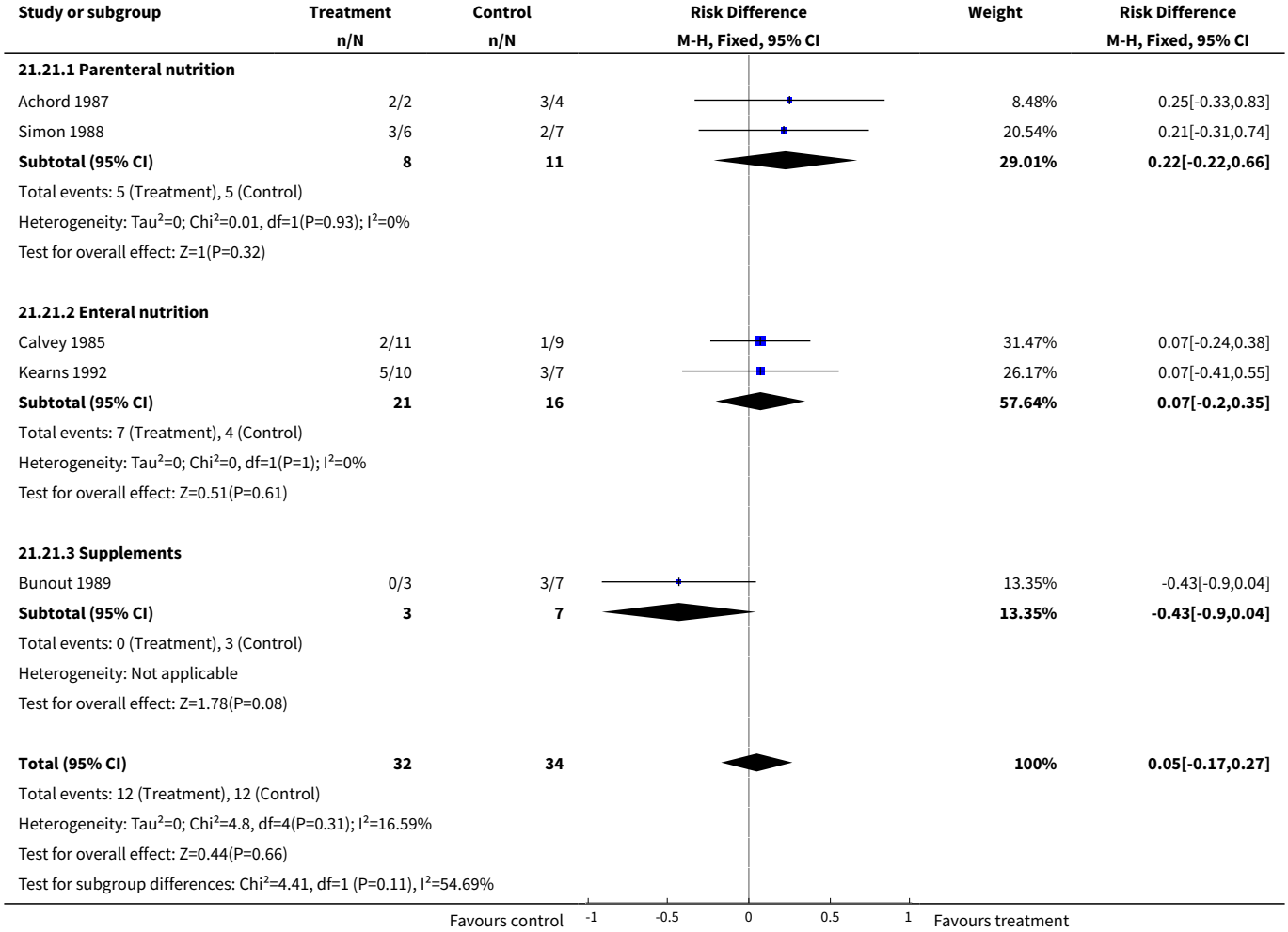
Analysis 21.20. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 20 Abstracts excluded - all trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.20.1 Parenteral nutrition					
Achord 1987	2/2	3/4		4.8%	0.25[-0.33,0.83]
Simon 1988	3/6	2/7		11.63%	0.21[-0.31,0.74]
Subtotal (95% CI)	**8**	**11**		**16.43%**	**0.22[-0.22,0.66]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.93); I^2=0%					
Test for overall effect: Z=1(P=0.32)					
21.20.2 Enteral nutrition					
Calvey 1985	6/21	1/9		22.68%	0.17[-0.11,0.46]
Kearns 1992	5/10	3/7		14.82%	0.07[-0.41,0.55]
Subtotal (95% CI)	**31**	**16**		**37.5%**	**0.13[-0.12,0.39]**
Total events: 11 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.15, df=1(P=0.7); I^2=0%					
Test for overall effect: Z=1.03(P=0.3)					



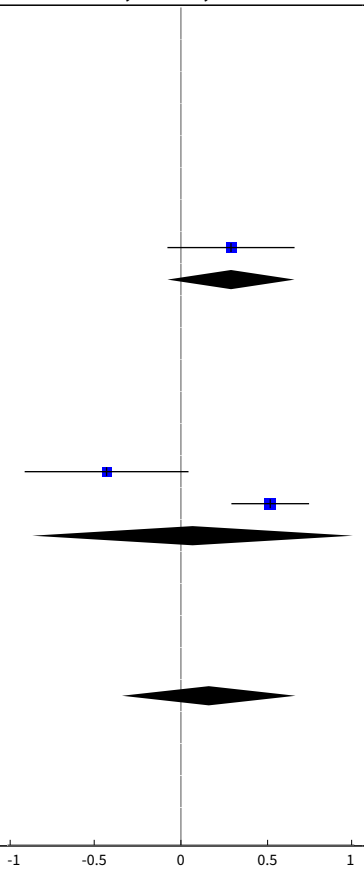


Analysis 21.21. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 21 Abstracts excluded - standard amino acids.



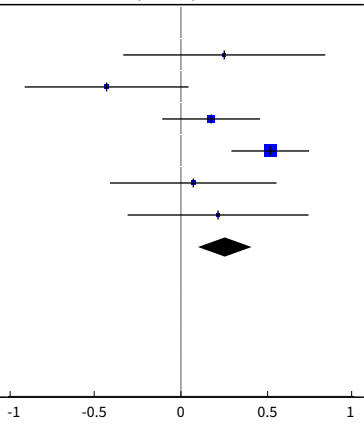
Analysis 21.22. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 22 Abstracts excluded - BCAAs.

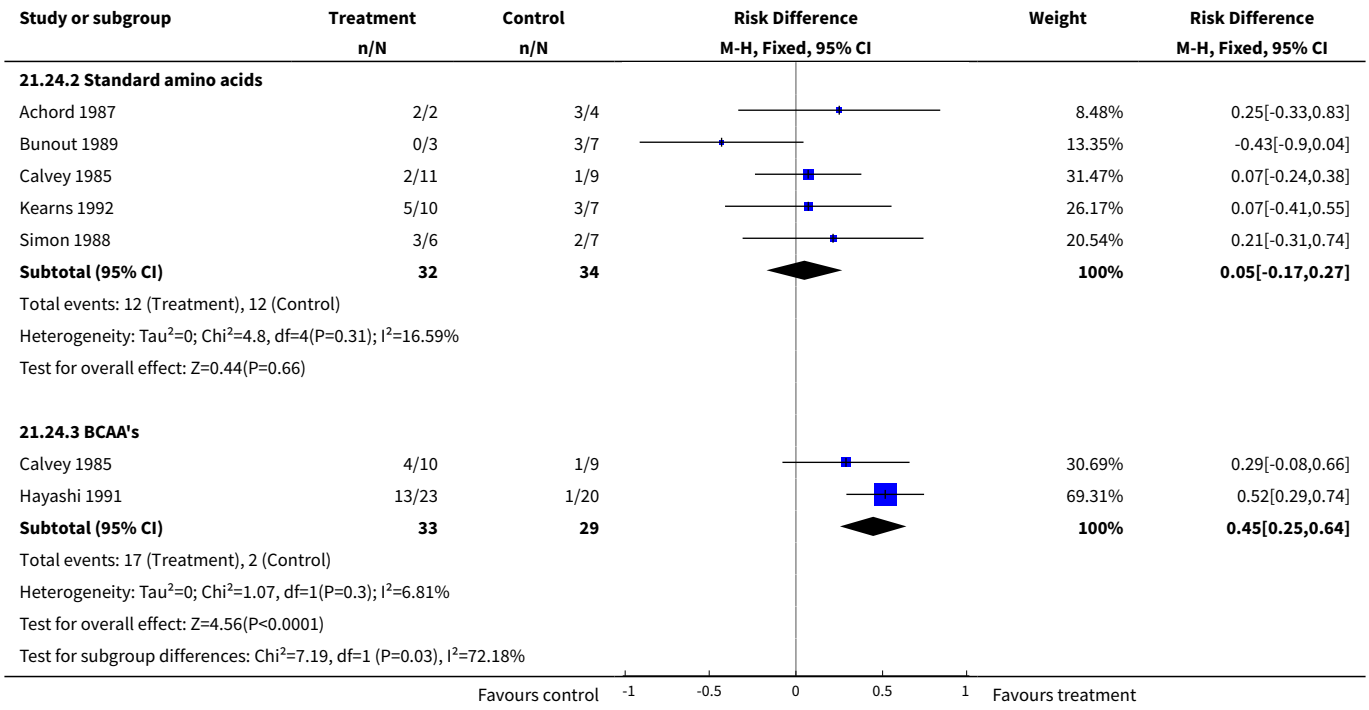
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
21.22.1 Parenteral nutrition					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
21.22.2 Enteral nutrition					
Calvey 1985	4/10	1/9		33.11%	0.29[-0.08,0.66]
Subtotal (95% CI)	**10**	**9**		**33.11%**	**0.29[-0.08,0.66]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					
21.22.3 Supplements					
Bunout 1989	0/3	3/7		29.63%	-0.43[-0.9,0.04]
Hayashi 1991	13/23	1/20		37.25%	0.52[0.29,0.74]
Subtotal (95% CI)	**26**	**27**		**66.89%**	**0.07[-0.86,0.99]**
Total events: 13 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0.41; Chi^2=12.55, df=1(P=0); I^2=92.03%					
Test for overall effect: Z=0.14(P=0.89)					
Total (95% CI)	**36**	**36**		**100%**	**0.16[-0.34,0.66]**
Total events: 17 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0.16; Chi^2=12.59, df=2(P=0); I^2=84.12%					
Test for overall effect: Z=0.63(P=0.53)					
Test for subgroup differences: Chi^2=0.19, df=1 (P=0.66), I^2=0%					



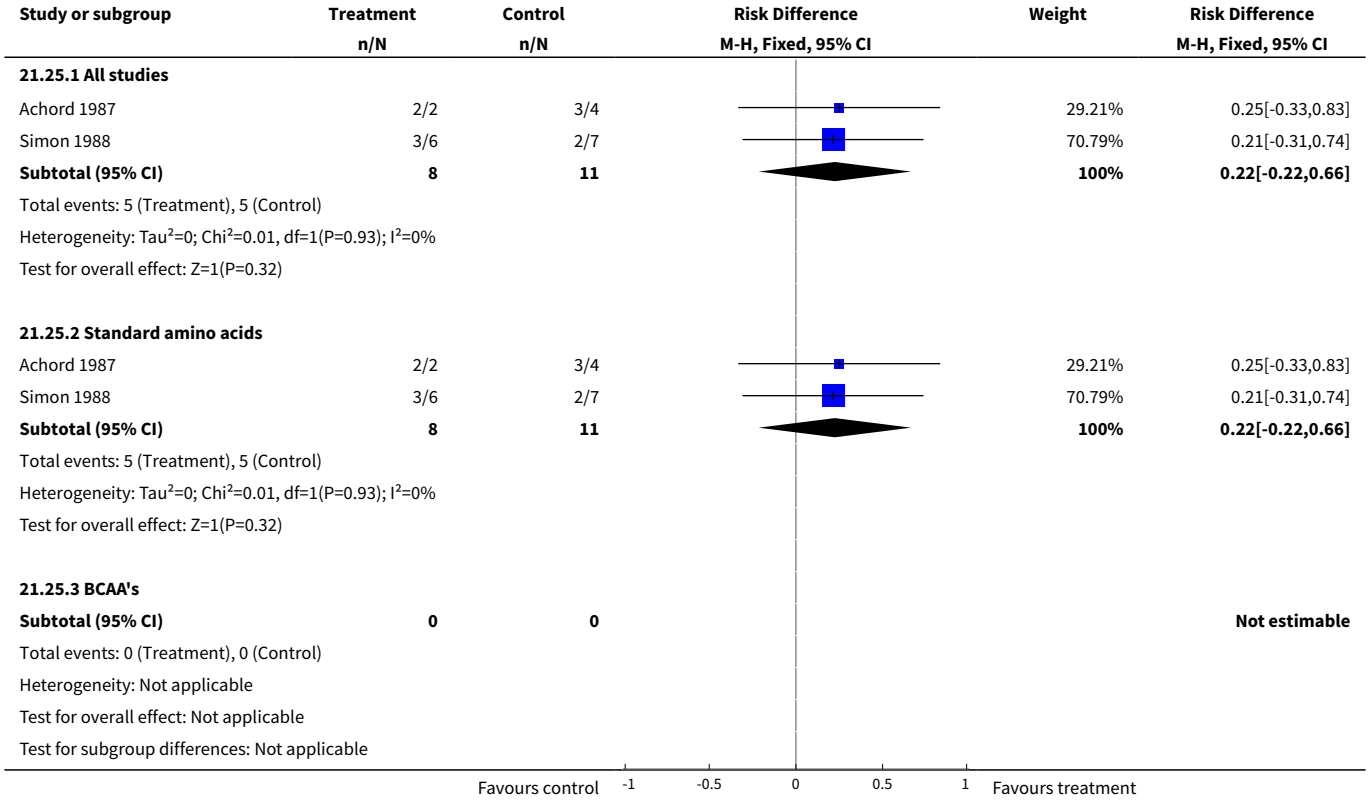
Analysis 21.24. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 24 ITT - All trials - best case scenario - no changes made because all patients reported.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.24.1 All studies					
Achord 1987	2/2	3/4		4.8%	0.25[-0.33,0.83]
Bunout 1989	0/3	3/7		7.56%	-0.43[-0.9,0.04]
Calvey 1985	6/21	1/9		22.68%	0.17[-0.11,0.46]
Hayashi 1991	13/23	1/20		38.51%	0.52[0.29,0.74]
Kearns 1992	5/10	3/7		14.82%	0.07[-0.41,0.55]
Simon 1988	3/6	2/7		11.63%	0.21[-0.31,0.74]
Subtotal (95% CI)	**65**	**54**		**100%**	**0.25[0.1,0.41]**
Total events: 29 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=14.13, df=5(P=0.01); I^2=64.61%					
Test for overall effect: Z=3.21(P=0)					





Analysis 21.25. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 25 ITT - Parenteral nutrition trials - best-case scenario - no changes made because all patients reported.

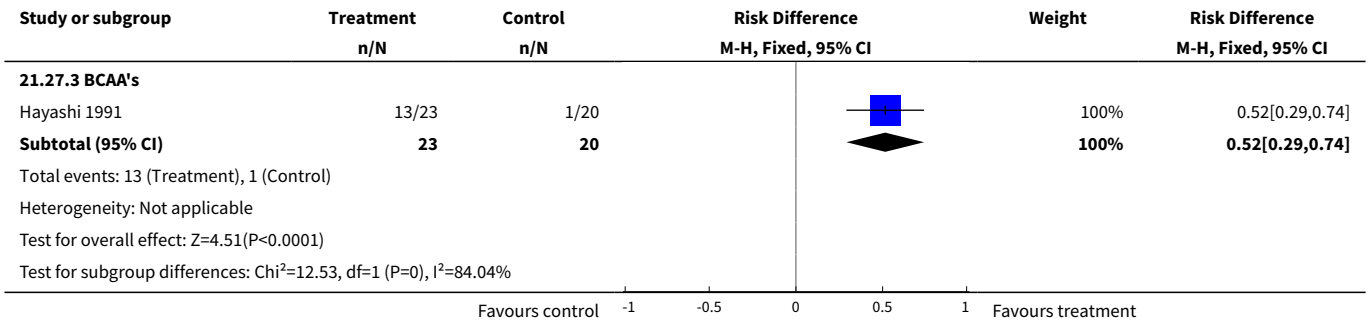


Analysis 21.26. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 26 ITT - Enteral nutrition trials - best-case scenario - no changes made because all patients reported.

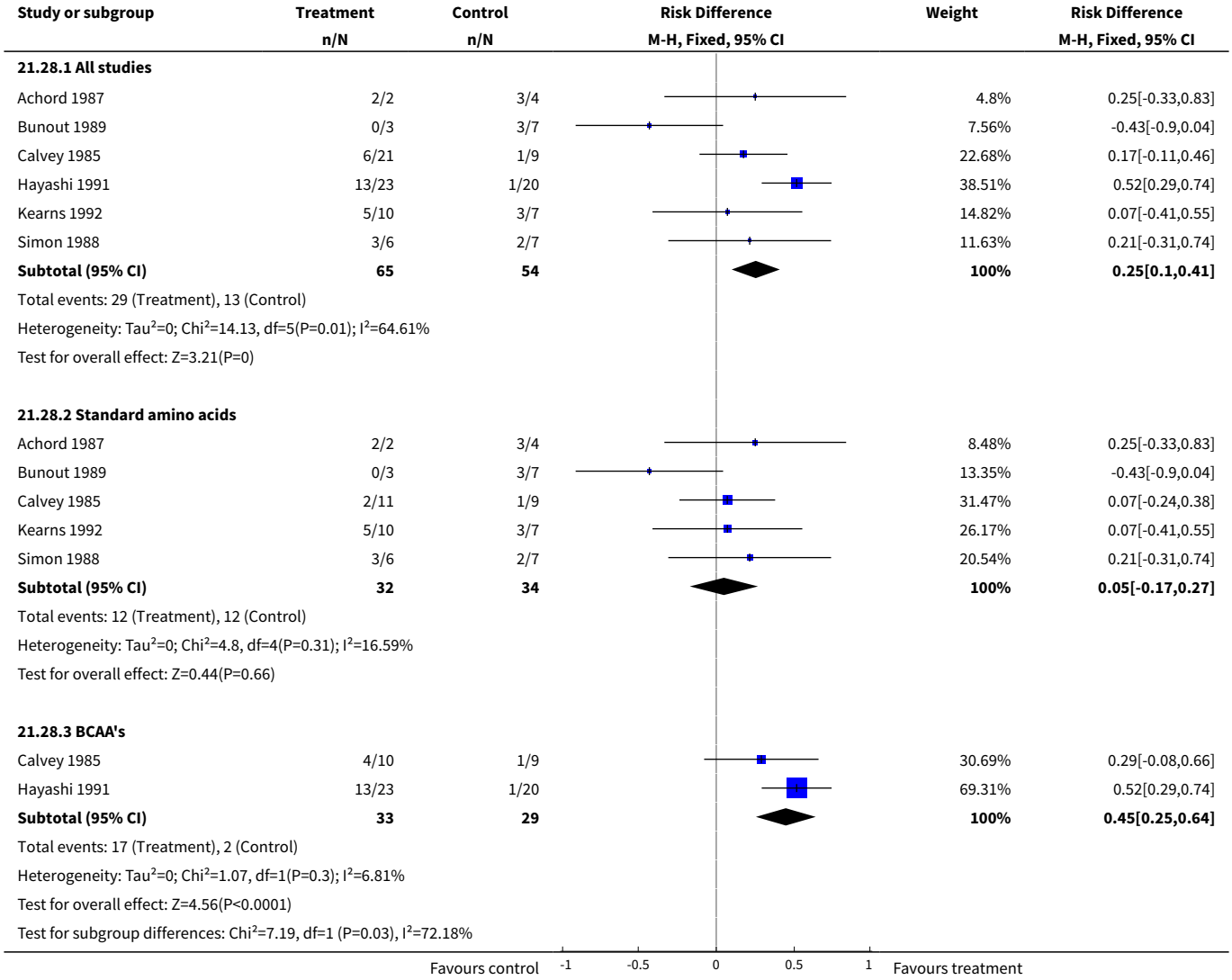
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.26.1 All studies					
Calvey 1985	6/21	1/9		60.47%	0.17[-0.11,0.46]
Kearns 1992	5/10	3/7		39.53%	0.07[-0.41,0.55]
Subtotal (95% CI)	**31**	**16**		**100%**	**0.13[-0.12,0.39]**
Total events: 11 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.15, df=1(P=0.7); I^2=0%					
Test for overall effect: Z=1.03(P=0.3)					
21.26.2 Standard amino acids					
Calvey 1985	2/11	1/9		54.59%	0.07[-0.24,0.38]
Kearns 1992	5/10	3/7		45.41%	0.07[-0.41,0.55]
Subtotal (95% CI)	**21**	**16**		**100%**	**0.07[-0.2,0.35]**
Total events: 7 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%					
Test for overall effect: Z=0.51(P=0.61)					
21.26.3 BCAA's					
Calvey 1985	4/10	1/9		100%	0.29[-0.08,0.66]
Subtotal (95% CI)	**10**	**9**		**100%**	**0.29[-0.08,0.66]**
Total events: 4 (Treatment), 1 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					
Test for subgroup differences: Chi^2=0.88, df=1 (P=0.65), I^2=0%					

Analysis 21.27. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 27 ITT - Supplement trials - best-case scenario - no changes made because all patients reported.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.27.1 All studies					
Bunout 1989	0/3	3/7		16.41%	-0.43[-0.9,0.04]
Hayashi 1991	13/23	1/20		83.59%	0.52[0.29,0.74]
Subtotal (95% CI)	**26**	**27**		**100%**	**0.36[0.15,0.57]**
Total events: 13 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=12.55, df=1(P=0); I^2=92.03%					
Test for overall effect: Z=3.34(P=0)					
21.27.2 Standard amino acids					
Bunout 1989	0/3	3/7		100%	-0.43[-0.9,0.04]
Subtotal (95% CI)	**3**	**7**		**100%**	**-0.43[-0.9,0.04]**
Total events: 0 (Treatment), 3 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.78(P=0.08)					

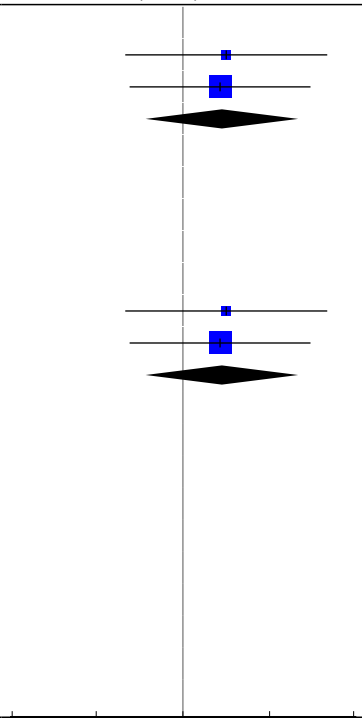


Analysis 21.28. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 28 ITT - All trials - worst-case scenario - no changes made because all patients reported.



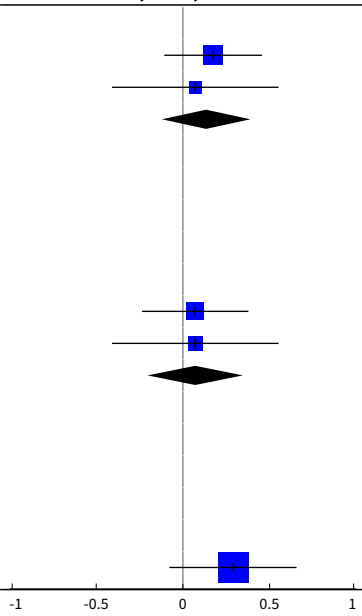
Analysis 21.29. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 29 ITT - Parenteral nutrition trials - worst-case scenario - no changes made because all patients reported.

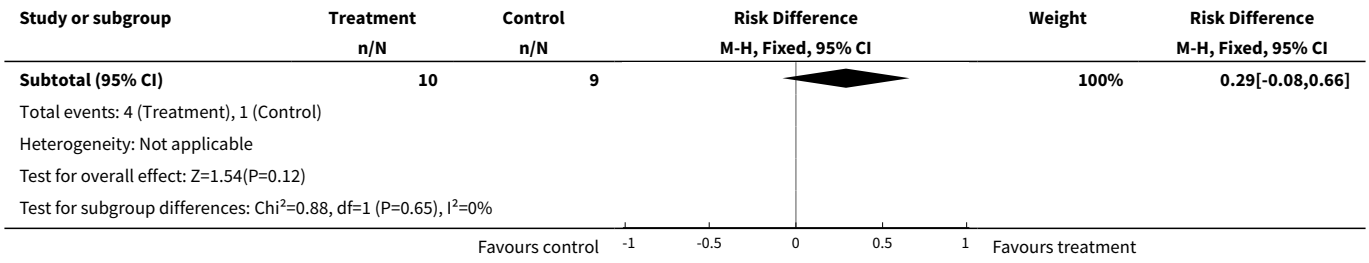
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.29.1 All studies					
Achord 1987	2/2	3/4		29.21%	0.25[-0.33,0.83]
Simon 1988	3/6	2/7		70.79%	0.21[-0.31,0.74]
Subtotal (95% CI)	**8**	**11**		**100%**	**0.22[-0.22,0.66]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.93); I^2=0%					
Test for overall effect: Z=1(P=0.32)					
21.29.2 Standard amino acids					
Achord 1987	2/2	3/4		29.21%	0.25[-0.33,0.83]
Simon 1988	3/6	2/7		70.79%	0.21[-0.31,0.74]
Subtotal (95% CI)	**8**	**11**		**100%**	**0.22[-0.22,0.66]**
Total events: 5 (Treatment), 5 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.93); I^2=0%					
Test for overall effect: Z=1(P=0.32)					
21.29.3 BCAA's					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					



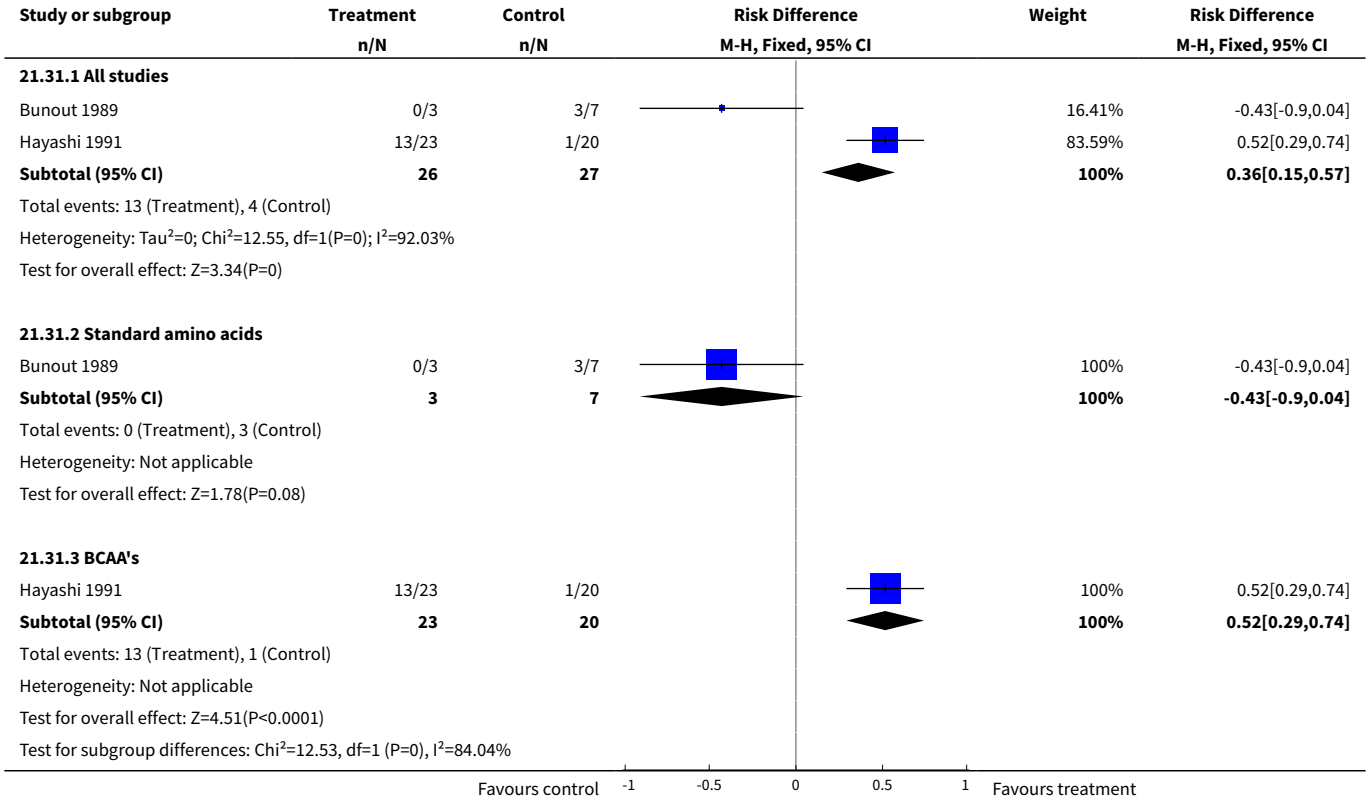
Analysis 21.30. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 30 ITT - Enteral nutrition trials - worst-case scenario - no changes made because all patients reported.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
21.30.1 All studies					
Calvey 1985	6/21	1/9		60.47%	0.17[-0.11,0.46]
Kearns 1992	5/10	3/7		39.53%	0.07[-0.41,0.55]
Subtotal (95% CI)	**31**	**16**		**100%**	**0.13[-0.12,0.39]**
Total events: 11 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.15, df=1(P=0.7); I^2=0%					
Test for overall effect: Z=1.03(P=0.3)					
21.30.2 Standard amino acids					
Calvey 1985	2/11	1/9		54.59%	0.07[-0.24,0.38]
Kearns 1992	5/10	3/7		45.41%	0.07[-0.41,0.55]
Subtotal (95% CI)	**21**	**16**		**100%**	**0.07[-0.2,0.35]**
Total events: 7 (Treatment), 4 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%					
Test for overall effect: Z=0.51(P=0.61)					
21.30.3 BCAA's					
Calvey 1985	4/10	1/9		100%	0.29[-0.08,0.66]





Analysis 21.31. Comparison 21 Resolution of encephalopathy - absolute risk difference (ARD), Outcome 31 ITT - Supplement trials - worst-case scenario - no changes made because all patients reported.



Comparison 22. Infections - absolute risk difference (ARD)

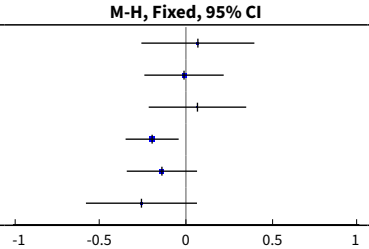
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All studies	15	793	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.13, -0.02]
2 Trials with total numbers (Meng) excluded	14	749	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.14, -0.03]
3 Parenteral nutrition	2	164	Risk Difference (M-H, Fixed, 95% CI)	-0.10 [-0.22, 0.03]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Medical trials	1	40	Risk Difference (M-H, Fixed, 95% CI)	0.2 [0.01, 0.39]
3.2 Surgical trials	1	124	Risk Difference (M-H, Fixed, 95% CI)	-0.19 [-0.35, -0.04]
4 Enteral nutrition	6	267	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.19, 0.03]
4.1 Medical trials	4	176	Risk Difference (M-H, Fixed, 95% CI)	-0.03 [-0.16, 0.11]
4.2 Surgical trials	2	91	Risk Difference (M-H, Fixed, 95% CI)	-0.18 [-0.35, -0.01]
5 Supplements	7	362	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.14, 0.00]
5.1 Medical trials	4	268	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.15, -0.00]
5.2 Surgical trials	3	94	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.21, 0.13]
6 Medical trials	9	484	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.10, 0.03]
7 Surgical trials	6	309	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.24, -0.05]
8 Alcoholic hepatitis	2	115	Risk Difference (M-H, Fixed, 95% CI)	-0.14 [-0.30, 0.02]
9 Cirrhosis	7	336	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.13, 0.04]
9.1 Parenteral nutrition	1	40	Risk Difference (M-H, Fixed, 95% CI)	0.2 [0.01, 0.39]
9.2 Enteral nutrition	3	112	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.20, 0.13]
9.3 Supplements	3	184	Risk Difference (M-H, Fixed, 95% CI)	-0.10 [-0.21, 0.00]
10 HCC	2	208	Risk Difference (M-H, Fixed, 95% CI)	-0.13 [-0.22, -0.03]
10.1 Parenteral nutrition	1	124	Risk Difference (M-H, Fixed, 95% CI)	-0.19 [-0.35, -0.04]
10.2 Enteral nutrition	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.3 Supplements	1	84	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.09, 0.04]
11 Abstracts excluded	14	738	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.13, -0.02]
12 Abstracts excluded	14	738	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.13, -0.02]
12.1 Parenteral nutrition	2	164	Risk Difference (M-H, Fixed, 95% CI)	-0.10 [-0.22, 0.03]
12.2 Enteral nutrition	5	212	Risk Difference (M-H, Fixed, 95% CI)	-0.06 [-0.18, 0.05]
12.3 Supplements	7	362	Risk Difference (M-H, Fixed, 95% CI)	-0.07 [-0.14, 0.00]
13 Surgical trials excluding transplants	5	278	Risk Difference (M-H, Fixed, 95% CI)	-0.13 [-0.23, -0.03]
14 Parenteral nutrition - best-case scenario	2	190	Risk Difference (M-H, Fixed, 95% CI)	-0.23 [-0.35, -0.11]

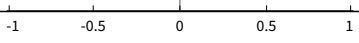
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Medical trials	1	40	Risk Difference (M-H, Fixed, 95% CI)	0.2 [0.01, 0.39]
14.2 Surgical trials	1	150	Risk Difference (M-H, Fixed, 95% CI)	-0.35 [-0.49, -0.21]
15 Parenteral nutrition - worst-case scenario	2	190	Risk Difference (M-H, Fixed, 95% CI)	0.04 [-0.08, 0.16]
15.1 Medical trials	1	40	Risk Difference (M-H, Fixed, 95% CI)	0.2 [0.01, 0.39]
15.2 Surgical trials	1	150	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.15, 0.15]
16 Enteral nutrition - best-case scenario	6	298	Risk Difference (M-H, Fixed, 95% CI)	-0.17 [-0.27, -0.07]
16.1 Medical trials	4	184	Risk Difference (M-H, Fixed, 95% CI)	-0.08 [-0.21, 0.06]
16.2 Surgical trials	2	114	Risk Difference (M-H, Fixed, 95% CI)	-0.32 [-0.46, -0.17]
17 Enteral nutrition - worst-case scenario	6	298	Risk Difference (M-H, Fixed, 95% CI)	0.04 [-0.06, 0.15]
17.1 Medical trials	4	184	Risk Difference (M-H, Fixed, 95% CI)	0.01 [-0.12, 0.15]
17.2 Surgical trials	2	114	Risk Difference (M-H, Fixed, 95% CI)	0.09 [-0.08, 0.26]
18 Supplements - best-case scenario	7	401	Risk Difference (M-H, Fixed, 95% CI)	-0.16 [-0.23, -0.10]
18.1 Medical trials	4	286	Risk Difference (M-H, Fixed, 95% CI)	-0.13 [-0.21, -0.06]
18.2 Surgical trials	3	115	Risk Difference (M-H, Fixed, 95% CI)	-0.24 [-0.40, -0.09]
19 Supplements - worst-case scenario	7	401	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.05, 0.10]
19.1 Medical trials	4	286	Risk Difference (M-H, Fixed, 95% CI)	-0.00 [-0.08, 0.07]
19.2 Surgical trials	3	115	Risk Difference (M-H, Fixed, 95% CI)	0.09 [-0.06, 0.25]

Analysis 22.1. Comparison 22 Infections - absolute risk difference (ARD), Outcome 1 All studies.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		4.47%	0.07[-0.26,0.39]
Calvey 1985	11/42	6/22		7.43%	-0.01[-0.24,0.22]
DeLedinghen 1997	2/12	1/10		2.81%	0.07[-0.21,0.35]
Fan 1994	11/64	22/60		15.93%	-0.19[-0.35,-0.04]
Foschi 1986	4/28	9/32		7.68%	-0.14[-0.34,0.06]
Hasse 1995	3/14	8/17		3.95%	-0.26[-0.58,0.06]



Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Hirsch 1993	2/26	9/25		6.56%	-0.28[-0.5,-0.07]
Ishikawa 2010	2/11	3/13		3.07%	-0.05[-0.37,0.27]
Meng 1999	8/21	9/23		5.65%	-0.01[-0.3,0.28]
Mikagi 2011	0/13	1/13		3.34%	-0.08[-0.27,0.11]
Nakaya 2007	0/19	0/19		4.89%	0[-0.1,0.1]
Naveau 1986	4/20	0/20		5.14%	0.2[0.01,0.39]
Norman 2008	16/26	22/29		7.05%	-0.14[-0.39,0.1]
Poon 2004	0/41	1/43		10.8%	-0.02[-0.09,0.04]
Sievert 1999	10/61	7/34		11.23%	-0.04[-0.21,0.12]
Total (95% CI)	**414**	**379**		**100%**	**-0.08[-0.13,-0.02]**
Total events: 80 (Treatment), 105 (Control)					
Heterogeneity: Tau^2=0; Chi^2=23.99, df=14(P=0.05); I^2=41.64%					
Test for overall effect: Z=2.8(P=0.01)					

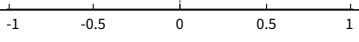


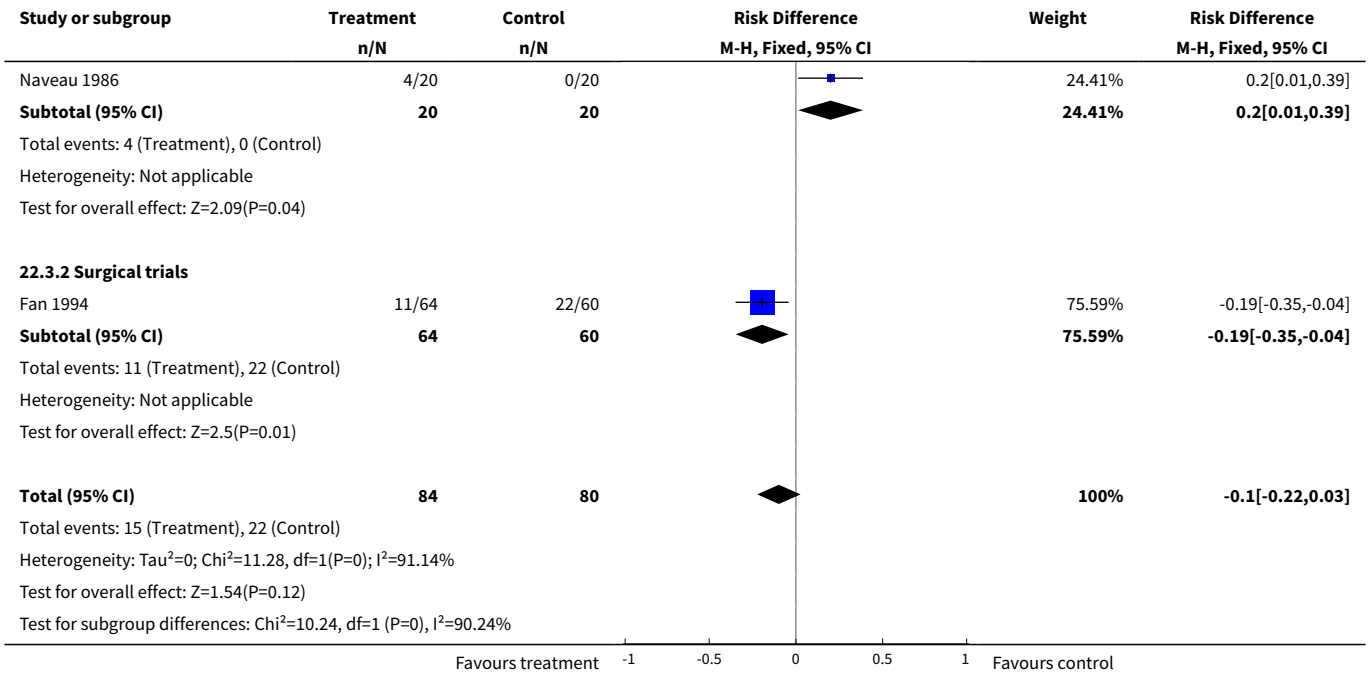
Analysis 22.2. Comparison 22 Infections - absolute risk difference (ARD), Outcome 2 Trials with total numbers (Meng) excluded.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		4.74%	0.07[-0.26,0.39]
Calvey 1985	11/42	6/22		7.87%	-0.01[-0.24,0.22]
DeLedinghen 1997	2/12	1/10		2.97%	0.07[-0.21,0.35]
Fan 1994	11/64	22/60		16.89%	-0.19[-0.35,-0.04]
Foschi 1986	4/28	9/32		8.14%	-0.14[-0.34,0.06]
Hasse 1995	3/14	8/17		4.19%	-0.26[-0.58,0.06]
Hirsch 1993	2/26	9/25		6.95%	-0.28[-0.5,-0.07]
Ishikawa 2010	2/11	3/13		3.25%	-0.05[-0.37,0.27]
Mikagi 2011	0/13	1/13		3.54%	-0.08[-0.27,0.11]
Nakaya 2007	0/19	0/19		5.18%	0[-0.1,0.1]
Naveau 1986	4/20	0/20		5.45%	0.2[0.01,0.39]
Norman 2008	16/26	22/29		7.48%	-0.14[-0.39,0.1]
Poon 2004	0/41	1/43		11.44%	-0.02[-0.09,0.04]
Sievert 1999	10/61	7/34		11.9%	-0.04[-0.21,0.12]
Total (95% CI)	**393**	**356**		**100%**	**-0.08[-0.14,-0.03]**
Total events: 72 (Treatment), 96 (Control)					
Heterogeneity: Tau^2=0; Chi^2=24.51, df=13(P=0.03); I^2=46.96%					
Test for overall effect: Z=2.91(P=0)					

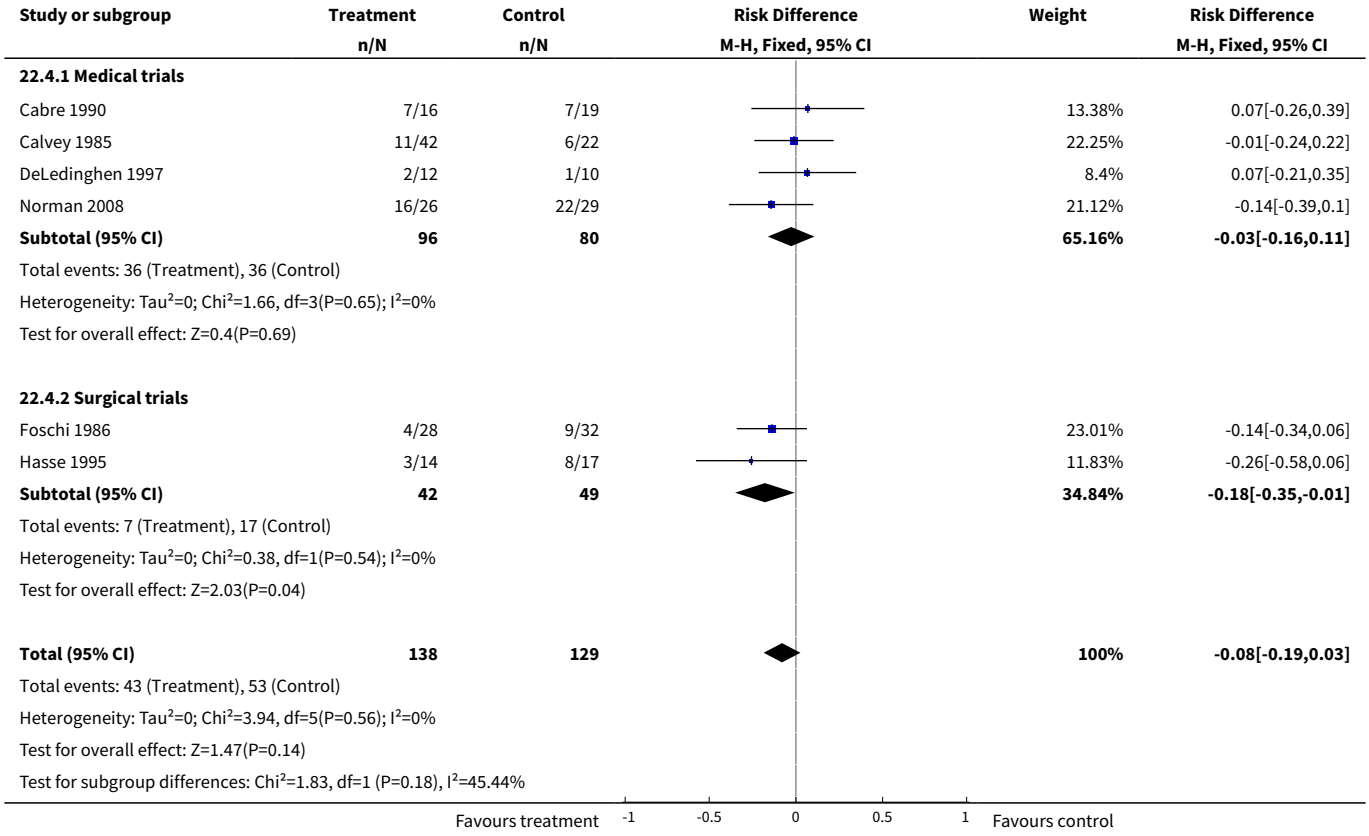
Analysis 22.3. Comparison 22 Infections - absolute risk difference (ARD), Outcome 3 Parenteral nutrition.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
22.3.1 Medical trials					



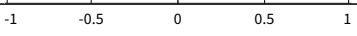


Analysis 22.4. Comparison 22 Infections - absolute risk difference (ARD), Outcome 4 Enteral nutrition.



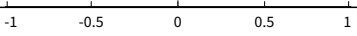
Analysis 22.5. Comparison 22 Infections - absolute risk difference (ARD), Outcome 5 Supplements.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
22.5.1 Medical trials					
Hirsch 1993	2/26	9/25		14.4%	-0.28[-0.5,-0.07]
Nakaya 2007	0/19	0/19		10.73%	0[-0.1,0.1]
Poon 2004	0/41	1/43		23.72%	-0.02[-0.09,0.04]
Sievert 1999	10/61	7/34		24.67%	-0.04[-0.21,0.12]
Subtotal (95% CI)	**147**	**121**		**73.52%**	**-0.08[-0.15,-0]**
Total events: 12 (Treatment), 17 (Control)					
Heterogeneity: Tau^2=0; Chi^2=8.97, df=3(P=0.03); I^2=66.57%					
Test for overall effect: Z=2.04(P=0.04)					
22.5.2 Surgical trials					
Ishikawa 2010	2/11	3/13		6.73%	-0.05[-0.37,0.27]
Meng 1999	8/21	9/23		12.4%	-0.01[-0.3,0.28]
Mikagi 2011	0/13	1/13		7.34%	-0.08[-0.27,0.11]
Subtotal (95% CI)	**45**	**49**		**26.48%**	**-0.04[-0.21,0.13]**
Total events: 10 (Treatment), 13 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.2, df=2(P=0.91); I^2=0%					
Test for overall effect: Z=0.45(P=0.65)					
Total (95% CI)	**192**	**170**		**100%**	**-0.07[-0.14,0]**
Total events: 22 (Treatment), 30 (Control)					
Heterogeneity: Tau^2=0; Chi^2=7.85, df=6(P=0.25); I^2=23.61%					
Test for overall effect: Z=1.87(P=0.06)					
Test for subgroup differences: Chi^2=0.17, df=1 (P=0.68), I^2=0%					



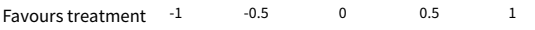
Analysis 22.6. Comparison 22 Infections - absolute risk difference (ARD), Outcome 6 Medical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		7.4%	0.07[-0.26,0.39]
Calvey 1985	11/42	6/22		12.3%	-0.01[-0.24,0.22]
DeLedinghen 1997	2/12	1/10		4.65%	0.07[-0.21,0.35]
Hirsch 1993	2/26	9/25		10.86%	-0.28[-0.5,-0.07]
Nakaya 2007	0/19	0/19		8.1%	0[-0.1,0.1]
Naveau 1986	4/20	0/20		8.52%	0.2[0.01,0.39]
Norman 2008	16/26	22/29		11.68%	-0.14[-0.39,0.1]
Poon 2004	0/41	1/43		17.88%	-0.02[-0.09,0.04]
Sievert 1999	10/61	7/34		18.6%	-0.04[-0.21,0.12]
Total (95% CI)	**263**	**221**		**100%**	**-0.04[-0.1,0.03]**
Total events: 52 (Treatment), 53 (Control)					
Heterogeneity: Tau^2=0; Chi^2=13.58, df=8(P=0.09); I^2=41.09%					
Test for overall effect: Z=1.06(P=0.29)					



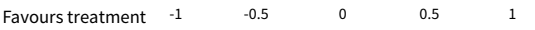
Analysis 22.7. Comparison 22 Infections - absolute risk difference (ARD), Outcome 7 Surgical trials.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Fan 1994	11/64	22/60		40.21%	-0.19[-0.35,-0.04]
Foschi 1986	4/28	9/32		19.39%	-0.14[-0.34,0.06]
Hasse 1995	3/14	8/17		9.97%	-0.26[-0.58,0.06]
Ishikawa 2010	2/11	3/13		7.74%	-0.05[-0.37,0.27]
Meng 1999	8/21	9/23		14.25%	-0.01[-0.3,0.28]
Mikagi 2011	0/13	1/13		8.44%	-0.08[-0.27,0.11]
Total (95% CI)	**151**	**158**		**100%**	**-0.14[-0.24,-0.05]**
Total events: 28 (Treatment), 52 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.53, df=5(P=0.77); I^2=0%					
Test for overall effect: Z=2.95(P=0)					



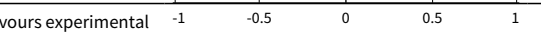
Analysis 22.8. Comparison 22 Infections - absolute risk difference (ARD), Outcome 8 Alcoholic hepatitis.

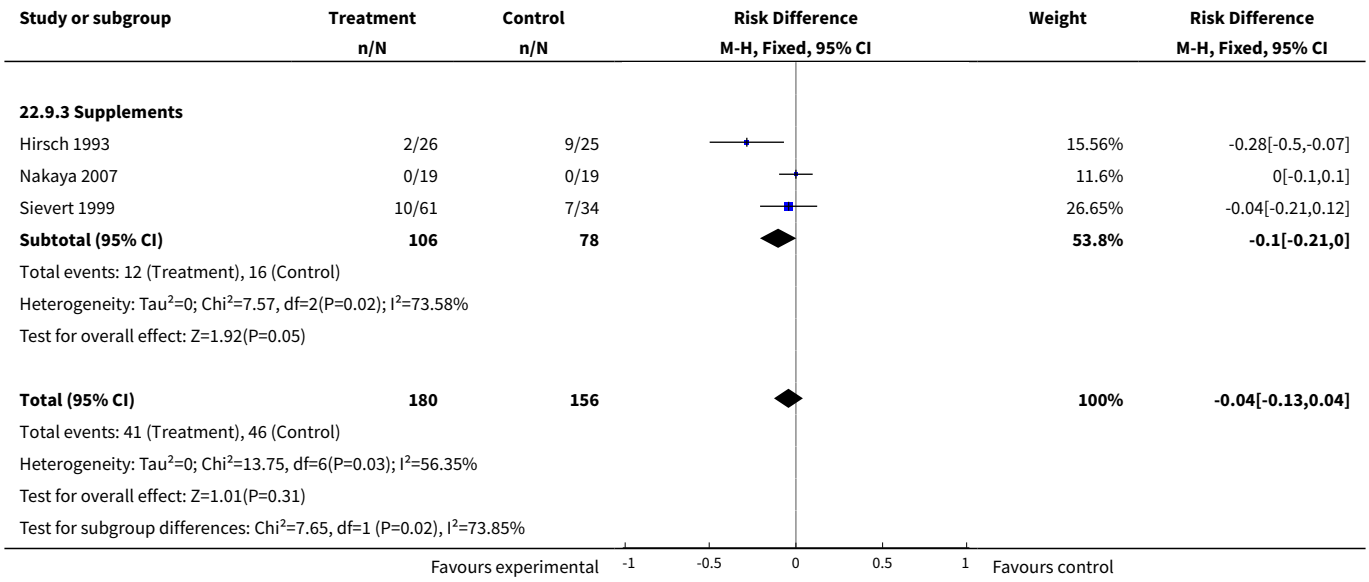
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Calvey 1985	11/42	6/22		53.11%	-0.01[-0.24,0.22]
Hirsch 1993	2/26	9/25		46.89%	-0.28[-0.5,-0.07]
Total (95% CI)	**68**	**47**		**100%**	**-0.14[-0.3,0.02]**
Total events: 13 (Treatment), 15 (Control)					
Heterogeneity: Tau^2=0; Chi^2=2.95, df=1(P=0.09); I^2=66.06%					
Test for overall effect: Z=1.72(P=0.09)					



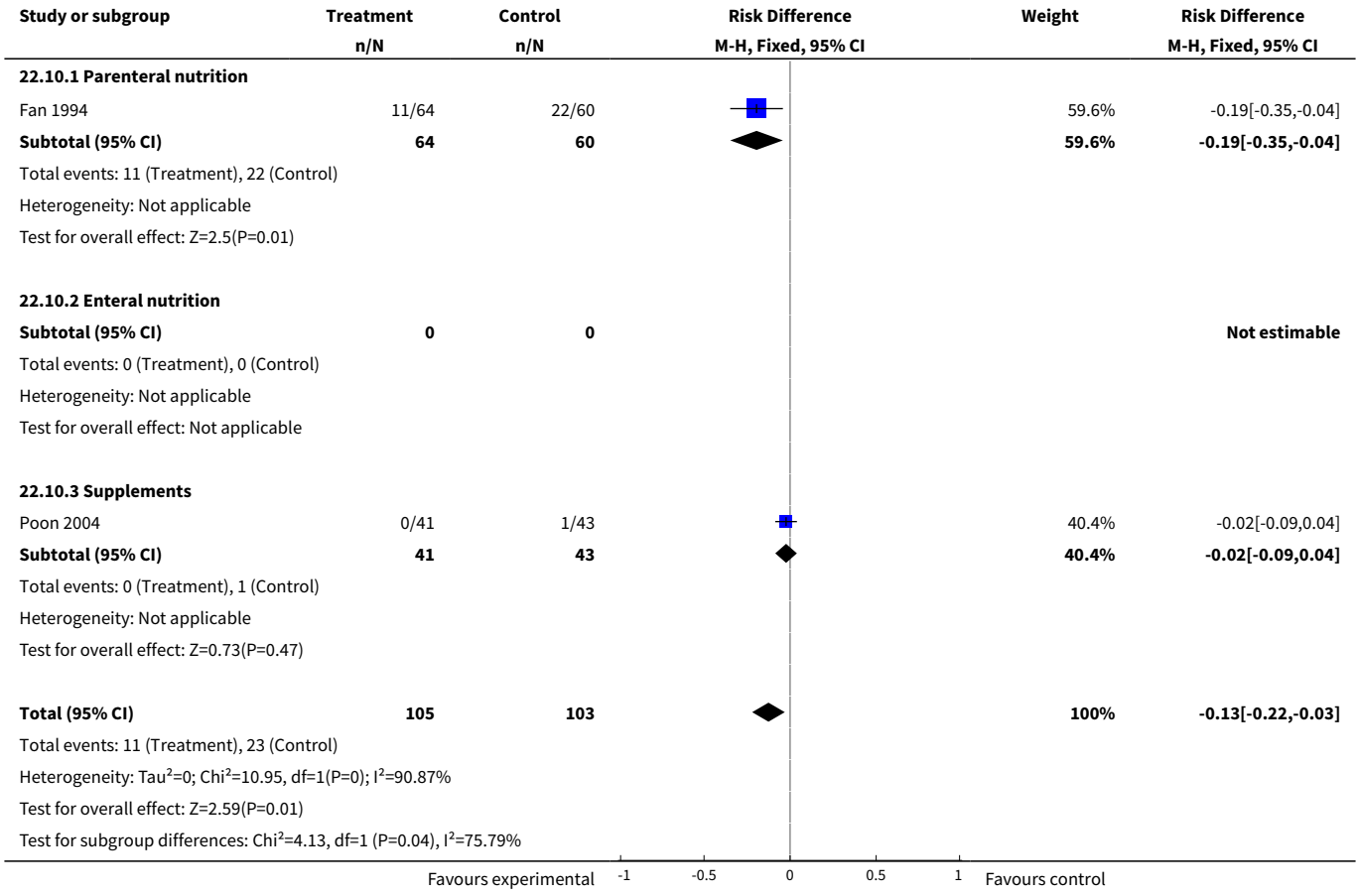
Analysis 22.9. Comparison 22 Infections - absolute risk difference (ARD), Outcome 9 Cirrhosis.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
22.9.1 Parenteral nutrition					
Naveau 1986	4/20	0/20		12.21%	0.2[0.01,0.39]
Subtotal (95% CI)	**20**	**20**		**12.21%**	**0.2[0.01,0.39]**
Total events: 4 (Treatment), 0 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.09(P=0.04)					
22.9.2 Enteral nutrition					
Cabre 1990	7/16	7/19		10.6%	0.07[-0.26,0.39]
DeLedinghen 1997	2/12	1/10		6.66%	0.07[-0.21,0.35]
Norman 2008	16/26	22/29		16.73%	-0.14[-0.39,0.1]
Subtotal (95% CI)	**54**	**58**		**33.99%**	**-0.04[-0.2,0.13]**
Total events: 25 (Treatment), 30 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.66, df=2(P=0.44); I^2=0%					
Test for overall effect: Z=0.42(P=0.67)					



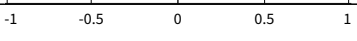


Analysis 22.10. Comparison 22 Infections - absolute risk difference (ARD), Outcome 10 HCC.



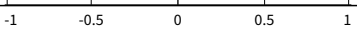
Analysis 22.11. Comparison 22 Infections - absolute risk difference (ARD), Outcome 11 Abstracts excluded.

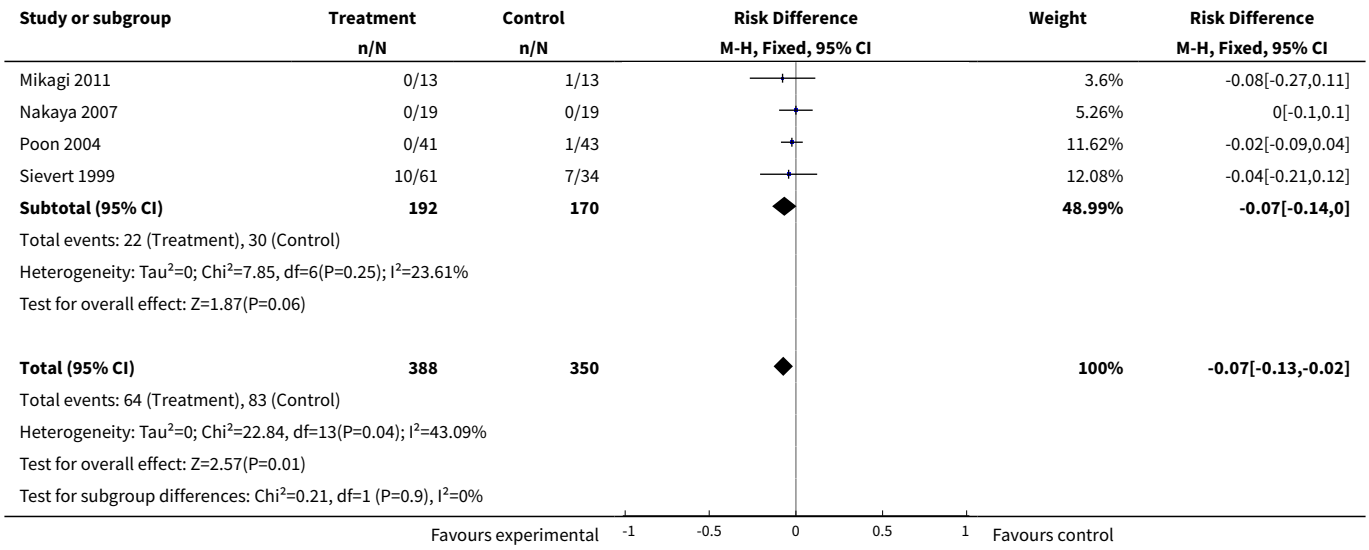
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Cabre 1990	7/16	7/19		4.81%	0.07[-0.26,0.39]
Calvey 1985	11/42	6/22		7.99%	-0.01[-0.24,0.22]
DeLedinghen 1997	2/12	1/10		3.02%	0.07[-0.21,0.35]
Fan 1994	11/64	22/60		17.14%	-0.19[-0.35,-0.04]
Foschi 1986	4/28	9/32		8.27%	-0.14[-0.34,0.06]
Hasse 1995	3/14	8/17		4.25%	-0.26[-0.58,0.06]
Hirsch 1993	2/26	9/25		7.05%	-0.28[-0.5,-0.07]
Ishikawa 2010	2/11	3/13		3.3%	-0.05[-0.37,0.27]
Meng 1999	8/21	9/23		6.08%	-0.01[-0.3,0.28]
Mikagi 2011	0/13	1/13		3.6%	-0.08[-0.27,0.11]
Nakaya 2007	0/19	0/19		5.26%	0[-0.1,0.1]
Naveau 1986	4/20	0/20		5.54%	0.2[0.01,0.39]
Poon 2004	0/41	1/43		11.62%	-0.02[-0.09,0.04]
Sievert 1999	10/61	7/34		12.08%	-0.04[-0.21,0.12]
Total (95% CI)	**388**	**350**		**100%**	**-0.07[-0.13,-0.02]**
Total events: 64 (Treatment), 83 (Control)					
Heterogeneity: Tau^2=0; Chi^2=22.84, df=13(P=0.04); I^2=43.09%					
Test for overall effect: Z=2.57(P=0.01)					



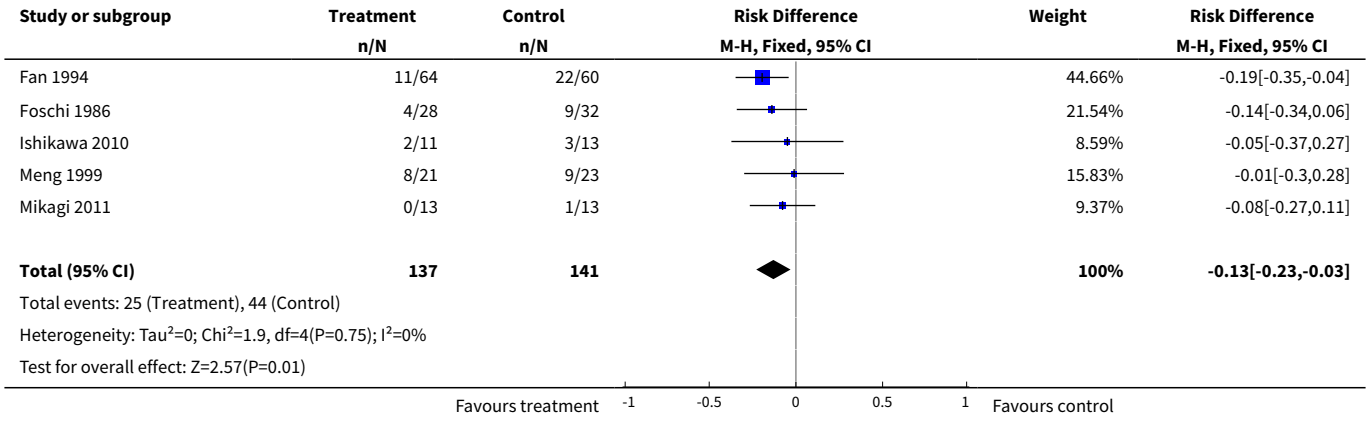
Analysis 22.12. Comparison 22 Infections - absolute risk difference (ARD), Outcome 12 Abstracts excluded.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
22.12.1 Parenteral nutrition					
Fan 1994	11/64	22/60		17.14%	-0.19[-0.35,-0.04]
Naveau 1986	4/20	0/20		5.54%	0.2[0.01,0.39]
Subtotal (95% CI)	**84**	**80**		**22.68%**	**-0.1[-0.22,0.03]**
Total events: 15 (Treatment), 22 (Control)					
Heterogeneity: Tau^2=0; Chi^2=11.28, df=1(P=0); I^2=91.14%					
Test for overall effect: Z=1.54(P=0.12)					
22.12.2 Enteral nutrition					
Cabre 1990	7/16	7/19		4.81%	0.07[-0.26,0.39]
Calvey 1985	11/42	6/22		7.99%	-0.01[-0.24,0.22]
DeLedinghen 1997	2/12	1/10		3.02%	0.07[-0.21,0.35]
Foschi 1986	4/28	9/32		8.27%	-0.14[-0.34,0.06]
Hasse 1995	3/14	8/17		4.25%	-0.26[-0.58,0.06]
Subtotal (95% CI)	**112**	**100**		**28.33%**	**-0.06[-0.18,0.05]**
Total events: 27 (Treatment), 31 (Control)					
Heterogeneity: Tau^2=0; Chi^2=3.58, df=4(P=0.47); I^2=0%					
Test for overall effect: Z=1.05(P=0.29)					
22.12.3 Supplements					
Hirsch 1993	2/26	9/25		7.05%	-0.28[-0.5,-0.07]
Ishikawa 2010	2/11	3/13		3.3%	-0.05[-0.37,0.27]
Meng 1999	8/21	9/23		6.08%	-0.01[-0.3,0.28]

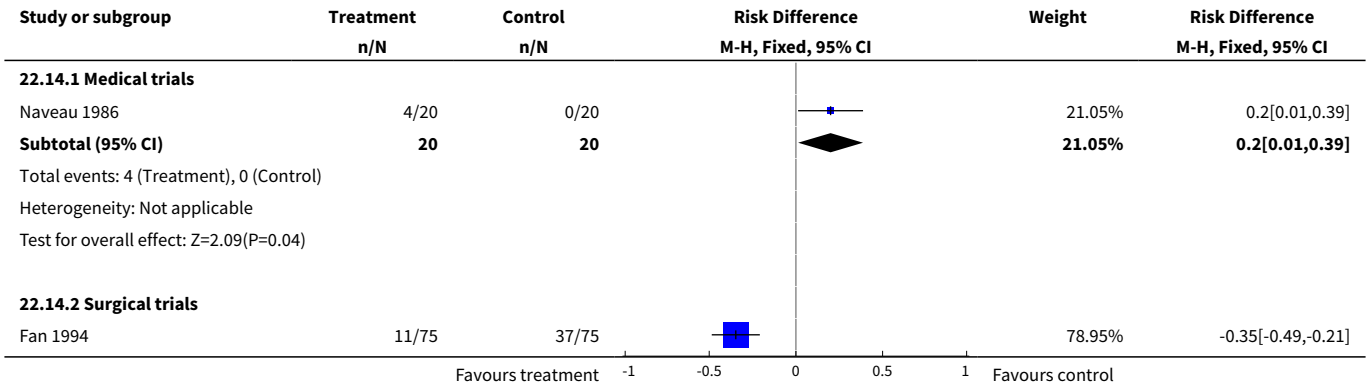


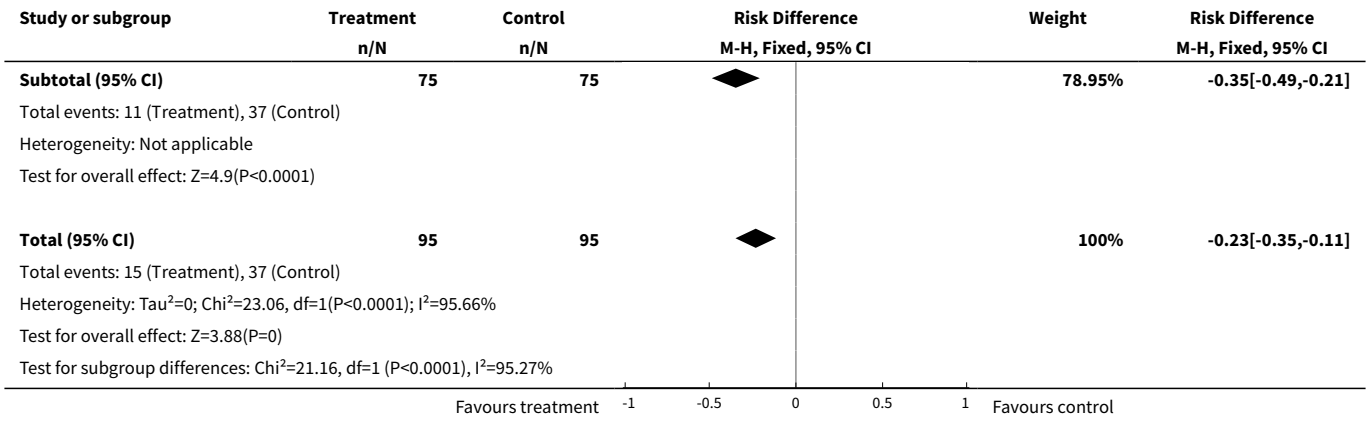


Analysis 22.13. Comparison 22 Infections - absolute risk difference (ARD), Outcome 13 Surgical trials excluding transplants.

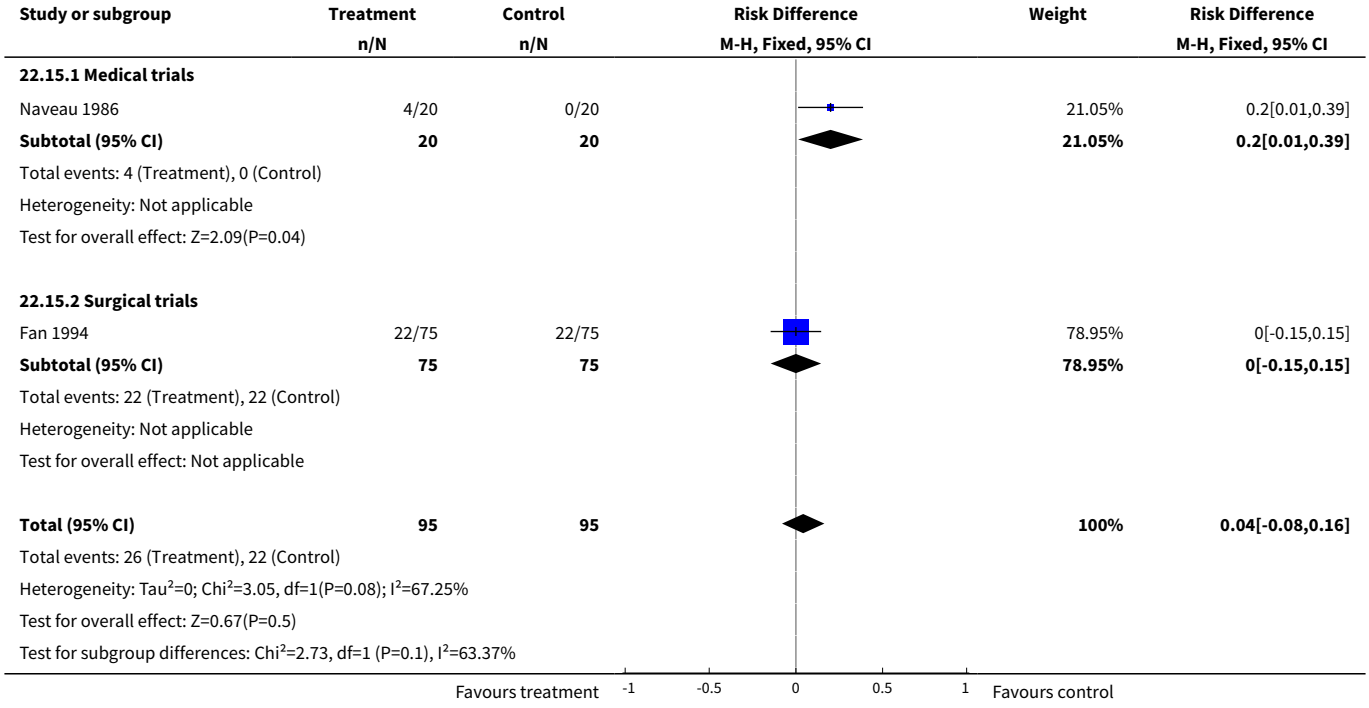


Analysis 22.14. Comparison 22 Infections - absolute risk difference (ARD), Outcome 14 Parenteral nutrition - best-case scenario.

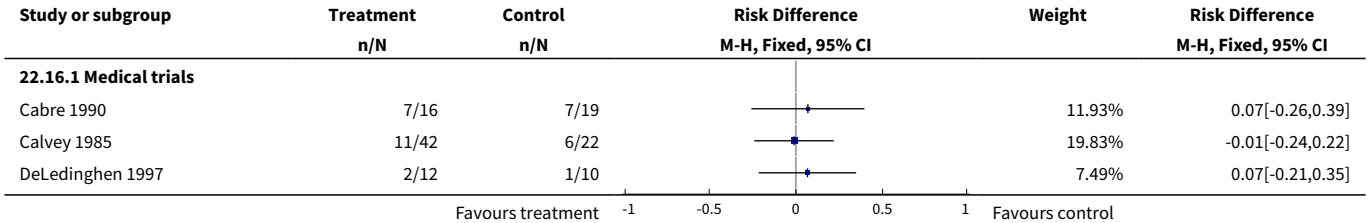


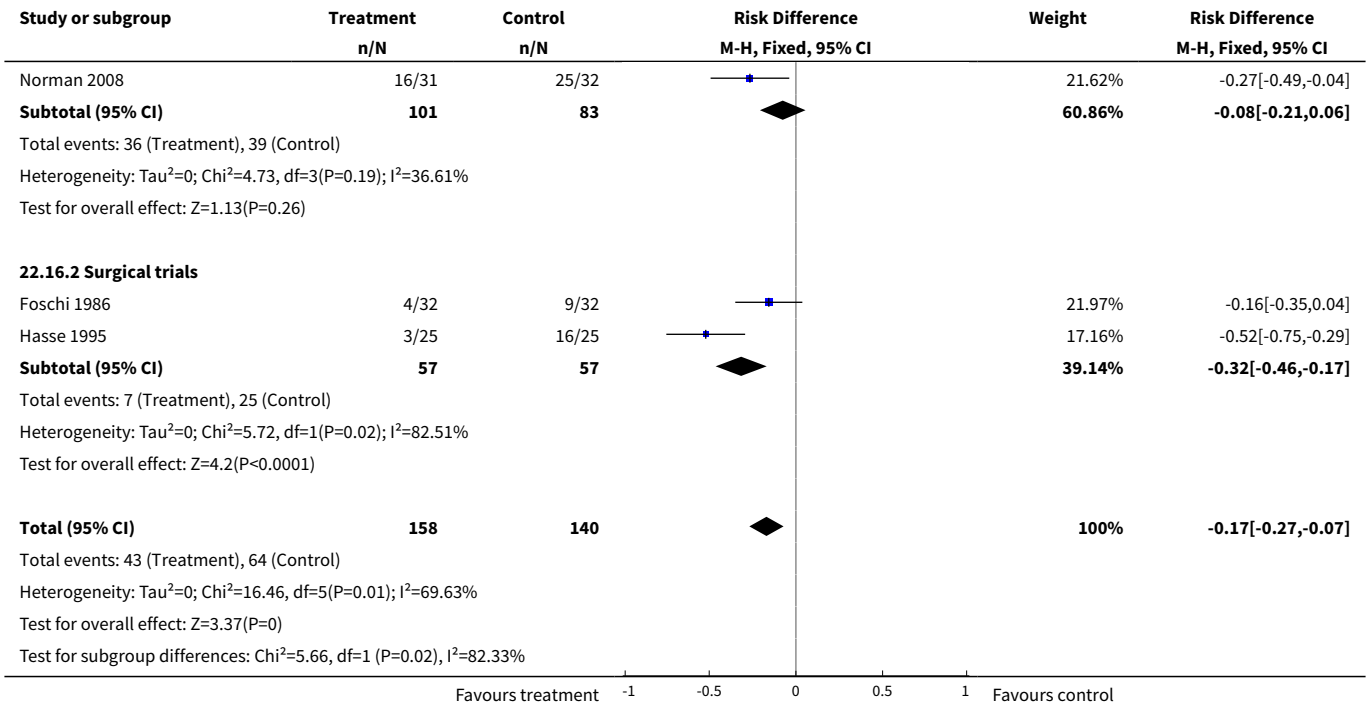


Analysis 22.15. Comparison 22 Infections - absolute risk difference (ARD), Outcome 15 Parenteral nutrition - worst-case scenario.

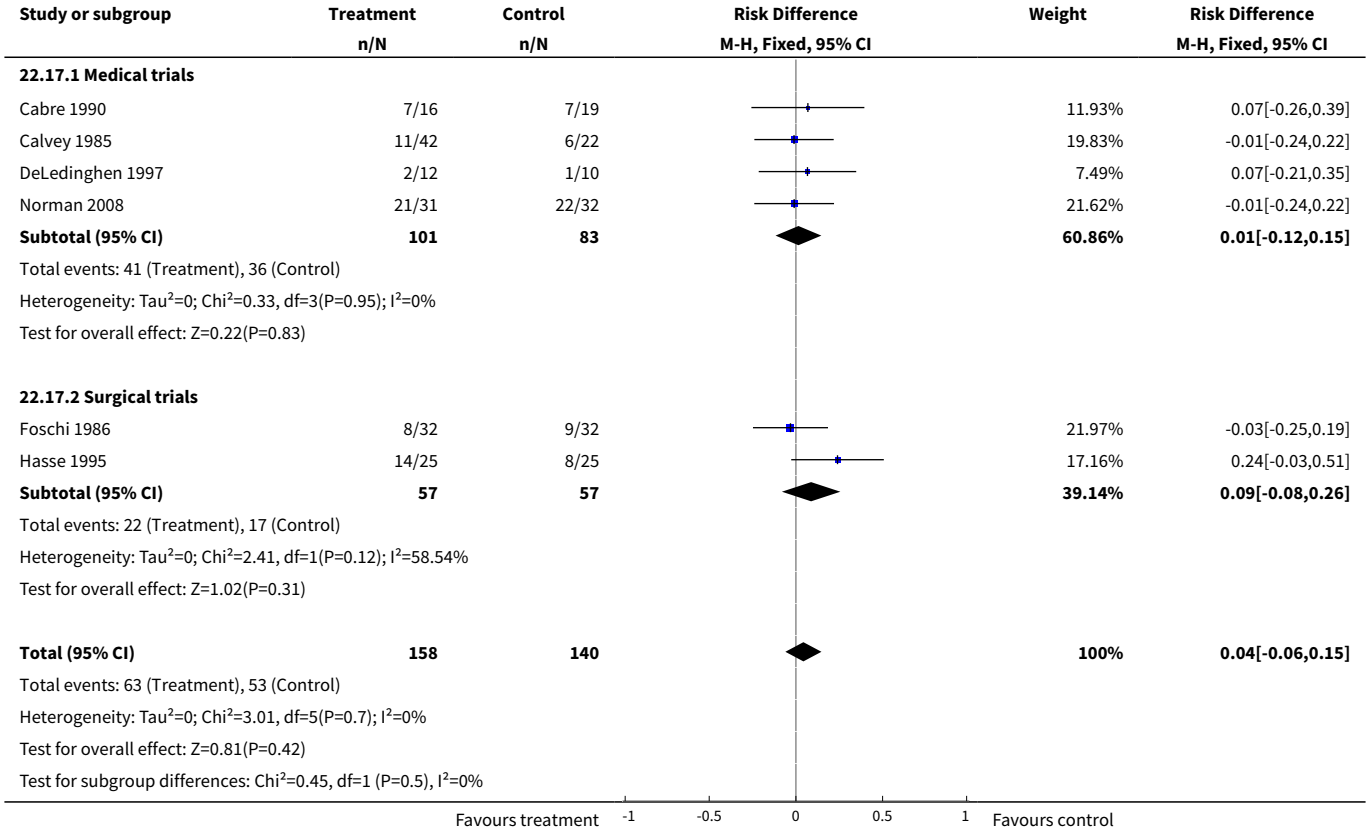


Analysis 22.16. Comparison 22 Infections - absolute risk difference (ARD), Outcome 16 Enteral nutrition - best-case scenario.



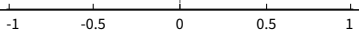


Analysis 22.17. Comparison 22 Infections - absolute risk difference (ARD), Outcome 17 Enteral nutrition - worst-case scenario.



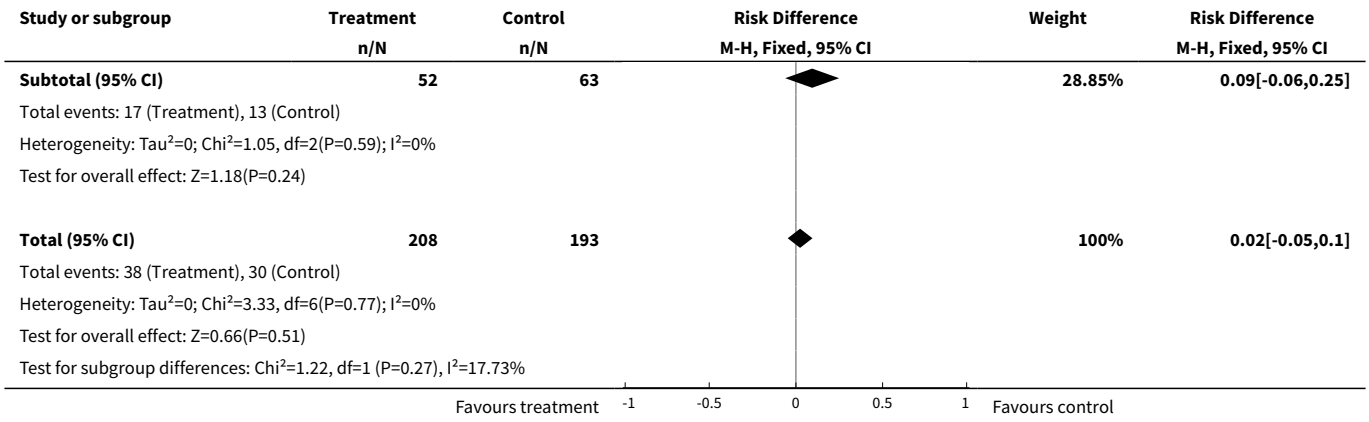
Analysis 22.18. Comparison 22 Infections - absolute risk difference (ARD), Outcome 18 Supplements - best-case scenario.

Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
22.18.1 Medical trials					
Hirsch 1993	2/32	17/33		16.61%	-0.45[-0.64,-0.26]
Nakaya 2007	0/19	0/19		9.71%	0[-0.1,0.1]
Poon 2004	0/44	2/44		22.5%	-0.05[-0.12,0.03]
Sievert 1999	10/61	7/34		22.32%	-0.04[-0.21,0.12]
Subtotal (95% CI)	**156**	**130**		**71.15%**	**-0.13[-0.21,-0.06]**
Total events: 12 (Treatment), 26 (Control)					
Heterogeneity: Tau^2=0; Chi^2=24.78, df=3(P<0.0001); I^2=87.89%					
Test for overall effect: Z=3.55(P=0)					
22.18.2 Surgical trials					
Ishikawa 2010	2/11	3/13		6.09%	-0.05[-0.37,0.27]
Meng 1999	8/25	11/25		12.78%	-0.12[-0.39,0.15]
Mikagi 2011	0/16	13/25		9.98%	-0.52[-0.73,-0.31]
Subtotal (95% CI)	**52**	**63**		**28.85%**	**-0.24[-0.4,-0.09]**
Total events: 10 (Treatment), 27 (Control)					
Heterogeneity: Tau^2=0; Chi^2=9, df=2(P=0.01); I^2=77.77%					
Test for overall effect: Z=3.05(P=0)					
Total (95% CI)	**208**	**193**		**100%**	**-0.16[-0.23,-0.1]**
Total events: 22 (Treatment), 53 (Control)					
Heterogeneity: Tau^2=0; Chi^2=44.03, df=6(P<0.0001); I^2=86.37%					
Test for overall effect: Z=4.69(P<0.0001)					
Test for subgroup differences: Chi^2=1.56, df=1 (P=0.21), I^2=35.99%					



Analysis 22.19. Comparison 22 Infections - absolute risk difference (ARD), Outcome 19 Supplements - worst-case scenario.

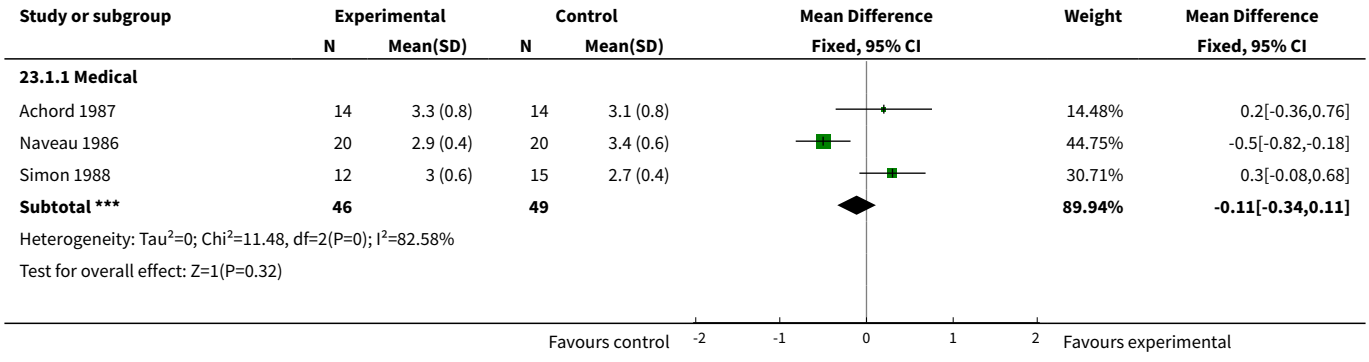
Study or subgroup	Treatment n/N	Control n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
22.19.1 Medical trials					
Hirsch 1993	8/32	9/33		16.61%	-0.02[-0.24,0.19]
Nakaya 2007	0/19	0/19		9.71%	0[-0.1,0.1]
Poon 2004	3/44	1/44		22.5%	0.05[-0.04,0.13]
Sievert 1999	10/61	7/34		22.32%	-0.04[-0.21,0.12]
Subtotal (95% CI)	**156**	**130**		**71.15%**	**-0[-0.08,0.07]**
Total events: 21 (Treatment), 17 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.5, df=3(P=0.68); I^2=0%					
Test for overall effect: Z=0.1(P=0.92)					
22.19.2 Surgical trials					
Ishikawa 2010	2/11	3/13		6.09%	-0.05[-0.37,0.27]
Meng 1999	12/25	9/25		12.78%	0.12[-0.15,0.39]
Mikagi 2011	3/16	1/25		9.98%	0.15[-0.06,0.35]

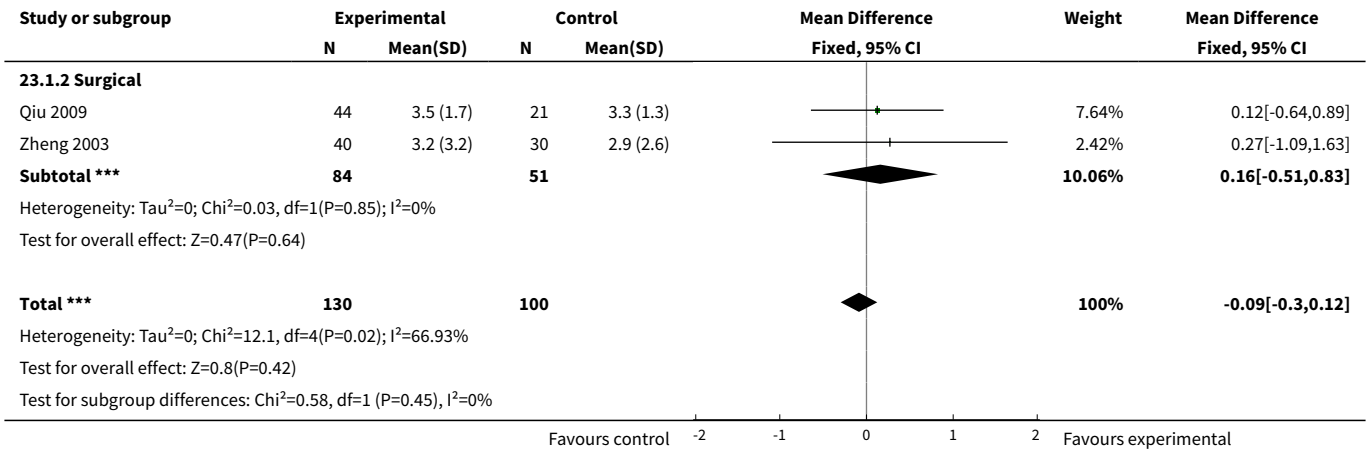


Comparison 23. Serum albumin

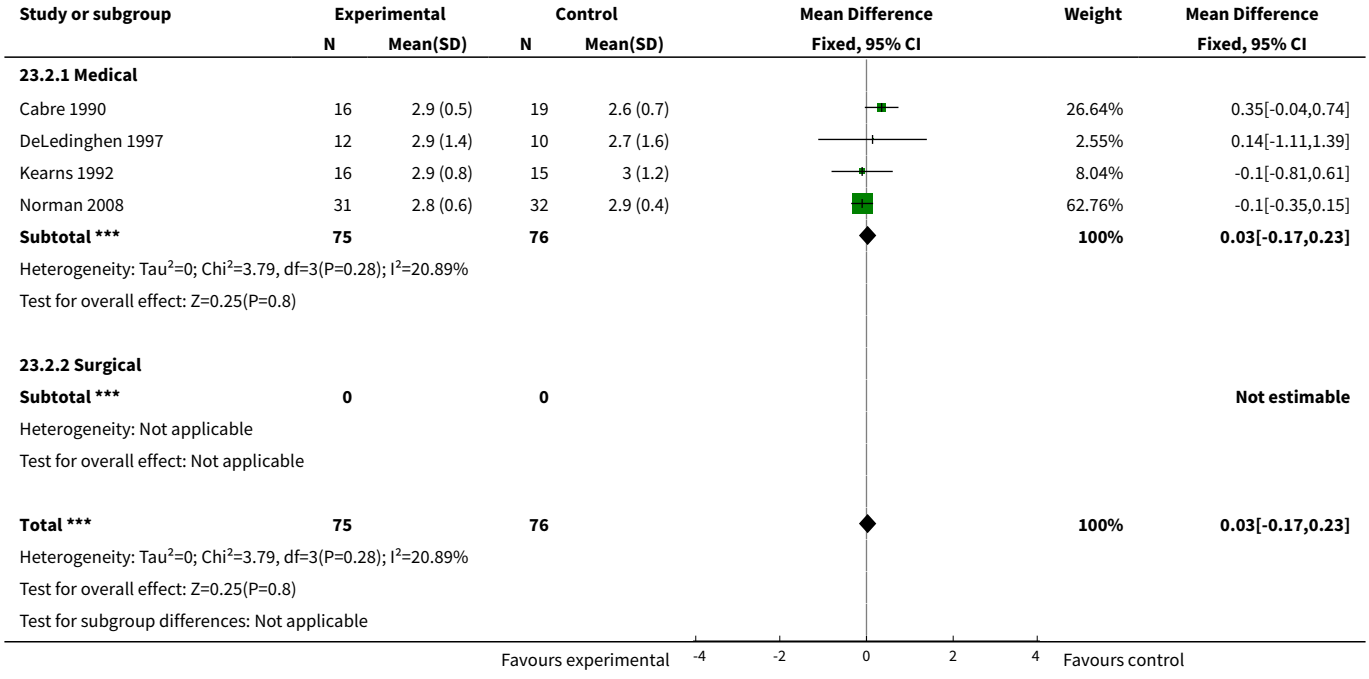
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parenteral nutrition	5	230	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.30, 0.12]
1.1 Medical	3	95	Mean Difference (IV, Fixed, 95% CI)	-0.11 [-0.34, 0.11]
1.2 Surgical	2	135	Mean Difference (IV, Fixed, 95% CI)	0.16 [-0.51, 0.83]
2 Enteral nutrition	4	151	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.17, 0.23]
2.1 Medical	4	151	Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.17, 0.23]
2.2 Surgical	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Supplements	9	477	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.18, 0.00]
3.1 Medical	9	477	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.18, 0.00]
3.2 Surgical	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 23.1. Comparison 23 Serum albumin, Outcome 1 Parenteral nutrition.

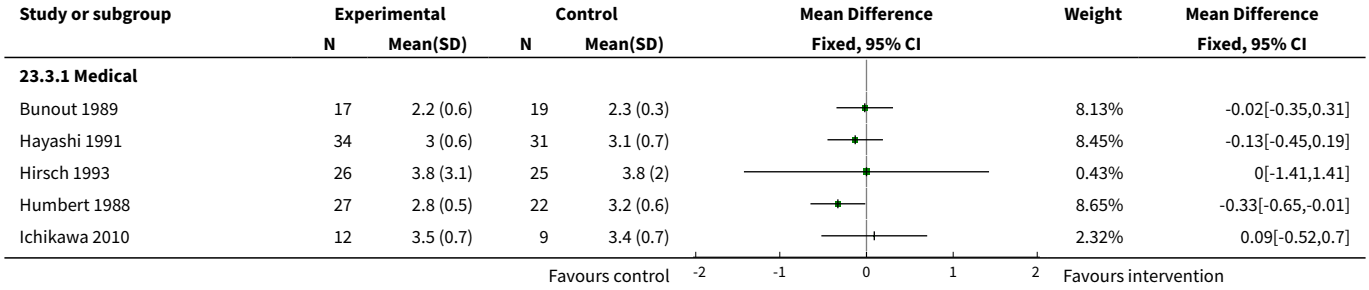


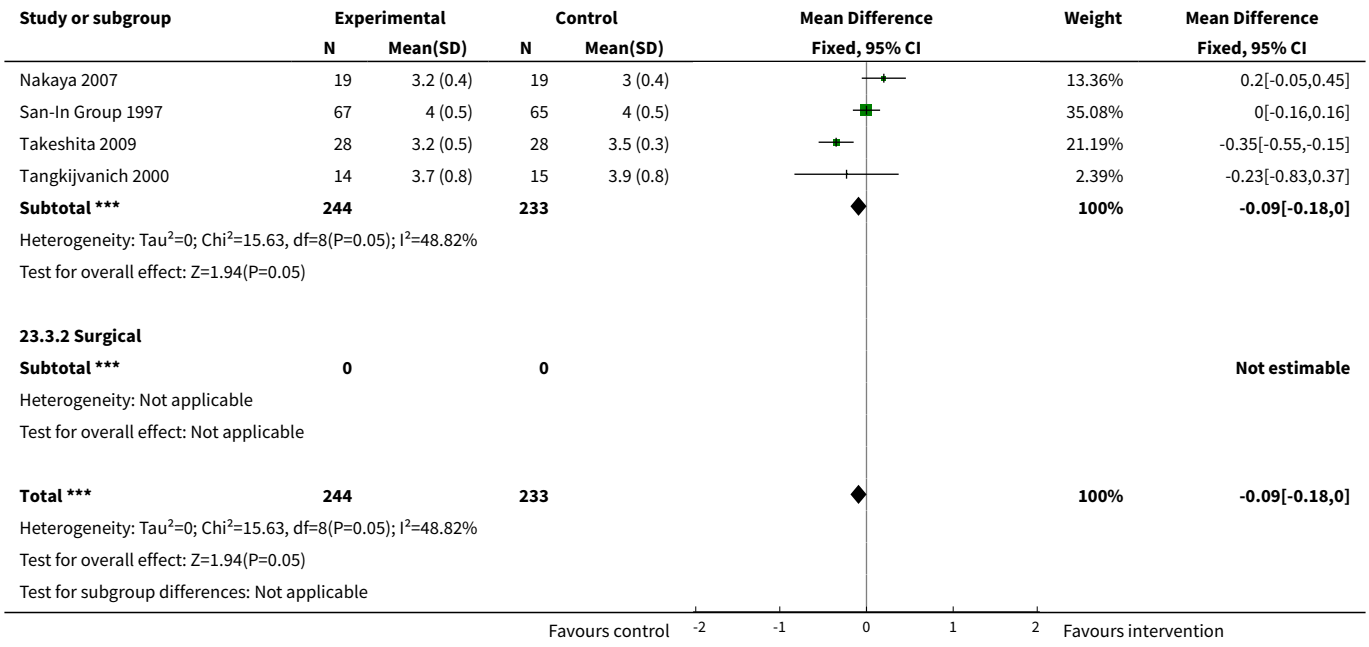


Analysis 23.2. Comparison 23 Serum albumin, Outcome 2 Enteral nutrition.



Analysis 23.3. Comparison 23 Serum albumin, Outcome 3 Supplements.





ADDITIONAL TABLES

Table 1. Details of included studies

Category of nutritional support	Category of patient	Number trials	Publication status (full papers/abstracts)	Disease states	Total number patients (range)
Parenteral nutrition	Medical	4	4/0	Alcoholic hepatitis, alcoholic cirrhosis.	170 (21 to 69)
	Surgical	5	5/0	Resectable hepatocellular carcinoma, portocaval shunt, liver transplantation, various surgeries in patients with cirrhosis.	333 (20 to 150)
Enteral nutrition	Medical	7	4/3	Malnourished cirrhotics, alcoholic hepatitis, alcoholic liver disease, stabilized variceal bleeding, awaiting transplantation in hospital, decompensated cirrhosis.	279 (22 to 64)
	Surgical	2	2/0	Obstructive jaundice, liver transplantation.	114 (50, 64)
Supplements	Medical	14	11/3	Cirrhosis (± malnutrition, encephalopathy, other evidence of decompensation), alcoholic hepatitis, hepatocellular carcinoma (unresectable or postoperative resection).	1003 (15 to 233)
	Surgical	5	5/0	Resection of hepatocellular carcinoma or a variety of benign and malignant liver tumours, liver transplantation.	285 (38 to 82)

APPENDICES

Appendix 1. Search strategies

Database	Span of Search	Search strategy
Cochrane Hepato-Biliary Group Controlled Trials Register	January 18, 2012	(alimentation OR 'branched chain amino acids' OR BCAA OR 'Dietary disorder*' OR 'Enteral nutrition' OR Enterostom* OR 'Fat emulsion' or 'formulated food*' OR Gastrostom* OR Hyperalimentation* OR 'Hypocaloric alimentation*' OR 'Hypocaloric nutrition' OR 'Intragastric feed*' OR 'Intragastric nutrition' OR Nutrition OR 'Nutrition diseases' OR 'Nutrition disorders' OR 'Nutrition supplement*' OR 'Parenteral nutrition' OR 'Percutaneous endoscopic gastrostom*' OR 'Peripheral parenteral nutrition' OR 'Permissive underfeeding' OR 'Post-pyloric feeding' OR 'Post-pyloric nutrition' OR 'Protein hydrolysate' OR 'Supplemental feed*' OR 'Total parenteral nutrition') AND ('Alcoholic liver disease*' OR Ascites OR Cirrhosis OR 'Esophageal varic*' OR Hepat* OR Liver OR Varic*)
Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*	Issue 4, 2011	#1 MeSH descriptor Feeding Methods explode all trees #2 MeSH descriptor Nutrition Therapy explode all trees #3 MeSH descriptor Enterostomy explode all trees #4 MeSH descriptor Fat Emulsions, Intravenous explode all trees #5 MeSH descriptor Food, Formulated explode all trees #6 MeSH descriptor Gastrostomy explode all trees #7 MeSH descriptor Nutrition Disorders explode all trees #8 MeSH descriptor Protein Hydrolysates explode all trees #9 alimentation OR branched chain amino acids OR BCAA OR Dietary disorder* OR Enteral nutrition OR Enterostom* OR Fat emulsion or formulated food* OR Gastrostom* OR Hyperalimentation* OR Hypocaloric alimentation* OR Hypocaloric nutrition OR Intragastric feed* OR Intragastric nutrition OR Nutrition OR Nutrition diseases OR Nutrition disorders OR Nutrition supplement* OR Parenteral nutrition OR Percutaneous endoscopic gastrostom* OR Peripheral parenteral nutrition OR Permissive underfeeding OR Post-pyloric feeding OR Post-pyloric nutrition OR Protein hydrolysate OR Supplemental feed* OR Total parenteral nutrition #10 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9) #11 MeSH descriptor Liver Diseases explode all trees #12 MeSH descriptor Fibrosisexplode all trees #13 MeSH descriptor Ascitesexplode all trees #14 MeSH descriptor Liver Transplantation explode all trees #15 MeSH descriptor Varicose Veins explode all trees #16 Alcoholic liver disease* OR Ascites OR Cirrhosis OR Esophageal varic* OR Hepat* OR Liver OR Varic* #17 (#11 OR #12 OR #13 OR #14 OR #15 OR #16) #18 (#10 AND #17)
MEDLINE (Ovid SP)	1948 to January 18, 2012	1. exp Feeding Methods/ 2. exp Nutrition Therapy/ 3. exp Enterostomy/ 4. exp Fat Emulsions, Intravenous/ 5. exp Food, Formulated/ 6. exp Gastrostomy/ 7. exp Nutrition Disorders/ 8. exp Protein Hydrolysates/ 9. (alimentation or branched chain amino acids or BCAA or Dietary disorder$ or Enteral nutrition or Enterostom$ or Fat emulsion or formulated food$ or Gastrostom$ or Hyperalimentation$ or Hypocaloric alimentation$ or Hypocaloric nutrition or Intragastric feed$ or Intragastric nutrition or Nutrition or Nutrition diseases or Nutrition disorders or Nutrition supplement$ or Parenteral nutrition or Percutaneous endoscopic gastrostom$ or Peripheral parenteral nutrition or Permissive underfeeding or Post-pyloric feeding or Post-pyloric nutrition or Protein hydrolysate or Supplemental feed$ or Total parenteral nu-

(Continued)

		trition).mp. [mp=title, original title, abstract, name of substance word, subject heading word] 10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 11. exp Liver Diseases/ 12. exp Fibrosis/ 13. exp Ascites/ 14. exp Liver Transplantation/ 15. exp Varicose Veins/ 16. (Alcoholic liver disease$ or Ascites or Cirrhosis or Esophageal varic$ or Hepat$ or Liver or Varic$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] 17. 11 or 16 or 13 or 12 or 15 or 14 18. 10 and 17 19. (random$ or blind$ or placebo$ or meta-analysis).mp. [mp=title, original title, abstract, name of substance word, subject heading word] 20. 18 and 19
EMBASE (Ovid SP)	From 1980 to January 18, 2012	1. exp Diet Therapy/ 2. exp Artificial Feeding/ 3. exp Enterostomy/ 4. exp Lipid Emulsion/ 5. exp Gastrostomy/ 6. exp Nutrition/ 7. exp Nutritional Disorder/ 8. exp Diet Supplementation/ 9. exp Percutaneous Endoscopic Gastrostomy/ 10. exp Protein Hydrolysate/ 11. (alimentation or branched chain amino acids or BCAA or Dietary disorder$ or Enteral nutrition or Enterostom$ or Fat emulsion or formulated food$ or Gastrostom$ or Hyperalimentation$ or Hypocaloric alimentation$ or Hypocaloric nutrition or Intragastric feed$ or Intragastric nutrition or Nutrition or Nutrition diseases or Nutrition disorders or Nutrition supplement$ or Parenteral nutrition or Percutaneous endoscopic gastrostom$ or Peripheral parenteral nutrition or Permissive underfeeding or Post-pyloric feeding or Post-pyloric nutrition or Protein hydrolysate or Supplemental feed$ or Total parenteral nutrition).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] 12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 13. exp Liver Disease/ 14. exp Ascites/ 15. exp Esophagus Varices/ 16. exp Hepatic Encephalopathy/ 17. exp Liver Cancer/ 18. exp Liver Failure/ 19. exp Liver Transplantation/ 20. exp Liver/ 21. (Alcoholic liver disease$ or Ascites or Cirrhosis or Esophageal varic$ or Hepat$ or Liver or Varic$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] 22. 21 or 17 or 20 or 15 or 14 or 18 or 13 or 16 or 19 23. 22 and 12 24. (random$ or blind$ or placebo$ or meta-analysis).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] 25. 24 and 23
Science Citation Index Expanded (http://portal.isiknowledge.com/por-	From 1900 to January 18, 2012	# 4 (#3 AND #2 AND #1) # 3 TS=(random* OR blind* OR placebo* OR meta-analysis) # 2 TS=('Alcoholic liver disease*' OR Ascites OR Cirrhosis OR 'Esophageal varic*' OR Hepat* OR Liver OR Varic*)

(Continued)

tal.cgi?DestApp=WOS&Func=Frame)		# 1TS=(alimentation OR 'branched chain amino acids' OR BCAA OR 'Dietary disorder*' OR 'Enteral nutrition' OR Enterostom* OR 'Fat emulsion' or 'formulated food*' OR Gastrostom* OR Hyperalimentation* OR 'Hypocaloric alimentation*' OR 'Hypocaloric nutrition' OR 'Intragastric feed*' OR 'Intragastric nutrition' OR Nutrition OR 'Nutrition diseases' OR 'Nutrition disorders' OR 'Nutrition supplement*' OR 'Parenteral nutrition' OR 'Percutaneous endoscopic gastrostom*' OR 'Peripheral parenteral nutrition' OR 'Permissive underfeeding' OR 'Post-pyloric feeding' OR 'Post-pyloric nutrition' OR 'Protein hydrolysate' OR 'Supplemental feed*' OR 'Total parenteral nutrition')
Clinicaltrials.gov	November 14, 2011	'Liver disease" AND 'Nutrition'

CONTRIBUTIONS OF AUTHORS

RK designed the review and wrote the protocol; RK was involved in screening the computer searches to identify pertinent articles, deciding on the eligibility of each trial identified, abstracting the data from each eligible trial, entering the data into RevMan, and writing the report. AA assisted in the writing of the protocol and was involved in screening the computer searches for identifying pertinent articles, deciding on the eligibility of each trial, abstracting the data, and writing the report. TL was involved in deciding on the eligibility of each trial identified, abstracting the data, and writing the report.

DECLARATIONS OF INTEREST

Neither RK, AA, or TL have any real or potential conflict of interest with any party (commercial or third party payers). There was no external or internal funding source that sponsored this review.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- None, Not specified.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. Emma Metcalfe was unable to participate as author and her name was dropped from the review.

2. Because over 8000 titles were initially identified, RK alone reviewed all of the titles. A sample of 500 were sent to AA, who did not identify any trials that were not also identified by RK. It was therefore assumed that the RK review was adequate and RK alone subsequently reviewed all of the titles from subsequent literature searches.

3. Jaundice, as defined by a serum bilirubin $\geq$ 3 mg%, was added as a secondary outcome and was considered as representing a manifestation of hepatic morbidity.

4. When not specified in the paper, alcoholic hepatitis was defined as a history of recent alcohol usage in a patient who presented with decompensated (one or more of jaundice, variceal bleeding, ascites, encephalopathy, coagulopathy) liver disease.

5. The subgroup and sensitivity analyses were only performed for the outcomes for which meta-analyses were available.

6. The results were reported from the fixed-effect model unless one, but not the other, model found a significant difference, in which case the results of both models were reported.

7. It was initially intended to assess individual disease states, including 'alcoholic liver disease' and 'non-alcoholic liver disease'. However, each category contained patients with a variety of different diagnoses. As the intent of the analysis was to assess particular diseases, these two analyses were not done. However, a separate category, namely patients with cirrhosis, was added.

8. At the Cochrane Colloquium in Keystone, Colorado, in 2010, a policy was adopted that baseline imbalance and early stopping no longer be routinely considered in the assessment of the risk of bias of trials. These two domains were eliminated from among those considered in assessing risk of bias, although the information, already collected, was retained in the description of each trial.

9. In accordance with Cochrane Hepato-Biliary Group policy, the primary outcomes were changed to mortality, morbidity, quality of life, and adverse events; the other outcomes became secondary ones.

10. Because immediate postoperative nutritional support in surgical trials in non-transplanted patients was to be considered, any trials assessing perioperative (including immediate postoperative) nutritional interventions were included. The word 'preoperative' in the protocol was changed to 'perioperative'.

11. At the request of an external reviewer, the serum albumin was also assessed . However, since this was a post hoc analysis of a continuous outcome in one specific application and done by request, we did not include albumin as another secondary outcome in the systematic review as a whole. Furthermore, we did not view the serum albumin as a marker of nutrition since it is influenced by the underlying liver disease as well as by circulating cytokines.

12. Because two trials with factorial designs were identified, it was decided to use only the data from the groups receiving the nutritional intervention and the group receiving neither intervention if possible; but, if the data were only available from the combined groups, to use those instead.

13. Because surgical trials in patients without cirrhosis would not be expected to observe postoperative ascites or encephalopathy, it was decided to add postoperative complications as the primary morbidity outcome in such situations.

INDEX TERMS

Medical Subject Headings (MeSH)

Ascites [prevention & control]; Enteral Nutrition [*methods]; Hepatic Encephalopathy [therapy]; Infection; Liver Diseases [*therapy]; Parenteral Nutrition [*methods]; Postoperative Complications [prevention & control]; Randomized Controlled Trials as Topic

MeSH check words

Humans