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Nutritional therapy for reducing disability and improving activities of daily living in people after stroke (Review)

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TABLE OF CONTENTS

[Intervention Review]

Nutritional therapy for reducing disability and improving activities of daily living in people after stroke

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ABSTRACT

Background

Stroke patients often face disabilities that significantly interfere with their daily lives. Poor nutritional status is a common issue amongst these patients, and malnutrition can severely impact their functional recovery post-stroke. Therefore, nutritional therapy is crucial in managing stroke outcomes. However, its effects on disability, activities of daily living (ADL), and other critical outcomes have not been fully explored.

Objectives

To evaluate the effects of nutritional therapy on reducing disability and improving ADL in patients after stroke.

Search methods

We searched the trial registers of the Cochrane Stroke Group, CENTRAL, MEDLINE (from 1946), Embase (from 1974), CINAHL (from 1982), and AMED (from 1985) to 19 February 2024. We also searched trials and research registries (ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform) and reference lists of articles.

Selection criteria

We included randomised controlled trials (RCTs) that compared nutritional therapy with placebo, usual care, or one type of nutritional therapy in people after stroke. Nutritional therapy was defined as the administration of supplemental nutrients, including energy, protein, amino acids, fatty acids, vitamins, and minerals, through oral, enteral, or parenteral methods. As a comparator, one type of nutritional therapy refers to all forms of nutritional therapies, excluding the specific nutritional therapy defined for use in the intervention group.

Data collection and analysis

We used Cochrane's Screen4Me workflow to assess the initial search results. Two review authors independently screened references that met the inclusion criteria, extracted data, and assessed the risk of bias and the certainty of the evidence using the GRADE approach. We

calculated the mean difference (MD) or standardised mean difference (SMD) for continuous data and the odds ratio (OR) for dichotomous data, with 95% confidence intervals (CIs). We assessed heterogeneity using the I^2 statistic. The primary outcomes were disability and ADL. We also assessed gait, nutritional status, all-cause mortality, quality of life, hand and leg muscle strength, cognitive function, physical performance, stroke recurrence, swallowing function, neurological impairment, and the development of complications (adverse events) as secondary outcomes.

Main results

We identified 52 eligible RCTs involving 11,926 participants. Thirty-six studies were conducted in the acute phase, 10 in the subacute phase, three in the acute and subacute phases, and three in the chronic phase. Twenty-three studies included patients with ischaemic stroke, three included patients with haemorrhagic stroke, three included patients with subarachnoid haemorrhage (SAH), and 23 included patients with ischaemic or haemorrhagic stroke including SAH. There were 25 types of nutritional supplements used as an intervention. The number of studies that assessed disability and ADL as outcomes were nine and 17, respectively.

For the intervention using oral energy and protein supplements, which was a primary intervention in this review, six studies were included. The results for the seven outcomes focused on (disability, ADL, body weight change, all-cause mortality, gait speed, quality of life, and incidence of complications (adverse events)) were as follows: There was no evidence of a difference in reducing disability when 'good status' was defined as an mRS score of 0 to 2 (for 'good status': OR 0.97, 95% CI 0.86 to 1.10; 1 RCT, 4023 participants; low-certainty evidence). Oral energy and protein supplements may improve ADL as indicated by an increase in the FIM motor score, but the evidence is very uncertain (MD 8.74, 95% CI 5.93 to 11.54; 2 RCTs, 165 participants; very low-certainty evidence). Oral energy and protein supplements may increase body weight, but the evidence is very uncertain (MD 0.90, 95% CI 0.23 to 1.58; 3 RCTs, 205 participants; very low-certainty evidence). There was no evidence of a difference in reducing all-cause mortality (OR 0.57, 95% CI 0.14 to 2.28; 2 RCTs, 4065 participants; low-certainty evidence). For gait speed and quality of life, no study was identified. With regard to incidence of complications (adverse events), there was no evidence of a difference in the incidence of infections, including pneumonia, urinary tract infections, and septicaemia (OR 0.68, 95% CI 0.20 to 2.30; 1 RCT, 42 participants; very low-certainty evidence). The intervention was associated with an increased incidence of diarrhoea compared to usual care (OR 4.29, 95% CI 1.98 to 9.28; 1 RCT, 4023 participants; low-certainty evidence) and the occurrence of hyperglycaemia or hypoglycaemia (OR 15.6, 95% CI 4.84 to 50.23; 1 RCT, 4023 participants; low-certainty evidence).

Authors' conclusions

We are uncertain about the effect of nutritional therapy, including oral energy and protein supplements and other supplements identified in this review, on reducing disability and improving ADL in people after stroke. Various nutritional interventions were assessed for the outcomes in the included studies, and almost all studies had small sample sizes. This led to challenges in conducting meta-analyses and reduced the precision of the evidence. Moreover, most of the studies had issues with the risk of bias, especially in terms of the absence of blinding and unclear information. Regarding adverse events, the intervention with oral energy and protein supplements was associated with a higher number of adverse events, such as diarrhoea, hyperglycaemia, and hypoglycaemia, compared to usual care. However, the quality of the evidence was low. Given the low certainty of most of the evidence in our review, further research is needed. Future research should focus on targeted nutritional interventions to reduce disability and improve ADL based on a theoretical rationale in people after stroke and there is a need for improved methodology and reporting.

PLAIN LANGUAGE SUMMARY

Nutritional therapy for reducing disability and improving activities of daily living in people after stroke

Key messages

° Nutritional therapy using oral energy and protein supplements may improve daily activities (very uncertain evidence).

° Nutritional therapy using oral energy and protein supplements may not reduce disability (uncertain evidence).

° We identified various types of nutritional interventions for disabilities and daily activities. More high-quality studies are needed to determine the effect of each type of nutritional therapy on disability and daily activities in people after stroke.

What is stroke?

A stroke occurs when the blood supply to part of your brain is interrupted or reduced. There are three main types of strokes: an ischaemic stroke, which happens when a blood clot blocks or narrows an artery leading to the brain; a haemorrhagic stroke, which occurs when a blood vessel in the brain bursts, causing bleeding in the brain; and a subarachnoid haemorrhage, which occurs when there is bleeding in the space between the brain and the surrounding membrane (subarachnoid space).

What is nutritional therapy?

Nutrition therapy is an intervention using nutrients such as protein, vitamins, and energy for daily meals and/or between meals, and includes nutrition care based on the condition of each patient. People with and after a disease often receive nutritional therapy.

Why is a specific focus needed on nutritional therapy in people after stroke?

Stroke patients easily get malnutrition because they do not receive enough energy and nutrients as a result of impairments. Stroke patients often experience physical and cognitive issues, and nutritional status may affect their improvement.

What did we want to find out?

We wanted to find out whether nutritional therapy reduces disability and improves daily activities in people after stroke.

What did we do?

We searched the medical literature for all randomised trials conducted on nutritional therapy in people after stroke. We also assessed whether nutritional therapy is safe in terms of unwanted effects. We compared and summarised the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We identified 52 studies that involved 11,926 participants. Thirty-six studies with acute stroke patients were conducted (within 14 days from stroke onset), 10 with subacute stroke patients (within 6 months, from 14 days after stroke onset), three with acute and subacute stroke patients, and three with chronic stroke patients (after 6 months from stroke onset). The stroke type investigated was ischaemic in 23 studies, haemorrhagic in three studies, subarachnoid haemorrhage (SAH) in three studies, and ischaemic or haemorrhagic stroke including SAH in 23 studies. We identified 25 types of nutritional intervention in this review. The number of studies that assessed disability and ADL as outcomes were 9 and 17, respectively.

For the primary intervention of using oral energy and protein supplements, we identified six studies.
We found that nutritional therapy using oral energy and protein supplements:

- may not reduce disability; however, the evidence is uncertain

- may improve daily activities; however, the evidence is very uncertain

For other outcomes, nutritional therapy using oral energy and protein supplements:

- may improve nutritional status in weight gain; however, the evidence is very uncertain

- may not decrease the risk of death from any cause; however, the evidence is uncertain

- were associated with an increased incidence of both diarrhoea and either hyperglycaemia (a condition where there is too much sugar (glucose) in the blood) or hypoglycaemia (a condition where there is too little sugar (glucose) in the blood); however, the evidence is uncertain

We did not find any studies with oral energy and protein supplements that reported walking speed and quality of life.

What were the limitations of the evidence?

We are not confident of the evidence for reducing disability and improving daily activities for the following reasons:

- Patients in most studies were aware of the intervention they were receiving.

- Healthcare providers and outcome assessors were aware of the interventions the patients were receiving.

- Most studies that assessed ADL(activities of daily living) did not describe their methods in sufficient detail.

- The effect may differ according to stroke type, time from stroke onset, and nutritional status at the start of nutritional therapy, but we could not assess those differences sufficiently due to the small number of studies.

How up-to-date is this evidence?

The evidence is current to 19 February 2024.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings

Patient or population: stroke patients
Setting: inpatient and rehabilitation centres
Intervention: oral nutritional supplements (energy and protein)
Comparison: no supplements

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Nutritional therapy				
Primary outcome: Disability: good status (mRS 0 to 2) Scale: 0 to 6 (lower is better) Follow-up: 6 months	411 per 1000	404 per 1000	OR 0.97 (0.86 to 1.10)	4023 (1 study)	⊕⊕⊖⊖ **Low**[a]	Stroke phase: 1 acute Stroke type; 1 mixed (ischaemic and haemorrhagic) population
Primary outcome: ADL: FIM-Motor score at end of intervention phase Scale: 13 to 91 (higher is better) Follow-up: 3.5 to 8 weeks	The mean score in the control group: 43.33 to 54.1 (range)	MD 8.74 higher (5.93 higher to 11.54 higher)	–	165 (2 studies)	⊕⊖⊖⊖ **Very low**[b]	Stroke phase: 1 acute and subacute, 1 subacute Stroke type: 2 mixed (ischaemic and haemorrhagic) population
Gait: gait speed	No evidence identified					
Nutritional status during intervention phase: change in body weight Higher is better Follow-up: 21 to 30 days	The mean change in the control group: 0.70 to 1.68 (range)	MD 0.90 higher (0.23 lower to 1.58 higher)	–	205 (3 studies)	⊕⊖⊖⊖ **Very low**[c]	Stroke phase: 1 acute and subacute, 2 subacute Stroke type: 1 ischaemic, 1 mixed (iscahemic and haemorrhagic) population, 1 not reported

Death: all-cause mortality Lower is better Follow-up: 3 to 6 months	125 per 1000	119 per 1000	OR 0.57 (0.14 to 2.28)	4065 (2 studies)	⊕⊕⊖⊖ **Low**[d]	Stroke phase: 2 acute Stroke type: 2 mixed (ischaemic and haemorrhagic) population
Complications: infections (pneumonia, urinary tract, and septicaemias) Lower is better Follow-up: 12 weeks	524 per 1000	429 per 1000	OR 0.68 (0.20 to 2.30)	42 (1 studies)	⊕⊖⊖⊖ **Very low**[e]	Stroke phase: 1 acute Stroke type: 1 mixed (ischaemic and haemorrhagic) population
QOL: EQ-5D	No evidence identified					

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
ADL: activity of daily living; **CI:** confidence interval; **EQ-5D:** EuroQol-5 Dimension; **FIM:** Functional Independence Measure; **GRADE:** Grading of Recommendations, Assessment, Development and Evaluation; **mRS:** modified Rankin Scale: **QOL:** quality of life: **OR:** odds ratio.
GRADE Working Group grades of evidence
High certainty: further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty: we are very uncertain about the estimate.
[a] Downgraded two levels due to very serious concerns about risk of bias: high risk of bias in blinding participants and personnel and outcome assessment
[b] Downgraded two levels due to very serious concerns about risk of bias: high risk of bias in blinding participants and personnel and outcome assessment and other sources of bias (the last author was an employee of a nutrition products company related to the study) (1 study) and selecting reportings (2 studies) Downgraded one level due to serious concerns about imprecision: small sample size
[c] Downgraded two levels due to very serious concerns about risk of bias: High risk of bias in other sources of bias (1 study) and allocation concealment (2 study). Downgraded one level due to serious concerns about inconsistency: high heterogeneity. Downgraded one level due to serious concerns about imprecision: small sample size
[d] Downgraded one level due to serious concerns about inconsistency: high heterogeneity. Downgraded one level due to serious concerns about imprecision: the confidence interval including no effect and the benefit.
[e] Downgraded two levels due to very serious concerns about risk of bias: high risk of bias in blinding participants and personnel and outcome assessment. Downgraded one level due to serious concerns about imprecision: small sample size.

BACKGROUND

Description of the condition

Stroke is the second leading cause of death and disability-adjusted life-years (DALYs) worldwide, which represents the sum of the years of life lost due to premature mortality (YLLs) and the years of 'healthy' life lost due to disability (YLDs) (GBD 2017 DALYs and HALE Collaborators 2018). From 1991 to 2013, the mortality rates and DALYs of stroke have decreased, but the YLDs and prevalence rates have increased globally (Barker 2015). This decrease in the mortality rate of stroke can be attributed to the advances in emergency and acute care technology, which consequently results in an increase in the percentage of disabled patients. Many stroke survivors experience physical, cognitive, communication, and/or emotional impairments. Of these, 25% to 74% need some assistance or full assistance in activities of daily living (ADL) (Anderson 1995; Kalra 2007). This has led to an increasing need for rehabilitation to help patients live and cope with the post-stroke conditions. Neurological disorders bear the third-highest need for rehabilitation in patients 65 years or older, with stroke being the most common cause (Cieza 2021). In terms of cost, the total annual direct healthcare expenditure for the treatment and management of stroke patients is expected to increase from USD 71.55 billion in 2012 to USD 183.13 billion in 2030, due to increasing prevalence in the USA (Gorelick 2019). Due to such a large global burden, strategies for improving disability care are important.

Nutritional status is a major issue in stroke patients. The frequency of malnutrition after stroke is reported to be up to 62% (Foley 2009). Several observational studies have shown that malnutrition is associated with poor outcomes in stroke patients, such as greater dependence on help with ADLs and an increased likelihood of death (Dávalos 1996; FOOD Trial Collaboration 2003; Gariballa 1998; Yoo 2008). In addition, malnourished patients had more infections and bedsores (Gariballa 1998; Yoo 2008). These studies imply that a decline in nutritional status is a significant issue in stroke patients, and it is important to identify and treat these patients in the early stage of stroke. Malnutrition typically refers to insufficient protein-energy intake due to an imbalance of energy and protein supply (Foley 2009). Because of this, metabolic requirements exceed nutritional intake (Foley 2009). In addition, the role of vitamins, minerals, and other essential nutrients has attracted attention in terms of neuroprotective and neuroplastic effects (Aquilani 2011; Daubail 2012; Kalueff 2007).

Some risk factors for malnutrition in patients with stroke include dysphagia, perception deficits, cognitive dysfunction, and reduced level of consciousness (Burgos 2018; Chen 2019). Acute stroke patients have a high incidence of dysphagia (37% to 78%) (Foley 2009; Martino 2005). Although the exact mechanism of developing malnutrition is unclear, insufficient energy intake during hospitalisation has been reported (Lieber 2018). The nutritional status of patients with stroke can deteriorate during hospitalisation. It has been estimated that acute stroke patients consumed 80% to 91% of their energy requirements in this setting (Foley 2009). For example, stroke patients had an increase in protein-energy malnutrition from 16.3% at admission to 26.4% after one week and to 35% after two weeks of hospitalisation (Bouziana 2011). Stroke patients with dysphagia suffered higher malnutrition during the post-acute phase than during the acute phase (Foley 2009).

In recent years, stroke-related sarcopenia, which is a geriatric syndrome characterised by decreased skeletal muscle mass or quality and muscle strength of the limbs, has attracted attention due to associated poor outcomes associated (Li 2020; Scherbakov 2014). The prevalence of sarcopenia amongst stroke patients is high and estimated at approximately 42% (Su 2020). Although the exact mechanism of developing sarcopenia in stroke patients is unknown, malnutrition is one possible cause (Cruz 2019; Knops 2013).

Description of the intervention

We are interested in the effect of nutritional therapy (with a focus on energy and protein, and other nutrients) and its outcome in stroke patients compared with usual care. In the guidelines published by the European Society for Clinical Nutrition and Metabolism, nutritional therapy for stroke patients has been described as medical nutritional therapy, which encompasses interventions using oral nutritional supplements, enteral tube feeding, parenteral nutrition, and individualised nutritional therapy based on the condition of each patient (Burgos 2018).

Most guidelines on stroke management address nutrition management (Japan Stroke Society 2019; National Stroke Foundation 2017; NICE 2019; Powers 2019; Winstein 2016), and recommend supplements for patients who are malnourished or at risk of malnutrition. However, the routine use of nutritional supplements has not been shown to be beneficial in these guidelines based on a single randomised controlled trial (RCT) (Dennis 2005). For patients with inadequate or unsafe oral intake, the guidelines recommend early enteral feeding.

How the intervention might work

Stroke patients can easily develop malnutrition due to insufficient energy and nutrient intake. An association between malnutrition and poor outcomes has been reported in patients with stroke (Dávalos 1996; FOOD Trial Collaboration 2003; Gariballa 1998; Yoo 2008). Preventing protein-energy malnutrition may lead to better motor function outcomes after stroke (Matwee 2020). An adequate amount of protein and energy is necessary to maintain muscle mass and encourage its synthesis in cancer patients (Ford 2022). Vitamins and minerals may improve or maintain muscle mass and function, and nutritional intervention is a promising treatment for sarcopenia (Khor 2014; Malafarina 2012; Nakamura 2020; Van Dronkelaar 2018). Given these findings, nutritional therapy is a potential intervention for improving the outcome of patients after stroke, thereby reducing patient and caregiver burden, and consequently decreasing stroke-related healthcare expenditure.

Why it is important to do this review

Disability due to stroke is a global health problem. Nutritional status is one of the focused aspects related to the outcomes of stroke patients, and most stroke guidelines have recommendations regarding nutritional therapy. Although the assessment and intervention for nutrition are described as important in the guidelines, details such as the type of nutrients and their effects have not been sufficiently addressed. A Cochrane Review published in 2012 investigated the effects of interventions for dysphagia involving nutritional support for energy and protein (Geeganage 2012). An updated review published in 2018 did not include the effects of nutritional support (Bath 2018). A comprehensive review

of the effects of nutritional therapy plays a crucial role in enhancing stroke management strategies.

OBJECTIVES

To evaluate the effect of nutritional therapy on disability and activities of daily living (ADL) in stroke patients.

METHODS

Criteria for considering studies for this review

Types of studies

Studies that met the following criteria were included: individual randomised controlled trials (RCTs), cluster-RCTs, and cross-over trials, regardless of the language and publication status. We excluded quasi-RCTs that used a quasi-random method of allocating participants to different intervention groups.

Types of participants

We included patients with all types of stroke, at all levels of severity, at all stages post-stroke (acute, subacute, or chronic), and at any age. We also included participants with subarachnoid haemorrhage. We excluded studies with participants of mixed aetiology (e.g. stroke and traumatic brain injury) unless data were available for stroke survivors only.

Types of interventions

We included trials that compared nutritional therapy with placebo, usual care, or one type of nutritional therapy. Nutritional therapy was described as being administered orally and/or enterally via a tube or stoma, using additional energy, protein, fatty acids, amino acids, vitamins, and/or minerals. We also included parenteral nutritional therapy provided through a central venous line or peripheral intravenous line. For parenteral and enteral nutrition therapies, we included total and supplemental nutrition. We also included individualised nutritional therapy, tailored to meet the specific conditions and needs of each individual (e.g. an intervention using energy with/without protein, taking into consideration an individual's nutritional status and activity level). We excluded a comprehensive intervention in which nutritional therapy was not the main component (e.g. lifestyle intervention). We have also excluded whole-food-based interventions (e.g. fruit juice, soy products, Mediterranean diet). Therefore, this review focuses on specific nutrient-based supplements or oral nutritional supplements. Regarding comparators, one type of nutritional therapy refers to any other variety of nutritional interventions distinct from the nutritional therapy defined as the intervention, including comparisons between low and high doses of the therapy. This approach entails comparing the specified nutritional therapy in the intervention group against all other varieties of nutritional therapies.

Types of outcome measures

All outcomes of interest were assessed at the end of intervention and scheduled follow-up.

Primary outcomes

- Disability: assessed using tools such as the modified Rankin Scale (mRS) (Bonita 1988);
- Activities of daily living (ADL): assessed using tools such as the Barthel Index (BI) (Collin 1988), Katz Index of Activities of Daily Living (Katz 1970), and Functional Independence Measure (FIM) (Keith 1987). The FIM consists of the motor score and cognitive score, but only the motor score was considered as an ADL when data were available.

Secondary outcomes

- Gait: assessed using gait speed and walk distance defined in minutes (e.g. 6-minute walk test (Butland 1982));
- Nutritional status: determined by physical measurements such as a change in body weight, muscle mass, thickness of the triceps skinfold, and arm muscle circumference;
- Death (all-cause);
- Incidence of complications: determined by the number of complications (adverse events) including infections, pneumonia, pressure sores, sarcopenia, diarrhoea, hyperglycaemia, kidney failure, liver failure, vomiting, gastrointestinal haemorrhage, and sepsis recorded;
- Quality of life (QOL): measured using tools such as the Stroke Specific Quality of Life (SS-QOL) (Williams 1999) and EuroQol-5 Dimension (EQ-5D) (Rabin 2001);
- Muscle strength: measured using grip or leg strength;
- Cognitive function: assessed using tools such as the FIM cognitive score (Keith 1987);
- Physical performance: assessed using tools such as the Fugl-Meyer Assessment (Fugl-Meyer 1975) and Short Physical Performance Battery (Guralnik 1994);
- Stroke recurrence: as defined by the study investigators;
- Neurological impairment: assessed using tools such as NIHSS (National Institutes of Health Stroke Scale) score (Brott 1989);
- Swallowing function: assessed using tools such as the Dysphagia Outcome and Severity Scale (O'Neil 1999), and the Penetration-Aspiration Scale (Rosenbek 1996). We also accepted a water swallow test as a screening test for dysphagia.

Search methods for identification of studies

See the 'Specialized Register' information available at the Cochrane Stroke Group website. We searched for trials in all languages and arranged for the translation of relevant articles where necessary.

Electronic searches

Working with the Cochrane Stroke Group's Information Specialist, we searched the Cochrane Stroke Group's Trials Register and the following electronic databases:

- MEDLINE Ovid (1946 to 19 February 2024) (Appendix 1);
- Cochrane Central Register of Controlled Trials (CENTRAL; last searched 19 February 2024) in the Cochrane Library (Appendix 2);
- Embase Ovid (1974 to 19 February 2024) (Appendix 3);
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1982 to 19 February 2024) (Appendix 4);
- AMED Ovid (Allied and Complementary Medicine; 1985 to 19 February 2024) (Appendix 5).

All search strategies combined adaptations of the sensitive search strategy for identifying RCTs designed by Cochrane (Lefebvre 2021)

with the Cochrane Stroke Group's search strategy for identifying stroke studies.

Searching other resources

In an effort to identify further published, unpublished, and ongoing trials, we conducted the following searches.

We searched the following registries to identify ongoing trials without date limits on 19 February 2024:

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov/);
- World Health Organization (WHO) International Clinical Trials Registry Platform (who.int/ictrp/en/) (Appendix 6).

The bibliographies of included studies and any relevant systematic review identified were checked for further references to relevant trials, and Google Scholar was used for forward tracking of important articles (scholar.google.co.uk/):

- The original authors were contacted for clarification and further data if the trial reports were unclear;
- Where necessary, experts/professionals/trial investigators/representative bodies and organisations in the field were contacted to obtain additional information on relevant trials;
- Dissertations and conference abstracts were included.

Data collection and analysis

Selection of studies

We used Cochrane's Screen4Me workflow to help assess the search results from the databases of MEDLINE, Embase, CINAHL, and AMED. We used two components of Screen4Me: a service that matches records in the search results with those already screened in Cochrane Crowd and labelled as either an 'RCT' or 'Not an RCT', and the RCT classifier, a machine learning model that distinguishes RCTs from non-RCTs. For more information about Screen4Me and the evaluations that have been done, please go to the Screen4Me webpage on the Cochrane Information Specialist's portal: https://community.cochrane.org/organizational-info/resources/resourcesgroups/information-specialists-portal. In addition, more detailed information regarding evaluations of the Screen4Me components, can be found in the following publications: Marshall 2018, Noel-Storr 2020, Noel-Storr 2021, Thomas 2021.

The search results from the stroke group register, CENTRAL, WHO ICTRP, and ClinicalTrials.gov were added to the records identified through Screen4Me. Any two review authors (from KS, MN, RM, EN, KM, TM, NT, or EH) independently and in duplicate screened titles and abstracts of the studies obtained from the searches and excluded irrelevant reports using Covidence (Covidence). We retrieved the full-text articles for the remaining studies, and the two review authors independently screened the full-text articles and identified studies for inclusion and recorded reasons for exclusion of studies deemed ineligible. We resolved any disagreements through discussion or, if required, we consulted a third review author. We collated multiple reports of the same study so that each study was the unit of interest in the review. We recorded the selection process and completed a PRISMA flow diagram (Page 2021).

Data extraction and management

Any two review authors (from KS, MN, or EN) independently and in duplicate extracted data from the included studies using a standard data extraction form. We resolved any differences in opinion between the review authors through discussion and, where necessary, by consulting a third review author. We extracted information pertaining to the following aspects in line with the Template for Intervention Description and Replication (TIDieR) checklist and guide (Hoffmann 2014).

- Basic trial characteristics: study design, number of participants, author names, year, country, funding, conflicts of interest, and inclusion and exclusion criteria including nutritional status at baseline;
- Participant characteristics: age, sex, stroke type, severity, and stroke phase;
- Intervention: type and dose of nutrients, delivery route (oral, enteral, or parenteral), co-intervention, intervention period, and timing;
- Intervention characteristics of the control group;
- Outcome data: dropouts, primary and secondary outcomes as well as the time points reported;
- Information needed for the risk of bias assessment.

Assessment of risk of bias in included studies

Any two review authors (from KS, MN, or EN) independently and in duplicate assessed the risk of bias for each included study using RoB 1 as described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (Higgins 2011). We resolved any disagreements by discussion or by involving another review author. We assessed the risk of bias according to the following domains.

- Random sequence generation;
- Allocation concealment;
- Blinding of participants and personnel;
- Blinding of outcome assessment;
- Incomplete outcome data;
- Selective outcome reporting;
- Other bias.

We judged the risk of bias for each domain as low risk, unclear, or high risk, and provided information from the study report together with a justification for our judgement in the risk of bias tables. We produced a risk of bias graph to illustrate the potential biases within each of the included studies. The risk of bias for each individual study can be located in the Characteristics of included studies table, and the Risk of Bias Summary and Risk of Bias graph can be located in Figure 1 and Figure 2, respectively.

Figure 1. Risk of bias summary

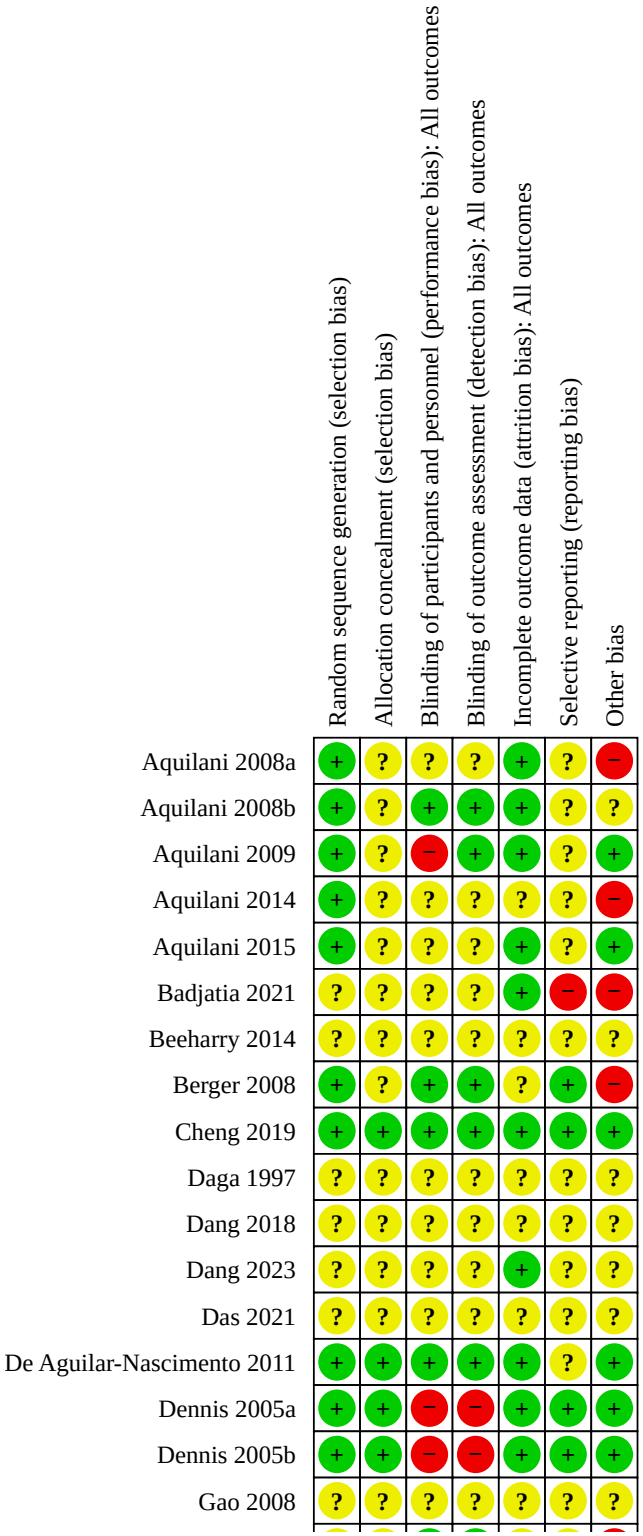


Figure 1. (Continued)

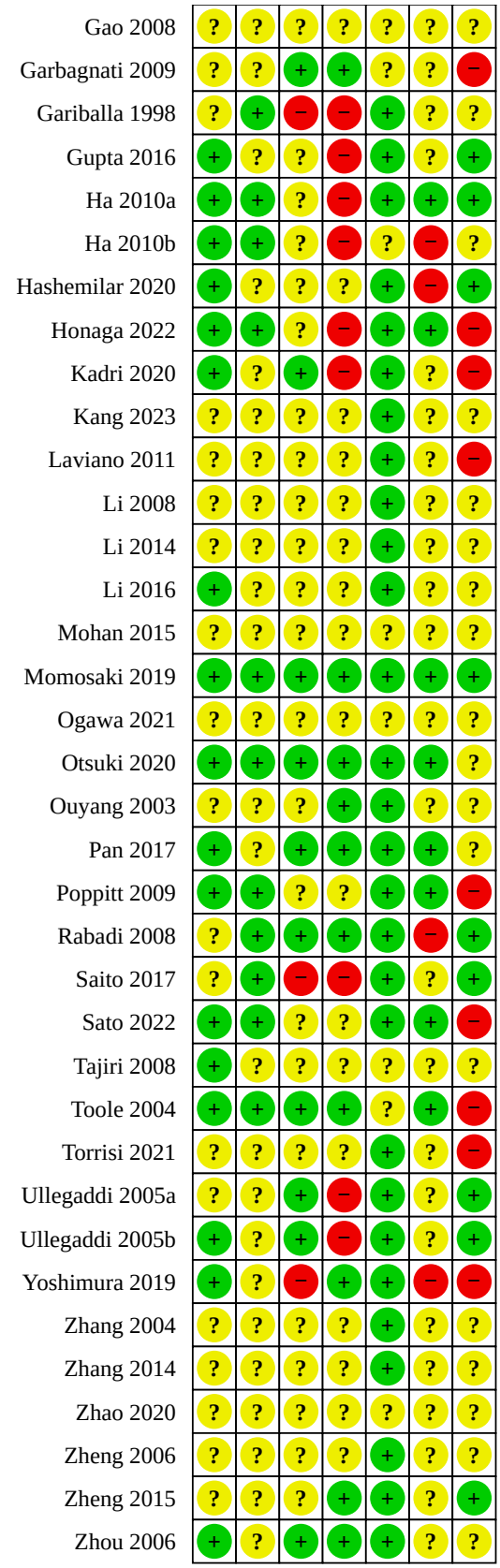
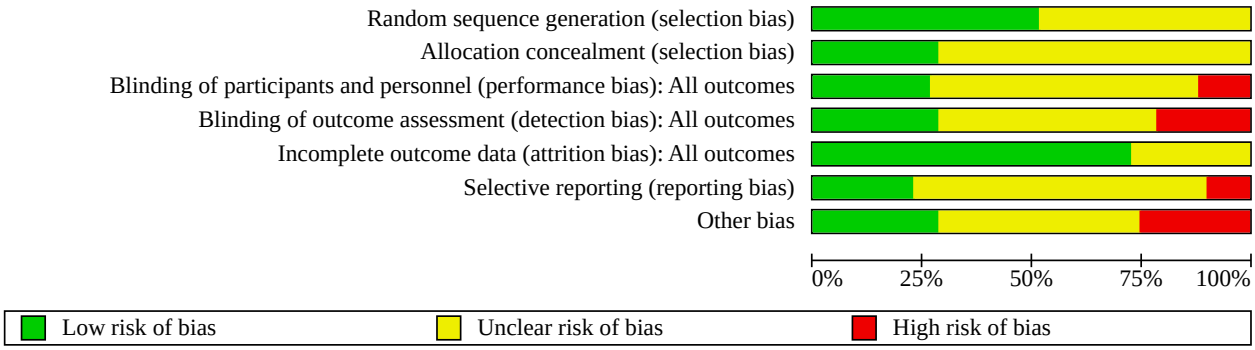


Figure 2. Risk of bias graph



Measures of treatment effect

For binary outcomes, we estimated the odds ratio (OR) and its 95% confidence interval (CI). For continuous variables, we estimated the standardised mean differences with 95% CIs (if studies measure the same outcome using different tools) or used mean differences and 95% CIs (when all studies used the same measurement tool). If a study provided the data as a median and interquartile range (IQR), we converted the data to mean and standard deviation (SD) for large studies (with more than 100 participants in each group). For trials with smaller sample sizes, we did not further consider median and interquartile range data, with the assumption that the data were skewed and not normally distributed (Higgins 2021; Wan 2014).

Unit of analysis issues

In standard RCTs, we treated individual participants as the unit of analysis. In the case of cluster-RCTs, we planned to treat the clusters as the unit of analysis. We planned to extract, where available, a direct estimate of the required effect from an analysis that properly accounted for the cluster design. We planned to perform an assumed intraclass correlation analysis between clusters if required information was available (Higgins 2021). However, if we could not extract such information, we planned to conduct a mean imputation for the missing information, which could attain better efficiency compared with multiple-imputation-based methods. In the case of cross-over trials, we planned to use only data from the first phase.

Dealing with missing data

We emailed the corresponding authors of the studies to request missing data. If missing data were not provided, we explored the effect of excluding the study in a sensitivity analysis, if necessary. We described the reasons for the missing data (e.g. withdrawal from the study or loss to follow-up). We critically appraised the management of missing data in each study (Higgins 2022).

When a study provided data on a log scale, we converted the data using the exponential scale, when necessary (Higgins 2022). When a study did not report SD but reported a mean value and 95% CI at follow-up, we calculated the SD using the equation described in Chapter 6 of the *Cochrane Handbook* version 6.3 (Higgins 2022). When we converted the data at baseline and follow-up into the change value and its SD, we used the equation with an estimated correlation coefficient from a previous study, as described in Chapter 6 in the *Cochrane Handbook* version 6.3 (Higgins 2022). When a study reported the data by group (e.g. sex), we converted the data into combined data using the average value.

Assessment of heterogeneity

Clinical heterogeneity

We initially considered all included studies to assess the clinical heterogeneity. We inspected all studies for participants who were clearly outliers or for unpredictable situations. In such cases, we discussed the situations or participants and did not include those studies in the meta-analyses.

Methodological heterogeneity

We initially considered all included studies to judge for methodological heterogeneity. We inspected all studies for methodological outliers.

Statistical heterogeneity

Visual inspection

We visually inspected graphs to investigate the possibility of statistical heterogeneity.

Employing the I^2 statistic

We investigated the heterogeneity between studies by considering the I^2 statistic. The I^2 statistic provides an estimate of the degree of inconsistency thought to be due to chance (Higgins 2003). The importance of the I^2 statistic depends on the magnitude and direction of the effects, as well as the strength of the evidence for heterogeneity. We interpreted the I^2 statistic estimate as follows: 0% to 25% as unimportant, 25% to 50% as moderate, 50% to 75% as substantial, and ≥ 75% as considerable (Higgins 2022). When there was considerable heterogeneity in the primary outcomes, we explored the reasons for the heterogeneity.

Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of the results (Egger 1997), as described in Chapter 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.3 (Higgins 2022). We are aware that funnel plots may be useful in investigating reporting biases but

are of limited power to detect small-study effects; we planned to use these if we found ten or more studies for any outcomes. We did not use funnel plots for outcomes where there were 10 or fewer studies, or where all studies were of similar size (Peters 2008).

Data synthesis

Where we considered studies that compared nutritional therapy with placebo or usual care to be sufficiently similar, we performed a meta-analysis by pooling the appropriate data within Cochrane's Review Manager Web (RevMan Web 2023). We pooled data by each type of nutritional therapy (e.g. protein, energy, or vitamin D) with a nutritional route (oral, enteral, or parenteral). We used a random-effects model in the presence of considerable heterogeneity between studies; otherwise, we used a fixed-effect model for meta-analysis. For studies where meta-analysis was not possible, we summarised the data narratively. We followed intention-to-treat (ITT) principles, where we analysed participants in their randomised group regardless of the intervention received. When a study reported the data for each paretic and not-paretic side, we did not combine those data, as they were heterogeneous.

Subgroup analysis and investigation of heterogeneity

We expected that the variables below would introduce heterogeneity into the analyses. To investigate this, we performed the following prespecified subgroup analyses for the outcomes.

- Stroke phase: acute (within 14 days from stroke onset), subacute (within 6 months, from 14 days after stroke onset), and chronic (after 6 months from stroke onset) (Geeganage 2012; Minhas 2022);
- Type of stroke: ischaemic and haemorrhagic;
- Nutritional status at baseline: malnutrition and/or malnutrition risk, defined as inclusion criteria by study authors.

Sensitivity analysis

To explore the influence of the factors listed below, we planned to carry out sensitivity analyses for primary outcomes only. We excluded the studies identified in each sensitivity analysis and discussed their differences with the main analysis.

Risk of bias

We analysed the effect of excluding studies that were judged as having a high risk of bias for primary outcomes (see Assessment of risk of bias in included studies). We considered a study as having a high risk of bias if the following criteria were not met.

- Random sequence generation;
- Allocation concealment;
- Blinding of outcome assessment.

Imputed values

We analysed the effects of excluding data from studies where we used imputed values in intraclass correlation analysis to calculate the design effect in cluster-RCTs (see Unit of analysis issues), or where means or SDs were imputed.

Attrition rate

We excluded studies with differences in attrition between groups that exceeded 10%.

Summary of findings and assessment of the certainty of the evidence

We created a summary of findings table to capture the outcomes at the final follow-up from interventions with oral nutritional supplements of energy-protein, which can be a primary intervention for malnutrition in stroke patients (Foley 2009).

- Disability (primary outcome);
- ADL (primary outcome);
- Gait: gait speed;
- Nutritional status: change in body weight;
- Death: all-cause;
- Incidence of complications (adverse events);
- QOL: EQ-5D score.

We used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of a body of evidence as it related to the studies that contributed data to the meta-analyses for the prespecified outcomes (Atkins 2004). We used the methods and recommendations described in Chapter 14 of the *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.3 (Higgins 2022) and the GRADE Handbook (Schünemann 2013) using the GRADEpro GDT software (GRADEpro GDT). We justified all decisions to downgrade the certainty of the evidence in the footnotes, and we made comments to aid the readers' understanding of the review, where necessary.

RESULTS

Description of studies

We identified randomised controlled trials comparing nutritional therapy with control in people after stroke. See Included studies; Excluded studies.

Studies awaiting classification are shown in Studies awaiting classification.

Ongoing studies are shown in Ongoing studies.

The flow diagram depicting the entire process of study selection, including the Screen4Me assessment, is shown in Figure 3.

Figure 3. Prisma flow diagram

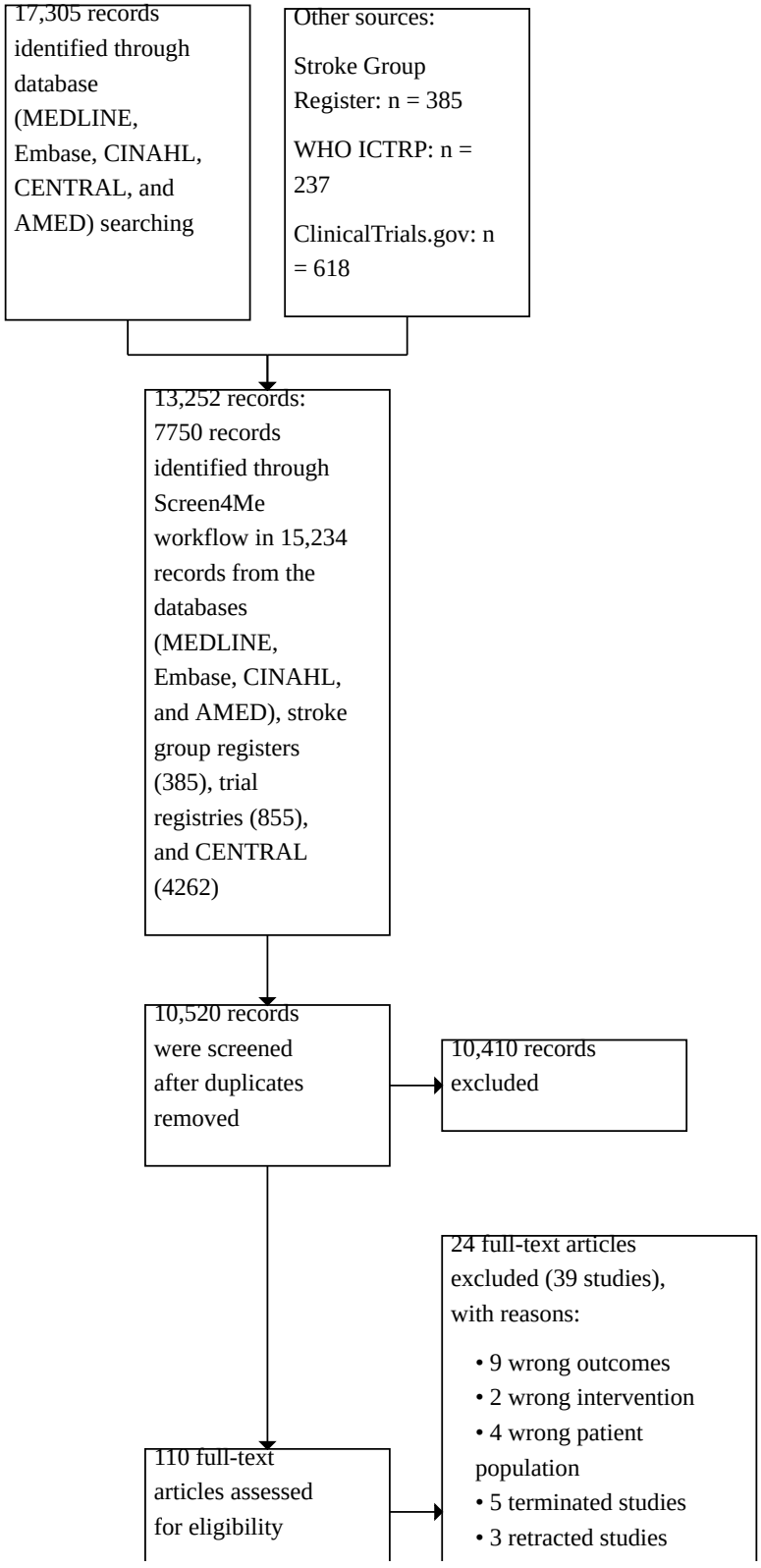
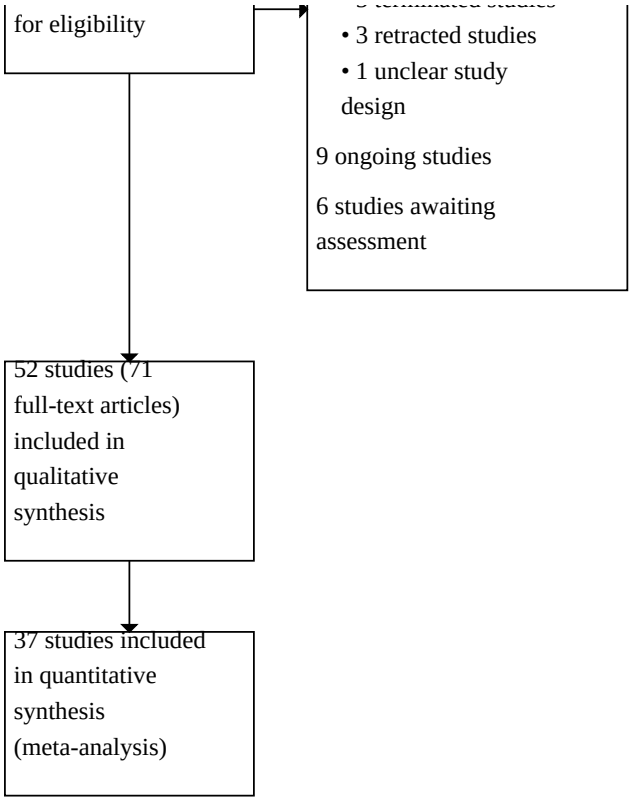


Figure 3. (Continued)



Results of the search

The initial search yielded 18,545 results. We employed the Cochrane Screen4Me to identify potential records of RCTs from MEDLINE, Embase, CINAHL, and AMED, resulting in 7750 records. After removing duplicate records from Screen4Me (7750), stroke group registers (385), trial registries (855), and CENTRAL (4262), 10,520 records were screened. From these, 110 records were selected for full-text assessment based on our predefined inclusion/exclusion criteria.

Included studies

Fifty-two studies involving 11,926 participants were included. The included studies were conducted in Europe (16 studies: Italy 9, Russia 1, Switzerland 1, Norway 2, UK 3), North America (2 studies: USA 2), South America (2 studies: Chile 1, Brazil 1), East Asia (22 studies: Taiwan 2, Japan 6, China 14), South Asia (3 studies: India 3), Southeast Asia (2 studies: Indonesia 1, Malaysia 1), Western Asia (1 study: Iran 1), Oceania (1 study: New Zealand 1), and multiple countries (3 studies). Most of the studies were conducted in Europe, especially Italy, and East Asia, especially in China. The average or median age in a group or overall population ranged from 48 years of age (Saito 2017) to 80.8 years of age (Yoshimura 2019). Amongst the included studies, 32 out of 52 (62%) included older participants aged over 65 years, based on either the mean or median age across all participants or across all groups in a study. Five studies were reported as conference abstracts (Beeharry 2014; Dang 2018; Das 2021; Mohan 2015; Ogawa 2021). See Included studies.

Stroke phase and setting

Thirty-six studies were conducted in the acute phase (within 14 days from stroke onset), 10 in the subacute phase (≥ 15 days and < 6 months from stroke onset), three in the acute and subacute phases, and only three in the chronic phase (≥ 6 months from stroke onset) (Cheng 2019; Poppitt 2009; Sato 2022). Almost all studies (50 studies) were conducted amongst inpatients, with only two amongst outpatients (Cheng 2019; Toole 2004).

Stroke type

Twenty-three studies were conducted amongst patients with ischaemic stroke, three amongst patients with haemorrhagic stroke (Laviano 2011; Zhang 2004), three amongst patients with subarachnoid haemorrhage (Badjatia 2021; Berger 2008; Saito 2017), and 23 amongst a mixed-stroke population (ischaemic or haemorrhagic stroke).

Malnutrition or malnutrition risk as an inclusion criterion

Six studies included patients with malnutrition or malnutrition risk, as defined by the authors (Gariballa 1998; Ha 2010a; Ha 2010b; Laviano 2011; Rabadi 2008; Yoshimura 2019). Two studies used the Malnutrition Universal Screening Tool to assess nutritional risk (Ha 2010a; Ha 2010b). One study assessed hypoalbuminemia (Laviano 2011). One study used anthropometric evidence of undernutrition (Gariballa 1998). One study used weight loss (Rabadi 2008). One study included patients with sarcopenia, defined using the 2014 Asian Working Group for Sarcopenia consensus (Yoshimura 2019).

Stroke severity

Of 36 studies that included acute stroke patients, 16 reported the severity using a stroke-specific assessment tool. Most of the studies included patients with mild-to-moderately severe stroke based on the NIHSS score.

We have summarised the characteristics in the included studies in Table 1.

Interventions

We identified 14 intervention comparisons using oral supplements, nine using enteral supplements, two using oral or enteral supplements, two using parenteral supplements, two using parenteral or enteral supplements, and one using oral and parenteral supplements. There were 25 types of nutritional supplements used as an intervention. Thirty-three studies used standard of care as a comparator, 11 used placebo, and eight used another nutrient or a different nutrient dose. The length of intervention ranged from five days to two years, but most of the studies had an intervention phase that lasted approximately one to three months. The characteristics of the interventions in the included studies are summarised in Table 2.

Outcomes

In the 52 studies included, we identified the outcomes of disability (9) and ADL (17) as primary outcomes. Secondary outcomes included gait (4), all-cause mortality (18), quality of life (5), muscle mass (5), muscle strength (5), cognitive function (4), physical performance (4), stroke recurrence (7), swallowing function (4), neurological impairment (12), and incidence of complications (adverse events) (27).

Disability: Eight used the mRS and one used Glasgow Outcome Scale Extended for assessment.

ADL: Four studies used FIM motor score, BI in seven, and FIM total score specifically for ADL in three studies. Three studies did not specify the assessment tool used.

Gait: Assessments included gait speed (2) and walking capacity (3).

Nutritional status: Assessments included body weight (10), triceps skinfold thickness (6), calf circumference (3), thigh muscle cross-sectional area (1), lean mass (1), skeletal muscle index (2), thigh circumference (1), mid-upper arm circumference (3), arm muscular circumference (5), and decreased nutritional status (2).

Quality of life: Assessments included NeuroQoL short-form (1), EQ-5D (2), and SF-36 (2).

Muscle strength: Assessments included grip strength (4) and knee-extensor strength (1).

Cognitive function: Assessments included FIM cognition score (2), MMSE score (1), and Montreal Cognitive Assessment score (1).

Physical performance: Assessments included Fugl-Meyer Assessment (2), Timed Up and Go (2), Berg Balance Scale (1), Short Performance Physical Battery score (1), 30-second chair test (1), and Rivermead Mobility Index (1).

Swallowing function: Assessments included the water swallow test (1) and Dysphagia Outcome and Severity Scale (2). One study reported better swallowing function as an outcome but did not report the assessment tool.

Neurological impairment: Assessments included the NIHSS score (12), and Canadian Neurological Score (1). One study assessed good neurologic performance using a combination of NIHSS, BI, and mRS scores.

Incidence of complications (adverse events): of 27 studies that reported complications, seven reported no occurrence of complications, while the remainder reported one or more complications during the intervention phase. We did not find any complications of liver failure and sarcopenia in this review.

Excluded studies

We excluded 24 studies for various reasons. See Excluded studies. The main reason for exclusion was that the outcomes did not align with our specified criteria. Out of 24 studies, eight were excluded because they reported biological outcomes instead of the clinical outcomes we were interested in, representing the most common reason for exclusion. Furthermore, five studies were from registries where the trial was terminated early, representing the second most common reason for exclusion.

Ongoing studies

We identified nine ongoing studies. See Ongoing studies.

Of these, two studies have included acute stroke patients (NCT04259307; NCT04386525), one has included acute and subacute stroke patients (DRKS00005577), one has included subacute stroke (UMIN000035365), one has included subacute and chronic stroke patients (NCT02347995), and one lacks the relevant information (IRCT20190305042937N1). Regarding stroke type, two studies have included ischaemic stroke (DRKS00005577; NCT04386525), one has included ischaemic or haemorrhagic stroke (IRCT20190305042937N1), and the others have not specified the relevant information. The planned interventions include amino acids (DRKS00005577), folic acids and vitamin D (IRCT20190305042937N1), energy (NCT04259307), and fatty acids (NCT04386525; UMIN000035365). Disability has been selected as an outcome in three studies (DRKS00005577; NCT04386525) and ADL in four studies (DRKS00005577; NCT04259307; NCT04386525; UMIN000035365). One study has included patients with malnutrition risk or malnutrition (MNA scores < 12) (NCT04259307), and one study has included patients with malnutrition (MNA Short-Form < 7 and BMI < 20.0 kg/m^2) (UMIN000035365).

Studies awaiting classification

We identified six studies awaiting classification. See Studies awaiting classification.

Of these, two studies assessed FIM (NCT04459091; UMIN000023954), one study assessed BI (ISRCTN11086312), and two studies assessed mRS (ISRCTN11086312; NCT04295044).

Risk of bias in included studies

Information on the risk of bias assessment is provided in the Included studies and is summarised in Figure 1 and Figure 2.

Of the 52 studies, only two studies were entirely at low risk of bias.

Allocation

Of the 52 studies, 27 were at low risk of bias for random sequence generation, and 15 were at low risk of bias for allocation, with none of the studies at high risk of bias in either category.

Blinding

Of the 52 studies, 15 studies were at low risk of bias, and five studies were at high risk of bias for blinding of participants and personnel.

Fifteen studies were at low risk of bias, and 11 studies were at high risk of bias for blinding of outcome assessment.

Incomplete outcome data

Of the 52 studies, 38 studies were at low risk of bias, and none of the studies were at high risk of bias.

Selective reporting

Of the 52 studies, 12 studies were at low risk of bias, and five studies were at high risk of bias. Two studies reported outcomes that were not listed in the registry, and three studies failed to report the outcomes that were listed in the registry.

Other potential sources of bias

Of the 52 studies, 15 were free of other potential sources of bias and were assessed as being at low risk of bias. Thirteen studies were at high risk of bias. We found a conflict of interest between the study and the product company in seven studies (Berger 2008; De Aguilar-Nascimento 2011; Honaga 2022; Laviano 2011; Poppitt 2009; Toole 2004; Yoshimura 2019, of which two studies had authors who were affiliated with a product company (Honaga 2022; Yoshimura 2019).

Effects of interventions

See: **Summary of findings 1** Summary of findings

In a table, we have summarised the findings of nutritional intervention using oral energy and protein supplements, which was the primary nutritional intervention in this review, as described in the background section. See Summary of findings 1.

Oral nutritional supplements (energy and protein) versus no supplements

Primary outcome: Disability

One study (Dennis 2005a) assessed disability using the mRS and identified 'good status' as having scores of 0 to 2. The study found no evidence of a difference in reducing disability at follow-up (for 'good status': OR 0.97, 95% CI 0.86 to 1.10; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.1)

Primary outcome: ADL

Three studies assessed ADL. In two studies (Rabadi 2008; Yoshimura 2019) , there was an effect in favour of the intervention for ADL assessed using the FIM motor score at the end of the intervention phase (MD 8.74, 95% CI 5.93 to 11.54; I^2 = 0%; 2 RCTs, 165 participants; very low-certainty evidence; Analysis 1.2). None of the studies met our criteria for the sensitivity analyses, specifically due to issues with missing data, high risk of bias, use of imputed data, and attrition rates. We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no evidence of a difference between the stroke phases (P = 0.72, I^2 = 0%; Analysis 1.2), and stroke type (P = 0.72, I^2 = 0%; Analysis 1.3). Subgroup analyses were not possible for nutritional status at baseline, as both studies included malnutrition or risk of malnutrition as inclusion criteria. One study reported ADL using BI with the median value and IQR (Gariballa 1998). We contacted the study author to obtain data on the mean value and SD, but received no response. The study reported that the trend of BI scores was similar between the groups at baseline (intervention group: median 45, IQR 20 to 58.75, control group: median 35, IQR 16.25 to 48.75) and follow-up (intervention group: median 90, IQR 60 to 93.75, control group: median 75, IQR 47 to 87.5).

Secondary outcome: Gait

Walking capacity

One study assessed walking capacity using the 2-minute walk test and the 6-minute walk test (Rabadi 2008). There was an effect in favour of the intervention for walking capacity assessed using the 2-minute walk test and 6-minute walk test at the end of the intervention phase (MD 63.92, 95% CI 29.49 to 98.35 for 2-minute walk test; MD 133.27, 95% CI 31.10 to 234.55 for 6-minute walk test; 1 RCT, 116 participants; low-certainty evidence; Analysis 1.5; Analysis 1.6).

Secondary outcome: Nutritional status

Body weight

Three studies assessed body weight (Aquilani 2008a; Aquilani 2008b; Rabadi 2008). There was an intervention effect on body weight change during the intervention phase (MD 0.90, 95% CI 0.23 to 1.58; I^2 = 0%; 3 RCTs, 205 participants; very low-certainty evidence; Analysis 1.8). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke phases (P = 0.96, I^2 = 0%; Analysis 1.8), stroke types (P = 0.61, I^2 = 0%; Analysis 1.9), and nutritional status at baseline (P = 0.61, I^2 = 0%; Analysis 1.10).

Triceps skinfold thickness

One study assessed triceps skinfold thickness (Li 2014). There was an effect in favour of the intervention for triceps skinfold thickness (TSF) at the end of the intervention phase (MD 2.30, 95% CI 0.92 to 3.68; 1 RCT, 148 participants; low-certainty evidence; Analysis 1.11).

Skeletal muscle index

One study reported SMI with the median and IQR (Yoshimura 2019). We contacted the study author to obtain data on the mean and SD. We received a response, but they did not accommodate our request. The study reported that there was a difference in SMI between the groups at the end of the intervention: intervention group median 5.9 (IQR 5.1 to 6.8), control group median 5.6 (IQR 4.9 to 6.4).

Secondary outcome: All-cause mortality

Two studies assessed all-cause mortality (Dennis 2005a; Gariballa 1998). There was no evidence of a difference in all-cause mortality at follow-up (OR 0.57, 95% CI 0.14 to 2.28; I^2 = 65%; 2 RCTs, 4065 participants; low-certainty evidence; Analysis 1.12). Subgroup analyses were not possible for the stroke phase, as both studies focused on the acute phase. There was no difference between stroke types (P = 0.09, I^2 = 65.4%; Analysis 1.13) and nutritional status at baseline (P = 0.09, I^2 = 65.4%; Analysis 1.14).

Secondary outcome: Muscle strength

Grip strength

One study assessed grip strength (Yoshimura 2019). There was an effect in favour of the intervention for grip strength at the end of the intervention (MD 4.90, 95% CI 2.31 to 7.49; 1 RCT, 49 participants; very low-certainty evidence; Analysis 1.7).

Secondary outcome: Cognitive function

Two studies reported cognitive function. One study reported the FIM cognition score with the median and IQR for each group (Yoshimura 2019). We contacted the study authors to obtain data on the mean and SD. We received a response, but they did not provide the requested data. The study reported that there was no difference at the end of the intervention (intervention group: median 26, IQR 12 to 13, control group: median 27, IQR 16 to 32). Another study reported the MMSE score using logarithm transformation at baseline and follow-up (Aquilani 2008a). We calculated the mean and SD using those data and inputted the data as the change score for each group. There was no evidence of a difference in the change in the MMSE score during the intervention phase (MD 3.68, 95% CI −8.67 to 16.03; 1 RCT, 48 participants; very low-certainty evidence; Analysis 1.16).

Secondary outcome: Stroke recurrence

One study assessed stroke recurrence (Dennis 2005a). There was no evidence of a difference in stroke recurrence at the end of the intervention phase (OR 1.16, 95% CI 0.77 to 1.75; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.15).

Secondary outcome: Neurological impairment

NIHSS

Two studies assessed NIHSS scores. One study (Li 2014) reported mean NIHSS scores and SDs at baseline and the end of the intervention, while another study (Aquilani 2008b) reported change in scores during the intervention phase. We converted the mean and SD to the mean change score and SD in each group for synthesis. There was an intervention effect in the change in NIHSS score during the intervention phase (MD −2.12, 95% CI −3.84 to −0.39; 2 RCTs, 190 participants; low-certainty evidence; Analysis 1.4). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke phases (P = 0.08, I^2 = 67%; Analysis 1.4). Subgroup analyses were not possible for stroke type, as both studies were conducted on ischaemic stroke, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Secondary outcome: Quality of life

One study reported the EQ-5D score with its median and IQR (Dennis 2005a). The study also reported mean differences between the groups. We contacted the study author to obtain the mean score and SD in each group, but no response was received. The median utility score for all patients, including those who died, was 0.52 (IQR 0.03 to 0.74) in both groups and there was no statistical difference (P = 0.96). The mean difference was 0.001 (95% CI -0.023 to 0.025) between the groups.

Secondary outcome: Incidence of complications (adverse events)

Pressure sores

One study reported the incidence of pressure sores (Dennis 2005a). There was no evidence of a difference in incidence of pressure sores during the intervention phase (OR 0.57, 95% CI 0.30 to 1.08; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.17).

Pneumonia

One study reported the incidence of pneumonia (Dennis 2005a). There was no evidence of a difference in incidence of pneumonia during the intervention phase (OR 1.13, 95% CI 0.88 to 1.47; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.19).

Urinary tract infection

One study reported the incidence of urinary tract infection (Dennis 2005a). There was no evidence of a difference in incidence of urinary tract infection during the intervention phase (OR 0.92, 95% CI 0.72 to 1.18; 1 RCT, 4023 participants; very low-certainty evidence; Analysis 1.20).

Infections: pneumonia, urinary tract, and septicaemia

One study reported the incidence of infections (pneumonia, urinary tract, and septicaemia)(Gariballa 1998). There was no evidence of a difference in this outcome during the intervention phase (OR 0.68, 95% CI 0.20 to 2.30; 1 RCT, 42 participants; very low-certainty evidence; Analysis 1.18).

Diarrhoea

One study reported the incidence of diarrhoea (Dennis 2005a). There was an intervention effect on incidence of diarrhoea during the intervention phase (OR 4.29, 95% CI 1.98 to 9.28; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.23).

Hyperglycaemia/Hypoglycaemia

One study reported the incidence of hyperglycaemia or hypoglycaemia (Dennis 2005a). There was an intervention effect on this outcome during the intervention phase (OR 15.6, 95% CI 4.84 to 50.23; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.21).

Gastrointestinal haemorrhage

One study reported the incidence of gastrointestinal haemorrhage (Dennis 2005a). There was no evidence of a difference in the incidence of gastrointestinal haemorrhage during the intervention phase (OR 1.56, 95% CI 0.86 to 2.82; 1 RCT, 4023 participants; low-certainty evidence; Analysis 1.22).

Oral nutritional supplements (vitamin D) versus no supplements

Primary outcome: Disability

One study reported disability using mRS and showed good status with scores of 0 to 2. The study found no evidence of a difference in reducing disability at the end of the intervention (for good status: OR 1.21, 95% CI 0.41 to 3.63; 1 RCT, 53 participants; low-certainty evidence; Gupta 2016; Analysis 2.1)

Primary outcome: ADL

Two studies reported ADL. One study (Momosaki 2019) reported ADL assessed using a change in the BI score, and another study (Torrisi 2021) reported the mean scores and SDs of the FIM total score at baseline and the end of the intervention phase. We converted these means and SDs to the mean value and SD of the FIM change score, respectively, as described in the Methods section. We used a correlation coefficient of 0.78, which was calculated using the SD of FIM change scores from one study (Rabadi 2008). There was no evidence of a difference in the change in ADL during the intervention phase (SMD 0.45, 95% CI −0.57 to 1.48; I^2 = 86%; 2 RCTs, 140 participants; very low-certainty evidence; Analysis 2.2). For the sensitivity analysis, even after excluding the one study (Torrisi 2021) that used imputed values, there was no evidence of a difference (MD −0.50, 95% CI −5.98 to 4.98; 1 RCT, 100 participants; Analysis 2.3). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was a difference between the stroke phases (P = 0.008, I^2 = 86%; Analysis 2.2), and types of stroke (P = 0.008, I^2 = 86%; Analysis 2.4). Subgroup analyses were not possible for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Secondary outcome: Nutritional status

Calf circumference

One study reported a change in calf circumference for each right foot and left foot (Momosaki 2019). We combined these data and calculated the mean and SD as a total. There was no evidence of a difference in calf circumference at the end of the intervention phase (MD 0.40, 95% CI −0.57 to 1.37; 1 RCT, 50 participants; moderate-certainty evidence; Analysis 2.5).

Secondary outcome: All-cause mortality

One study reported all-cause mortality (Gupta 2016). There was no evidence of a difference in all-cause mortality at the end of the intervention phase (OR 0.29, 95% CI 0.08 to 1.09; 1 RCT, 53 participants; moderate-certainty evidence; Analysis 2.6).

Secondary outcome: Muscle strength

Grip strength

One study reported a change in grip strength for both the right and left hand (Momosaki 2019). We combined the data for both hands and calculated the mean and SD as the overall total. There was no evidence of a difference in the change in grip strength at the end of the intervention (MD 0.50, 95% CI −0.85 to 1.85; 1 RCT, 100 participants; moderate-certainty evidence; Analysis 2.7).

Oral nutritional supplements (protein) versus no supplements

Primary outcome: Disability

Two studies reported disabilities using mRS. One study (Hashemilar 2020) found no evidence of a difference in disability at the end of the intervention (MD 0.21, 95% CI −0.42 to 0.84; 1 RCT, 42 participants; low-certainty evidence; Analysis 3.1). Another study (Badjatia 2021) reported mRS as the median value and IQR. We contacted the study authors to obtain the mean and SD, but no response was received. The study showed a lower score in the mRS in the intervention group (median 1, IQR 0 to 2) than in the control group (median 2, IQR 1 to 3) at follow-up.

Secondary outcome: Gait

Walking capacity

One study reported walking capacity (Cheng 2019). There was no evidence of a difference in walking capacity assessed using the 6-minute walk test at the end of the intervention phase (MD 6.10, 95% CI −15.40 to 27.60; 1 RCT, 20 participants; moderate-certainty evidence; Analysis 3.2).

Secondary outcome: Nutritional status

Quadriceps muscle atrophy

One study reported acute quadriceps muscle atrophy using a helical CT scan (Badjatia 2021). Scans started at the patella and ended at the femoral head. There was an effect in favour of the intervention on a proportion of quadriceps skeletal muscle atrophy at the end of the intervention (MD −6.00, 95% CI −7.95 to −4.05; 1 RCT, 118 participants; very low-certainty evidence; Analysis 3.3).

Lean mass

One study reported lean mass using dual-energy x-ray absorptiometry (Cheng 2019). There was no evidence of a difference in change in lean mass during the intervention phase (MD 795, 95% CI −542.13 to 2132.13; 1 RCT, 20 participants; moderate-certainty evidence; Analysis 3.4).

Secondary outcome: Quality of life

One study assessed QOL using the short-form NeuroQoL measurement tool and reported the score for each domain (Badjatia 2021). There was no evidence of a difference in the fatigue domain score at follow-up (MD −12.00, 95% CI −29.43 to 5.43; 1 RCT, 25 participants; very low-certainty evidence; Analysis 3.5). There was an effect on the lower extremity mobility domain score at follow-up (MD 17.00, 95% CI 1.64 to 32.36; 1 RCT, 25 participants; very low-certainty evidence; Analysis 3.6). There was no evidence of a difference in the cognition domain score at follow-up (MD 4.00, 95% CI −3.11 to 11.11; 1 RCT, 25 participants; very low-certainty evidence; Analysis 3.7).

Secondary outcome: Cognitive function

One study reported the Montreal Cognitive Assessment score with the median and IQR (Badjatia 2021). We contacted the study authors to obtain the mean and SD, but no response was received. The study reported that there was no difference in the Montreal Cognitive Assessment score between the groups at follow-up (intervention group median 29, IQR 24 to 29, control group median 26, IQR 23 to 29).

Secondary outcome: Physical performance

Lower extremity function

One study reported lower extremity function (Cheng 2019). There was no evidence of a difference in lower extremity function score in the Fugl-Meyer Assessment at the end of the intervention (MD 0.40, 95% CI −0.36 to 1.16; 1 RCT, 20 participants; moderate-certainty evidence; Analysis 3.8).

Timed Up & Go test

One study reported the Timed Up & Go test (Cheng 2019). There was no evidence of a difference in physical performance assessed using the Timed Up & Go test at the end of the intervention (MD −1.10,

95% CI −3.97 to 1.77; 1 RCT, 20 participants; moderate-certainty evidence; Analysis 3.9).

Berg Balance Scale

One study reported the Berg Balance Scale (Cheng 2019). There was a positive intervention effect on physical performance assessed using the Berg Balance Scale at the end of the intervention (MD 1.50, 95% CI 0.17 to 2.83; 1 RCT, 20 participants; moderate-certainty evidence; Analysis 3.10).

Short Performance Physical Battery score

One study reported the Short Performance Physical Battery score with the median and IQR (Badjatia 2021). We contacted the study authors to obtain the mean and SD, but no response was received. The study found a positive effect on the score at follow-up (intervention group median 12, IQR 10 to 12, control group median 9, IQR 4 to 12; P = 0.04).

Secondary outcome: Neurological impairment

NIHSS

One study reported the NIHSS (Hashemilar 2020). There was no evidence of a difference in change in NIHSS score during the intervention phase (MD −0.58, 95% CI −1.73 to 0.57; 1 RCT, 42 participants; low-certainty evidence; Analysis 3.13).

Secondary outcome: Cognitive function

One study reported the Montreal Cognitive Assessment score with the median and IQR (Badjatia 2021). We contacted the study author to obtain the mean and SD, but no response was received. The study reported that there was no difference in Montreal Cognitive Assessment score between the groups at follow-up (intervention group median 29, IQR 24 to 29, control group median 26, IQR 23 to 29).

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

One study reported the incidence of pneumonia (Badjatia 2021). There was no evidence of a difference in the incidence of pneumonia during the intervention phase (OR 0.18, 95% CI 0.01 to 4.25; 1 RCT, 25 participants; very low-certainty evidence; Analysis 3.11).

Urinary tract infection

One study reported the incidence of urinary tract infection (Badjatia 2021). There was no evidence of a difference in the incidence of urinary tract infection during the intervention phase (OR 0.53, 95% CI 0.10 to 2.98; 1 RCT, 25 participants; very low-certainty evidence; Analysis 3.12).

Vomiting

One study reported that there was no vomiting in either the intervention group or the control group (Badjatia 2021).

Oral nutritional supplements (protein and vitamin D) versus no supplements

Primary outcome: ADL

One study reported ADL (Honaga 2022). There was no evidence of a difference in ADL assessed using the FIM motor score at the end of the intervention phase (MD −1.30, 95% CI −10.38 to 7.78; 1 RCT, 50 participants; very low-certainty evidence; Analysis 4.1).

Secondary outcome: Gait

Gait speed

Two studies reported gait speed (Honaga 2022; Sato 2022). There was no evidence of a difference in gait speed assessed using the 10-metre walk test at the end of the intervention (MD −0.03, 95% CI −0.21 to 0.14; I^2 = 0%; 2 RCTs, 65 participants; very low-certainty evidence; Analysis 4.2). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no evidence of a difference between the stroke phases (P = 0.34, I^2 = 0%; Analysis 4.2). Subgroup analyses were not possible for the stroke type, as both studies were conducted on ischaemic and haemorrhagic stroke, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Secondary outcome: Walking capacity

One study reported walking capacity (Sato 2022). No evidence of a difference was identified in walking capacity assessed using the 6-minute walk test at the end of the intervention phase (MD 46.00, 95% CI −68.51 to 160.51; 1 RCT, 15 participants; low-certainty evidence; Analysis 4.3).

Secondary outcome: Nutritional status

Body weight

One study reported body weight (Sato 2022). There was no evidence of a difference in body weight at the end of the intervention (MD −2.50, 95% CI −10.75 to 5.75; 1 RCT, 15 participants; low-certainty evidence; Analysis 4.11).

Thigh muscle area

One study reported cross-sectional areas of the thigh muscle (Honaga 2022). The thigh muscle area was measured using a six-detector row CT scanner at 20 cm above the upper edge of the patella. The outcomes were total area, normal area (normal-density muscle), and an area with fat infiltration (low-density muscle) on the paretic and non-paretic sides. There was no evidence of a difference in these areas at the end of the intervention phase (total area on the paretic side: MD −5.60, 95% CI −18.92 to 7.72; total area on the non-paretic side: MD −7.40, 95% CI −20.64 to 5.84; normal area on the paretic side: MD −3.10, 95% CI −13.46 to 7.26; normal area on the non-paretic side: MD −4.20, 95% CI −14.30 to 5.90; area with fat infiltration on the paretic side: MD −2.50, 95% CI −6.63 to 1.63; area with fat infiltration on the non-paretic side: MD −3.10, 95% CI −7.49 to 1.29; very low-certainty evidence; Analysis 4.5; Analysis 4.6; Analysis 4.7; Analysis 4.8; Analysis 4.9; Analysis 4.10).

Skeletal muscle index

One study reported skeletal muscle index (Honaga 2022). There was no evidence of a difference in change in skeletal muscle index at the end of the intervention phase (MD −0.06, 95% CI −0.40 to 0.28; 1 RCT, 50 participants; very low-certainty evidence; Analysis 4.4).

Secondary outcome: Muscle strength

Grip strength

One study reported grip strength for each paretic and non-paretic side (Honaga 2022). There was no evidence of a difference in grip

strength at the end of the intervention (paretic side: MD −3.40, 95% CI −8.25 to 1.45; non-paretic side: MD −0.30, 95% CI −5.33 to 4.73; 1 RCT, 50 participants; very low-certainty evidence; Analysis 4.12; Analysis 4.13).

Knee-extensor strength

One study reported knee-extensor strength for both the paretic and non-paretic sides (Sato 2022). There was no evidence of a difference in the knee-extensor strength at the end of the intervention (paretic side: MD 2.80, 95% CI −7.65 to 13.25; non-paretic side: MD 4.70, 95% CI −3.96 to 13.36; 1 RCT, 15 participants; low-certainty evidence; Analysis 4.14; Analysis 4.15).

Secondary outcome: Physical performance

Timed Up & Go test

One study reported the Timed Up & Go test (Honaga 2022). There was no evidence of a difference in physical performance assessed using the Timed Up & Go test at the end of the intervention (MD −2.30, 95% CI −6.05 to 1.45; 1 RCT, 50 participants; very low-certainty evidence; Analysis 4.17).

30-second chair test

One study reported the 30-second chair test (Honaga 2022). There was no evidence of a difference in physical performance assessed using the 30-second chair test at the end of the intervention (MD −2.30, 95% CI −6.05 to 1.45; 1 RCT, 50 participants; very low-certainty evidence; Analysis 4.16).

Oral nutritional supplements (vitamin C and vitamin D) versus no supplements

Secondary outcome: Stroke recurrence

One study reported stroke recurrence (Ullegaddi 2005a). There was no evidence of a difference in stroke recurrence at follow-up (OR 0.48, 95% CI 0.04 to 5.66; 1 RCT, 48 participants; low-certainty evidence; Analysis 5.1).

Secondary outcome: Incidence of complications (adverse events)

Infections (pneumonia, urinary tract infection, and septicaemia)

One study reported the outcome narratively (Ullegaddi 2005a). We contacted the study authors to obtain data, but no response was received. The study found that there was no difference between the groups at the end of the intervention.

Oral nutritional supplements (zinc) versus no supplements

Secondary outcome: Nutritional status

Body weight

One study reported body weight at the end of the intervention with the mean and 95% CI (Aquilani 2009). We calculated its SD from 95% CIs. There was no evidence of a difference in body weight at the end of the intervention (MD 1.90, 95% CI −7.63 to 11.43; 1 RCT, 26 participants; low-certainty evidence; Analysis 6.2).

Secondary outcome: Neurological impairment

NIHSS

One study reported the NIHSS score with a mean and 95% CI (Aquilani 2009), and we calculated its SD from 95% CIs. There was no evidence of a difference in the NIHSS score at the end of the intervention (MD 0.00, 95% CI − 3.12 to 3.12; 1 RCT, 26 participants; low-certainty evidence; Analysis 6.1)

Oral nutritional supplements (fatty acids) versus no supplements

Secondary outcome: Quality of life

One study that used omega-3 polyunsaturated fatty acids reported QOL using SF-36 (Poppitt 2009). There was no evidence of a difference in the physical component scale at follow-up (MD −0.10, 95% CI −4.06 to 3.86; 1 RCT, 102 participants; low-certainty evidence; Analysis 7.1). There was no evidence of a difference in the mental component scale at follow-up (MD −1.00, 95% CI −5.10 to 3.10; 1 RCT, 102 participants; low-certainty evidence; Analysis 7.2).

Oral nutritional supplements (vitamin E) versus no supplements

Primary outcome: ADL

One study assessed ADL using BI but did not report the score (Daga 1997). We contacted the study authors to obtain data, but received no response. This study reported no difference in the BI scores between the groups at the end of the intervention and follow-up.

Oral whey protein supplements versus oral casein supplements

Secondary outcome: All-cause mortality

One study reported the mortality rate in each group (De Aguilar-Nascimento 2011). There was no evidence of a difference in all-cause mortality at follow-up (whey protein group 30%, casein group 26.7%; P = 1.00).

Oral high-dose multivitamin (vitamin B group) supplements versus low-dose multivitamin supplements

Secondary outcome: All-cause mortality

One study reported the mortality rate and found no evidence of a difference between the high-dose group (99/1827 deaths) and the low-dose group (117/1853 deaths) at follow-up (Toole 2004).

Secondary outcome: Stroke recurrence

One study reported ischaemic stroke recurrence. There was no evidence of a difference between the high-dose group (152/1827) and the low-dose group (148/1853) at the end of the intervention (Toole 2004).

Oral nutritional supplements (vitamin E and vitamin C) versus oral nutritional supplements (fatty acids) versus oral nutritional supplements (vitamin E, vitamin C, and fatty acids) versus no supplements

Primary outcome: ADL

One study addressed ADL using BI scores amongst four groups at the end of the intervention and reported no evidence of a difference (vitamin E and vitamin C group 77.78 ± 19.06; fatty acid group 83.85 ± 22.66; vitamin E and vitamin C and fatty acids 80.50 ± 19.06; and placebo 73.64 ± 24.50; Garbagnati 2009).

Secondary outcome: All-cause mortality

One study reported the number of deaths, but only four participants died at follow-up in the overall population (Garbagnati

2009). The study showed that there was no difference between groups.

Secondary outcome: Physical performance

One study assessed the Rivermead Mobility Index score and found no difference at the end of the intervention (vitamin E and vitamin C group 9.89 ± 4.57, fatty acids group 11.20 ± 4.91, vitamin E and vitamin C and fatty acids group 11.60 ± 4.57, placebo 10.18 ± 4.60; Garbagnati 2009).

Oral vitamin A supplements versus oral vitamin D supplements versus oral vitamin A and vitamin D supplements versus no supplements

Secondary outcome: Neurological impairment

One study reported the NIHSS score at the end of the intervention in four groups (vitamin A 10.30 ± 1.59, vitamin D 10.40 ± 1.23, vitamin A and D 6.00 ± 1.52, placebo 11.75 ± 1.29), and the greatest decrease was found in the vitamin A and D group (Kadri 2020).

Oral vitamin E and vitamin C supplements versus vitamin B supplements versus combined vitamin E, vitamin C, and vitamin B supplements versus no supplements

Secondary outcome: Incidence of complications (adverse events)

Infections (pneumonia, urinary tract infection, and septicaemia)

One study reported the proportion of participants who developed infections (Ullegaddi 2005b). We contacted the study authors to obtain more data, but no response was received. The study found that there was no difference in the proportion of participants with infections amongst the groups.

Secondary outcome: Stroke recurrence

One study assessed reinfarctions and reported the results narratively (Ullegaddi 2005b). We contacted the study author to obtain more data, but no response was received. The study found that there was no difference in the number of reinfarctions amongst the groups.

Oral sodium (Na) supplements versus potassium (K) supplements versus potassium/magnesium (K/Mg) supplements

Secondary outcome: All-cause mortality

One study assessed the mortality effects of salts formulated with three nutrients: sodium (Na)-based, potassium (K)-based, and potassium/magnesium (K/Mg)-based (Pan 2017). There was no difference in the number of deaths amongst the groups at the end of the intervention (sodium (Na) group 1/99, potassium (K) group 0/97, and potassium/magnesium (K/Mg) group 2/95).

Secondary outcome: Neurological impairment

One study assessed good neurologic performance, which was defined as a score of 0 on NIHSS, a score of 100 on BI, and 0 or 1 on mRS (Pan 2017). Compared to the sodium (Na) group and potassium (K) group, the potassium/magnesium (K/Mg) group demonstrated better neurologic performance at the end of the intervention (OR 2.25, 95% CI 1.09 to 4.67; P = 0.029).

Secondary outcome: Stroke recurrence

One study reported only the number of stroke recurrences in each group (sodium (Na) group 1/99, potassium (K) group 2/97, and potassium/magnesium (K/Mg) group 2/95) (Pan 2017).

Early enteral nutrition versus control

Primary outcome: Disability

Four studies reported disability using mRS, of which two (Dennis 2005b; Zheng 2015) defined 'good status' as mRS scores of 0 to 3. The studies found no evidence of a difference in reducing disability at follow-up (for 'good status': OR 1.37, 95% CI 0.76 to 2.46; I^2 = 62%; 2 RCTs, 1005 participants; very low-certainty evidence; Analysis 8.1). None of the studies met our criteria for the sensitivity analyses, specifically due to issues with missing data, high risk of bias, use of imputed data, and attrition rates. Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase; for the stroke type, since both studies focused on ischaemic stroke and intracerebral haemorrhage; and for nutritional status at baseline, as neither study included malnutrition nor the risk of malnutrition as inclusion criteria. Two studies reported the outcome using mRS or NIHSS narratively. We contacted the study authors to obtain data, but no response was received. One study reported no difference between the groups (Dang 2018), while another study reported that the intervention group had a lower score at the end of the intervention (P < 0.05) (Kang 2023).

Primary outcome: ADL

Five studies reported ADL. A meta-analysis of two studies (Zhao 2020; Zheng 2015) revealed no evidence of a difference in ADL assessed using the BI score at the end of the intervention phase (MD 0.66, 95% CI −1.94 to 3.26; I^2 = 60%; 2 RCTs, 224 participants; very low-certainty evidence; Analysis 8.2). None of the studies met our criteria for the sensitivity analyses, specifically due to issues with missing data, high risk of bias, use of imputed data, and attrition rates. We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no evidence of a difference between the stroke types (P = 0.11, I^2 = 59.8%; Analysis 8.3). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria. One study reported ADL as a categorical variable (Zhang 2004). There was no evidence of a difference in ADL (categorised as 'independent') at the end of the intervention phase (OR 1.79, 95% CI 0.70 to 4.60; 1 RCT, 72 participants; low-certainty evidence; Analysis 8.4). Two studies reported ADL narratively. We contacted the study authors to obtain more data, but no responses were received. One study reported no evidence of a difference in ADL, without specifying the measurement tools used (Dang 2018), while another study reported that the intervention group had a higher score than the control group in BI scores at the end of the intervention (Kang 2023).

Secondary outcome: Nutritional status

Triceps skinfold thickness

Three studies reported triceps skinfold thickness (Ouyang 2003; Zhao 2020; Zheng 2015). There was an effect in favour of the intervention for TSF at the end of the intervention phase (MD 0.98, 95% CI 0.51 to 1.46; I^2 = 0%; 3 RCTs, 286 participants; low-certainty

evidence; Analysis 8.8). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.93, I^2 = 0%; Analysis 8.9). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Arm muscular circumference

Three studies reported arm muscular circumference (AMC) but did not specify the method used for assessment (Ouyang 2003; Zhao 2020; Zheng 2015). There was an effect in favour of the intervention on AMC at the end of the intervention phase (MD 1.45, 95% CI 0.68 to 2.22; I^2 = 63%; 3 RCTs, 286 participants; low-certainty evidence; Analysis 8.10). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.07, I^2 = 63.1%; Analysis 8.11). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Secondary outcome: Swallowing function

Water swallow test

One study reported swallowing function using a water swallow test, but failed to specify which specific tool was used (Li 2016). There was an intervention effect on the water swallow test score at the end of the intervention phase (MD −0.29, 95% CI −0.44 to −0.14; 1 RCT, 112 participants; low-certainty evidence; Analysis 8.12).

Better swallowing function

One study assessed swallowing function but did not report the tool used for the assessment (Dang 2018). The study reported the results narratively. We contacted the study authors to obtain more information, but no response was received. The study found that the intervention group had better function compared to the control group, but there was no evidence of a difference.

Secondary outcome: Neurological impairment

NIHSS score

Two studies reported the NIHSS (Zhao 2020; Zheng 2015). There was an intervention effect on the NIHSS score at the end of the intervention (MD −1.09, 95% CI −1.84 to −0.34; I^2 = 0%; 2 RCTs, 224 participants; low-certainty evidence; Analysis 8.5). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.41, I^2 = 0%; Analysis 8.6). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Improvement in NIHSS score

One study reported the number of participants who showed a ≥ 90% decrease in the NIHSS score from baseline (Li 2016). There was an intervention effect on the improvement of NIHSS score at the end of the intervention (OR 3.94, 95% CI 1.72 to 9.00; 1 RCT, 112 participants; low-certainty evidence; Analysis 8.7).

Secondary outcome: All-cause mortality

Three studies reported all-cause mortality (Dennis 2005b; Zhang 2004; Zheng 2015). There was no evidence of a difference in all-cause mortality at follow-up (OR 0.53, 95% CI 0.27 to 1.07; I^2 = 51%; 3 RCTs, 1077 participants; low-certainty evidence; Analysis 8.13). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.13, I^2 = 51.2%; Analysis 8.14). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Secondary outcome: Stroke recurrence

One study reported stroke recurrence (Dennis 2005b). There was no evidence of a difference in stroke recurrence at follow-up (OR 0.64, 95% CI 0.33 to 1.25; 1 RCT, 859 participants; moderate-certainty evidence; Analysis 8.15).

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

Four studies reported the incidence of pneumonia (Dennis 2005b; Zhang 2004; Zhao 2020; Zheng 2015). There was no evidence of a difference in incidence of pneumonia during the intervention phase (OR 0.59, 95% CI 0.28 to 1.24; I^2 = 71%; 4 RCTs, 1155 participants; very low-certainty evidence; Analysis 8.16). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was a difference between stroke types (P = 0.02, I^2 = 70.9%; Analysis 8.17). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Urinary tract infection

Four studies reported the incidence of urinary tract infection (Dennis 2005b; Zhao 2020; Zheng 2015). There was no evidence of a difference in incidence of urinary tract infection during the intervention phase (OR 0.99, 95% CI 0.70 to 1.39; I^2 = 0%; 3 RCTs, 1083 participants; low-certainty evidence; Analysis 8.18). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.79, I^2 = 0%; Analysis 8.19). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Intestinal infection

Two studies reported the incidence of intestinal infection (Zhang 2004; Zheng 2015). There was no evidence of a difference in incidence of intestinal infection during the intervention phase (OR 0.32, 95% CI 0.07 to 1.37; I^2 = 57%; 2 RCTs, 218 participants; low-certainty evidence; Analysis 8.20). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.13, I^2 = 56.7%; Analysis 8.21). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute

phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Sepsis

One study reported the incidence of sepsis (Zhang 2004). There was no evidence of a difference in incidence of sepsis during the intervention phase (OR 0.20, 95% CI 0.02 to 1.91; 1 RCT, 72 participants; low-certainty evidence; Analysis 8.22).

Pressure sores

Two studies reported the incidence of pressure sores (Dennis 2005b; Zheng 2015). There was no evidence of a difference in incidence of pressure sores during the intervention phase (OR 0.63, 95% CI 0.08 to 4.76; I^2 = 51%; 2 RCTs, 1005 participants; low-certainty evidence; Analysis 8.23). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase; or for stroke type, since both studies focused on ischaemic stroke and intracerebral haemorrhage; and for nutritional status at baseline, as neither study included malnutrition nor the risk of malnutrition as inclusion criteria.

Vomiting

One study reported the incidence of vomiting (Ouyang 2003). There was an intervention effect on incidence of vomiting during the intervention phase (OR 0.19, 95% CI 0.05 to 0.79; 1 RCT, 62 participants; low-certainty evidence; Analysis 8.24).

Diarrhoea

Two studies reported the incidence of diarrhoea (Zhao 2020; Dennis 2005b). There was no evidence of a difference in incidence of diarrhoea during the intervention phase (OR 1.35, 95% CI 0.67 to 2.73; I^2 = 0%; 2 RCTs, 937 participants; moderate-certainty evidence; Analysis 8.25).

Gastrointestinal haemorrhage

Two studies reported the incidence of gastrointestinal haemorrhage (Dennis 2005b; Ouyang 2003; Zhang 2004). There was no evidence of a difference in incidence of gastrointestinal haemorrhage during the intervention phase (OR 0.79, 95% CI 0.47 to 1.33; I^2 = 87%; 3 RCTs, 993 participants; very low-certainty evidence; Analysis 8.26). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria. There was a difference between stroke types (P = 0.0004, I^2 = 87.1%; Analysis 8.27).

Renal problems

One study reported the incidence of renal problems (Dennis 2005b). There was no evidence of a difference in incidence of renal problems during the intervention phase (OR 1.00, 95% CI 0.37 to 2.70; 1 RCT, 859 participants; moderate-certainty evidence; Analysis 8.28).

Pulmonary infections, electrolyte disturbances, gastrointestinal symptoms, and cardiac failure

One study reported the complications rate of pulmonary infections, electrolyte disturbances, gastrointestinal symptoms, and cardiac failure in each group. The rate of the intervention group was 17.14%, while it was 42.86% in the control group (P < 0.05) (Kang 2023).

Enteral nutritional supplements (energy and protein) versus no supplements

Secondary outcome: All-cause mortality

One study reported the mortality rate (Li 2014). We contacted the study author to obtain more data, but received no response. The study reported a positive effect of the intervention (intervention group 15.3%, control group 21.2%).

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

One study reported the proportion of participants who developed pneumonia (Li 2014). We contacted the study author to obtain the number of cases, but no response was received. The study found that there was a positive effect on reducing the proportion of participants who developed pneumonia during the intervention phase (intervention group 41.3%, control group 63.2%).

Enteral nutritional supplement (protein) versus no supplement

Secondary outcome: All-cause mortality

One study reported mortality narratively (Zhou 2006). We contacted the study author to obtain more data, but no response was received. The study reported that mortality was lower in the intervention group than in the control group at follow-up.

Enteral high-protein nutrition versus low-protein nutrition

Primary outcome: Disability

One study used enteral nutrition formulas with different protein-calorie ratios (Gao 2008). This study assessed disability using mRS and reported good status with scores of 1 to 4. The reported number of participants with a good status was 16/30 (54%) in the intervention group and 10/30 (38%) in the control group at the end of the intervention, and there was no evidence of a difference.

Secondary outcome: All-cause mortality

One study reported the proportion of participants who survived (Gao 2008). We contacted the study authors to obtain more data, but no response was received. The study showed no difference in mortality rate at follow-up (intervention group 10.3%, control group 15.4%).

Secondary outcome: Incidence of complications (adverse events)

Vomiting

One study reported that four out of 30 patients in the intervention group and one out of 30 patients in the control group vomited, without providing further details (Gao 2008).

Secondary outcome: Nutritional status

Calf circumference

One study assessed calf circumference at the end of the intervention in three groups (one group with high protein and two groups with low protein) (Zhang 2014). The study reported that calf circumferences in the groups with low protein were smaller than those in the group with high protein (high-protein group: 36.04 ±

5.11, low-protein group A: 30.17 ± 6.6, low-protein group B: 30.48 ± 5.54).

Arm circumference

One study assessed arm circumference at the end of the intervention in three groups (one group with high protein and two groups with low protein) (Zhang 2014). The study reported that arm circumference in the groups with low protein was smaller than that in the high-protein group (high-protein group: 32.11 ± 6.78, low-protein group A: 26.47 ± 3.88, low-protein group B: 26.31 ± 5.09).

Secondary outcome: Incidence of complications (adverse events)

Diarrhoea

One study reported that one out of 30 participants experienced diarrhoea in both the intervention and control groups (Gao 2008).

Enteral nutrition (high energy and multi-nutrients) versus no supplements

Secondary outcome: Nutritional status

Arm muscular circumference

One study assessed AMC using the equation "mid-arm circumference – (0.314 × TSF)" (Zheng 2006). There was no evidence of a difference in AMC at the end of the intervention phase (MD 1.70, 95% CI −5.89 to 9.29; 1 RCT, 54 participants; low-certainty evidence; Analysis 9.1).

Triceps skinfold thickness

One study assessed triceps skinfold thickness (Zheng 2006). There was an effect in favour of the intervention for TSF at the end of the intervention phase (MD 1.70, 95% CI 0.21 to 3.19; 1 RCT, 54 participants; low-certainty evidence; Analysis 9.2).

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

One study reported the incidence of pneumonia (Zheng 2006). There was no evidence of a difference in incidence of pneumonia during the intervention phase (OR 0.41, 95% CI 0.11 to 1.59; 1 RCT, 54 participants; low-certainty evidence; Analysis 9.3).

Urinary tract infection

One study reported the incidence of urinary tract infection (Zheng 2006). There was no evidence of a difference in incidence of urinary tract infection during the intervention phase (OR 0.64, 95% CI 0.10 to 4.17; 1 RCT, 54 participants; low-certainty evidence; Analysis 9.4).

Intestinal infection

One study reported the incidence of intestinal infection (Zheng 2006). There was no evidence of a difference in incidence of intestinal infection during the intervention phase (OR 0.31, 95% CI 0.03 to 3.16; 1 RCT, 54 participants; low-certainty evidence; Analysis 9.5).

Pressure sores

One study reported the incidence of pressure sores (Zheng 2006). There was no evidence of a difference in incidence of pressure sores during the intervention phase (OR 0.32, 95% CI 0.01 to 8.24; 1 RCT, 54 participants; low-certainty evidence; Analysis 9.6).

Enteral nutritional supplements (energy) versus no supplements

Primary outcome: ADL

One study reported an ADL score; however, the assessment tool was not reported (Li 2008). There was an effect in favour of the intervention on the ADL score at the end of the intervention phase (MD 10.68, 95% CI 6.35 to 15.1; 1 RCT, 54 participants; very low-certainty evidence; Analysis 10.1).

Secondary outcome: Neurological impairment

NIHSS

Two studies reported NIHSS scores (Dang 2023; Li 2008). There was an intervention effect on the NIHSS score at the end of the intervention (MD −2.35, 95% CI −2.55 to −2.15; 2 RCTs, 134 participants; low-certainty evidence; Analysis 10.2). We analysed the subgroups according to stroke phase, stroke type, and nutritional status at baseline. There was no difference between stroke types (P = 0.76, I^2 = 0%; Analysis 10.3). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for nutritional status at baseline, since neither included malnutrition nor risk of malnutrition as inclusion criteria.

Secondary outcome: Physical performance

Fugl-Meyer Assessment

One study reported the Fugl-Meyer Assessment score (Dang 2023). There was an intervention effect on the Fugl-Meyer Assessment score at the end of the intervention (MD 16.27, 95% CI 13.58 to 18.96; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.4).

Secondary outcome: Quality of life

SF-36: Physiological function score

One study reported the physiological function score (Dang 2023). There was an intervention effect on the physiological function score at the end of the intervention (MD 12.48, 95% CI 9.11 to 15.85; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.5).

SF-36: Role function score

One study reported the role function score (Dang 2023). There was an intervention effect on the role function score at the end of the intervention (MD 7.11, 95% CI 4.04 to 10.18; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.6).

SF-36: Physical pain score

One study reported the physical pain score (Dang 2023). There was an intervention effect on the physical pain score at the end of the intervention (MD 12.02, 95% CI 8.65 to 15.39; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.7).

SF-36: General health score

One study reported the general health score (Dang 2023). There was an intervention effect on the general health score at the end of the intervention (MD 7.88, 95% CI 5.13 to 10.63; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.8).

SF-36: Mental health score

One study reported the mental health score (Dang 2023). There was an intervention effect on the mental health score at the end of the

intervention (MD 8.71, 95% CI 6.14 to 11.28; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.9).

SF-36: Energy score

One study reported the energy score (Dang 2023). There was an intervention effect on the energy score at the end of the intervention (MD 7.12, 95% CI 4.30 to 9.94; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.10).

SF-36: Social function score

One study reported the social function score (Dang 2023). There was an intervention effect on the social function score at the end of the intervention (MD 9.53, 95% CI 6.05 to 13.1; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.11).

SF-36: Emotional function score

One study reported the emotional function score (Dang 2023). There was an intervention effect on the emotional function score at the end of the intervention (MD 14.51, 95% CI 11.49 to 17.53; 1 RCT, 80 participants; low-certainty evidence; Analysis 10.12).

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

One study reported the incidence of pneumonia (Li 2008). There was no evidence of a difference in incidence of pneumonia during the intervention phase (OR 0.40, 95% CI 0.11 to 1.44; 1 RCT, 54 participants; low-certainty evidence; Analysis 10.13).

Urinary tract infection

One study reported the incidence of urinary tract infection (Li 2008). There was no evidence of a difference in incidence of urinary tract infection during the intervention phase (OR 0.58, 95% CI 0.14 to 2.47; 1 RCT, 54 participants; low-certainty evidence; Analysis 10.14).

Intestinal infection

One study reported the incidence of intestinal infection (Li 2008). There was no evidence of a difference in incidence of intestinal infection during the intervention phase (OR 0.78, 95% CI 0.14 to 4.25; 1 RCT, 54 participants; low-certainty evidence; Analysis 10.15).

Enteral nutritional supplements (fatty acids) versus no supplements

Secondary outcome: Incidence of complications (adverse events)

Pressure sores

One study reported the incidence of pressure sores (Ogawa 2021). There was no evidence of a difference in incidence of pressure sores during the intervention phase in a study using eicosapentaenoic acid (OR 0.10, 95% CI 0.00 to 2.28; 1 RCT, 20 participants; low-certainty evidence; Analysis 11.1).

Enteral individualised nutritional therapy versus control

Secondary outcome: All-cause mortality

One study assessed the effect of individualised nutritional therapy using an indirect calorimeter and reported the result narratively (Das 2021). We contacted the study authors to obtain more data, but no response was received. The study reported that there was no difference in mortality in the ICU between the groups.

Enteral essential amino acids and fatty acids-enriched nutrition versus enteral protein (nonessential amino acids-based)-enriched nutrition

Secondary outcome: All-cause mortality

One study reported the mortality rate at the end of the intervention and found that there was no difference in the number of deaths between the groups, with both groups having two deaths each (Tajiri 2008).

Secondary outcome: Neurological impairment

One study reported the NIHSS scores at the end of the intervention and the change scores with the median values (Tajiri 2008). We contacted the study authors to obtain data on the means and SDs, but no response was received. The study reported that there was no difference in the scores at the end of the intervention (intervention group median 15, control group median 16) and the change scores (intervention group median −2, control group median −1) between the groups.

Secondary outcome: Incidence of complications (adverse events)

Diarrhoea or vomiting

One study reported the number of people with diarrhoea or vomiting and reported no difference between the two groups (Tajiri 2008). The number of people with diarrhoea or vomiting in the amino acids and fatty acids-enriched nutrition group was four out of 26, and, in the protein-enriched nutrition group, it was two out of 15.

Oral or enteral nutritional supplements (essential amino acids) versus no supplements

Primary outcome: ADL

Two studies using essential amino acids reported ADL using the total FIM score. We contacted the study authors to obtain the FIM motor score, but received no response. In one study (Aquilani 2014), there was no evidence of a difference in ADL at the end of the intervention phase (MD −12.60, 95% CI −32.33 to 7.13; 1 RCT, 38 participants; very low-certainty evidence; Analysis 12.1). Another study did not report the scores (Aquilani 2015). The study reported that the FIM scores were similar between the groups.

Secondary outcome: Nutritional status

Body weight

Two studies using essential amino acids assessed body weight. In one study (Aquilani 2014), there was no evidence of a difference in body weight at the end of the intervention (MD 3.80, 95% CI −2.56 to 10.16; 1 RCT, 38 participants; low-certainty evidence; Analysis 12.2). Another study reported body weight narratively (Aquilani 2015). We contacted the study author to obtain data, but received no response. The study reported that body weight was similar between the groups at the end of the intervention.

Secondary outcome: Swallowing function

Dysphagia Outcome and Severity Scale score

Two studies using essential amino acids assessed the Dysphagia Outcome and Severity Scale score, which was based on an objective examination. In one study (Aquilani 2014), there was an intervention effect on the Dysphagia Outcome and Severity Scale

at the end of the intervention (MD −1.30, 95% CI −2.35 to −0.25; 1 RCT, 38 participants; very low-certainty evidence; Analysis 12.3). Another study reported the outcome narratively (Aquilani 2015). We contacted the study authors to obtain more data, but no response was received. The study found that the Dysphagia Outcome and Severity Scales were similar between the groups at the end of the intervention phase.

Improvement in Dysphagia Outcome and Severity Scale score

One study using essential amino acids reported the number of participants who improved on the Dysphagia Outcome and Severity Scale (Aquilani 2015). There was no evidence of a difference at the end of the intervention phase (OR 0.63, 95% CI 0.16 to 2.42; 1 RCT, 42 participants; low-certainty evidence; Analysis 12.4).

Oral or enteral individualised nutritional therapy versus control

Primary outcome: ADL

One study reported ADL (Otsuki 2020). There was no evidence of a difference in ADL assessed using the FIM score at follow-up (MD 8.60, 95% CI −0.74 to 17.94; 1 RCT, 128 participants; moderate-certainty evidence; Analysis 13.1).

Secondary outcome: Nutritional status

Body weight

Three studies reported a change in body weight. One study reported that separately for men and women (Ha 2010b), and we calculated it as a total for a synthesis. Based on two studies (Otsuki 2020; Ha 2010b), there was an effect in favour of the intervention for body weight at follow-up and the end of the intervention (MD 1.07, 95% CI 0.10 to 2.04; I^2 = 33%; 2 RCTs, 252 participants; very low-certainty evidence; Analysis 13.2). Subgroup analyses were not possible for the stroke phase, as both studies were conducted during the acute phase, and for stroke type, since both studies were conducted on cerebral infarction, cerebral haemorrhage, or subarachnoid haemorrhage. There was no difference between the nutritional status at baseline (P = 0.22, I^2 = 33.2%; Analysis 13.3). One study reported the proportion of participants who lost ≥ 5% of their body weight at follow-up: 20.7% in the intervention group and 36.4% in the control group, showing no difference (Ha 2010a).

Thigh circumference

One study assessed thigh circumference for each paretic and non-paretic side (Otsuki 2020). There was an effect in favour of the intervention for thigh circumference on both the paretic and non-paretic sides at follow-up (paretic side: MD 2.10, 95% CI 0.59 to 3.61, non-paretic side: MD 1.80, 95% CI 0.12 to 3.48; 1 RCT, 128 participants; moderate-certainty evidence; Analysis 13.4; Analysis 13.5).

Calf circumference

One study reported calf circumference for each paretic and non-paretic side (Otsuki 2020). There was an effect in favour of the intervention for calf circumference on the paretic and non-paretic sides at follow-up (paretic side: MD 1.40, 95% CI 0.25 to 2.55, non-paretic side: MD 1.60, 95% CI 0.38 to 2.82; 1 RCT, 128 participants; moderate-certainty evidence; Analysis 13.6, Analysis 13.7).

Arm circumference

Two studies reported arm circumference. One study reported that for each paretic and non-paretic side (Otsuki 2020). There was an effect in favour of the intervention on arm circumference on both the paretic and non-paretic sides at follow-up (paretic side: MD 1.60, 95% CI 0.44 to 2.76, non-paretic side: MD 1.80, 95% CI 0.63 to 2.97; 1 RCT, 128 participants; moderate-certainty evidence: Analysis 13.8; Analysis 13.9). Another study reported arm circumference that was measured on the dominant or non-dominant arm (Ha 2010b). The study reported these separately for men and women, and we calculated the arm circumference by combining the data of men and women to show the results. There was an intervention effect on arm circumference (MD 0.15, 95% CI 0.05 to 0.25; 1 RCT, 124 participants; very low-certainty evidence; Analysis 13.10).

Arm muscular circumference

One study assessed AMC using the equation "mid-arm circumference − (0.314 × TSF)" on the dominant or non-paretic arm (Ha 2010b). The study reported the data for men and women separately, and we combined the data of both genders to calculate the overall AMC. There was no evidence of a difference in the AMC (MD 0.00, 95% CI −0.09 to 0.09; 1 RCT, 124 participants; very low-certainty evidence; Analysis 13.11).

Triceps skinfold thickness

One study assessed a change in TSF (Ha 2010b). The study reported that separately for men and women, and we combined these data to calculate it as a total. There was an intervention effect on the change in body weight (MD 0.25, 95% CI 0.09 to 0.41; 1 RCT, 124 participants; very low-certainty evidence; Analysis 13.12).

Secondary outcome: Cognitive function

One study reported the FIM cognition score (Otsuki 2020). There was no evidence of a difference in the cognitive score at follow-up (MD 2.90, 95% CI −0.49 to 6.29; 1 RCT, 128 participants; moderate-certainty evidence; Analysis 13.13).

Secondary outcome: Quality of life

One study assessed QOL using the EQ-5D score and reported the score for each domain (Ha 2010a). We contacted the study authors to obtain the total score, but no response was received. There was no evidence of a difference in the improvement of mobility scores at follow-up (OR 0.92, 95% CI 0.37 to 2.30; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.14). There was no evidence of a difference in the improvement of self-care scores at follow-up (OR 1.13, 95% CI 0.48 to 2.64; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.15). There was no evidence of a difference in the improvement of usual activities scores at follow-up (OR 1.79, 95% CI 0.70 to 4.56; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.16). There was no evidence of a difference in the improvement of pain or discomfort scores at follow-up (OR 1.16, 95% CI 0.44 to 3.01; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.17). There was no evidence of a difference in the improvement of anxiety or depression scores at follow-up (OR 0.59, 95% CI 0.23 to 1.51; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.18). The study also reported EQ-5D VAS scores with median values and ranges. The study reported a difference between the intervention group and the control group in the change in EQ-5D VAS scores after three months (intervention

group median 10, range -80 to 60; control group median 0, range -35 to 70; P = 0.009).

Secondary outcome: Muscle strength

Grip strength

One study reported grip strength (Ha 2010a). There was an intervention effect on grip strength at follow-up (MD 2.60, 95% CI 1.30 to 3.90; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.19).

Secondary outcome: Neurological impairment

Canadian Neurological Score

One study using enteral individualised nutritional therapy reported the Canadian Neurological Score narratively (Das 2021). We contacted the study authors to obtain more data but no response was received. The study reported that the score was similar between the groups.

Secondary outcome: All-cause mortality

One study reported all-cause mortality (Ha 2010a). There was no evidence of a difference in all-cause mortality at follow-up (OR 0.92, 95% CI 0.49 to 1.17; 1 RCT, 170 participants; low-certainty evidence; Analysis 13.20).

Early parenteral nutrition versus control

Primary outcome: ADL

One study reported ADL as a dichotomous variable (independent or not); however, the assessment tool was not reported (Zhang 2004). We contacted the study authors to obtain more information, but no response was received. There was no evidence of a difference in ADL at the end of the intervention (OR 0.84, 95% CI 0.32 to 2.25; 1 RCT, 69 participants; very low-certainty evidence; Analysis 14.1).

Secondary outcome: All-cause mortality

One study reported mortality (Zhang 2004). There was no evidence of a difference in all-cause mortality at follow-up (OR 0.96, 95% CI 0.33 to 2.82; 1 RCT, 69 participants; moderate-certainty evidence; Analysis 14.2).

Secondary outcome: Quality of life

One study reported the EQ-5D scores with their median values (Dennis 2005b). We contacted the study authors to obtain the mean values and SDs, but no response was received. The study found no difference in the EQ-5D scores between the groups when including the dead participants (median 0.0 in both groups; P = 0.76) and when excluding them (intervention group 0.08, control group 0.15; P = 0.35).

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

One study reported the incidence of pneumonia (Zhang 2004). There was no evidence of a difference in incidence of pneumonia during the intervention phase (OR 0.66, 95% CI 0.25 to 1.75; 1 RCT, 69 participants; low-certainty evidence; Analysis 14.3).

Intestinal infection

One study reported the incidence of intestinal infection (Zhang 2004). There was no evidence of a difference in incidence of intestinal infection during the intervention phase (OR 1.10, 95% CI 0.39 to 3.07; 1 RCT, 69 participants; low-certainty evidence; Analysis 14.4).

Sepsis

One study reported the incidence of sepsis (Zhang 2004). There was no evidence of a difference in incidence of sepsis during the intervention phase (OR 1.25, 95% CI 0.31 to 5.11; 1 RCT, 69 participants; low-certainty evidence; Analysis 14.5).

Parenteral nutritional supplements (amino acids) versus no supplements

Secondary outcome: Nutritional status

Decreased nutritional status

Two studies reported decreased nutritional status. One study assessed nutritional status using anthropometric and laboratory indicators but did not provide detailed information on the methods used (Beeharry 2014). We included this study because the assessment of nutritional status included anthropometric indicators. There was an effect in favour of the intervention on the decreased nutritional status at the end of the intervention (OR 0.17, 95% CI 0.04 to 0.75, 1 RCT, 37 participants; low-certainty evidence; Analysis 15.1). Another study only stated "nutritional status" without specifying how it was assessed (Mohan 2015). We contacted the study authors to obtain more information but received no response. The study reported that none of the participants in the intervention group had decreased nutritional status, while 76% of the control group did.

Secondary outcome: All-cause mortality

One study reported the mortality rate at follow-up (Mohan 2015). We contacted the study authors to obtain more data, but no response was received. The study reported that the mortality rate was 40% in the intervention group and 67% in the control group.

Parenteral (selenium, zinc, vitamin C, and vitamin B1) and enteral (vitamin E) supplements versus no supplements

Secondary outcome: Incidence of complications (adverse events)

Pneumonia

One study reported the incidence of pneumonia (Berger 2008). There was no evidence of a difference in incidence of pneumonia during the intervention phase (OR 0.21, 95% CI 0.03 to 1.47; 1 RCT, 21 participants; low-certainty evidence; Analysis 16.1).

Enteral or parenteral amino-acid supplements versus protein supplements

Secondary outcome: All-cause mortality

One study reported the mortality rate (Laviano 2011). We contacted the study authors to obtain more data but received no response. The study found no difference in mortality rates between the intervention group (60%) and the control group (77%).

Secondary outcome: Incidence of complications (adverse events)

Urinary tract infection

One study reported the incidence of urinary tract infection (Laviano 2011). There was no difference in the number of participants who

developed urinary tract infections between the groups at the end of the intervention (intervention group 2/10, control group 4/10).

Hyperglycaemia

One study reported that blood glucose levels were not different between the groups at the end of the intervention phase (amino-acid group 103 ± 21 mg/dL, protein group 119 ± 37 mg/dL) (Laviano 2011). However, this study reported that blood glucose levels were reduced only in the intervention group at the end of the intervention compared to the baseline (P = 0.01).

Oral and parenteral supplements (fatty acids) versus no supplements

Primary outcome: Disability

One study used omega-3 polyunsaturated fatty acids in the intervention group (Saito 2017). This study assessed disability using the Glasgow Outcome Scale Extended score and showed poor status using scores of 1 to 4. The study found no evidence of a difference in disability at the end of the intervention phase (OR 0.61, 95% CI 0.17 to 2.16; 1 RCT, 41 participants; very low-certainty evidence; Analysis 17.1).

Secondary outcome: Stroke recurrence

One study reported stroke recurrence (Saito 2017). There was no evidence of a difference in stroke recurrence at follow-up in a study using omega-3 polyunsaturated fatty acids (OR 0.38, 95% CI 0.10 to 1.45; 1 RCT, 41 participants; very low-certainty evidence; Analysis 17.2).

DISCUSSION

Summary of main results

This review aimed to evaluate the effects of nutritional therapy on reducing disability and improving ADL in patients after stroke. We identified six nutritional interventions for disability: oral supplements of energy and protein, vitamin D, protein, fatty acids, enteral high-protein nutrition, and early enteral nutrition. For ADL, we identified 12 nutritional interventions. For oral supplements, these included: nutritional supplements of energy and protein; vitamin D; vitamin E; a combination of vitamin E and vitamin C; fatty acids; protein; and a combination of vitamin E, vitamin C, and fatty acids. Other interventions were: early enteral nutrition; enteral energy supplements; oral or enteral supplements of amino acids; oral or enteral individualised nutritional therapy; and early parenteral nutrition. There were nine studies assessing the effect on disability and 17 studies evaluating the effect on ADL. Overall, there was no evidence of a difference in reducing disability, but the certainty of the evidence was very low or low (very low for early enteral nutrition and oral fatty acid supplements, low for oral energy and protein supplements, oral vitamin D supplements, oral protein supplements, and enteral high-protein nutrition). Therefore, whether nutritional therapy reduces disability in people after stroke remains uncertain. The effect on ADL varied depending on the type of intervention. Oral energy and protein supplements improved ADL at the end of the intervention phase; however, the certainty of the evidence was very low. The certainty of the evidence of the others was very low or moderate (very low for oral vitamin D supplements, oral protein and vitamin D supplements, oral vitamin E supplements, oral or enteral amino acids supplements, oral supplements of vitamin E and vitamin C, oral fatty acids supplements, oral supplements of vitamin E, vitamin C, and fatty acids, early enteral nutrition, enteral energy supplements, and early parenteral nutrition, moderate for oral or enteral individualised nutrition therapy). Therefore, whether nutritional therapy improves ADL in people after stroke remains uncertain.

Overall completeness and applicability of evidence

Participants

Most studies assessed the effect of nutritional therapy in a mixed-stroke population including patients with ischaemic or haemorrhagic stroke (24 studies) or just in the ischaemic stroke population (23 studies). A few studies focused on patients with SAH (three studies) or haemorrhagic stroke (three studies). The existence of many studies with mixed-stroke populations suggests that the theoretical rationale for disease pathophysiology is insufficient. Regarding the stroke phase, 36 studies assessed stroke patients in the acute phase; three in the acute and subacute phases; 10 in the sub-acute phase; and only three in the chronic phase. Almost all studies were conducted amongst inpatients, with only two being conducted amongst outpatients. Only six studies included participants with malnutrition risk or malnutrition defined by the study authors, four of which assessed patients in the acute phase; one in the acute and subacute phases; and one in the subacute phase. Evidence on the effects of nutritional therapy in patients with haemorrhagic stroke, including SAH, chronic stroke, and malnutrition, is very limited. Furthermore, there is a lack of evidence for its use in outpatients.

Nine studies assessed disability. Seven of these assessed patients in the acute phase, and one in the subacute phase. Three studies were conducted amongst patients with ischaemic stroke, one on those with SAH, and four on a mixed-stroke population. Seventeen studies assessed ADL. Of these, nine were conducted in the acute phase, one in the acute and subacute phases, and seven in the subacute phase. Twenty-three studies were conducted amongst patients with ischaemic stroke, six on those with haemorrhagic stroke including SAH, and 23 on a mixed-stroke population. The effect of nutritional therapy may differ depending on the stroke type, stroke phase, and participants' baseline nutritional status. The variation in these factors reduces the generalisability of the evidence in this review. The results of this review should be carefully applied in clinical practice, considering these characteristics.

Interventions

We identified various interventions that assessed the effects of nutritional therapy. We classified the types of intervention based on nutritional routes and supplements. There were seven types of nutritional routes used in the studies (oral, 22 studies; oral or enteral, 5 studies; oral or enteral or parenteral, 1 study; oral or parenteral, 1 study; enteral, 19 studies; enteral or parenteral, 2 studies; parenteral, 2 studies). In this review, 25 types of nutritional supplements were identified: protein (nine studies); early enteral nutrition (eight studies); energy and protein (six studies); amino acids (six studies); fatty acids (four studies); individualised nutritional therapy (three studies); vitamin D (four studies); protein and vitamin D (two studies); vitamin E and vitamin C (two studies); vitamin B (two studies); amino acid and fatty acid (one study); energy (two studies); energy and multi-nutrients (one study); zinc (one study); vitamin A (one study); vitamin A and vitamin D (one study); vitamin D and vitamin C

(one study); a combination of vitamin E, vitamin B, and zinc (one study); a combination of vitamin E, vitamin C, and fatty acids (one study); a combination of vitamin E, vitamin C, and vitamin B (one study); sodium (one study); potassium (one study); magnesium and potassium (one study); and early parenteral nutrition (one study). We synthesised the data based on the type of route and supplement, but this led to low certainty in almost all comparisons owing to the small sample sizes. Future studies should focus on one type of nutritional therapy based on a theoretical rationale. This will help establish nutritional management for people after stroke. The comparators in the included studies were usual care, placebo, or other supplements (usual care, 33 studies; placebo, 11 studies; other supplements, 8 studies). Most studies used usual care as a comparator; therefore, the findings of this review may be clinically applicable in this regard.

Outcomes

All outcomes that we aimed to find in this review were reported in the included studies. Disability and ADL as primary outcomes were reported in nine and 17 studies, respectively. We identified the following secondary outcomes: gait (5 studies), nutritional status (33 studies), mortality (17 studies), complications (26 studies), QOL (5 studies), muscle strength (5 studies), cognitive function (5 studies), physical performance (6 studies), swallowing function (4 studies), and neurological impairment (12 studies). There were 11 types of measurements as the outcome of nutritional status (body weight, 8 studies; triceps skinfold thickness, 6 studies; calf circumference, 3 studies; arm muscular circumference, 5 studies; arm circumference, 3 studies; skeletal muscle mass index, 2 studies; thigh muscle area, 1 study; thigh circumference, 1 study; lean mass, 1 study; skeletal muscle atrophy, 1 study; and decreased nutritional status, 1 study). When applying the findings in this review to clinical practice, the type of nutritional status that is important as an outcome for people after stroke should be considered. Concerning the QOL data in five studies, four reported the data with median values, and one reported the data with mean values. Future studies should provide data with mean values and SD for synthesis. Moreover, future studies should consider the type of QOL that is important as an outcome. One study used a disease-specific QOL measure (the short-form NeuroQoL). Two studies employed a profile-based QOL measure (SF-36). Meanwhile, three studies utilised a preference-based QOL measure (EQ-5D). This measure assesses value in the general population and is mainly used for economic evaluation. All types of QOL are useful in clinical settings and society. Regarding physical performance in seven studies, we found six types of measurement tools: the Timed Up and Go test (2 studies), Berg Balance Scale (1 study), Short Performance Physical Battery (1 study), 30-second chair test (1 study), Fugl-Meyer Assessment (2 studies), and Rivermead Mobility Index (1 study). We could not synthesise the data owing to a single study for each type of nutritional therapy. More data on physical performance are required in future studies. For swallowing function in four studies, three studies used the Dysphagia Outcome and Severity Scale score. The Dysphagia Outcome and Severity Scale score is useful as an outcome because it is based on objective assessment. Conversely, other objective assessments such as the Penetration-Aspiration Scale (Rosenbek 1996) based on a videofluoroscopic swallowing study using an X-ray film would also be useful in confirming the functional improvement of swallowing.

Quality of the evidence

We assessed the quality of evidence in the meta-analyses using the GRADE approach. The quality of evidence for the primary outcomes ranged from very low to low certainty for disability and from very low to moderate certainty for ADL. Risk of bias and imprecision were the main domains that led to the downgrading of the evidence for primary outcomes in all nutritional therapies identified in this review.

Risk of bias

The main reason for downgrading was the blinding of the outcome of disability. Of the six studies on disability that assessed the quality of evidence, two had a high risk of bias in the domain of blinding participants and personnel. Furthermore, three studies exhibited a high risk of bias in the domain of blinding outcome assessment. Of the eight studies on ADL that assessed the quality of evidence, the main reasons for downgrading were insufficient information available from published reports and blinding. Three studies had unclear bias in most domains, and two had a high risk of bias in the blinding domains: the participants and personnel domain in one study and the outcome assessment domain in another.

Imprecision

Of the five intervention comparisons for which we judged the quality of evidence for disability, four intervention comparisons had small sample sizes. For ADL, all intervention comparisons for which we judged the quality of evidence had small sample sizes. This led to a downgrading of our confidence in the evidence.

Overall, our confidence in the evidence was low, mainly because of the risk of bias and imprecision. At present, there is insufficient high-quality evidence to support any generalised conclusions regarding the effect of nutritional therapy on disability and ADL in people after stroke. Future research should be designed to improve trial quality and reduce the risk of bias.

Potential biases in the review process

We performed a systematic literature search of multiple literature and trial databases. Despite this process, there is still a chance that we missed a relevant trial (e.g. trials published in grey literature sources) throughout our search process. Some studies reported the outcome narratively or as median values. We contacted the study authors to obtain data for synthesis, but the response rate was very low. This might have caused bias in the effects of the intervention on the outcomes of this review. However, we found that almost all outcomes in these studies had the same direction of effect as in the studies in the meta-analyses. We did not restrict inclusion of studies by language and translated languages, except English and Japanese, to English, supported by a translation expert, thereby minimising bias. We categorised the interventions using the nutrition route and supplements (e.g. oral amino acids and enteral fatty acids). Two independent reviewers, consulting with a registered dietitian as needed, classified all the interventions and discussed any differences that arose. These are the strengths of this review.

Agreements and disagreements with other studies or reviews

We conducted a similar systematic review, which we published in 2019 (Sakai 2019). We evaluated the effects of nutritional therapy

using energy and protein on ADL, all-cause mortality, incidence of infections, disability, walking ability, falls, stroke recurrence, and QOL. Our previous review identified a positive effect of intervention using oral energy and protein on ADL in one study (Rabadi 2008). In this review, we identified an additional study and synthesised this study and the previous study. A meta-analysis using two studies also showed a positive effect on ADL in this review. Our previous review identified no evidence of a difference using early enteral nutrition in ADL using one study (Zheng 2015). This review included one additional study and showed no evidence of a difference in ADL, similar to the results of the previous review. For disability, we identified three studies (Dennis 2005a; Dennis 2005b; Zheng 2015) using energy and protein in our previous review, and one additional study that reported the outcome narratively (Dang 2018) was included in this review. The results of the additional study were the same as those of the previous review, with no evidence of a difference in disability. For infections, we synthesised the number of all infections defined by the study author in our previous review using three studies (Boselli 2012; Gariballa 1998; Zheng 2015), of which we did not include one study in this review because it included patients with brain injury (Boselli 2012). In this review, we did not synthesise the number of all infections due to the heterogeneity between infections reported in the included studies. In the previous review, we found a positive reduction in the incidence of infections. However, we found no evidence of a difference in the incidence of pneumonia, urinary tract infection, intestinal infection, and infections of pneumonia, urinary tract, and septicaemia in this review, except for one study that used enteral energy and protein supplements and reported a positive effect on the incidence of pneumonia (Li 2014). For all-cause mortality, there was no evidence of a difference in our previous study using three studies (Dennis 2005a; Dennis 2005b; Ha 2010a). There were 16 intervention comparisons for all-cause mortality in this review, and none of the comparisons showed an intervention effect, except for one study that used enteral energy and protein supplements (Li 2014). Regarding walking capacity, we found only one study in our previous review (Rabadi 2008) and two additional studies in this review (Cheng 2019; Sato 2022). The intervention using oral energy and protein supplements in one study had an intervention effect on walking capacity (Rabadi 2008), but we found no evidence of a difference in that outcome in studies using oral protein supplements (Cheng 2019) and oral protein and vitamin D supplements (Sato 2022). For stroke recurrence, there was no evidence of a difference similar to that observed in our previous review. For QOL, we found three studies (Dennis 2005a; Dennis 2005b; Ha 2010a), but we could not synthesise the data because of insufficient reports in our previous review. In this review, we found three additional studies (Badjatia 2021; Dang 2023; Poppitt 2009) but could not synthesise the studies due to different interventions and insufficient reports. Two studies showed no evidence of a difference in QOL, consistent with the findings of the previous review, while one study indicated a difference between the groups (Dang 2023). In this review, we assessed the effects of various nutritional therapy and outcomes, including nutritional status, muscle strength, cognitive function, swallowing function, physical performance, and complications. Thus, this review assessed the effects of nutritional therapy more comprehensively than our previous review.

A previous Cochrane review that assessed the effects of nutritional supplementation with protein and energy in patients with acute and subacute (within six months from onset) stroke revealed no evidence of a difference in case fatality, all-cause mortality, or dependent status (Geeganage 2012). We observed no evidence of a difference in all-cause mortality and dependent status in the meta-analyses of the interventions with protein and energy, similar to the previous review. This review encompassed a wider range of nutritional interventions, evaluated more outcomes, and included a larger patient population than the previous review. It also extended its scope to cover patients with chronic stroke. This review provides more evidence on nutritional therapy for people after stroke than that provided by the previous review.

AUTHORS' CONCLUSIONS

Implications for practice

This review shows low-certainty evidence that nutritional therapy may not improve disability but may improve ADL in people after stroke when nutritional therapy is conducted using oral energy and protein supplements. Given the minimal clinically important difference in the FIM motor scores, the improvement in ADL cannot be considered clinically relevant (Beninato 2006). There is continued uncertainty about who might benefit the most from nutritional therapy using oral energy and protein supplements, especially for types of stroke. However, current evidence indicates that patients in the acute or subacute phase who are at risk of malnutrition or are malnourished benefit from nutritional therapy with oral energy and protein supplements during hospitalisation.

We found that various types of nutrients were used in nutritional therapy to reduce disability and improve ADL. Although this review found that nutritional supplements (e.g. vitamin D, amino acids, and fatty acids) other than oral energy and protein supplements showed no effect, clinicians should be aware of the uncertainty of all findings presented here. This implies that the true effect may differ substantially.

Oral energy and protein supplements may lead to an increased incidence of diarrhoea, as well as higher rates of hyperglycaemia or hypoglycaemia. Although this finding was supported by low-certainty evidence, clinicians should particularly note these adverse events during nutritional therapy using oral energy and protein supplements. For other adverse events, the evidence, ranging from very low to low certainty, suggests that the number of events experienced by both the intervention and control groups was similar. Given the uncertainty of the evidence, clinicians are advised to also monitor for additional adverse events.

Implications for research

We recommend that future studies investigating the effects of nutritional therapy on people after stroke should:

- ensure nutrients and co-intervention are investigated based on a theoretical rationale;
- include patients based on stroke type, stroke phase, baseline nutritional status, and stroke severity based on theoretical rationale;
- include careful assessment and complete reporting of adverse events;
- ensure complete intervention descriptions to allow easy interpretation of the results and generalisation;
- ensure complete reporting of results to allow pooling of quantitative data;

- endeavour to conduct a trial with a low risk of bias via rigorous methodological development and clear reporting.

When developing future trials, trial development guidelines such as the Stroke Recovery and Rehabilitation Roundtable Trials Development Framework can be useful in providing high-quality evidence on nutritional therapy (Bernhardt 2019).

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REFERENCES

References to studies included in this review

Aquilani 2008a *{published data only}*

Aquilani R, Scocchi M, Boschi F, Viglio S, Iadarola P, Pastoris O, et al. Effect of calorie-protein supplementation on the cognitive recovery of patients with subacute stroke. *Nutritional Neuroscience* 2008;**11**(5):235-40.

Aquilani 2008b *{published data only}*

Aquilani R, Scocchi M, Iadarola P, Franciscone P, Verri M, Boschi F, et al. Protein supplementation may enhance the spontaneous recovery of neurological alterations in patients with ischaemic stroke. *Clinical Rehabilitation* 2008;**22**:1042-50.

Aquilani 2009 *{published data only}*

Aquilani R, Baiardi P, Scocchi M, Iadarola P, Verri M, Sessarego P, et al. Normalization of zinc intake enhances neurological retrieval of patients suffering from ischemic strokes. *Nutritional Neuroscience* 2009;**12**(5):219–25.

Aquilani 2014 *{published data only}*

Aquilani R, Boselli M, D'Antona G, Baiardi P, Boschi F, Viglio S, et al. Unaffected arm muscle hypercatabolism in dysphagic subacute stroke patients: the effects of essential amino acid supplementation. *BioMed Research International* 2014;**2014**:964365.

Aquilani 2015 *{published data only}*

Aquilani R, Emilio B, Dossena M, Baiardi P, Testa A, Boschi F, et al. Correlation of deglutition in subacute ischemic stroke patients with peripheral blood adaptive immunity: essential amino acid improvement. *International Journal of Immunopathology and Pharmacology* 2015;**28**(4):576–83.

Badjatia 2021 *{published data only}*

Badjatia N, Sanchez S, Haymore J, Judd G, Motta M, Parikh G, et al. Impact of neuromuscular electrical stimulation and high protein supplementation on recovery after subarachnoid hemorrhage. *Neurocritical Care (Conference: 17th Annual Meeting, Neurocritical Care Society)* 2019;**31**(Suppl 1):1–341.

* Badjatia N, Sanchez S, Judd G, Hausladen R, Hering D, Motta M, et al. Neuromuscular electrical stimulation and high-protein supplementation after subarachnoid hemorrhage: a single-center phase 2 randomized clinical trial. *Neurocritical Care* 2021;**35**(1):46–55.

Beeharry 2014 *{published data only}*

Beeharry S, Petrova MV, Butrov AV, Storchai M. The role of high protein nutritional support on the nutritional status and in correcting hyper-catabolic syndrome in patients suffering from ischemic stroke. *Clinical Nutrition* 2014;**33**:S67.

Berger 2008 *{published data only}*

Berger MM, Soguel L, Shenkin A, Revelly JP, Pinget C, Baines M, et al. Influence of early antioxidant supplements on clinical evolution and organ function in critically ill cardiac surgery, major trauma, and subarachnoid hemorrhage patients. *Critical Care* 2008;**12**(4):R101.

Cheng 2019 *{published data only}*

Cheng YH, Wei L, Chan WP, Hsu CY, Huang SW, Wang H, et al. Effects of protein supplementation on aerobic training-induced gains in cardiopulmonary fitness, muscle mass, and functional performance in chronic stroke: a randomized controlled pilot study. *Clinical Nutrition* 2020;**39**(9):2743-50.

Daga 1997 *{published data only}*

Daga MK, Madhuchhanda, Mishra TK, Mohan A. Lipid peroxide, beta-carotene and alpha-tocopherol in ischaemic stroke and effect of exogenous vitamin E supplementation on outcome. *Journal of the Association of Physicians of India* 1997;**45**(11):843–6.

Dang 2018 *{published data only}*

Dang Y, Zhang G. Effects of early enteral nutrition on sub-acute ischemic stroke via gut microbiota reconstruction: a randomized controlled trial. *Journal of Gastroenterology and Hepatology* 2018;**33**(Suppl 4):219.

Dang 2023 *{published data only}*

Dang J, Li G, Wu Q, Pian G, Wang Z. Impacts of evidence-based nursing combined with enteral nutrition on nutritional status and quality of life in acute cerebral infarction patients: a randomized controlled trial. *Perfusion* 2023;**Vol not reported**:2676591231223910. [DOI: 10.1177/02676591231223910]

Das 2021 *{published data only}*

Das KC, Dube SK, Rath GP, Jena BR, Roy H, Bithal P, et al. Nutrition in stroke patients: comparison of indirect calorimetry vs. standard weight-based regimen. *Anesthesia and Analgesia* 2021;**133**(Suppl 2):956.

De Aguilar-Nascimento 2011 *{published data only}*

De Aguilar-Nascimento JE, Prado Silveira BR, Dock-Nascimento DB. Early enteral nutrition with whey protein or casein in elderly patients with acute ischemic stroke: a double-blind randomized trial. *Nutrition* 2011;**27**(4):440-4.

Dennis 2005a *{published data only}*

Dennis M, Lewis S, Cranswick G, Forbes J, FOOD Trial Collaboration. FOOD: a multicentre randomised trial evaluating feeding policies in patients admitted to hospital with a recent stroke. *Health Technology Assessment* 2006;**10**(2):1-120.

* Dennis MS, Lewis SC, Warlow C. Routine oral nutritional supplementation for stroke patients in hospital (FOOD): a multicentre randomised controlled trial. *Lancet* 2005;**365**(9461):755-63.

Dennis MS. The FOOD trial 1 - results of a multicentre RCT comparing outcomes of stroke patients given routine oral nutritional supplements in addition to normal hospital diet with those given normal hospital diet alone. *Stroke* 2004;**35**(6):e200.

Dennis MS. The FOOD trial 1 - results of a multicentre RCT evaluating the effects of routine oral nutritional supplements on hospitalised stroke patients. *Cerebrovascular Diseases* 2004;**17**(Suppl 5):39.

Prosser-Loose EJ, Paterson PG. The FOOD Trial Collaboration: nutritional supplementation strategies and acute stroke outcome. *Nutrition Reviews* 2006;**64**(6):289-94.

Dennis 2005b *{published data only}*

* Dennis MS, Lewis SC, Warlow C. Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial. *Lancet* 2005;**365**(9461):764-72.

Dennis MS. The FOOD trial 2 - results of a multicentre RCT comparing early versus delayed enteral tube feeding after acute stroke. *Cerebrovascular Diseases* 2004;**17**(Suppl 5):39.

Dennis MS. The FOOD trial 2 - results of a multicentre RCT comparing outcomes of dysphagic acute stroke patients fed early via an enteral tube with those where enteral feeding was avoided for at least a week. *Stroke* 2004;**35**(6):e286.

Teasell R, Foley N. Results from the FOOD trial. *Lancet Neurology* 2005;**4**(5):267.

Gao 2008 *{published data only}*

Gao JX, Su YY. Effects of two enteral nutrition formulas with equal calorie and different carbohydrate on plasma glucose in acute stroke patients: a randomized controlled study. *Chinese Journal of Clinical Nutrition* 2008;**4**:209-15.

Garbagnati 2009 *{published data only}*

Garbagnati F, Cairella G, De Martino A, Multari M, Scognamiglio U, Venturiero V, et al. Is antioxidant and n-3 supplementation able to improve functional status in poststroke patients? Results from the Nutristroke Trial. *Cerebrovascular Diseases* 2009;**27**(4):375–83.

Gariballa 1998 *{published data only}*

Gariballa SE, Parker SG, Taub N, Castleden CM. A randomized, controlled, a single-blind trial of nutritional supplementation after acute stroke. *Journal of Parenteral and Enteral Nutrition* 1998;**22**(5):315–9.

Gupta 2016 *{published data only}*

Gupta A, Prabhakar S, Modi M, Bhadada SK, Kalaivani M, Lal V, et al. Effect of vitamin D and calcium supplementation on ischaemic stroke outcome: a randomised controlled open-label trial. *International Journal of Clinical Practice* 2016;**70**(9):764–70.

Ha 2010a *{published data only}*

Ha L, Hauge T, Iversen PO. Individualised nutritional supplementation improves quality of life in elderly patients hospitalised with acute stroke; a randomised controlled trial. *Stroke* 2009;**40**(4):e237-e238.

* Ha L, Hauge T, Spenning AB, Iversen PO. Individual, nutritional support prevents undernutrition, increases muscle strength and improves QoL among elderly at nutritional risk hospitalized for acute stroke: a randomized, controlled trial. *Clinical Nutrition* 2010;**29**(5):567–73.

Iversen PO, Ha L, Blomhoff R, Hauge T, Veierød MB. Baseline oxidative defense and survival after 5-7 years among elderly stroke patients at nutritional risk: follow-up of a randomized, nutritional intervention trial. *Clinical Nutrition* 2015;**34**(4):775-8.

Ha 2010b *{published data only}*

Ha L, Hauge T, Iversen PO. Body composition in older acute stroke patients after treatment with individualized, nutritional supplementation while in hospital. *BMC Geriatrics* 2010;**10**:75.

Hashemilar 2020 *{published data only}*

Hashemilar M, Khalili M, Rezaeimanesh N, Sadeghi Hokmabadi E, Rasulzade S, Shamshirgaran SM, et al. Effect of whey protein supplementation on inflammatory and antioxidant markers, and clinical prognosis in acute ischemic stroke (TNS trial): a randomized, double blind, controlled, clinical trial. *Advanced Pharmaceutical Bulletin* 2020;**10**(1):135–40.

Honaga 2022 *{published data only}*

Honaga K, Mori N, Akimoto T, Tsujikawa M, Kawakami M, Okamoto T, et al. Investigation of the effect of nutritional supplementation with whey protein and vitamin D on muscle mass and muscle quality in subacute post-stroke rehabilitation patients: a randomized, single-blinded, placebo-controlled trial. *Nutrients* 14;**3**:685.

Kadri 2020 *{published data only}*

Kadri A, Sjahrir H, Juwita Sembiring R, Ichwan M. Combination of vitamin A and D supplementation for ischemic stroke: effects on interleukin-1s and clinical outcome. *Medicinski Glasnik: official publication of the Medical Association of Zenica-Doboj Canton, Bosnia and Herzegovina* 2020;**17**(2):425–32.

Kang 2023 *{published data only}*

Kang T, Xue Y, Yang Q, Lei Q. Analysis of the effect of early nutritional support on clinical treatment and prognosis of emergency patients with severe intracerebral hemorrhage. *Panminerva Medica* 2023;**65**(3):424–5.

Laviano 2011 *{published data only}*

Laviano A, Aghilone F, Colagiovanni D, Fiandra F, Giambarresi R, Tordiglione P, et al. Metabolic and clinical effects of the supplementation of a functional mixture of amino acids in cerebral hemorrhage. *Neurocritical Care* 2011;**14**(1):44–9.

Li 2008 *{published data only}*

Li MY, Xia F, Su JH. Effect of enteral nutrition support on prognosis in patients with severe acute stroke. *Journal of Clinical Neurology (China)* 2008;**21**(3):171-3.

Li 2014 *{published data only}*

Li Y, Pei Y, Sun M. Effects of early enteral nutrition support on the nutritional status and outcomes of patients with post-stroke dysphagia [Chinese]. *Chinese Journal of Clinical Nutrition* 2014;**22**(6):334-8.

Li 2016 *{published data only}*

Li Y, Dai J, Zhang S, Li X-Z. Clinical value of early enteral nutrition support in patients with acute cerebral infarction accompanied with dysphagia. *World Chinese Journal of Digestology* 2016;**24**(4):618-22.

Mohan 2015 *{published data only}*

Mohan R, Beeharry S, Petrova MV, Butrov AV. Correction of protein-energy malnutrition in mechanically ventilated patients suffering from severe ischemic stroke. *Clinical Nutrition* 2015;**34**:S33.

Momosaki 2019 *{published data only}*

Momosaki R, Abo M, Urashima M. Vitamin D supplementation and post-stroke rehabilitation: a randomized, double-blind, placebo-controlled trial. *Nutrients* 11;**6**:1295.

Ogawa 2021 *{published data only}*

Ogawa K. Effect of enteral nutrition with eicosapentaenoic acids for prevention of bedsores in cerebrovascular disease patients. *Clinical Nutrition ESPEN* 2021;**46**:S763.

Otsuki 2020 *{published and unpublished data}*

Otsuki I, Himuro N, Tatsumi H, Mori M, Niiya Y, Kumeta Y, et al. Individualized nutritional treatment for acute stroke patients with malnutrition risk improves functional independence measurement: a randomized controlled trial. *Geriatrics & Gerontology International* 2020;**20**(3):176–82.

Ouyang 2003 *{published data only}*

Ouyang HM, Wang XH, Song HQ. Applied research on early enteral nutrition in patiens with severe cerebral infarction. *Chinese Journal of Clinical Rehabilitation* 2003;**7**(28):3836-7.

Pan 2017 *{published data only}*

Pan WH, Lai YH, Yeh WT, Chen JR, Jeng JS, Bai CH, et al. Intake of potassium-and magnesium-enriched salt improves functional outcome after stroke: a randomized, multicenter, double-blind controlled trial. *American Journal of Clinical Nutrition* 2017;**106**(5):1267–73.

Poppitt 2009 *{published data only}*

Poppitt SD, Howe CA, Lithander FE, Silvers KM, Lin RB, Croft J, et al. Effects of moderate-dose omega-3 fish oil on cardiovascular risk factors and mood after ischemic stroke: a randomized, controlled trial. *Stroke* 2009;**40**:11.

Rabadi 2008 *{published data only}*

Bergstrom N. Intensive nutritional supplementation improved functional outcome after stroke. *Evidence-Based Nursing* 2009;**12**:85.

* Rabadi MH, Coar PL, Lukin M, Lesser M, Blass JP. Intensive nutritional supplements can improve outcomes in stroke rehabilitation. *Neurology* 2008;**71**(23):1856-61.

Saito 2017 *{published data only}*

Saito G, Zapata R, Rivera R, Zambrano H, Rojas D, Acevedo H, et al. Long-chain omega-3 fatty acids in aneurysmal subarachnoid hemorrhage: a randomized pilot trial of pharmaconutrition. *Surgical Neurology International* 2017;**8**:304.

Sato 2022 *{published data only}*

Sato C, Kamijo YI, Sakurai Y, Araki S, Sakata Y, Ishigame A, et al. Three-week exercise and protein intake immediately after exercise increases the 6-min walking distance with simultaneously improved plasma volume in patients with chronic cerebrovascular disease: a preliminary prospective study. *BMC Sports Science, Medicine & Rehabilitation* 2022;**14**(1):38.

Tajiri 2008 *{published data only}*

* Tajiri H, Mori T, Iwata T, Miyazaki Y, Nakazaki M. Short-term clinical outcome following gastrointestinal tube feeding of immunonutritionoriented (IMPACT®) or protein-oriented food (PEMVest®) in acute stroke management [Japanese]. *Japanese Journal of Stroke* 2011;**33**(3):305-12. [DOI: https://doi.org/10.3995/jstroke.33.305]

Tajiri H, Mori T, Iwata T, Nakazaki M. Short-term clinical outcome following gastro-intestinal tube feeding by immunonutrition-oriented or protein-oriented food in acute stroke management. Preliminary results. *International Journal of Stroke* 2008;**3 (Suppl 1)**:239.

Toole 2004 *{published data only}*

Spence JD, Bang H, Chambless LE, Stampfer MJ. Vitamin intervention for stroke prevention trial. An efficacy analysis. *Stroke; Journal of Cerebral Circulation* 2005;**36**(11):2404-9.

Spence JD, Blake C, Landry A, Fenster A. Measurement of carotid plaque and effect of vitamin therapy for total homocysteine. *Clinical Chemistry and Laboratory Medicine* 2003;**41**(11):1498-504.

Spence JD, Howard VJ, Chambless LE, Malinow MR, Pettigrew LC, Stampfer M, et al. Vitamin intervention for stroke prevention (VISP) trial: rationale and design. *Neuroepidemiology* 2001;**20**(1):16-25.

* Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, et al. Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the vitamin intervention for stroke prevention (VISP) randomized controlled trial. *JAMA* 291;**5**:565–75.

Torrisi 2021 *{published data only}*

Torrisi M, Bonanno L, Formica C, Arcadi FA, Cardile D, Cimino V, et al. The role of rehabilitation and vitamin D supplementation on motor and psychological outcomes in poststroke patients. *Medicine* 2021;**100**(45):e27747.

Ullegaddi 2005a *{published data only}*

Ullegaddi R, Powers HJ, Gariballa SE. Antioxidant supplementation enhances antioxidant capacity and mitigates oxidative damage following acute ischaemic stroke. *European Journal of Clinical Nutrition* 2005;**59**(12):1367–73.

Ullegaddi 2005b *{published data only}*

Gariballa S, Ullegaddi R. Riboflavin status in acute ischaemic stroke. *European Journal of Clinical Nutrition* 2007;**61**(10):1237-40.

* Ullegaddi R, Powers HJ, Gariballa SE. Antioxidant supplementation with or without B-group vitamins after acute ischemic stroke: a randomized controlled trial. *Journal of Parenteral and Enteral Nutrition* 2006;**30**(2):2.

Yoshimura 2019 *{published and unpublished data}*

Yoshimura Y, Bise T, Shimazu S, Shiraishi A. A randomized-controlled trial of leucine-enriched amino-acid mixtures on muscle mass, strength, and physical performance in post-stroke patients with sarcopenia. *Clinical Nutrition* 2017;**36**:s198.

* Yoshimura Y, Bise T, Shimazu S, Tanoue M, Tomioka Y, Araki M, et al. Effects of a leucine-enriched amino acid supplement on muscle mass, muscle strength, and physical function in post-stroke patients with sarcopenia: a randomized controlled trial. *Nutrition* 2019;**58**:1–6.

Zhang 2004 *{published data only}*

Zhang JJ, Dong WF, Gu SJ, Zhang J, Xuan HF, Xie RL. Clinical study on the early nutrition support in postoperative patients with critical hypertensive intracerebral hemorrhage [Chinese]. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue* 2004;**16**(9):552-5.

Zhang 2014 *{published data only}*

Zhang L, Li Z, Luo B, Li Z, Lei Min, Jing Y. Effects of different intakes of protein on nutritional status in severe stroke patients [Chinese]. *Wei Sheng Yan Jiu* 2014;**43**(6):929-32.

Zhao 2020 *{published data only}*

Zhao S, Wang B, Geng S, Zhao X, Wang W, Xie L, et al. Impact of early enteral nutrition on nutritional indicators in patients with severe cerebrovascular disease [Chinese]. *Chinese Journal of Clinical Nutrition* 2020;**28**(4):232-7.

Zheng 2006 *{published data only}*

Zheng TH, Wang SS, Chen ZL, Yang JD, Zhao HF, Cheng L, et al. The effect of early enteral nutrition support on immunological function in patients with acute stroke [Chinese]. *Chinese Journal of Cerebrovascular Diseases* 2006;**3**(8):356-60.

Zheng 2015 *{published data only}*

Zheng T, Zhu X, Liang H, Huang H, Yang J, Wang S. Impact of early enteral nutrition on short term prognosis after acute stroke. *Journal of Clinical Neuroscience* 2015;**22**(9):1473-6.

Zhou 2006 *{published data only}*

Zhou CP, Su YY. Effect of the equal non-protein-calorie but different protein intake on enteral nutritional metabolism in 51 patients with severe stroke: a randomized controlled study [Chinese]. *Chinese Journal of Clinical Nutrition* 14;**6**:351-5.

References to studies excluded from this review

Cavalieri 2012 *{published data only}*https://doi.org/10.1111/j.1468-1331.2012.03887.x

Cavalieri M, Chen C, Mok V, De Freitas GR, Homayoon N, Grazer A, et al. B-vitamins and cerebral small vessel disease: the VITATOPS MRI substudy. *European Journal of Neurology* 2012;**19**:25.

Ikeda 2020 *{published data only}*10.3390/nu12071928

Ikeda T, Morotomi N, Kamono A, Ishimoto S, Miyazawa R, Kometani S, et al. The effects of timing of a leucine-enriched amino acid supplement on body composition and physical function in stroke patients: a randomized controlled trial. *Nutrients* 2020;**12**(7):1-9.

Kang 2010 *{published data only}*10.4162/nrp.2010.4.5.393

Kang Y, Lee HS, Paik NJ, Kim WS, Yang M. Evaluation of enteral formulas for nutrition, health, and quality of life among stroke patients. *Nutrition Research and Practice* 2010;**4**(5):393-9.

Liu 2015 *{published data only}*10.1111/ijs.12017

Liu X, Shi M, Xia F, Han J, Liu Z, Wang B, et al. The China Stroke Secondary Prevention Trial (CSSPT) protocol: a double-blinded, randomized, controlled trial of combined folic acid and B vitamins for secondary prevention of stroke. *International Journal of Stroke* 2015;**10**(2):264-8.

Martin 2019 *{published data only}*https://doi.org/10.1177/1747493019858233

Martin J, Murphy A, McNamara E, Wilton D, Martin L. Medical nutrition therapy to improve nutrition and fluid intake in patients with dysphagia. In: International Journal of Stroke. Vol. 14(1 Supplement). 2019:13.

Missaoui 2021 *{published data only}*10.1111/ene.14975

Missaoui M, Hassine A, Naija S, Emna J, Ben Amor S. Effect of vitamin D supplementation on anxiety-depressive disorder at six months of stroke: a randomized clinical trial. *European Journal of Neurology* 2021;**28**(Suppl 1):864.

Nakamura 2011 *{published data only}*https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000006995

UMIN000005915. Antioxidant nutrients enhanced diet effect on stroke study. https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000006995 (accessed prior to 24 July 2024).

Narasimhan 2017 *{published data only}*10.7860/JCDR/2017/24299.9346

Narasimhan S, Balasubramanian P. Role of vitamin D in the outcome of ischemic stroke - a randomized controlled trial. *India Journal of Clinical and Diagnostic Research* 2017;**11**(2):CC06-CC10.

NCT01810263 *{published data only}*

NCT01810263. The efficacy of intensive nutritional supplement[s] in patient[s] with stroke. https://ClinicalTrials.gov/show/NCT01810263 (date first received 2012).

NCT02982668 *{published data only}*

NCT02982668. Optimizing early enteral nutrition in severe stroke. https://ClinicalTrials.gov/show/NCT02982668 (date first received November 30, 2016).

Oonuma 2019 *{published data only}*10.1161/str.50.suppl_1.TP481

Oonuma Y, Tanno Y, Chiba N, Mori T. Rapid improvement of malnutrition following treatment by leucine-enhanced branched chain amino acid in severe acute stroke patients fed with enteral nutrition. In: American Heart Association/American Stroke Association 2019 International Stroke Conference and State-of-the-Science Stroke Nursing Symposium 2019. Vol. 50 (Supplement 1). 2019:481.

Sato 2005a *{published data only}*10.1001/jama.293.9.1082

Sato Y, Honda Y, Iwamoto J, Kanoko T, Satoh K. Effect of folate and mecobalamin on hip fractures in patients with stroke: a randomized controlled trial. *Journal of the American Medical Association* 2005;**293**(9):1082-8.

Sato 2005b *{published data only}*10.1159/000087203

Sato Y, Iwamoto J, Kanoko T, Satoh Kei. Low-dose vitamin D prevents muscular atrophy and reduces falls and hip fractures in women after stroke: a randomized controlled trial. *Cerebrovascular Diseases* 2005;**20**(3):187-92.

Shen 2020 *{published data only}*10.1177/0300060520949657

Shen H, Zhan B. Effect of vitamin E on stroke-associated pneumonia. *Journal of International Medical Research* 2020;**48**(9):300060520949657.

Solodov 2010 *{published data only}*10.1007/s00134-010-2000-8

Solodov AA, Petrikov SS, Titova YV, Zinkin VY, Krylov VV. Enteral nutrition with glutamin supplementation vs standard enteral formula in patients with intracranial hemorrhages. *Intensive Care Medicine* 2010;**36**(Suppl 2):S300.

Sugiyama 2005 *{published data only}*

Sugiyama T, Tanaka H, Taguchi T, Sato Y, Iwamoto J, Kanoko T, et al. Folate and vitamin B12 for hip fracture prevention after stroke. *Journal of the American Medical Association* 2005;**294**(7):792.

UMIN000019589 *{published data only}*https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000022615

UMIN000019589. A randomized trial to evaluate the efficacy of branched-chain amino acid fortified supplements in post-stroke rehabilitation patients. https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000022615 (date received 2015).

UMIN000025075 *{published data only}*https://center6.umin.ac.jp/cgi-open-bin/icdr_e/ctr_view.cgi?recptno=R000028843

UMIN000025075. Effects of early enteral nutrition in acute stroke patients: an open-label randomized study. https://center6.umin.ac.jp/cgi-open-bin/icdr_e/ctr_view.cgi?recptno=R000028843 (date received 2016).

Witham 2009 *{published data only}*10.1111/j.1747-4949.2009.00354.x

Witham MD, Dove FJ, Sugden JA, Doney A, Struthers AD. Does vitamin D supplementation improve markers of vascular health in stroke patients? A randomised controlled trial. *International Journal of Stroke* 2009;**4**(Suppl 2):21.

Wuyanti 2005 *{published data only}*10.13181/mji.v14i1.169

Wuyanti S, Sayogo S, Ahmad SA. The effect of high protein enteral nutrition on protein status in acute stroke patients. *Medical Journal of Indonesia* 2005;**14**(1):37-43.

Xia 2014 *{published data only}*10.1016/j.jocn.2013.11.043

Xia X-S, Li X, Wang L, Wang J-Z, Ma J-P, Wu C-J. Supplementation of folic acid and vitamin B12 reduces plasma levels of asymmetric dimethylarginine in patients with acute ischemic stroke. *Journal of Clinical Neuroscience* 2014;**21**(9):1586-90.

Yousefian 2019 *{published data only}*10.29333/ejgm/94224

Yousefian M, Sadegi SRGP, Sakaki M. Vitamin D supplements' effect on expediting the weaning process in patients with the stroke. *Electronic Journal of General Medicine* 2019;**16**(2):1-5.

Zavertailo 2010 *{published data only}*20919542

Zavertailo LL, Semenkova GV, Leiderman IN. Effect of an original enteral feeding protocol on clinical outcome indicators in patients with acute cerebral damage of vascular and traumatic genesis. *Anesteziologiia i Reanimatologiia* 2010;**4**:35-8.

Zhong 2014 *{published data only}*https://explore.bl.uk/primo_library/libweb/action/display.do?tabs=detailsTab&gathStatTab=true&ct=display&fn=search&doc=ETOCRN3

Zhong G-Y, Li Y-H, Ma L-P, Huang C-P. Early enteral nutrition and nursing care for prevention of complications of severe cerebrovascular diseases. *World Chinese Journal of Digestology* 2014;**22**(11):1612-15.

References to studies awaiting assessment

CTRI 2020/03/024293 *{published data only}*

CTRI/2020/03/024293. Impact of MTHFR, MS and CBS genes polymorphisms and vitamin B6, B9 & B12 supplementations on hyperhomocysteinemia among ischemic stroke patients. https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2020/03/024293 (date received 2020).

ISRCTN11086312 *{published data only}*

ISRCTN11086312. Effect of vitamin D supplementation on the functional efficiency of patients after stroke. https://www.isrctn.com/ISRCTN11086312 (date received February 16, 2023).

NCT03637270 *{published data only}*

NCT03637270. Incorporating supplementary protein into rehabilitative exercise (INSPIRE Trial) for patients with chronic stroke. https://clinicaltrials.gov/ct2/show/NCT03637270 (date received August 18, 2018).

NCT04295044 *{published data only}*

NCT04295044. Effect of high protein diet in stroke patients with low muscle mass. https://clinicaltrials.gov/ct2/show/NCT04295044 (date received 2018).

NCT04459091 *{published data only}*

NCT04459091. Effects of supplementation with amino essential acids on circulating albumin levels in patients with cerebral ictus in rehabilitation phase. https://clinicaltrials.gov/ct2/show/NCT04459091 (date received 2018).

UMIN000023954 *{published data only}*

UMIN000023954. Efficacy of nutrition management for acute stroke patients with malnutrition risk: a randomized controlled study. https://rctportal.niph.go.jp/detail/um?trial_id=UMIN000023954# (date received 2016).

References to ongoing studies

CTRI/2023/11/060377 *{published data only}*

CTRI/2023/11/060377. A study to know whether Vitamin D supplementation can improve the disability due to stroke in 90 days in patients with low levels of vitamin D in blood. https://ctri.nic.in/Clinicaltrials/pmaindet2.php?EncHid=OTYwNDc=&Enc=&userName=Vitamin%20D (date received November 26, 2023).

DRKS00005577 *{published data only}*

DRKS00005577. Effect of essential amino acids on muscle size and strength in patients with acute ischemic stroke during rehabilitation - AMINOS. https://trialsearch.who.int/Trial2.aspx?TrialID=DRKS00005577 (date received 2014).

* Scherbakov N, Ebner N, Sandek A, Meisel A, Haeusler KG, Von Haehling S, et al. Influence of essential amino acids on muscle mass and muscle strength in patients with cerebral stroke during early rehabilitation: protocol and rationale of a randomized clinical trial (AMINO-Stroke Study). *BMC Neurology* 2016;**16**:10.

IRCT20190305042937N1 *{published data only}*

IRCT20190305042937N1. Clinical trial comparison of the effect of folic acid and vitamin D supplementation in the prevention of cerebrovascular attacks in patients referred to Shahid Beheshti Hospital in 3 months. https://en.irct.ir/trial/40282 (date received 2019).

NCT02347995 *{published data only}*

NCT02347995. Resistive training combined with nutritional therapy after stroke (REPS). https://www.clinicaltrials.gov/study/NCT02347995 (date received January 15, 2015).

NCT04259307 *{published data only}*

NCT04259307. Effect of intensive nutritional support on functional recovery in subacute stroke patient. https://clinicaltrials.gov/ct2/show/NCT04259307 (date received February 4, 2020).

NCT04386525 *{published data only}*

NCT04386525. The potential effect of omega3 supplement in fish oil on infarcted areas in the brain and improvement of neurological functions of ischemic stroke patients. https://clinicaltrials.gov/ct2/show/NCT04386525 (date received 2020).

NCT05474105 *{published data only}*

NCT05474105. Multi-nutrient supplementation as a therapeutic intervention in ischaemic stroke (MUST-IS). https://classic.clinicaltrials.gov/ct2/show/NCT05474105 (date received July 26, 2022).

NCT05728229 *{published data only}*

NCT05728229. Effects of nutrition on post stroke fatigue (NUTRE-S). https://classic.clinicaltrials.gov/ct2/show/NCT05728229 (date received February 15, 2023).

UMIN000035365 *{published data only}*

UMIN000035365. Effects of medium-chain triglyceride on ghrelin activation, food intake, activity of daily living and muscle mass in older malnourished patients with stroke. https://center6.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&recptno=R000040301&type=summary&lang (date received 2018).

Additional references

Anderson 1995

Anderson CS, Linto J, Stewart-Wynne EG. A population-based assessment of the impact and burden of caregiving for long-term stroke survivors. *Stroke* 1995;**26**(5):843-9.

Aquilani 2011

Aquilani R, Sessarego P, Iadarola P, Barbieri A, Boschi F. Nutrition for brain recovery after ischemic stroke: an added value to rehabilitation. *Nutrition in Clinical Practice* 2011;**26**(3):339-45.

Atkins 2004

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al, GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**(7454):1490.

Barker 2015

Barker-Collo S, Bennett DA, Krishnamurthi RV, Parmar P, Feigin VL, Naghavi M, et al. Sex differences in stroke incidence, prevalence, mortality and disability-adjusted life years: results from the Global Burden of Disease Study 2013. *Neuroepidemiology* 2015;**45**(3):203-14.

Bath 2018

Bath PM, Lee HS, Everton LF. Swallowing therapy for dysphagia in acute and subacute stroke. *Cochrane Database of Systematic Reviews* 2018, Issue 10. Art. No: CD000323. [DOI: 10.1002/14651858.CD000323.pub3]

Beninato 2006

Beninato M, Gill-Body KM, Salles S, Stark PC, Black-Schaffer RM, Stein J. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. *Archives of Physical Medicine and Rehabilitation* 2005;**87**(1):32–9.

Bernhardt 2019

Bernhardt J, Hayward KS, Dancause N, Lannin NA, Ward NS, Nudo RJ, et al. A stroke recovery trial development framework: consensus-based core recommendations from the Second Stroke Recovery and Rehabilitation Roundtable. *Neurorehabilitation and Neural Repair* 2019;**33**(11):959–69.

Bonita 1988

Bonita R, Beaglehole R. Recovery of motor function after stroke. *Stroke* 1988;**19**:1497-500.

Boselli 2012

Boselli M, Aquilani R, Baiardi P, Dioguardi FS, Guarnaschelli C, Achilli MP, et al. Supplementation of essential amino acids may reduce the occurrence of infections in rehabilitation patients with brain injury. *Nutrition in Clinical Practice* 2012;**27**:99–113.

Bouziana 2011

Bouziana SD, Tziomalos K. Malnutrition in patients with acute stroke. *Journal of Nutrition and Metabolism* 2011;**2011**:167898.

Brott 1989

Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. *Stroke* 1989;**20**(7):864-70.

Burgos 2018

Burgos R, Bretón I, Cereda E, Desport JC, Dziewas R, Genton L, et al. ESPEN guideline clinical nutrition in neurology. *Clinical Nutrition* 2018;**37**(1):354-96.

Butland 1982

Butland RJ, Pang J, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. *British Medical Journal* 1982;**284**(6329):1607–8.

Chen 2019

Chen N, Li Y, Fang J, Lu Q, He L. Risk factors for malnutrition in stroke patients: a meta-analysis. *Clinical Nutrition* 2019;**38**(1):127-35.

Cieza 2021

Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T. Global estimates of the need for rehabilitation based on the global burden of disease study 2019: a systematic analysis for the global burden of disease study 2019. *Lancet* 2021;**396**(10267):2006-17.

Collin 1988

Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *International Disability Studies* 10;**2**:61–3.

Covidence [Computer program]

Covidence. Melbourne, Australia: Veritas Health Innovation, 2022. Available at covidence.org (accessed 1 March 2022).

Cruz 2019

Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al, Writing group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the extended group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. *Age and Ageing* 2019;**48**(1):16-31.

Daubail 2012

Daubail B, Jacquin A, Guilland JC, Hervieu M, Osseby GV, Rouaud O, et al. Serum 25-hydroxyvitamin D predicts severity and prognosis in stroke patients. *European Journal of Neurology* 2013;**20**(1):57-61.

Dennis 2005

Dennis MS, Lewis SC, Warlow C, FOOD Trial Collaboration. Routine oral nutritional supplementation for stroke patients in hospital (FOOD): a multicentre randomised controlled trial. *Lancet* 2005;**365**(9461):755-63.

Dávalos 1996

Dávalos A, Ricart W, Gonzalez-Huix F, Soler S, Marrugat J, Molins A, et al. Effect of malnutrition after acute stroke on clinical outcome. *Stroke* 1996;**27**(6):1028-32.

Egger 1997

Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629-34.

Foley 2009

Foley NC, Salter KL, Robertson J, Teasell RW, Woodbury MG. Which reported estimate of the prevalence of malnutrition after stroke is valid? *Stroke* 2009;**40**(3):e66-74.

FOOD Trial Collaboration 2003

FOOD Trial Collaboration. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD trial. *Stroke* 2003;**34**(6):1450-6.

Ford 2022

Ford KL, Arends J, Atherton PJ, Engelen MPKJ, Gonçalves TJM, Laviano A, et al. The importance of protein sources to support muscle anabolism in cancer: an expert group opinion. *Clinical Nutrition* 2022;**41**(1):192–201.

Fugl-Meyer 1975

Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. *Scandinavian Journal of Rehabilitation* 1975;**7**(1):13-31.

Gariballa 1998

Gariballa SE, Parker SG, Taub N, Castleden CM. Influence of nutritional status on clinical outcome after acute stroke. *American Journal of Clinical Nutrition* 1998;**68**(2):275–81.

GBD 2017 DALYs and HALE Collaborators 2018

GBD 2017 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease study 2017. *Lancet* 2018;**392**(10159):1859-922.

Geeganage 2012

Geeganage C, Beavan J, Ellender S, Bath PMW. Interventions for dysphagia and nutritional support in acute and subacute stroke. *Cochrane Database of Systematic Reviews* 2012, Issue 10. Art. No: CD000323. [DOI: 10.1002/14651858.CD000323.pub2]

Gorelick 2019

Gorelick PB. The global burden of stroke: persistent and disabling. *Neurology* 2019;**18**(5):417–8.

GRADEpro GDT [Computer program]

GRADEpro GDT. Version accessed on December 1, 2022. Hamilton (ON): McMaster University (developed by Evidence Prime), 2022. Available at gradepro.org.

Guralnik 1994

Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology* 1994;**49**(2):M85–M94.

Higgins 2003

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557-60.

Higgins 2011

Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration 2011. Available from training.cochrane.org/handbook/archive/v5.1.

Higgins 2021

Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 6.2 (updated February 2021). Cochrane 2021. Available from www.training.cochrane.org/handbook/archive/v6.2.

Higgins 2022

Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated August 2022). Cochrane 2022. Available from www.training.cochrane.org/handbook/archive/v6.3.

Hoffmann 2014

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;**348**:g1687.

Japan Stroke Society 2019

Japan Stroke Society. Japanese guidelines for the management of stroke 2015; 2019. jsts.gr.jp/img/guideline2015_tuiho2019_10.pdf (accessed 1 March 2022).

Kalra 2007

Kalra L, Langhorne P. Facilitating recovery: evidence for organized stroke care. *Journal of Rehabilitation Medicine* 2007;**39**(2):97-102.

Kalueff 2007

Kalueff AV, Tuohimaa P. Neurosteroid hormone vitamin D and its utility in clinical nutrition. *Current Opinion in Clinical Nutrition and Metabolic Care* 2007;**10**(1):12–9.

Katz 1970

Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970;**10**(1):20-30.

Keith 1987

Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. *Advances in Clinical Rehabilitation* 1987;**1**:6–18.

Khor 2014

Khor SC, Abdul Karim N, Ngah WZ, Yusof YA, Makpol S. Vitamin E in sarcopenia: current evidence on its role in prevention and treatment. *Oxidative Medicine and Cellular Longevity* 2014;**2014**:914853.

Knops 2013

Knops M, Werner CG, Scherbakov N, Fiebach J, Dreier JP, Meisel A, et al. Investigation of changes in body composition, metabolic profile and skeletal muscle functional capacity in ischemic stroke patients: the rationale and design of the Body Size in Stroke Study (BoSSS). *Journal of Cachexia, Sarcopenia and Muscle* 2013;**4**(3):199–207.

Kondrup 2003

Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clinical nutrition* 2003;**22**(3):321-36.

Lefebvre 2021

Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf M-I, et al. Technical Supplement to Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston MS, Li T, Page MJ, et al, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 6.2 (updated February 2021). Cochrane 2021. Available from www.training.cochrane.org/handbook/archive/v6.2.

Li 2020

Li W, Yue T, Liu Y. New understanding of the pathogenesis and treatment of stroke-related sarcopenia. *Biomedicine & Pharmacotherapy* 2020;**131**:110721.

Lieber 2018

Lieber AC, Hong E, Putrino D, Nistal DA, Pan JS, Kellner CP. Nutrition, energy expenditure, dysphagia, and self-efficacy in stroke rehabilitation: a review of the literature. *Brain Sciences* 2018;**8**(12):218.

Malafarina 2012

Malafarina V, Uriz-Otano F, Iniesta R, Gil-Guerrero L. Effectiveness of nutritional supplementation on muscle mass in treatment of sarcopenia in old age: a systematic review. *Journal of the American Medical Directors Association* 2012;**14**(1):10–7.

Marshall 2018

Marshall IJ, Noel-Storr A, Kuiper J, Thomas J, Wallace BC. Machine learning for identifying randomized controlled trials: an evaluation and practitioner's guide. *Research Synthesis Methods* 2018;**9**(4):602-14.

Martino 2005

Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke* 2005;**36**(12):2756-63.

Matwee 2020

Matwee LK, Alaverdashvili M, Muir GD, Farthing JP, Bater SA, Paterson PG. Preventing protein-energy malnutrition after cortical stroke enhances recovery of symmetry in forelimb use

during spontaneous exploration. *Applied Physiology, Nutrition, and Metabolism* 2020;**45**(9):1015–21.

Minhas 2022

Minhas JS, Chithiramohan T, Wang X, Barnes SC, Clough RH, Kadicheeni M, et al. Oral antiplatelet therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2022, Issue 1. Art. No: CD000029. [DOI: 10.1002/14651858.CD000029.pub3]

Nakamura 2020

Nakamura S, Sato Y, Kobayashi T, Kaneko Y, Ito E, Soma T, et al. Vitamin D protects against immobilization-induced muscle atrophy via neural crest-derived cells in mice. *Scientific Reports* 10;**1**:12242.

National Stroke Foundation 2017

National Stroke Foundation. Clinical Guidelines for Stroke Management 2017. clinicalguidelines.gov.au/portal/2585/clinical-guidelines-stroke-management-2017 (accessed 1 March 2022).

NICE 2019

National Institute for Health and Care Excellence (NICE). Stroke and transient ischaemic attack in over 16s: diagnosis and initial management, NICE guideline (NG128). www.nice.org.uk/guidance/ng128 (accessed 1 March 2022).

Noel-Storr 2020

Noel-Storr AH, Dooley G, Wisniewski S, Glanville J, Thomas J, Cox S, et al. Cochrane centralised search service showed high sensitivity identifying randomized controlled trials: a retrospective analysis. *Journal of Clinical Epidemiology* 2020;**127**:142-50.

Noel-Storr 2021

Noel-Storr A, Dooley G, Elliott J, Steele E, Shemilt I, Mavergames C, et al. An evaluation of Cochrane Crowd found that crowdsourcing produced accurate results in identifying randomized trials. *Journal of Clinical Epidemiology* 2021;**133**:130-9.

O'Neil 1999

O'Neil KH, Purdy M, Falk J, Gallo L. The dysphagia outcome and severity scale. *Dysphagia* 1999;**14**(3):139-45.

Page 2021

Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ* 2021;**372**:n160.

Peters 2008

Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *Journal of Clinical Epidemiology* 2008;**61**(10):991-6.

Powers 2019

Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019. Update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2019;**50**(12):e344-e418.

Rabin 2001

Rabin R, De Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Annals of Medicine* 2001;**33**(5):337–43.

RevMan Web 2023 [Computer program]

Cochrane Collaboration Review Manager Web (RevManWeb). Version Version 4.23.0. Cochrane Collaboration, 2023. Available at revman.cochrane.org. (accessed 8 January 2023).

Rosenbek 1996

Rosenbek JC, Robbins JA, Roecker EB. A penetration-aspiration scale. *Dysphagia* 1996;**11**:93–8.

Scherbakov 2014

Scherbakov N, Sandek A, Doehner W. Stroke-related sarcopenia: specific characteristics. *Journal of the American Medical Directors Association* 2015;**16**(4):272–6.

Schünemann 2013

Schünemann H, Brożek J, Guyatt G, Oxman A, editor(s). Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach (updated October 2013). GRADE Working Group, 2013. Available from gdt.gradepro.org/app/handbook/handbook.html (accessed 1 March 2022).

Su 2020

Su Y, Yuki M, Otsuki M. Prevalence of stroke-related sarcopenia: a systematic review and meta-analysis. *Journal of Stroke and Cerebrovascular Diseases* 2020;**29**(9):105092.

Thomas 2021

Thomas J, McDonald S, Noel-Storr A, Shemilt I, Elliott J, Mavergames C, et al. Machine learning reduced workload with minimal risk of missing studies: development and evaluation of a randomized controlled trial classifier for Cochrane Reviews. *Journal of Clinical Epidemiology* 2021;**133**:140-51.

Van Dronkelaar 2018

Van Dronkelaar C, Van Velzen A, Abdelrazek M, Van der Steen A, Weijs PJM, Tieland M. Minerals and sarcopenia: the role of calcium, iron, magnesium, phosphorus, potassium, selenium, sodium, and zinc on muscle mass, muscle strength, and physical performance in older adults: a systematic review. *Journal of the American Medical Directors Association* 2018;**19**(1):6–11.

Wan 2014

Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Medical Research Methodology* 2014;**14**:135.

Williams 1999

Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a stroke-specific quality of life scale. *Stroke* 1999;**30**(7):1362-9.

Winstein 2016

Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2016;**47**(6):e98-e169.

Yoo 2008

Yoo SH, Kim JS, Kwon SU, Yun SC, Koh JY, Kang DW. Undernutrition as a predictor of poor clinical outcomes in acute ischemic stroke patients. *Archives of Neurology* 2008;**65**(1):39–43.

References to other published versions of this review

Sakai 2019

Sakai K, Kinoshita S, Tsuboi M, Fukui R, Momosaki R, Wakabayashi H. Effects of nutrition therapy in older stroke patients undergoing rehabilitation: a systematic review and meta-analysis. *Journal of Nutrition, Health & Aging* 2019;**23**(1):21-6.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Aquilani 2008a

Study characteristics	
Methods	Setting: single-centre, Italy Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 48 Gender (men/women): 27/21 Mean age (SD): Intervention 73 (6.2) control 71 (8.5) Stroke phase: subacute Type of baseline stroke: ischaemic Inclusion criteria: no cognitive dysfunction, as shown by a score of < 20 in the Mini-Mental State Examination (MMSE), independent in their alimentation Exclusion criteria: patients who were aphasic or had chronic renal failure and/or diabetes on hypoglycaemic therapy Stroke severity: not reported
Interventions	Intervention group: energy-protein supplementation - 200 mL mixture providing 250 kcal energy, 20 g proteins, 28.2 g carbohydrates, and 7 g lipids between meals/ day Control group: spontaneous alimentation Co-interventions: not reported Duration of treatment: 21 days Compliance: not reported Intervention route: oral

Aquilani 2008a *(Continued)*

Outcomes	• Body weight • MMSE Time points: at 21 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	A randomisation list was available to the principal investigator. It was unclear how the list was managed and its impact on the outcome.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	High risk	Difference in body weight at the baseline

Aquilani 2008b

Study characteristics

Methods	Setting: single-centre, Italy Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 42 Gender (men/women): 27/15 Mean age (SD): All 66.4 (11) Stroke phase: acute and subacute (range 12–20 days after stroke onset) Type of baseline stroke: ischaemic

Aquilani 2008b *(Continued)*

	Inclusion criteria: alimentation-independent, admitted to a rehabilitation unit after an acute cerebrovascular stroke Exclusion criteria: chronic renal failure, diabetes, or taking hypoglycaemic drugs Stroke severity: not reported
Interventions	Intervention group: energy and protein - The formula (200 mL) provided 250 Kcal energy, 20 g proteins, 28 g carbohydrates, and 7 g lipids. - Once between meals Control group: spontaneous alimentation Co-interventions: not reported Duration of treatment: 21 days Compliance: not reported Intervention route: oral
Outcomes	• Body weight • NIH Stroke Scale score Time points: at 21 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	The randamasion list was available to the principal investigator. It was unclear how the list was managed and its impact on the outcome.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The patients/caregivers and physician who evaluated the neurological test, apart from the one who prescribed the supplementation, were blinded to the supplements themselves."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The patients/caregivers and physician who evaluated the neurological test, apart from the one who prescribed the supplementation, were blinded to the supplements themselves."
Incomplete outcome data (attrition bias) All outcomes	Low risk	One participant lost due to myocardial infarction in the intervention group
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

Aquilani 2009

Study characteristics	
Methods	Setting: single-centre, Italy Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 26 Gender (men/women): 17/9 Mean age (SD): intervention 74 (8.0) control 72 (6.5) Stroke phase: subacute Type of baseline stroke: ischaemic Inclusion criteria: an adequate energy-protein intake (energy ≥ 24 kcal/kg, protein > 0.8 g/kg) and low Zn^{2+} intake (lower than 67% of recommended daily allowance; the RDA for Zn^{2+} is 10 mg/day) Exclusion criteria: not stated Stroke severity: NIHSS: intervention group mean 13.5 (95% CI 11.3 to 14.8), control group: mean 12.1 (95% CI 10.5 to 14.1)
Interventions	Intervention group: Zn^{2+} - 10 mg elemental Zn^{2+}/day at 10 am as an emulsion of zinc sulfate Control group: placebo Co-interventions: not stated Duration of treatment: 30 days Compliance: not reported Intervention route: oral
Outcomes	• NIHSS • Body weight Time points: 30 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	Randomisation list was available to the principal investigator. It was unclear how the list was managed and its impact on the outcome.

Aquilani 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome unlikely to be biassed by blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	It was unclear how the trial was funded.

Aquilani 2014

Study characteristics	
Methods	Setting: single-centre, Italy Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 38 Gender (men/women): 29/9 Mean age (SD): all 69.7(69.7) Stroke phase: subacute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: dysphagic subacute stroke patients (< 3 months after acute cerebrovascular event) admitted to our rehabilitation centre. The reason for patient admission was due to rehabilitation for dysphagia and hemiplegia. Exclusion criteria: chronic heart failure, acute coronary syndrome, acute or chronic renal failure (creatinine clearance < 30 mg/100 m), cancer surgery, pressure ulcer, diabetes (on oral hypoglycaemic or insulin treatment), dysthyroidism, and on steroid therapy Stroke severity: not reported
Interventions	Intervention group: essential amino acid Nutrition mixture supplement that provided 8 g of EAAs/d (4 g in the morning + 4 g in the afternoon diluted in half a glass of water until patient discharge) Control group: placebo Co-interventions: rehabilitative treatment adapted to each individual patient (therapeutic exercise with a personal physiotherapist for 60 minutes, five days a week). Speech therapy, occupational therapy (activities of daily living, vocational, perceptual, and functional activity training), and recreational activity were also performed depending on individual needs.

Aquilani 2014 *(Continued)*

	Duration of treatment: until patient discharge (mean 38 ± 4 days) Compliance: Rehabilitation nurses assisted each patient with their oral diet during placebo or EAA intake to be sure of the patient compliance. Intervention route: oral
Outcomes	• FIM • DOSS • Body weight Time points: at the patient's discharge from rehabilitation (mean 42 ± 4 days from admission)
Notes	Declaration of interests: none Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	Randomisation list was available to the principal investigator. It was unclear how the list was managed and its impact on the outcome.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: blinded Personnel: the nurses were blinded, but there was no reporting about other healthcare providers.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The first author, who interpreted all results, was blinded, but there was no reporting about outcome assessors.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	High risk	Imbalanced baseline characteristics

Aquilani 2015

Study characteristics

Methods	Setting: single-centre, Italy Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 42

Aquilani 2015 *(Continued)*

	Gender (men/women): 27/15 Mean age (SD): all 71 (9) Stroke phase: subacute Type of baseline stroke: ischaemic Inclusion criteria: ischaemic strokes and dysphagic patients Exclusion criteria: on steroid therapy, or had cancer or nephrotic syndrome Stroke severity: not reported
Interventions	Intervention group: essential amino acid - 8 g/d of EAAs (4 g in the morning + 4 g in the afternoon diluted in half a glass of water) Control group: placebo Co-interventions: the centre rehabilitative protocol, which consisted of performing passive, active, and active-assistive range-of-motion exercise coordination, and assistive ambulation with devices or support. The duration of the treatment by the same therapist was 60 min a day for 5 days a week. Moreover, all patients underwent speech and occupational therapy. Duration of treatment: 35 days Compliance: not reported Intervention route: oral or enteral
Outcomes	• FIM • Body weight • DOSS • Improved dysphagia Time points: 38 ± 1 days
Notes	Declaration of interests: none Funding statement: Quote "no specific grant" Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: blinded Personnel: not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome assessor: not reported

Aquilani 2015 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	No other sources of bias were found.

Badjatia 2021

Study characteristics	
Methods	Setting: single-centre, USA Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 26 Gender (men/women): 11/15 Mean age (SD): all 59(11) Stroke phase: acute Type of baseline stroke: SAH Inclusion criteria: 1) diagnosis of aneurysmal SAH; 2) aneurysmal repair within 48 h of ictus; 3) age >18 years; 4)expected stay in the NCCU > 72 h; 5) admission Hunt Hess Grade ≥ 2; 6) modifed Fisher score > 1 Exclusion criteria: 1) diagnosis of SAH from trauma, rupture of an arteriovenous malformation, neoplasm, vasculitis, or other secondary causes; 2) unlikely to survive 1-week post-haemorrhage either due to impending brain death or likely request for withdrawal of care; 3) unlikely to remain in the ICU for more than 7 days; 4) body mass index < 15 or > 40 kg/m^2; 5)allergy to whey protein; 6) evidence of lower extremity paresis or spasticity within 48 h of injury; 7) pre-morbid modifed Rankin Score > 1; 8) known pregnancy, malignancy, inflammatory disorder, neuromuscular disorder or renal failure; 9) ongoing seizure activity as assessed clinically or by electrographic detection on continuous electroencephalogram (cEEG) at time of enrolment; 10) prisoner
Interventions	Intervention group: protein - a whey protein powder with a total dose of at least 3 g leucine/feeding to achieve a goal of 1.75 g/kg/day, 3 times daily Control group: SOC - protein: 1.2–1.4 g/kg/day Co-interventions: neuromuscular electrical stimulation (intervention group) Duration of treatment: until post -bleed day 14 Compliance: monitored (control group 0.88 ± 0.36 g/kg/ day vs intervention group 1.51 ± 0.47 g/kg/day) Intervention route: oral
Outcomes	• Muscle atrophy: acute quadriceps muscle atrophy • Hospital-acquired infection

Badjatia 2021 *(Continued)*

	• mRS • MoCA • Short survey of Neuro-QoL questionnaires Time points: 14 days and 90 days
Notes	Declaration of interests: not reported Funding statement: Quote: "This study was supported by the Baltimore VAMC—Maryland Exercise and Robotics Center of Excellence (NB). Investing in Clinical Neurocritical Care Research (INCLINE) grant from the Neurocritical Care Society (NB). VA RR&D Senior Research Career Scientist Award (ASR), National Institutes of Health. The NMES device (L300 Plus® system) used in this study was given at no cost to the investigators by Bioness, Inc (Valencia, CA)." Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	High risk	Planned outcome in the protocol was only "Change in cross-sectional area of the quadriceps muscle as measured by CT scan at the end of study period".
Other bias	High risk	The NMES device (L300 Plus® system) used in this study was given at no cost to the investigators by the product company.

Beeharry 2014

Study characteristics

Methods	Setting: single-centre, Russia Design: RCT, 2 arms, parallel assignment Recruitment period: 2013-2014
Participants	Sample size: 37 Gender (men/women): 21/16

Beeharry 2014 *(Continued)*

	Mean age (SD): all 73.4 (6.2) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: ischaemic stroke Exclusion criteria: not reported Stroke severity: not reported
Interventions	Intervention group: amino-acid + energy - Enteral nutrition (hyper-caloric, 1 mL = 1.5 kcal, protein = 76 g/L) according to energy expenditure measured by indirect calorimeter + parenteral infusion of amino-acid according to protein loss Control group: energy only - Enteral nutrition (hyper-caloric, 1 mL = 1.5 kcal, protein = 76 g/L) according to energy expenditure measured by indirect calorimeter Co-interventions: not reported Duration of treatment: not reported Compliance: not reported Intervention route: enteral and parenteral
Outcomes	• Nutritional status Nutritive status was assessed using anthropometric and laboratory indicators. No information about anthropometric indicators Time points: during ICU stay, day not reported
Notes	Conference abstract Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported

Beeharry 2014 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Berger 2008

Study characteristics	
Methods	Setting: single-centre, Switzerland Design: RCT, 2 arms, parallel assignment Recruitment period: January 2003-September 2004
Participants	Sample size: 21 Gender (men/women): 5/16 Mean age (SD): all 54(9) Stroke phase: acute Type of baseline stroke: SAH Inclusion criteria: deemed likely by the medical team to require at least 48 hours of ICU treatment, severe subarachnoid haemorrhage (SAH) (that is, World Federation of Neurological Surgeons grades 3, 4, and 5) Exclusion criteria: liver cirrhosis or major burns, and life expectancy of less than 48 hours or a lack of commitment to full aggressive care (anticipated withholding or withdrawing of treatment in 48 hours) Stroke severity: not reported
Interventions	Intervention group: antioxidant supplement Parenteral: zinc (60–30 mg/day), selenium (540.4–270.2 µg), vitamin C (2700-1600 mg), vitamin B1 (305–102.5 mg), vitamin E (12.8–6.4) + standard care (100 mg thiamine and 500 mg vitamin C/day) AND Enteral: vitamin E(600-300 mg) Control group: Parenteral; 100 mg thiamine and 500 mg vitamin C/day Co-interventions: not reported Duration of treatment: 5 days An initial loading dose (double dose for 2 days) and 3 days of therapeutic dose Compliance: not reported Intervention route: enteral and parenteral

Berger 2008 *(Continued)*

Outcomes	• Infection: pneumonia Time points: three months
Notes	Declaration of interests: The study was supported by a grant from Fresenius Kabi AG (Bad Homburg, Germany) to the department that partly financed the salary of an author (no direct payment) and the provision of the study micronutrients. Three authors have given conferences and lectures supported by the same company. Two authors have also delivered conferences sponsored by Nestlé (Vevey, Switzerland) and by B. Braun (Melsungen, Germany). Funding statement: as stated above Protocol: Clinical Trials.gov RCT Register: NCT00515736

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random list was used.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote:"Patients, clinicians, and investigators were blinded to the treatment."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote:"Patients, clinicians, and investigators were blinded to the treatment."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Authors did not report about the loss to follow-up in participants with SAH.
Selective reporting (reporting bias)	Low risk	Protocol available. All prespecified outcomes were reported.
Other bias	High risk	Competing interests were reported.

Cheng 2019

Study characteristics

Methods	Setting: multicentre, Taiwan Design: RCT, 2 arms, parallel assignment Recruitment period: September 2017–May 2018
Participants	Sample size: 20 Gender (men/women): 14/4 (after exclusion of dropouts, not reported as ITT analysis) Mean age (SD): all 58.8 (7.1) (after exclusion of dropouts, not reported as ITT analysis)

Cheng 2019 *(Continued)*

	Stroke phase: chronic Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: (1) stroke exceeding 6 months, (2) aged between 20 and 75 years, (3) able to walk for 30 min independently with or without orthosis, and (4) able to perform cycling ergometry training Exclusion criteria: (1) contraindications to or difficulties performing exercises, (2) unable to coordinate with intervention because of cognitive or emotional problems, and (3) malnutrition Stroke severity: not reported
Interventions	Intervention group: protein - A 40-g serving of the protein supplement which was made from isolate soy protein which contained 23.2 g of protein, 11 g of carbohydrates, and 144.2 kcal - 20 g of protein supplement immediately before and after each training session Control group: placebo Co-interventions: not reported Duration of treatment: 21.4 ± 1.9 (range, 18-24) intervention sessions Compliance: not reported Intervention route: oral
Outcomes	• TUG • 6-min WT • Total lean mass • BBS • Fugl-Meyer assessment (leg subscale) Time points: at 8 weeks
Notes	Declaration of interests: none Funding statement: a grant (MOST 107-2320-B-038-016) from the Ministry of Science and Technology, Taiwan, and research Grants for Newly Hired Faculty (105-6204-012-112) Taipei Medical University Protocol: Clinical Trials.gov RCT Register: NCT03244527

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Performed by a central coordinator
Allocation concealment (selection bias)	Low risk	Performed by a central coordinator
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blinded. Nutritional supplements were sealed in paper bags coded with serial numbers upon production. Only the central coordinator was given the coding book.
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded.

Cheng 2019 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	One for each group with the same reason
Selective reporting (reporting bias)	Low risk	One dropped out because of prostate surgery in each group.
Other bias	Low risk	No other sources of bias were found.

Daga 1997

Study characteristics	
Methods	Setting: single-centre, India Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 27 Gender (men/women): not reported Mean age (SD): not reported Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: suffered a cerebrovascular event and presenting within the first 24 hours of the episode. Only patients with CT-proven infarct were included. Exclusion criteria: (l) obvious cause for embolic ischaemic stroke, (2) very large lesions on CT scan or very small lesions (in eluding lacunar infarcts), and (3) TIA Stroke severity: not reported
Interventions	Intervention group: vitamin E (300 mg/day) Control group: placebo Co-interventions: not reported Duration of treatment: 15 days Compliance: not reported Intervention route: oral
Outcomes	• Barthel index Time points: at 15 days and 6 weeks
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Daga 1997 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Dang 2018

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 22 Gender (men/women): not reported Mean age (SD): not reported Stroke phase: subacute Type of baseline stroke: ischaemic Inclusion criteria: ischaemic stroke Exclusion criteria: not reported Stroke severity: not reported
Interventions	Intervention group: early enteral nutrition Control group: daily diet

Dang 2018 *(Continued)*

	Co-interventions: stroke-specified rehabilitation intervention including physical training, occupational training, and swallow training Duration of treatment: not reported Compliance: not reported Intervention route: enteral
Outcomes	• mRS • Activity of daily living • Swallowing function Time points: at 4 weeks
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Dang 2023

Study characteristics

Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment

Dang 2023 *(Continued)*

	Recruitment period: January 2021 to December 2022
Participants	Sample size: 80 Gender (men/women): 45/35 Mean age (SD): intervention 61.02 (6.61) control 60.52 (6.58) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: diagnosed with ACI by head CT or MRI. GCS scores are below 8 points. Exclusion criteria: patients with severe limb dysfunction, abnormal heart, liver and kidney function, aphasia and unconsciousness Stroke severity: NIHSS score: control group 8.57 ± 0.86, intervention group 8.60 ± 0.87
Interventions	Intervention group: enteral energy The enteral nutritional emulsion (Total Protein and Fibre, TPF) produced by Fresenius Kabivari Pharmaceutical Co., Ltd. 400 mL (520 kcal) per day, and 30 mL/h was pumped on the first day, and 50 mL/h was pumped every day thereafter. Control group: routine diet intervention + health education, psychological counselling, posture nursing, and individual functional exercise guidance Co-interventions: evidence-based nursing Duration of treatment: not reported Compliance: not reported Intervention route: enteral
Outcomes	• NIHSS • Physical performance: Fugl-Meyer Assessment score • QOL: SF-36 Time points: stated "after intervention"
Notes	Declaration of interests: no potential conflicts of interest Funding statement: no financial support Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias)	Unclear risk	Not reported

Dang 2023 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	None
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	Baseline data were insufficient.

Das 2021

Study characteristics	
Methods	Setting: single-centre, India Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 12 Gender (men/women): not reported Mean age (SD): not reported Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: ischaemic stroke patients requiring > 48 hrs of mechanical ventilation above 40 years of age Exclusion criteria: not reported Stroke severity: not reported
Interventions	Intervention group: individualised nutrition (energy) - Enteral nutrition based on energy requirement calculated by indirect calorimeter Control group: SOC - Enteral nutrition based on energy requirement calculated by standard weight-based measurements Co-interventions: not reported Duration of treatment: not reported Compliance: not reported Intervention route: enteral
Outcomes	• Mortality • Complications

Das 2021 *(Continued)*

	• Canadian neurological score Time points: not reported
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

De Aguilar-Nascimento 2011

Study characteristics

Methods	Setting: single-centre, Brazil Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 31 Gender (men/women): 12/19 Median age [range]: 74 [65–90] Stroke phase: acute Type of baseline stroke: ischaemic

De Aguilar-Nascimento 2011 *(Continued)*

	Inclusion criteria: admitted to the ICU due to acute ischaemic stroke, elderly (above 65 years old), admission due to acute ischaemic stroke, initiation of early (no longer than 48 hours after admission) enteral nutrition, and an APACHE II score between 8 and 30 Exclusion criteria: change of diagnosis, modification of the nutritional route to parenteral nutrition, fewer than three consecutive days on enteral nutrition, immune suppressive conditions (AIDS, chronic corticoid use, immune-suppressive drugs), chronic obstructive pulmonary disease (PCO2 > 45 mm Hg on admission), renal failure requiring peritoneal or haemodialysis, or creatinine > 2.5 mg/dL, hepatic dysfunction or cirrhosis or bilirubin > 3 mg % on admission, and death in the first 5 days of hospitalisation Stroke severity: APACHE II: intervention group: median 16.5 (range 8–26) control group: median 18 (range 8–28)
Interventions	Intervention group: whey protein - 35 kcal/kg/d and 1.2 g of protein/kg/d with a formula containing hydrolysed whey protein Control group: casein - 35 kcal/kg/d and 1.2 g of protein/kg/d with a standard formula containing hydrolysed casein Co-interventions: early nasogastric feeding for both groups Duration of treatment: 5 days Compliance: not reported Intervention route: enteral
Outcomes	• Mortality during the ICU stay Time points: during the ICU stay
Notes	Declaration of interests: partially funded by Nestle Health Nutrition, which donated the whole provision of Peptamen 1.5 for enteral feeding Funding statement: as stated above Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: ”A table of random numbers generated"
Allocation concealment (selection bias)	Low risk	Quote: ”Group assignments were sealed in opaque envelopes and opened sequentially by the investigators".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Outcome unlikely to be biassed by blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome unlikely to be biassed by blinding
Incomplete outcome data (attrition bias)	Low risk	Five in the intervention group and one in the control group due to a change of diagnosis (four cases, all in the intervention group) and fewer than 3 days of

De Aguilar-Nascimento 2011 *(Continued)*

All outcomes		enteral feeding (two cases, one for each group). It was not likely to affect the outcome.
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	No other sources of bias were found.

Dennis 2005a

Study characteristics	
Methods	Setting: multicentre, UK, India, Italy, New Zealand, Australia, Belgium, Brazil, Canada, Czech Republic, Denmark, Hong Kong, Poland, Portugal, Republic of Ireland, Turkey Design: RCT, 2 arms, parallel assignment Recruitment period: November 1996–July 2003
Participants	Sample size: 4023 Gender (men/women): 2149/1874 Mean age (SD): intervention 71 (12) control 71 (13) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: patients admitted with a recent stroke (first or recurrent stroke no more than 7 days before admission), passed their swallow screen, the responsible clinician was uncertain whether to use oral nutritional supplements Exclusion criteria: patients with subarachnoid haemorrhage Stroke severity: not reported
Interventions	Intervention group: energy and protein - Normal hospital diet plus oral protein energy supplements, which was equivalent to 360 mL at 6.27 kJ/mL and 62.5 g/L in protein every day Control group: normal hospital diet - The nutritional composition of the normal hospital diet or the diets of individual patients was not measured. Co-interventions: not reported Duration of treatment: until discharge Compliance: not reported Intervention route: oral
Outcomes	• mRS • Death • EUROQoL • Infection (pneumonia and urinary infection) • Pressure sores

Dennis 2005a *(Continued)*

	Time points: mRS, death, EUROQoL: at 6 months after enrolment Infection and pressure sores: during hospitalisation
Notes	Declaration of interests: none Funding statement: Quote "grants from the Health Technology Assessment Board of NHS Research and Development in UK, the Stroke Association, the Chief Scientist Office of the Scottish Executive, and Chest, Heart and Stroke Scotland. The Royal Australasian College of Physicians supported the trial in Hawkes Bay, New Zealand. The views expressed in this report are those of the authors and do not necessarily represent those of the funding source". Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Quote: ”Baseline data were obtained from a telephone call to the international coordinating centre at randomisation. Allocation was concealed until it was given."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: ”Neither the randomising clinician, the clinical team, nor patients were unaware of treatment allocation".
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: ”review was not explicitly done unaware of baseline nutritional status or treatment allocation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Seven in the intervention group and four in the control group were lost. It was unlikely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	The protocol was published.
Other bias	Low risk	No other sources of bias were found.

Dennis 2005b

Study characteristics

Methods	Setting: multicentre (Australia, Belgium, Brazil, Canada, Czech Republic, Denmark, Hong Kong, India, Italy, New Zealand, Portugal, Republic of Ireland, Singapore, Turkey, UK) Design: RCT, 2 arms, parallel assignment Recruitment period: November 1996-July 2003
Participants	Sample size: 859 Gender (men/women): 394/465

Dennis 2005b *(Continued)*

	Mean age (SD): intervention 76 (11) control 76 (11) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: patients with dysphagia admitted to a participating hospital with a recent (within 7 days before admission) stroke (first-ever or recurrent) could be enroled if the responsible clinician was uncertain of the best feeding policy. Exclusion criteria: patients with subarachnoid haemorrhage Stroke severity: not reported
Interventions	Intervention group: early enteral nutrition - Started enteral tube feeding (via the clinician's preferred tube) as soon as possible Control group: avoid tube feeding - Avoid any enteral tube feeding for at least 7 days Patients who were not tube fed were given parenteral fluids either intravenously or subcutaneously, but not nutrition. Co-interventions: not reported Duration of treatment: within 7 days Compliance: they did not monitor patients' daily intake of nutrients. Intervention route: enteral
Outcomes	• Mortality • mRS: death or poor outcome (score 4-5) • Recurrent strokes • Infections (pneumonia and urinary infection) • Pressure sores • EUROQoL Time points: at 6 months
Notes	Declaration of interests: none Funding statement: Quote "supported with grants from the Health Technology Assessment Board of NHS Research and Development in UK, the Stroke Association, the Chief Scientist Office of the Scottish Executive and Chest, Heart and Stroke Scotland. The trial was supported in Singapore by the Singapore Medical Research Council and by the Royal Australasian College of Physicians in Hawkes Bay, New Zealand. The views expressed in this report are those of the authors and do not necessarily represent those of the funding sources". Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote in another FOOD trial report: "A central 24-hour telephone randomisation service was provided for this trial".

Dennis 2005b *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote in another FOOD trial report: ”It was impossible to guess the allocation given the use of minimisation to balance treatments between groups."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: ”review was not explicitly done unaware of baseline nutritional status or treatment allocation."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: ”review was not explicitly done unaware of baseline nutritional status or treatment allocation."
Incomplete outcome data (attrition bias) All outcomes	Low risk	None in the intervention group and two in the control group were lost. It was unlikely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	The protocol was published.
Other bias	Low risk	No other sources of bias were found.

Gao 2008

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: January 2007–January 2008
Participants	Sample size: 60 Gender (men/women): 41/19 Mean age (SD): intervention 63.17 (12.68) control 67.47 (12.33) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: 1) severe stroke (Glasgow Coma Score < 12), 2) within 5 days after stroke onset, 3) having dysphagia Exclusion criteria: patients with diabetes mellitus with ketosis, abnormal protein metabolism, or hypoproteinemia Stroke severity: APACHEⅡ: high-protein group 14.0 ± 4.77, low-protein group 13.90 ± 4.99
Interventions	Intervention group: protein (high-protein enteral nutrition) - Calorie ratio of protein, carbohydrate, and fat: 20:45:35 - Non-protein calories were the same in both groups. Control group: diabetes-specific enteral nutrition - Calorie ratio of protein, carbohydrate, and fat: 15:53:32 Co-interventions: not reported

Gao 2008 *(Continued)*

	Duration of treatment: not reported, but during hospitalisation Compliance: not reported Intervention route: enteral
Outcomes	• Mortality Time points: at 3 months
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Garbagnati 2009

Study characteristics

Methods	Setting: single-centre, Italy Design: RCT, 3 arms, parallel assignment Recruitment period: June 2004–February 2006
Participants	Sample size: 72 Gender (men/women): 47/25

Garbagnati 2009 *(Continued)*

	Mean age (SD): All 65.3 (12.9) Stroke phase: subacute Type of baseline stroke: ischaemic Inclusion criteria: stroke survivors admitted to a rehabilitation unit for the rehabilitation of sequelae of their first ischaemic stroke Exclusion criteria: onset-admission interval > 60 days, haemorrhagic lesions and the presence of other chronic disabling pathologies and/or medical conditions that would contraindicate physical therapy, and inability or refusal to give consent Stroke severity: Canadian Neurological Scale (mean ± SD): group 1, 5.5 ± 2.5, group 2, 6.3 ± 1.8, group 3, 5.9 ± 1.8, placebo, 5.6 ± 2.5
Interventions	Intervention group 1: vitamin (antioxidant supply) - 290 mg vitamin E, 240 mg vitamin C, 150 mg polyphenols and 19 mg carotene Intervention group 2: fatty acid - n–3 polyunsaturated fatty acid supply (500 mg) Intervention group 3: vitamins and fatty acid Co-interventions: rehabilitation Individual physiotherapy started within 24 hours from admission and was performed for 60 minutes twice a day (only once on Saturdays), 6 days a week, throughout the stay. After discharge and during the follow-up period, all patients performed home or ambulatory rehabilitative treatment (three 1-hour sessions/week). Duration of treatment: 12 months Compliance: monitored, but actual consumption was not reported Intervention route: oral
Outcomes	• Barthel Index • Rivermead Mobility Index • Mortality Time points: at 6 months and 12 months
Notes	Declaration of interests: not reported Sigma-Tau Health Science, Rome, supplied n–3 dietary supplements. Funding statement: supported by the Italian Ministry of Health Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Enrolled patients were randomized, by means of a specific list, into 4 groups". No information for a specific list
Allocation concealment (selection bias)	Unclear risk	Not reported

Garbagnati 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "no patient, research assistant, investigator, or any other medical or nursing staff could distinguish the placebo from the supplements during the study".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "no patient, research assistant, investigator or any other medical or nursing staff could distinguish the placebo from the supplements during the study".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Seven in the vitamin group, 0 in the fatty-acid group, six in the combination group, and seven in the placebo group were lost. The reasons for dropouts were not available in each group.
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	High risk	n–3 dietary supplements were supplied by a product company.

Gariballa 1998

Study characteristics	
Methods	Setting: single-centre, UK Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 42 Gender (men/women): 21/21 Mean age (SD): intervention 78 (10), control 80 (7) Stroke phase: acute Type of baseline stroke: cerebral haemorrhage and SAH Inclusion criteria: 1) being conscious during the first week after stroke onset, 2) anthropometric evidence of undernutrition defined as follows: triceps skinfold thickness (TSF) and midarm circumference ≦ 1 SD below the mean Exclusion criteria: active gastrointestinal disease, gastric surgery, biochemical evidence of hepatic or renal impairment, uncontrolled heart failure, diagnosed malignancy, sepsis, or persistent swallowing difficulty Stroke severity: not reported
Interventions	Intervention group: energy and protein - Received the hospital diet plus a twice daily (3:00 pm and 8:00 pm) oral nutritional supplement containing 600 kcal and 20 g protein Control group: hospital diet only Co-interventions: not reported Duration of treatment: for 4 weeks or until death or discharge Compliance: monitored

Gariballa 1998 *(Continued)*

	Energy intake: intervention group: 1807 ± 318 kcal/day, control group 1084 ± 343 kcal/day Protein intake: intervention group: 65.1 ± 13.8 g/day, control group 44.1 ± 12.8 g/day Intervention route: oral
Outcomes	• Mortality • Barthel Index • Infections (chest infections, urinary tract infections, and septicaemias). Not reported by each infection Time points: survival, Barthel scores taken at 2, 4, and 12 weeks Infections: during hospitalisation Mortality and Barthel Index: at 12 weeks (follow-up)
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation was used, but the method of generation was not reported.
Allocation concealment (selection bias)	Low risk	Quote: "Randomization blocks were kept separately by the dietitian, and allocation of patients to the treatment group was done by telephone."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The study was single-blind so that only the nurses and the patients themselves were aware of the group". "Barthel scores on a 100-point scale were recorded prospectively for each patient after assessment, discussion with the nurses in charge of that patient, and either by discussion or from the records documented by the multidisciplinary staff involved in the assessment and treatment of the patient."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The study was single-blind so that only the nurses and the patients themselves were aware of the group". "Barthel scores on a 100-point scale were recorded prospectively for each patient after assessment, discussion with the nurses in charge of that patient, and either by discussion or from the records documented by the multidisciplinary staff involved in the assessment and treatment of the patient."
Incomplete outcome data (attrition bias) All outcomes	Low risk	One participant lost in each group because of early discharge as a result of complete recovery. It was unlikely to affect the outcomes.
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

Gupta 2016

Study characteristics	
Methods	Setting: single-centre, India Design: RCT, 2 arms, parallel assignment Recruitment period: December 2011–March 2013
Participants	Sample size: 53 Gender (men/women): 37/16 Mean age (SD): all 60.4 (11.3) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: 1) presentation within 7 days of onset of first-ever ischaemic stroke, 2) prestroke modified Rankin Score (mRS) < 2, 3) age ≥ 35 years. Out of 73 patients who satisfied preliminary inclusion criteria, 4) who had vitamin D deficiency/insufficiency (serum 25 (OH)D levels < 75 nmol/L) Exclusion criteria: patients already on vitamin D and calcium supplementation, those with renal and hepatic impairment, and those who underwent thrombolysis Stroke severity: NIHSS: intervention group median 12 (range 3–25), control group median 12 (range 2–29)
Interventions	Intervention group: vitamin D - single intramuscular injection of 600,000 IU cholecalciferol followed by oral cholecalciferol 60,000 IU once a month Control group: usual care alone Co-interventions: one gram elemental calcium daily along with usual post-stroke care in the intervention group Duration of treatment: 6 months Compliance: not reported Intervention route: oral
Outcomes	• mRS • Mortality Time points: at 6 months
Notes	Declaration of interests: none Funding statement: no grant Protocol: not reported

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method

Gupta 2016 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote:"outcome assessment was done by a single investigator and was not blinded."
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of lost to follow-up was similar between the groups (four in the intervention group, five in the control group) and those reasons were not reported. It was unlikely to affect the outcomes.
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	No other sources of bias were found.

Ha 2010a

Study characteristics	
Methods	Setting: single-centre, Norway Design: RCT, 2 arms, parallel assignment Recruitment period: May 2005–December 2007
Participants	Sample size: 170 Gender (men/women): 60/64 (in completed patients, not reported by ITT analysis) Mean age (SD): intervention 78.5 (7.4), control 79.7 (6.8) (in completed patients) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: acute stroke patients aged > 65 years, patients who were at nutritional risk in the Malnutrition Universal Screening Tool (MUST) or undernourished (BMI ≦ 20 kg/m^2 and either triceps skinfold thickness or mid-upper arm muscle circumference < 15th percentile according to gender and age group) Exclusion criteria: patients with no confirmed stroke diagnosis, being critically ill, had severe dementia, could not be weighed, or had a planned discharge within 24 h after the first visit by the trial assessor Stroke severity: Scandinavian Stroke Scale: intervention: median 41 (IQR 6–58), control: median 42 (IQR 7–58)
Interventions	Intervention group: individualised nutrition - energy and protein according to individual intake and needs. Resting energy requirements were estimated with gender and age group specific equations from the WHO. Total energy need was calculated from an appropriate physical activity level factor (range: 1.25 to 1.40). The patients in the intervention group were given oral nutritional advice to prevent undernutrition or written nutritional advice if the patient was tube fed before discharge.

Ha 2010a *(Continued)*

	Control group: routine care - oral sip feedings or tube feeding at the discretion of the attending physician Co-interventions: not reported Duration of treatment: during hospitalisation Length of stay: median 12 days (intervention group), 13 days (control group) Compliance: monitored for the first 7 days of registration Intervention route: oral or enteral The number of patients who were tube fed: 11 (intervention group), 6 (control group)
Outcomes	• Weight loss ≥ 5% • EQ-5D questionnaire: the number of people with improvement in each subdomain and VAS score • Handgrip strength • Mortality (reported in the follow-up study) Time points: at 3 months
Notes	Declaration of interests: none Funding statement: supported by the Throne Holst Foundation for Nutrition Research Protocol: ClinicalTrials.gov NCT00163007

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Quote: "used sequentially numbered, non-transparent envelopes containing the treatment allocation information."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The assessors were not blinded to which treatment the patient was assigned at study entry".
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of lost to follow-up was one for each group with the reason, early discharge due to complete recovery. It was not likely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported.
Other bias	Low risk	No other sources of bias were found.

Ha 2010b

Study characteristics	
Methods	Setting: single-centre, Norway Design: RCT, 2 arms, parallel assignment Recruitment period: May 2005–December 2007
Participants	Sample size: 170 Gender (men/women): 60/64 (in completed patients, not reported by ITT analysis) Mean age (SD): intervention 78.5 (7.4), control 79.7(6.8) (in completed patients) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: 1) those with ischaemic stroke or cerebral haemorrhage, 2) at least one marker of nutritional risk present (either BMI ≤ 20 kg/m^2, or unintentional weight loss of ≥ 5% the previous 3–6 months, or poor nutritional intake for at least five days, or the risk of inadequate nutritional intake for the next five days) Exclusion criteria: patients being critically ill, had severe dementia, could not be weighed, or if there was planned discharge within 24 hours after the first visit by the trial assessor Stroke severity: ScandinavianStrokeScale: intervention group median 41 (range 6–58), control group: median 42 (range 7–58)
Interventions	Intervention group: individualised nutrition - energy and protein-enriched meals, or established oral energy and protein-rich sip feedings (with 0.8-1.5 kcal and 0.04-0.1 g protein per mL), or enteral tube feeding (with 1.0 kcal and 4.0 kcal per mL) according to the estimated individual nutritional intake and nutritional needs calculated according to the Schofield equations Control group: routine practice - no further assessment of nutritional intake or needs and treated without an individualised nutritional plan Co-interventions: not reported Duration of treatment: during hospitalisation Compliance: monitored only for the first week Intervention route: oral or enteral
Outcomes	• Body weight • Mid-upper arm circumference • Triceps skinfold thickness • Arm muscle circumference Time points: at 3 months
Notes	Declaration of interests: none Funding statement: supported by the South-Eastern Norway Regional Health Authority and Østfold Hospital Trust Protocol: ClinicalTrials.gov NCT00163007

Ha 2010b *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Sequentially numbered, non-transparent envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The assessors were not blinded to which treatment the patient was assigned at study entry. To minimize the possible bias from not blinding at baseline, the information about the allocated treatment was made inaccessible to the assessor at three-month follow-up".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "19 patients refused to attend three-month follow-up". The number of participants and reasons by group were not reported.
Selective reporting (reporting bias)	High risk	Protocol: No specific information about nutritional status at three months. Handgrip strength and quality of life in the trial were not reported.
Other bias	Unclear risk	No information on the number of participants who were randomised to the intervention group and the control group.

Hashemilar 2020

Study characteristics

Methods	Setting: single-centre, Iran Design: RCT, 2 arms, parallel assignment Recruitment period: February 2016–August 2018
Participants	Sample size: 42 Gender (men/women): 34/6 (in the study completed patients, not reported ITT analysis) Mean age (SD): intervention 65.73 (11.63), control 71.90 (5.91) (in the study completed patients, not reported ITT analysis) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: aged ≥ 40 years old, diagnosed with acute ischaemic stroke, the first-ever ischaemic stroke patient, the National Institutes of Health Stroke Scale (NIHSS) scores < 20, and with enteral feeding Exclusion criteria: being in a vegetative state, tissue plasminogen activator administration, chronic illness's presence (chronic renal failure requiring dialysis, hepatic failure and cirrhosis, epilepsy, cancer, gastrointestinal bleeding, uncontrolled diabetes mellitus, history of heart attacks three months before

Hashemilar 2020 *(Continued)*

	the study, chronic respiratory diseases, heart failure, and haematologic illnesses), change in diagnosis, parenteral feeding, enteral feeding for fewer than ten days, treatment with immunosuppressive medications, alcohol and drug abuse, lactose intolerance, and death at the time of admission first 10 days. Stroke severity: NIHSS: intervention group mean 7.36 (SD 4.28), control group: mean 5.28 (SD 4.57)
Interventions	Intervention group: protein - 20 g of their daily protein from whey protein Control group: routine hospital feeding - patients in the control group received routine hospital feeding that was kitchen-made, containing 25 kcal/kg energy and 1.5 g protein per day Co-interventions: not reported Duration of treatment: 3 weeks Compliance: not reported Intervention route: oral
Outcomes	• mRS • NIHSS Time points: at 3 weeks
Notes	Declaration of interests: none Funding statement: supported by the Vice Chancellor for Research of Tabriz University of Medical Sciences, Tabriz, Iran Protocol: Iranian Registry of Clinical Trials under IRCT2016061428450N1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind", but not reported who they were
Incomplete outcome data (attrition bias) All outcomes	Low risk	Withdrawal: intervention group n = 2, control group n = 0 The number and reasons were not likely to affect the results.
Selective reporting (reporting bias)	High risk	Protocol available. SF-36 was not reported.

Hashemilar 2020 *(Continued)*

Other bias	Low risk	No other sources of bias were found.

Honaga 2022

Study characteristics	
Methods	Setting: single-centre, Japan Design: RCT, 2 arms, parallel assignment Recruitment period: November 2015–November 2018
Participants	Sample size: 50 Gender (men/women): 30/15 (in the study completed patients, not ITT analysis) Mean age (SD): intervention 64.2 (8.9), control 61.3 (11.5) (in the study completed patients) Stroke phase: subacute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: age ≥ 40 years, hospital admission ≤ 2 weeks, with expected hospitalisation period ≥ 2 months, with functional independence measure (FIM) walk/wheelchair ≤ 4, social interaction ≥ 6, comprehension ≥ 5, and expression ≥ 5, with the ability to use a normal wheelchair Exclusion criteria: the presence of cognitive deficits, contraindications to exercise therapy due to complications or previous diseases, difficulty swallowing supplements, receiving parenteral or enteral nutrition, an estimated glomerular filtration rate < 60 mL/min/1.73 m^2, regular use of protein or vitamin D or citrus peel supplements, and serious allergy to foods or medicines Stroke severity: not reported
Interventions	Intervention group: protein + vitamin D - high-protein jelly type supplement (100 kcal, 15 g carbohydrate, 0 g fat, 10 g protein, and 20 µg vitamin D/pack) 2 packs/day Control group: placebo Co-interventions: conventional stroke rehabilitation Duration of treatment: 16 weeks If the subject was discharged before 16 weeks, the intervention was completed, and measurements were performed at that time. Compliance: monitored Consumption rates: intervention group 96.3 ± 3.1%, control group 95.6 ± 4.1% Intervention route: oral
Outcomes	• FIM motor score • 10–m walk speed; comfortable and maximum • Grip strength • Skeletal muscle index • Cross-sectional area of the thigh muscles • 30-s Chair test • Time Up and Go

Honaga 2022 *(Continued)*

	Time points: at 16 weeks
Notes	Declaration of interests: funded by Morinaga Milk Industry Co., Ltd. Four authors were employees of Morinaga Milk Industry Co., Ltd. Funding statement: as stated above Protocol: UMIN Clinical Trial Registry; UMINID: 000019360

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Quote: "Random allocation was performed by a person who was independent of the study."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: ”The subjects were blinded to group allocation", but it was not reported for health care providers.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Single-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intervention group: two participants with a discontinued protocol violation and one participant with data missing Control group: two participants with a discontinued protocol violation. The number lost to follow-up was not likely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported.
Other bias	High risk	Funded by Morinaga Milk Industry Co. Ltd. Four authors were employees of that company.

Kadri 2020

Study characteristics

Methods	Setting: single-centre, Indonesia Design: RCT, 4 arms, parallel assignment Recruitment period: March 2018–February 2019
Participants	Sample size: 120 Gender (men/women): 53/67 Mean age (SD): intervention; vitamin A + D 65.85 (4.23), vitamin A 66.85 (4.62), vitamin D 62.65 (5.66) Control 66.35 (5.30)

Kadri 2020 *(Continued)*

	Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: patients with acute ischaemic stroke diagnosed clinically and evidenced by neuroimaging examination, admitted to the hospital on day ≤ 3 after onset, and were > 18 years of age Exclusion criteria: patients with impaired liver function, impaired renal function (serum urea concentration > 2 mg/dL, nephrolithiasis), patients taking supplements containing vitamin A and D at the time of the study, hypercalcaemia, cardio-embolic stroke, and patients with sepsis and diabetes mellitus Stroke severity: NIHSS: vitamin A group mean 12.10 (SD 1.92), vitamin D group 13.20 (1.24), vitamin A + vitamin D 13.25 (1.61), placebo 13.15 (1.39)
Interventions	Intervention group: 1) vitamin A, 2) vitamin D, 3) vitamin A and vitamin D - vitamin A: 50,000 IU per week (5,000 IU vitamin A per tablet, ground and inserted into a capsule to make 50,000 IU dose) - vitamin D_3: 50,000 IU per week, using vitamin D_3 soft capsule (50,000 IU vitamin D_3 per capsule) - vitamin A + Vitamin D: 50,000 IU vitamin A combined with 50,000 IU vitamin D once a week Control group: placebo - capsules containing saccharose lactis as a placebo Co-interventions: standard physiotherapy Duration of treatment: 12 weeks Compliance: not reported Intervention route: oral
Outcomes	• NIHSS Time points: at 12 weeks
Notes	Declaration of interests: none Funding statement: no funding Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: ”Both the supplement and placebo were given in capsules of the same size, colour, and weight to ensure that patients were blinded toward the treatments."
Blinding of outcome assessment (detection bias)	High risk	Single-blind

Kadri 2020 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	High risk	The vitamin D level at the baseline was unbalanced.

Kang 2023

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: from July 2019 to July 2020
Participants	Sample size: 70 Gender (men/women): 40/30 Mean age (SD): intervention 66.84 (6.36), control 63.69 (5.87) Stroke phase: acute Type of baseline stroke: intracerebral haemorrhage Inclusion criteria: 1) all patients that had disturbance of consciousness and neurological impairment after examination by imaging films, 2) patients older than 50 years old Exclusion criteria: 1) patients with other major diseases and cancer, 2) patients with liver and kidney insufficiency, 3) patients with special constitution, 4) patients with diabetes complicated by severe complications, 5) patients with severe mental illness and language disorders Stroke severity: NIHSS was assessed, but not reported; was stated as "severe"
Interventions	Intervention group: early enteral nutrition The participants were given on the first day 1/4 of total energy, on the second day 1/2, and on the third day given full nutritional support. Control group: ordinary liquid food in the hospital, 4 to 6 times a day, 200 mL each time Co-interventions: all patients were given glycerol fructose, mannitol and other antihypertensive and dehydrating treatments, and acid-suppressing drugs were used to prevent stress ulcers. Duration of treatment: 14 days Compliance: not reported Intervention route: enteral
Outcomes	• NIHSS score • Barthel Index score Time points: at 7, 10 and 14 days of admission for NIHSS, 14 days for Barthel Index

Kang 2023 *(Continued)*

Notes	Declaration of interests: no conflict of interest Funding statement: the Basic Research of Natural Science in Shaanxi Province (2022JM-590) Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	None
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	Baseline data of participants were not available.

Laviano 2011

Study characteristics

Methods	Setting: single-centre, Italy Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 20 Gender (men/women): 10/10 Mean age (SD): intervention 56.8 (8.9), control 61.3 (12.2) Stroke phase: acute Type of baseline stroke: haemorrhagic Inclusion criteria: 1) age 18–75 years, 2) hypoalbuminemia (< 3.0 g/dL)

Laviano 2011 *(Continued)*

	Exclusion criteria: 1) any underlying disease influencing plasma albumin levels (i.e. liver cirrhosis, nephrotic syndrome, cancer, etc.), 2) renal failure, either requiring or not requiring extracorporeal dialysis, and 3) type 2 diabetes mellitus Stroke severity: APACHEII: intervention mean 21.5 (SD 6.7), control 24.6 (2.6)
Interventions	Intervention group: amino acids - patients received their 100% caloric requirements and 80% of nitrogen needs by total parenteral nutrition and received the remaining 20% of nitrogen requirements as the functional mixture of amino acids. - used 100 g amino/100 g acid product Control group: iso-nitrogenous standard protein - 88.5 g amino acid/100 g product Co-interventions: not reported Duration of treatment: 14 days Compliance: not reported Intervention route: enteral or parenteral
Outcomes	• Infection (urinary) • Mortality Time points: at 14 days
Notes	Declaration of interests: not reported Aminotrofic was generously supplied by Errekappa Euroterapici, Milan, Italy. Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One patient in the control group was excluded from the statistical analysis because of violation of the protocol." It was not likely to affect the outcomes.

Laviano 2011 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	High risk	Aminotrofic was supplied by a product company.

Li 2008

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: January 2002–August 2006
Participants	Sample size: 54 Gender (men/women): 32/22 Mean age (SD): intervention 73.3 (9.5), control 75.4 (10.4) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: < 72 hours from onset, disturbance of consciousness, dysphagia, positive for the dysphagia screening test using 30 mL water swallow test, NIHSS (National Institutes of Health Stroke Scale) 10 and over Exclusion criteria: patients with subarachnoid haemorrhage, serious endocrine and metabolic disorders, haematologic disorders, malignant tumours, chronic cardiopulmonary dysfunction, serious hepatic and renal dysfunction, peptic ulcer Stroke severity: NIHSS: intervention group mean 14.14 (SD 3.55), control group mean 13.78 (SD 4.23)
Interventions	Intervention group: energy - used high energy enteral nutrition (1 kcal/mL, 20～30 kcal/kg-day) Control group: usual care - the family managed the diet. The basic diet consists of milk, soy milk, soup, rice soup, vegetable juice, steamed egg custard, or homogenised soups Co-interventions: standard stroke treatment Duration of treatment: 21 days Compliance: not reported Intervention route: enteral
Outcomes	• NIHSS • ADL score • Infections (urinary and intestinal) Time points: NIHSS at 10 days and 21 days, ADL at 30 days, infections at 10 days and 21 days
Notes	Declaration of interests: not reported

Li 2008 *(Continued)*

	Funding statement: not reported
	Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Li 2014

Study characteristics

Methods	Setting: single-centre, China
	Design: RCT, 2 arms, parallel assignment
	Recruitment period: August 20013–July 2014
Participants	Sample size: 148
	Gender (men/women): 86/62
	Mean age (SD): all 64.1 (12.3)
	Stroke phase: acute
	Type of baseline stroke: ischaemic and haemorrhagic
	Inclusion criteria: NIHSS > 10, positive for the dysphagia screening test using a 30 mL water swallowing test.
	Exclusion criteria: not reported
	Stroke severity: NIHSS: intervention group mean 18. 8 (SD 3.6), control group: mean 19. 2 (SD 4.3)

Li 2014 *(Continued)*

Interventions	Intervention group: energy and protein - enteral nutrition was used. - no information on the amount of energy and protein Control group: standard diet - the family prepared chicken broth, fish broth, rice broth, milk, soy milk, fruit juice, vegetable juice, etc. Co-interventions: standard stroke treatment in both groups Duration of treatment: 21 days Compliance: not reported Intervention route: enteral
Outcomes	• Mortality • Infection: pneumonia • NIHSS • Triceps skinfold thickness Time points: 21 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Li 2016

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: April 2014–September 2015
Participants	Sample size: 112 Gender (men/women): 73/39 Mean age (SD): all 68.5 (5.1) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: patients with acute cerebral infarction complicated with dysphagia Exclusion criteria: patients with malignant tumours, haematologic systemic lesions, stress peptic ulcers, serious metabolic diseases, or endocrine disorders Stroke severity: not reported
Interventions	Intervention group: early enteral nutrition - gradually increased to about 2000 kcal/day - it was combined with amino acids (500 mL/day) (parenteral nutrition) Control group: parenteral nutrition - amino acids 500 mL/day, 1/5–1/3 of the non-protein calories were supplied by 20% fat emulsion and 10%–25% glucose solution. Co-interventions: not reported Duration of treatment: 1 month Compliance: not reported Intervention route: enteral
Outcomes	• NIHSS • Water swallow test score Time points: at 1 month
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported: not reported

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A randomisation list was used.

Li 2016 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	The patient's characteristics at baseline were not reported. Quote: ”non-significant“. It was unclear how the trial was funded.

Mohan 2015

Study characteristics	
Methods	Setting: single-centre, Malaysia Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 70 Gender (men/women): 31/39 Mean age (SD): all 74.6 (6.7) Stroke phase: acute phase Type of baseline stroke: ischaemic Inclusion criteria: mechanically ventilated patients suffering from severe ischaemic stroke Exclusion criteria: not reported Stroke severity: not reported
Interventions	Intervention group: amino acids - enteral nutrition: Isocal. formula + 40 g/L of protein according to energy expenditure measured by indirect calorimeter + parenteral infusion of amino acids according to protein loss Control group: no amino acids - enteral nutrition: Isocal. formula + 40 g/L of protein according to energy expenditure measured by indirect calorimeter only Co-interventions: not reported

Mohan 2015 *(Continued)*

	Duration of treatment: not reported Compliance: not reported Intervention route: parenteral
Outcomes	• Nutritive status assessed using anthropometric and laboratory indicators • Mortality Time points: at 15 days and 30 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Momosaki 2019

Study characteristics

Methods	Setting: multicentre, Japan (14 hospitals) Design: RCT, 2 arms, parallel assignment Recruitment period: January 2012 to July 2017
Participants	Sample size: 97

Momosaki 2019 *(Continued)*

	Gender (men/women): 68/29 Mean age (SD): intervention 67.6 (11.7), control 65.5 (11.7) Stroke phase: acute Type of baseline stroke: ischaemic, cerebral haemorrhage, and SAH Inclusion criteria: aged 20 years or older, had suffered a confirmed first hemiparetic stroke (infarct, intracerebral haemorrhage, or subarachnoid haemorrhage), had been admitted to a convalescent rehabilitation ward following acute treatment for stroke, and were deemed by the attending physiatrist to require 8 weeks of in-hospital rehabilitation Exclusion criteria: a history of calculi in the urinary tract, vitamin D3 or activated vitamin D supplementation before the stroke, osteoporosis, bone fracture, dysphagia, or another disorder that would make it difficult to take an oral vitamin D supplement, or an inability to participate in the study in the opinion of the attending physiatrist Stroke severity: not reported
Interventions	Intervention group: vitamin D - five capsules daily (providing 2000 IU of vitamin D3) at the same time after dinner Control group: placebo - capsules containing vehicle only (sesame oil, porcine gelatin, and glycerin) Co-interventions: rehabilitation Duration of treatment: 8 weeks Compliance: not reported Intervention route: oral
Outcomes	• Barthel index (gain and efficacy) • Brunnstrom stage • Hand grip strength • Calf circumference Time points: at 8 weeks
Notes	Declaration of interests: none Funding statement: no funding Protocol: UMIN000007002

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Central randomisation
Blinding of participants and personnel (performance bias)	Low risk	Quote:"Blinding of the patients, physiatrists, and the physical therapists who evaluated outcomes was maintained by bottle numbering until the data collection was complete and the database was locked for analysis".

Momosaki 2019 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote:"Blinding of the patients, physiatrists, and the physical therapists who evaluated outcomes was maintained by bottle numbering until the data collection was complete and the database was locked for analysis".
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of participants lost was one in the intervention group and two in the control group. The reasons were reported, and they were not likely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were reported.
Other bias	Low risk	No other sources of bias were found.

Ogawa 2021

Study characteristics	
Methods	Setting: single-centre, Japan Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 20 Gender (men/women): not reported Age: mean was not reported. Range: 55-85 Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: cerebrovascular infarction, patients showing critically impaired consciousness with GCS scores of 12 or less for whom four or more days of bed rest were prescribed Exclusion criteria: not reported Stroke severity: not reported
Interventions	Intervention group: fatty-acid - enteral nutrition-enriched Eicosapentaenoic Acid (EPA) Dose: not reported Control group: standard enteral nutrition (no enriched EPA) Co-interventions: not reported Duration of treatment: at least 14 days Compliance: not reported Intervention route: enteral
Outcomes	• Bedsores

Ogawa 2021 *(Continued)*

	Time points: at day 4, day 7, and day 14
Notes	Declaration of interests: none Funding statement: not reported Protocol: not reported Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Otsuki 2020

Study characteristics

Methods	Setting: single-centre, Japan Design: RCT, 2 arms, parallel assignment Recruitment period: September 2016 to December 2017
Participants	Sample size: 124 Gender (men/women): 50/74 Median age (IQR): intervention 78.5 (71–85), control 80.5 (75–86) Stroke phase: acute Type of baseline stroke: ischaemic, cerebral haemorrhage, and SAH

Otsuki 2020 *(Continued)*

	Inclusion criteria: stroke (i.e. cerebral infarction, cerebral haemorrhage, or subarachnoid haemorrhage), age > 65 years, with high risk for malnutrition, which was defined as a MUST score of ≥ 2 or serum albumin of ≤ 3.0 g/dL Exclusion criteria: those who were critically ill and difficult to save, had severe dementia, were at the terminal stage of other diseases, such as cancer, had a co-existing disease that required strict management, had liver cirrhosis, received albumin preparation, and were judged by the attending physician to be unsuitable for the study Stroke severity: NIHSS: intervention group median 8 (IQR 3–20), control group median 8.5 (IQR 3–16)
Interventions	Intervention group: individualised nutritional treatment - the daily caloric requirement was calculated by dietitians using the Harris–Benedict equation and according to the progress of patient rehabilitation; the stress coefficient ranged from 1.1 to 1.4, and the activity coefficient ranged from 1.0 to 1.4. Control group: body-weight-only based nutrition treatment - provided the daily caloric requirement, which was calculated as body weight (kg) × 25 kcal, according to the stroke department's protocol Co-interventions: rehabilitation Duration of treatment: during hospitalisation in an acute hospital - intervention group: median 28 days (21–39), control group: median 30 days (21–41) Compliance: monitored Energy intake: intervention group: median 1496 kcal/day (IQR 1200-1629), control group: median 1200 kcal/day (IQR 1085-1297) Protein intake: intervention group: median 59.7 g/day (IQR 60.6 – 71.9), control group: median 49.6g/day (IQR 41.5 – 58.5) Intervention route: oral or enteral
Outcomes	• FIM (motor score and cognitive score) • Body weight • Arm circumference • Thigh circumference • Calf circumference Time points: at the time of discharge from the recovery hospital (or at 3 months if patients were not discharged within 3 months) Length of stay: intervention group: median 28 days (21–39), control group: median 30 days (21–41)
Notes	Declaration of interests: none Funding statement: not reported Protocol: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method

Otsuki 2020 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "The sequence of treatment allocation was prepared from a computer-generated randomization list, which was managed by individuals who were not involved in the study. We obtained the allocation number by reporting eligible patients to the administrators."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients were blinded. The dietitians, nurses and physical therapists were not blinded, but this was unlikely to affect our primary outcome.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Primary outcome (FIM)assessors were blinded."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up: intervention group 19, control group 15 The reasons were similar between the two groups, and it was not likely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were reported.
Other bias	Unclear risk	It was unclear how the trial was funded.

Ouyang 2003

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: January 1999 to February 2003
Participants	Sample size: 62 Gender (men/women): 39/23 Mean age (SD): intervention 64.1 (9.02), control 62.55 (10.57) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: ischaemic stroke, neural function deficient scale ≥ 31 Exclusion criteria: died within 5 days from stroke onset Stroke severity: not reported
Interventions	Intervention group: early enteral feeding - started enteral nutrition after 48 hours from stroke onset - homogenised meal, milk mix, and elementary meal Control group: no early enteral nutrition - started on day 3-4 after stroke

Ouyang 2003 *(Continued)*

	Co-interventions: for the first week after initiation, gastroprokinetic agents (metoclopramide, domperidone, etc.) are administered for 2 weeks. Duration of treatment: not reported Compliance: not reported Intervention route: enteral
Outcomes	• Triceps skinfold thickness • Moveable arm muscular circumference Time points: at day 7, day 14, and day 28
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Pan 2017

Study characteristics

Methods	Setting: single-centre, Taiwan Design: RCT, 3 arms, parallel assignment Recruitment period: December 2009 to May 2013

Pan 2017 *(Continued)*

Participants	Sample size: 291 Gender (men/women): 185/106 Mean age (SD): K salt 64.4 (9.8), K/mg salt 64.7 (9.9), Na salt 64.8 (10.3) Stroke phase: acute and subacute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: 1) hospitalisation ≤ 1 month because of cerebral infarction or haemorrhage, 2) a modified Rankin scale (mRS) score of ≤ 4 at the time of discharge, 3) age ≥ 45 y, and 4) an agreement to prepare foods with salt provided by the project Exclusion criteria: 1) patients with poor kidney function (glomerular filtration rate < 60 mL/min), secondary hypertension, cancer, or liver diseases, 2) patients with eating disorders, 3) patients taking potassium-sparing medicines, or 4) patients consuming salt substitutes Stroke severity: NIHSS mean ± SD: K salt 2.3 ± 2.5, K/mg 2.2 ± 2.4, Na salt 2.3 ± 2.6
Interventions	Intervention group 1: potassium-enriched salt Intervention group 2: potassium and magnesium-enriched salt - a sufficient amount of salt (1 kg/month) was provided at the time of discharge and replenished at the 3-month outpatient visit. Control group: regular salt (sodium(Na) salt) Co-interventions: not reported Duration of treatment: 6 months Compliance: not reported Intervention route: oral
Outcomes	• Proportion of patients with good neurologic performance (NIHSS = 0, BI = 100, and mRS ≤ 1) Time points: at month 3 and month 6
Notes	Declaration of interests: none Funding statement: supported by grants from the Institute of Biomedical Sciences, Academia Sinica, and the Ministry of Health and Welfare Protocol: clinicaltrials.gov NCT02910427

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients were blinded. Blinding for healthcare providers was non reported, but it is unlikely to affect the outcome at 3 and 6 months.

Pan 2017 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Medical practitioners performing the patient evaluation and salt distribution were masked to the intervention group".
Incomplete outcome data (attrition bias) All outcomes	Low risk	The numbers of dropouts were similar between groups, and the reasons were also similar in each group.
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported.
Other bias	Unclear risk	It was unclear how the trial was funded.

Poppitt 2009

Study characteristics	
Methods	Setting: single-centre, New Zealand Design: RCT, 2 arms, parallel assignment Recruitment period: July 2004 to December 2005
Participants	Sample size: 102 Gender (men/women): 51/51 Mean age (SD): intervention 64 (10), control 65 (12) Stroke phase: chronic Type of baseline stroke: ischaemic Inclusion criteria: aged > 45 years, clinically stable, and with a history of CT-confirmed first-ever or recurrent ischaemic stroke of probable noncardioembolic aetiology, > 3 months before registration Exclusion criteria: intolerance/hypersensitivity to fish/fish oils, current use of fish oil supplements, malabsorptive bowel diseases Stroke severity: not reported
Interventions	Intervention group: fatty acid - 3 g/day fish oil supplement containing approximately 1.2 g/day total omega-3 polyunsaturated fatty acids each morning Control group: placebo - palm and soy oils Co-interventions: not reported Duration of treatment: 12 weeks Compliance: Compliance was assessed by capsule count - approximately 90% Intervention route: oral
Outcomes	• SF-36

Poppitt 2009 *(Continued)*

	Time points: at 12 weeks
Notes	Declaration of interests: An author has a consultancy relationship with Nutrition Labs New Zealand. The Maurice and Phyllis Paykel Trust, New Zealand, funded the LDL particle size and FAME analyses. Sea Dragon, New Zealand, provided the fish oil and Nutrition Laboratories, New Zealand, provided the placebo treatment and encapsulated the oils. Funding statement: as stated above Protocol: Australian Clinical Trials Registration: ACTRN12605000207617

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Quote: ”blinded for treatment with sequential allocation of packs to patients after confirmation of inclusion criteria"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It was just stated as "double-blind". Blinding was not reported for healthcare providers.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	It was just stated as "double-blind". Not reported who they were
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of dropouts and reasons were not likely to affect the outcomes (intervention group 4, control group 3).
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were reported.
Other bias	High risk	Unbalanced baseline characteristics

Rabadi 2008

Study characteristics

Methods	Setting: single-centre, USA Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 116 Gender (men/women): 68/48 Mean age (SD): intervention 75.0(10.58), control 73.58(13.02) Stroke phase: acute and subacute Onset to admission:

Rabadi 2008 *(Continued)*

	Intervention: mean 14.10 days (SD 11.23) Control: mean 16.36 days (SD 15.70) Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: 1) first acute stroke event within 4 weeks of admission to an inpatient rehabilitation facility, 2) haemorrhagic or ischaemic stroke, 3) significant weight loss as indicated by unintentional weight loss of at least 2.5% within 2 weeks following stroke onset, 4) medically stable from a cardiorespiratory standpoint that they could participate in their daily therapies, 5) ability to ingest food including supplements either orally or via the PEG tube Exclusion criteria: 1) patients with a prior documented history of alcohol abuse, renal and liver diseases, and malabsorption, 2) patients medically unstable or demented, 3) patients terminally ill (e.g. patients with stroke as a complication of a terminal cancer) Stroke severity: not reported
Interventions	Intervention group: energy and protein - supplement (240 calories, 11 g of proteins) added to normal hospital diet - the dose of each was 120 mL every 8 hours by mouth, accompanied by multivitamins with minerals. Control group: standard care - supplement (127 calories, 5 g of protein) added to normal hospital diet The dose was 120 mL every 8 hours by mouth, accompanied by multivitamins with minerals. Co-interventions: physical, occupational, speech therapy Duration of treatment: during hospitalisation (mean 25–26 days) Compliance: monitored. Quote: "Occasionally a dose was missed. When that happened, the treating physician would give the patient a make-up dose of the appropriate (but still blinded) preparation. This process led to excellent compliance." Intervention route: oral
Outcomes	• FIM: total score, motor score, cognitive score • 2-min walk test • 6-min walk test • Weight Time points: at discharge (mean 25–26 days)
Notes	Declaration of interests: none Funding statement: not reported Protocol: ClinicalTrials.gov NCT 00332800

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It was just stated as "block randomisation".
Allocation concealment (selection bias)	Low risk	Quote: "using sealed, opaque envelope"

Rabadi 2008 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "During the course of the study neither the patient nor the therapists providing therapy and assessing outcomes were aware of the groups to which their patients were assigned."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "During the course of the study neither the patient nor the therapists providing therapy and assessing outcomes were aware of the groups to which their patients were assigned."
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of patients withdrawn (7 in each group) and the reasons were the same between the groups.
Selective reporting (reporting bias)	High risk	FIM was specified in the protocol, but other outcomes (walk test, weight, and healed decubiti) were not specified.
Other bias	Low risk	No other sources of bias were found.

Saito 2017

Study characteristics	
Methods	Setting: multi-centre, Chile Design: RCT, 2 arms, parallel assignment Recruitment period: March 2013 to October 2016
Participants	Sample size: 41 Gender (men/women): 15/25 (in the study completed patients, not ITT analysis) Median age (SD): intervention 48 (20–67), control 53 (22–68) Stroke phase: acute Type of baseline stroke: SAH Inclusion criteria: aged 18–69 years, modified Fisher grade 3 or 4, SAH (short axis of cisternal blood on computed tomography ≥ 4 mm), admitted to the emergency department during the first 72 hours after the initial bleeding episode, had a ruptured intracranial aneurysm of the anterior circulation demonstrated by computed tomographic angiography (CTA) or digital subtraction angiography (DSA), required to be scheduled for surgical clipping no earlier than 5 hours after CTA/DSA diagnosis, World Federation of Neurological Surgeons (WFNS) grades 1 – 4, not having severe unstable acute or chronic systemic disturbances, nor received antiplatelets, anticoagulants or valproic acid during the 3 weeks before SAH. Exclusion criteria: a history of allergy to iodine contrast media, fish, or eggs; cerebral sequelae visible on admission CT Stroke severity: WFNS: intervention group 1 n = 8 (40%), 2 n = 8 (40%), 3 n = 1 (5%), 4 n = 3 (15%), control group: 1 n = 6 (30%), 2 n = 7 (35%), 3 n = 1 (5%), 4 n = 6 (30%)
Interventions	Intervention group: fatty-acid - the long-chain omega-3 polyunsaturated fatty acids (n-3 PUFAs) - administered intravenously (100 mL of the fish oil-based lipid emulsion, Omegaven 10%) for 5 consecutive days at first + 4 oral capsules (460 mg of EPA and 380 mg of DHA/capsule)/day

Saito 2017 *(Continued)*

	Control group: usual care alone - no supplementation Co-interventions: not reported Duration of treatment: 60 days after SAH Compliance: monitored. The actual consumption was not reported. Intervention route: oral and parenteral
Outcomes	• Glasgow Outcome Scale Extended score: poor (score 1 to 4: dead, vegetative, or severely disabled) or not • Cerebral infarction caused by delayed cerebral ischaemia (DCI) • Clinical deterioration by DCI Time points: at 90 days
Notes	Declaration of interests: none Funding statement: provided by the Public Health Care Service of the VI Region Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Low risk	Quote: ”using sequentially numbered opaque sealed envelopes"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open-label
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of participants and the reasons for lost to follow-up were similar between groups (intervention group 2, control group 3).
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	No other sources of bias were found.

Sato 2022

Study characteristics

Methods	Setting: single-centre, multicentre, Italy

Sato 2022 *(Continued)*

	Design: RCT, 2 arms, parallel assignment Recruitment period: June 2017 to December 2018
Participants	Sample size: 16 Gender (men/women): 8/8 Mean age (SD): intervention 76.1 (5.3), control 75.6 (6.9) Stroke phase: chronic Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: 1) patients who had chronic cerebrovascular disease for > 6 months, walked independently regardless of using foot orthosis or walking aids, and had normal cognitive function (Hasegawa dementia rating scale-revised score > 20), 2) patients could communicate effectively and understood the study objectives Even patients who used β-blockers were included if the resting heart rate was not low and increased over the target heart rate during exercise. Exclusion criteria: patients with brainstem stroke, bone and joint problems, heart or respiratory diseases that could worsen with walking, liver, or kidney diseases, poorly controlled diabetes, nephropathy stage 3 or higher, and/or drug allergy Stroke severity: not reported
Interventions	Intervention group: protein and vitamin D - protein-rich jelly (100 kcal, 10 g protein, 15 g carbohydrate, 0 g fat, 20 µg vitamin D, and 4 mg sodium in one pack) - two packs (120 g) of jelly within 30 min of the exercise session on a weekday. One pack of jelly on Saturday Control group: placebo - protein-free (90 kcal, 0 g protein, 18 g carbohydrate, 0 g fat, and 4–16 mg sodium in 125 g) Co-interventions: rehabilitation - underwent 11 sessions of rehabilitation programme per week for 3 weeks - each rehabilitation session lasted for one hour. The 1st session was conducted in the morning and the other in the afternoon on 5 weekdays per week, and only one session was conducted on Saturday morning per week. The rehabilitation programme consisted of standing/sitting exercises, aerobic exercise with a hand cycling ergometer, gait training on a treadmill, and stepping-stairs training. Borg's scale was 11–13. Duration of treatment: 3 weeks Compliance: not reported Intervention route: oral
Outcomes	• Body weight • 6-min walking distance • 10-m walking speed at optimum and maximum Time points: 3 weeks
Notes	Declaration of interests: none

Sato 2022 *(Continued)*

	Funding statement: grants from the Nachi-Katsuura Research Foundation
	Protocol: UMIN000028009

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	It was managed at another hospital.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It was double-blind, but not reported who were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	It was double-blind, but not reported who they were and for what outcomes were.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number of withdrawals: 1 in the intervention group, 0 in the control group. It was nounlikely to affect the outcomes.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were reported.
Other bias	High risk	Baseline imbalance

Tajiri 2008

Study characteristics

Methods	Setting: single-centre, Japan
	Design: RCT, 2 arms, parallel assignment
	Recruitment period: January 2007 to August 2007
Participants	Sample size: 41
	Gender (men/women): 22/19
	Mean age (SD): intervention 78.1 (10.6), control 77.2 (10.7)
	Stroke phase: acute
	Type of baseline stroke: ischaemic and haemorrhagic
	Inclusion criteria: required enteral tube feeding within 48 hours from admission due to dysphagia or disturbance of consciousness
	Exclusion criteria: 1) who suffered from gastrointestinal bleeding on admission or on the second day, 2) who suffered from serious pneumonia on admission or on the second day, and 3) who presented a coma state of 3 on the Glasgow coma scale on admission or on the second day

Tajiri 2008 *(Continued)*

	Stroke severity: NIHSS: intervention group median 16.9, control group median 17.7
Interventions	Intervention group 1: protein-enriched nutrition (enteral nutrition developed for older adults with malnutrition) - an enteral nutrition product: 1000–1200 kcal/day - product 100 mL: carbohydrate 140 g, protein 55 g (arginine 2.2 g, glutamine 9.5 g), lipid 27.8 g, (ω-3 fatty acid 1.64 g, EPA 0.67 g, DHA 0.46 g, ω-6:ω-3 2.7:1), nucleotide (g) none Intervention group 2: amino-acid, and fatty-acid-enriched nutrition (arginine, omega-3 fatty acids, EPA, and DHA) - product 100 mL: carbohydrate 134 g, protein 56 g (arginine 12.8 g, glutamine 3.8–5.6 g), lipid 28 g (ω-3 fatty acid 3.32 g, EPA 2 g, DHA 1.32 g, ω-6:ω-3 1:1), nucleotide 1.3 g - the energy was increased until the patient's required energy per day. Co-interventions: not reported Duration of treatment: 10 days Compliance: energy/day intervention 1: median 1000 kcal, intervention 2: median 1200 kcal Intervention route: enteral
Outcomes	Time points: during hospitalisation for death, NIHSS at day 10
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Coin toss was used.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

Toole 2004

Study characteristics	
Methods	Setting: multicentre 56 centres across the United States (n = 45), Canada (n = 10), and Scotland (n = 1) Design: RCT, 2 arms, parallel assignment Recruitment period: August 1997 to December 2001
Participants	Sample size: 3680 Gender (men/women): 2301/1379 Mean age (SD): intervention 66.4 (10.8), control 66.2 (10.8) Stroke phase: subacute Type of baseline stroke: ischaemic Inclusion criteria: nondisabling ischaemic stroke (mRS ≤ 3), onset ≤ 120 days, before randomisation, classified as ischaemic stroke, total homocysteine level ≥ 25th percentile for North American stroke population, age ≥ 35 years Exclusion criteria: potential sources of emboli (atrial fibrillation within 30 days of stroke, prosthetic cardiac valve, intracardiac thrombus or neoplasm, or valvular vegetation), other major neurological illness that would obscure evaluation of recurrent stroke, life expectancy < 2 years, requiring dialysis, untreated anaemia or untreated vitamin B12 deficiency, systolic blood pressure > 185 mm Hg or diastolic blood pressure > 105 mm Hg, refractory depression, severe cognitive impairment, or alcoholism or other substance abuse use within the last 30 days of medications that affect total homocysteine level (methotrexate, tamoxifen, levodopa, niacin, or phenytoin) or bile acid sequestrants that can decrease folate levels, any type of invasive cardiac instrumentation, or endarterectomy, stent placement, thrombectomy, or any other endovascular treatment of carotid artery within 30 days prior to randomisation or scheduled to be performed within 30 days after randomisation. Stroke severity: NIHSS: high-dose group mean 1.7 (SD 2.0), low-dose group mean 1.7 (SD 2.0)
Interventions	Intervention group: high-dose multivitamin - multivitamin: 25 mg of pyridoxine, 0.4 mg of cobalamin, and 2.5 mg of folic acid Control group: low-dose vitamin - 200 µg of pyridoxine, 6 µg of cobalamin, and 20 µg of folic acid Co-interventions: physicians provided the best available medical and surgical management to prevent recurrent stroke, which included risk factor control education and, usually, administration of aspirin, 325 mg/d in both groups. Duration of treatment: 2 years Compliance: 75% in both groups Intervention route: oral
Outcomes	• Recurrent stroke • Death Time points: 2 years
Notes	Declaration of interest: The raw materials for the vitamins were supplied by Roche Inc, Paramus, NJ.

Toole 2004 *(Continued)*

	Funding statement: supported by the National Institute of Neurological Disorders and Stroke grant
	Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method
Allocation concealment (selection bias)	Low risk	Central registration was used.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The reason for lost to follow-up was not reported. The number of participants with reasons: intervention group 133, control group 132
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were reported.
Other bias	High risk	The raw materials for the vitamins were supplied by a product company.

Torrisi 2021

Study characteristics

Methods	Setting: single-centre, Italy
	Design: RCT, 2 arms, parallel assignment
	Recruitment period: not reported
Participants	Sample size: 40
	Gender (men/women): the number was not reported; 53.3%/46.7%
	Mean age (SD): intervention 59.20 (11.38), control 62.07 (10.82)
	Stroke phase: subacute
	Type of baseline stroke: ischaemic and haemorrhagic
	Inclusion criteria: patients with ischaemic or haemorrhagic stroke outcomes that occurred between 30 and 60 days before and eligible for individual rehabilitation treatment
	Exclusion criteria: Mini-Mental State Examination < 15, patients with psychiatric diseases or treated with antidepressants, patients already on vitamin D supplementation, also in combination with calcium, multivitamins or other drugs, and medical conditions that did not allow the neurorehabilitation programme.

Torrisi 2021 *(Continued)*

	Stroke severity: not reported
Interventions	Intervention group: vitamin D - 2000 IU/day of oral cholecalciferol Control group: placebo Co-interventions: both groups: intensive neurorehabilitation consisting of motor and cognitive training. Specifically, motor modules included 4 daily rehabilitative sessions for 6 days a week, lasting about an hour. Cognitive rehabilitation included daily sessions based on exercises focused on the enhancement of attention and memory abilities. Psychotherapy and speech therapy was also supplied. Duration of treatment: 12 weeks Compliance: not reported Intervention route: oral
Outcomes	• FIM Time points: 12 weeks
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	It was just stated as "double-blind". Not reported who they were
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	It was just stated as "double blind". Not reported who they were
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	High risk	Baseline umbalance. It was unclear how the trial was funded.

Ullegaddi 2005a

Study characteristics	
Methods	Setting: single-centre, UK Design: RCT, 2 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 48 Gender (men/women): 24/24 Median age (IQR): intervention 76 (68–81), control 79 (73–84) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: acute ischaemic stroke patients admitted within 12 hours of symptom onset Exclusion criteria: patients with active gastrointestinal disease, psychiatric disorders, severe concurrent medical illness such as sepsis or acute renal failure, history of gout, supplemental vitamins, bleeding disorders, or inability or refusal to give consent Stroke severity: not reported
Interventions	Intervention group: vitamin C and vitamin D - daily oral supplementation of 800 IU (727 mg) a-tocopherol and 500 mg vitamin C Control group: no supplementation Co-interventions: not reported Duration of treatment: 14 days Compliance: 100% Intervention route: oral
Outcomes	• Infections (pneumonia, urinary tract infection, and septicemia) • Recurrent stroke Time points: at 3 months post-recruitment
Notes	Declaration of interests: not reported Funding statement: supported by a Grant from Sheffield Teaching Hospital NHS Trust. Protocol: not reported

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported

Ullegaddi 2005a *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Not reported, but outcome unlikely to be biassed by blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "investigators were not blinded as to the treatment vs nontreatment group".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	No other sources of bias were found.

Ullegaddi 2005b

Study characteristics	
Methods	Setting: single-centre, UK Design: RCT, 4 arms, parallel assignment Recruitment period: not reported
Participants	Sample size: 72 Gender (men/women): 51/21 Median age (IQR): intervention: vitamin E and vitamin C, 76 (68–81), vitamin B, 77 (68–81), vitamin E + vitamin C + vitamin B, 76 (66–82), control 79 (73–84) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: acute ischaemic stroke patients admitted within 12 hours of symptom onset Exclusion criteria: stroke patients with active gastrointestinal disease, severe concurrent medical or psychiatric illness, serum creatinine concentration 150 mol/L, history of gout, renal failure, supplemental vitamins, bleeding disorders, or inability or refusal to give consent Stroke severity: not reported
Interventions	Intervention group 1: vitamin E + vitamin C Oral 800 IU (727 mg) vitamin E, 500 mg vitamin C/day Intervention group 2: vitamin B B-group vitamins (5 mg folic acid, 5 mg vitamin B2, 50 mg vitamin B6, 0.4 mg vitamin B12)/day Intervention group 3: vitamin E + vitamin C + vitamin B Control group: no supplementation Co-interventions: not reported

Ullegaddi 2005b *(Continued)*

	Duration of treatment: 14 days Compliance: 100% Intervention route: oral
Outcomes	• Infections (pneumonia, urinary tract infection, and septicaemia) • Recurrent stroke Time points: at 1 week, 2 weeks, and 3 months
Notes	Declaration of interests: none Funding statement: supported by a grant from Sheffield Teaching Hospital NHS Trust Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Coin toss was used.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	This trial was open, but the outcome unlikely to be biassed by blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: ”Investigators were not blinded as to the treatment vs non-treatment group".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	No other sources of bias were found.

Yoshimura 2019

Study characteristics

Methods	Setting: single-centre, Japan Design: RCT, 2 arms, parallel assignment Recruitment period: September 2014 to April 2017
Participants	Sample size: 49

Yoshimura 2019 *(Continued)*

	Gender (men/women): 14/30 (in the study completed patients (n = 44), not ITT analysis) Mean age (SD): intervention 80.8 (7.1), control 78.9 (6.3) (in the study completed patients) Stroke phase: subacute Type of baseline stroke: ischaemic, haemorrhagic, and SAH Inclusion criteria: patients ≥ 65 y of age, undergoing convalescent rehabilitation, being medically stable, being able to stand up with or without aid, having sarcopenia, receiving appropriate nutrition (i.e. had adequate energy intake according to the requirements set by a registered dietitian) Exclusion criteria: being unconscious, having advanced dementia (Mini-Mental State Examination score ≤ 23) or delirium, an implanted pacemaker, obesity or overweight (body mass index [BMI] > 25 kg/m^2), an estimated glomerular filtration rate < 30 mL/min/1.73 m^2, swallowing difficulties, inability to rise from a chair with or without aid, inability to communicate or understand the purpose of the study, a contraindication for a high-protein diet such as severe renal dysfunction, and comorbidities such as kidney, liver, or heart failure Stroke severity: NIHSS at stroke onset, median (IQR): intervention 9 (6–19), control: median 8 (5–15)
Interventions	Intervention group: amino-acid - leucine-enriched amino acids containing jelly-type supplement - comprised 3 g of leucine 40% enriched essential amino acids and 9.7 g of carbohydrate - once daily within 30 min after the end of the sit-to-stand exercise Control group: no supplementation Co-interventions: patients in both groups underwent an eight-week post-stroke rehabilitation programme including physical, occupational, and speech-language therapy. In addition to the post-stroke rehabilitation programme, patients in both groups performed the sit-to-stand exercise. Duration of treatment: 8 weeks Compliance: not reported Intervention route: oral
Outcomes	• FIM motor score • FIM cognitive score • Skeletal Muscle Index • Grip strength Time points: at 8 weeks
Notes	Declaration of interests: Quote: ”The authors have no conflicts of interest to declare" but one author was an employee of a product company related to the intervention. Funding statement: not reported Protocol: UMIN Clinical Trials UMIN000015158

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a computer-generated method

Yoshimura 2019 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded medical staff assessed the outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The number lost to follow-up and the reasons were similar between the groups. Intervention group 3 (early discharge 1, withdrawal of consent 2), control group 2 (early discharge 1, withdrawal of consent 1)
Selective reporting (reporting bias)	High risk	Not all prespecified outcomes were reported.
Other bias	High risk	The last author is an employee of a nutrition product company related to the study, and it was stated that all authors contributed substantially to the conception and design of the study or the acquisition, analysis, or interpretation of data and the drafting or the revision of the article. Conflict of interest was not reported. It was unclear how the trial was funded.

Zhang 2004

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 3 arms, parallel assignment Recruitment period: 2001 to 2003
Participants	Sample size: 107 Gender (men/women): 76/31 Mean age (SD): all 59.6 (13.1) Stroke phase: acute Type of baseline stroke: haemorrhagic Inclusion criteria: 1) within 24 hours from stroke onset, 2) age 40–70 years Exclusion criteria: 1) other cerebral haemorrhagic diseases such as ruptured aneurysm, arteriovenous malformation, etc. 2) no pre-existing medical conditions that seriously affect nutrient metabolism, such as type 1 diabetes, hyperthyroidism, renal failure, gastrointestinal insufficiency, etc., 3) life expectancy less than 3 weeks Stroke severity: not reported
Interventions	Intervention group: Group 1: early enteral nutrition Group 2: early parenteral nutrition

Zhang 2004 *(Continued)*

	- started enteral or parenteral nutrition within 48 hours - resting metabolic expenditure (BEE) was calculated using the Harris-Benedict equation, and daily calorie supply was calculated by BEE x stress factor x 75%, with stress factors at 1.1, 1.3, and 1.5 according to patient severity Control group: late enteral nutrition - provided by liquid diets prepared by the hospital's nutrition department or homemade by family members - started enteral nutrition 5 days from admission Co-interventions: not reported Duration of treatment: maximum 5 days Compliance: not reported Intervention route: enteral and parenteral
Outcomes	• ADL • Mortality Time points: at 3 months
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Unclear risk	It was unclear how the trial was funded.

Zhang 2014

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 3 arms, parallel assignment Recruitment period: October 2011–December 2012
Participants	Sample size: 89 Gender (men/women): 58/31 Mean age (SD): all 61.9 (5.2) Stroke phase: acute Type of baseline stroke: ischaemic Inclusion criteria: within 48 hours from stroke onset, Glasgow Coma Scale 4–8, positive result (≥ score 3) for dysphagia screening test using 30 mL water swallowing test Exclusion criteria: patients with malignancy, serious hepatic or renal insufficiency, serious endocrine metabolic or haematologic disease, gastrointestinal stress ulcer within 48 hours of onset, subarachnoid haemorrhage, large volume cerebral haemorrhage, rapidly progressive disease amenable to surgical treatment
Interventions	Intervention group: high-dose protein 1.6 g/kg body weight Control group 1: protein 0.9 g/kg Control group 2: protein 1.2 g/kg Co-interventions: not reported Duration of treatment: 14 days Compliance: not reported Intervention route: enteral
Outcomes	• Arm circumference • Calf circumference Time points: at day 7 and day 14
Notes	Declaration of interests: not reported Protocol: not reported

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported

Zhang 2014 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

Zhao 2020

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: May 2017 to December 2018
Participants	Sample size: 78 Gender (men/women): 46/32 Mean age (SD): intervention 64.13 (8.13), control 65.13 (9.03) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: severe cerebrovascular disease, NIHSS score ≥ 17, age 40–80 years, within 12 hours of stroke onset, enteral tube feeding, Nutrition Risk Screening Score 2002 (NRS 2002) (Kondrup 2003) ≥ score 3 Exclusion criteria: patients with heart failure, pulmonary embolism, severe hepatic or renal insufficiency, gastrointestinal bleeding, shock or other severe dysfunction of other systems, enteral nutrition support for less than 4 weeks, fasting for ≥ 3 days during enteral nutrition, excessive obesity, excessive wasting or severe malnutrition prior to admission, dementia or mental disorders Stroke severity: NIHSS, mean ± SD: intervention group 18.25 ± 3. 12, control group 17. 81 ± 3. 09
Interventions	Intervention group: early enteral nutrition - started within 3 days after stroke onset Control group: late enteral nutrition - started from 4–7 days after stroke onset Co-interventions: not reported Duration of treatment: 4 weeks

Zhao 2020 *(Continued)*

	Compliance: not reported Intervention route: enteral
Outcomes	• Berthel Index • NIHSS • Infections • Arm muscle circumference • Triceps skinfold thickness Time points: at 2 weeks, 3 weeks, and 4 weeks
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Five participants were lost to follow-up. The number lost to follow-up and the reasons for each group were not reported.
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

Zheng 2006

Study characteristics

Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: July 2005 to May 2006

Zheng 2006 *(Continued)*

Participants	Sample size: 49 Gender (men/women): 32/17 Mean age (SD): all 71.4 (6.3) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: within 72 hours from stroke onset, a positive result for dysphagia screening test using 30 mL water swallowing test Exclusion criteria: patients with severe endocrine and metabolic disorders, haematologic disorders, malignant tumours, chronic cardiopulmonary insufficiency, severe hepatic dysfunction, renal dysfunction, and stress ulcers of the gastrointestinal tract. Patients receiving thrombolytic therapy Stroke severity: NIHSS, mean ± SD: intervention group 15.5 ± 0.8, control group 15.0 ± 0.8
Interventions	Intervention group: energy, protein, vitamins, minerals - high-energy enteral nutrition is prepared by a dietitian according to the patient's condition, weight, and nutritional status, and is adjusted to contain 46.5 g protein, 32 g fat, 133 g carbohydrate, 2361 mg sodium, 1087 mg potassium, and 4184 kj per 1000 mL Control group: standard enteral nutrition - the family managed enteral nutrition. The basic diet consists of milk, soy milk, fruit juice, vegetable juice, soup, rice, fried eggs, or a homogeneous mixture of these. Co-interventions: not reported Duration of treatment: 21 days Compliance: not reported Intervention route: enteral
Outcomes	• Triceps skinfold thickness • Arm muscle circumference • Infections Time points: at 21 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported

Zheng 2006 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

Zheng 2015

Study characteristics	
Methods	Setting: single-centre, China Design: RCT, 2 arms, parallel assignment Recruitment period: July 2011 to December 2013
Participants	Sample size: 146 Gender (men/women): 85/61 Mean age (SD): intervention 71.4 (9.3) control 71.8 (10.1) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: 1) cerebral infarction, intracranial haemorrhage, or both confirmed with a CT scan or MRI within 72 hours of onset; 2) all patients who met the diagnostic standard of the Fourth National Cerebrovascular Events Conference (Chinese Neuroscience Society and Chinese Neurosurgery Society); 3) patients who might have a medical history of stroke but no apparent neurological deficit remaining prior to the onset of the current stroke; 5) focal neurological signs and dysphagia Exclusion criteria: transient ischaemic attack, subarachnoid haemorrhage, severe endocrine or metabolic disorders, haematological disorders, malignancies, chronic lung and heart dysfunction, severe liver or kidney failure, stress ulcer of the digestive system, and those who died within a week of admission Stroke severity: NIHSS, mean ± SD: intervention group 12.53 ± 3.32, control group 13.21 ± 3.78
Interventions	Intervention group: early enteral nutrition - it was managed by nutritionists based on condition, body weight, and nutritional status. - energy requirements: 83.68–125.52 kJ/kg/day Control group: regular food - it was prepared by their families, which consisted of milk, soy milk, juice, vegetable juice, broth, congee, and eggs.

Zheng 2015 *(Continued)*

	Co-interventions: not reported Duration of treatment: 21 days Compliance: not reported Intervention route: enteral
Outcomes	• mRS • Berthel Index • NIHSS score • Infections (pneumonia, urinary tract, digestive tract, decubitus) • Death • Thickness of the triceps skinfold • Arm muscle circumference Time points: at day 7, day 21, and 90 days (mRS)
Notes	Declaration of interests: none Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: ”Two doctors, who were blinded to the treatment regimen, received training before the trial and started performing measurements after they reached a high inter-rater agreement".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Low risk	It was unclear how the trial was funded.

Zhou 2006

Study characteristics

Methods	Setting: single-centre, China

Zhou 2006 *(Continued)*

	Design: RCT, 2 arms, parallel assignment Recruitment period: January 2005 to January 2006
Participants	Sample size: 51 Gender (men/women): 29/22 Mean age (SD): all 65.69 (15.63) Stroke phase: acute Type of baseline stroke: ischaemic and haemorrhagic Inclusion criteria: within 5 days from stroke onset Exclusion criteria: patients with hepatic, renal, or thyroid disease, malignancy, or hypoalbuminemia affecting protein metabolism Stroke severity: not reported
Interventions	Intervention group: protein-enriched enteral nutrition - ratio of protein, sugar, and lipid = 20:45:35 Control group: standard enteral nutrition - ratio of protein, sugar, and lipid = 16:49:35 Co-interventions: not reported Duration of treatment: 14 days Compliance: not reported Intervention route: enteral
Outcomes	• Survival rate Time points: at 7 days, 14 days, 28 days, and 90 days
Notes	Declaration of interests: not reported Funding statement: not reported Protocol: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A randomisation list was used.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The outcomes were unlikely to be biassed by blinding.

Zhou 2006 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	The outcomes were unlikely to be biassed by blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0%
Selective reporting (reporting bias)	Unclear risk	No trial protocol was available.
Other bias	Unclear risk	It was unclear how the trial was funded.

ACI: acute cerebral infarction
ADL: activities of daily living
AIDS: acquired immunodeficiency syndrome
APACHE: acute physiology and chronic health evaluation
BBS: Berg balance scale
BEE: basal energy expenditure
BMI: body mass index
cEEG: continuous electroencephalogram
CT: computed tomography
CTA: computed tomographic angiography
DCI: cerebral infarction caused by delayed cerebral ischaemia
DHA: docosahexaenoic acid
DOSS: dysphagia outcome and severity scale
DSA: digital subtraction angiography
EAA: essential amino acids
EQ-5D: EuroQol-5 dimensions
EUROQOL: European Quality of Life
FIM: functional independence measure
GCS: Glasgow Coma Scale
ICU: intensive care unit
IQR: interquartile range
ITT: intention-to-treat
k: potassium
MMSE: Mini-Mental State Examination
MoCA: Montreal cognitive assessment
MRI: magnetic resonance imaging
mRS: modified Rankin Scale
MUST: malnutrition universal screening tool
Na: sodium
NCCU: neuroscience critical care unit
Neuro-QoL: neurological quality of life
NIH: National Institute of Health
NIHSS: National Institute of Health Stroke Scale
OH(D): 25-Hydroxyvitamin D
PCO2: partial pressure of carbon dioxide
PEG: percutaneous endoscopic gastrostomy
PUFA: polyunsaturated fatty acids
QOL: quality of life
RDA: recommended dietary allowance
SAH: subarachnoid haemorrhage
SOC: standard of care
SD: standard deviation
SF-36: Short Form (36) Health survey
TIA: transient ischaemic attack
TPF: total protein and fibre
TSF: triceps skinfold thickness

TUG: Timed Up and Go
VAS: visual analogue scale
WFNS: World Federation of Neurological Surgeons
WHO: World Health Organization
WT: walking test

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

Study	Reason for exclusion
Cavalieri 2012	Wrong patient population: including patients with TIA
Ikeda 2020	Wrong intervention: comparison of timing
Kang 2010	Wrong outcomes: biomarkers and caregiver's quality of life
Liu 2015	Terminated study
Martin 2019	Unclear study design, conference proceedings
Missaoui 2021	Wrong outcomes: depression
Nakamura 2011	Wrong outcomes: biological outcomes (antioxidant test)
Narasimhan 2017	Wrong intervention: no supplements. Intramuscular injection
NCT01810263	Terminated study
NCT02982668	Terminated study
Oonuma 2019	Wrong outcomes: biological outcomes
Sato 2005a	Retraction
Sato 2005b	Retraction
Shen 2020	Wrong outcomes: biological outcomes
Solodov 2010	Wrong patient population: including patients with trauma
Sugiyama 2005	Retracted study
UMIN000019589	Terminated study
UMIN000025075	Terminated study
Witham 2009	Wrong outcomes: biological outcomes
Wuyanti 2005	Wrong outcomes: biological outcomes
Xia 2014	Wrong outcomes: biological outcomes
Yousefian 2019	Wrong outcomes: biological outcomes, duration of intubation
Zavertailo 2010	Wrong patient population: patients with trauma
Zhong 2014	Wrong patient population: including patients with encephalitis

TIA: transient ischaemic attack

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

CTRI 2020/03/024293

Methods	Randomised, parallel, single-blind
Participants	Targeted enrolment: 90 participants Inclusion criteria: • Patients who have first-ever ischaemic stroke within 72 hours diagnosed by neurologist with the help of a CT/MRI report • Patients who have hyper-homocysteinemia at baseline • Patients who have normal renal function Exclusion criteria: • Patients who suffer from the diseases, migraine, Alzheimer's dementia, and Parkinson's disease. • Patients with recurrent ischaemic stroke with significant disabilities • Patients having a history of vitamin B6, B12, folic acid supplementation, sex hormonal preparations like androgens intake and treated for depression, dementia, 6 months prior to the attack of ischaemic stroke • Patients who have hypothyroidism, psoriasis, malignancies, rheumatoid disease • Patients who are on treatment with drugs like methotrexate, cyclosporine, theophylline, anticonvulsants like phenytoin, carbamazepine, lipid-lowering like cholestyramine, nicotinic acid derivatives (e.g. fenofibrate)
Interventions	• Vitamin B12 (methylcobalamine), vitamin B6 (pyridoxine), vitamin B9 (folic acid): vitamin B12: 0.02-1.5 mg, vitamin B9: 0.5-5 mg, vitamin B6: 2-50 mg • Standard hospital treatment
Outcomes	• Recurrence of stroke
Notes	Date of first enrolment (India) May 4, 2020 Date of study completion (India) 28/09/2021 Study completion: 28/09/2021 Last refreshed on: 17/10/2022

ISRCTN11086312

Methods	Randomised, parallel
Participants	Patients who had their first ischaemic stroke were admitted to the ward for early post-stroke rehabilitation
Interventions	• Vitamin D supplementation at a dose of 2000 IU every morning (at 7.30 a.m.) for 6 weeks • Without vitamin D supplementation
Outcomes	• NIHSS • ADL: Barthel Scale • Modified Rankin Scale 3 months after the intervention

ISRCTN11086312 *(Continued)*

Notes	

NCT03637270

Methods	Randomised, parallel, triple-blind
Participants	Targeted enrolment: 120 participants Inclusion criteria: • Chronic stroke > 6 months • Age: 20-75 y • Able to walk independently over 10 mins (with or without orthosis) • Able to use a stationary bike Exclusion criteria: • Physiological condition not stable, cognitive dysfunction, not able to coordinate with examiner or treatments • Not able to exercise due to severe cardiopulmonary dysfunction • Malnutrition (MNA < 11) • Severe obesity (BMI > 35) • Renal insufficiency • Unable to tolerate our cardiopulmonary exercise test (CPET) (e.g. too short stature to fit the machine, leg spasticity too strong to use pedals for cycling, unable to maintain 50 rpm at the beginning of CPET, indications for early termination of CPET based on the American College of Sport Medicine suggestions)
Interventions	• Dietary supplementation with protein-rich supplements immediately before and after each exercise training session • Dietary supplementation with carbohydrate-rich supplements immediately before and after each exercise training session
Outcomes	• Total body lean and fat mass • Timed up and go • Burg Balance Test • 6-minute walk test • Short Physical Performance Battery • Modified physical performance test
Notes	Estimated study completion date: April 19, 2023

NCT04295044

Methods	Randomised, parallel, single-blind (outcomes assessor)
Participants	Targeted enrolment: 100 participants Inclusion criteria: • 20 years to 99 years • Acute ischaemic stroke during hospitalisation • eGFR > 30; urine albumin creatinine ratio < 30 mg/g

NCT04295044 *(Continued)*

	• Urinary creatinine excretion rate (CER) < 1500 g/day Exclusion criteria: • Chronic kidney disease stage 4 or 5 (i.e. eGFR < 30) • Proteinuria (protein 1+ or more in urine routine) • Known impairment of functional status (mRS ≥ 2) prior to the index stroke • Refuse to participate in this study
Interventions	• High-protein diet: 1.8 g protein/kg • Normal protein diet
Outcomes	• Modified Rankin Scale [time frame: 3 months]
Notes	Estimated study completion date: March 31, 2021 Recruitment status: unknown Last update posted: March 4, 2020

NCT04459091

Methods	Randomised, parallel, triple-blind
Participants	Targeted enrolment: 125 participants Inclusion criteria: first episode of cerebral stroke, first taken into rehabilitation after hospitalisation in the acute department Exclusion criteria: neoplasia, long-term corticosteroid therapy (> 3 weeks) in the pre-event period and at the time of admission to the rehabilitation department
Interventions	• Essential amino acids • Placebo
Outcomes	• FIM Time frame: eight weeks
Notes	Actual study start date: January 10, 2018 Actual study completion date: September 15, 2018 Contact information: no information Location: Italy

UMIN000023954

Methods	Randomised, parallel, single-blind (patients)
Participants	Targeted enrolment: 128 Inclusion criteria: • Over 65 years old • Acute stroke

UMIN000023954 *(Continued)*

	• MUST (Malnutrition Universal Screening Tool) > score 2 or serum albumin < 3 g/dL Exclusion criteria: • Not stable • End of life • Severe dementia • Liver cirrhosis • Using albumin preparation
Interventions	• Individualised nutrition management • Not individualised nutrition management
Outcomes	• Functional Independence Measure • Handgrip strength • Walking speed • Modified Rankin Scale • Brunnstrom stage • Arm circumference • Thigh circumference • Calf circumference • Body weight
Notes	Status: Complete Last update posted: June 29, 2019

ADL: activities of daily living
BMI: body mass index
CER: creatinine excretion rate
CPET: cardiopulmonary exercise test
CT: computed tomography
eGFR: estimated Glomerular Filtration Rate
FIM: functional independence measure
MNA: mini-nutritional assessment
MRI: magnetic resonance imaging
mRS: modified Rankin Scale
MUST: malnutrition universal screening tool
NIHSS: National Institute of Health Stroke scale
rpm: revolutions per minute

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

CTRI/2023/11/060377

Study name	A study to know whether vitamin D supplementation can improve the disability due to stroke in 90 days in patients with low levels of vitamin D in blood
Methods	Randomised, parallel
Participants	Targeted enrolment: 86 Patients aged more than 40 years of either sex, presenting within 24 hours of the onset of symptoms and diagnosed with acute ischaemic stroke by a brain MRI/CT
Interventions	• Vitamin D 60,000 IU once weekly supplemented in acute ischaemic stroke patients with recorded vitamin D deficiency or insufficiency during admission for 8 weeks

CTRI/2023/11/060377 *(Continued)*

	• Placebo once weekly supplemented in acute ischaemic stroke patients with recorded vitamin D deficiency or insufficiency during admission for 8 weeks
Outcomes	• Modified Rankin score at admission and 90 days • Incidence of recurrent stroke within 90 days
Starting date	
Contact information	
Notes	Not yet recruiting

DRKS00005577

Study name	AMINO-Stroke study
Methods	Randomised, parallel, triple-blind
Participants	Targeted enrolment: 110 participants Inclusion criteria: • Patients > 45 years • Protocol article: Patients with ischaemic or haemorrhagic stroke within 8 weeks of enrolment (IC-TRP: ischaemic stroke after acute stroke) • Brain magnet resonance imaging or computer tomography demonstrating stroke • Motoric disability of an upper and /or lower limb (Rivermead Motor Assessment Gross Function > 1 and < 11) Exclusion criteria: • Clinically significant findings on physical examination or presence of clinically significant disease that would interfere with study evaluation in the opinion of the treating physicians • Participation in another clinical trial investigating a nutritional product • History of intolerance or allergic response to similar nutritional products or known hypersensitivity to essential amino acids • Clinical signs and symptoms of infection requiring antibiotic therapy at the time of enrolment that prevent completion of trial-related assessments as judged by the investigator • Transaminases (AST or ALT) > 3 times the upper limit of normal (ULN) • Severe renal dysfunction or nephrotic syndrome • Acquired immunodeficiency syndrome, HIV or hepatitis C infection • Current therapy with anabolic steroids or appetite stimulants • Current immunosuppressive therapy, heart transplantation, or renal dialysis • Life expectancy < 6 months
Interventions	• EAAs (4 grams, 3 times a day) for 4 weeks • Placebo
Outcomes	• Primary: physical performance according to the Rivermead motor assessment (RMA) gross function scale • Primary: muscle strength in a maximum hand grip strength test • Disability: mRS • Functional independence: BI • EQ-5D

DRKS00005577 *(Continued)*

	• Fugl-Meyer Score (motor functional domain) • Motor assessment scale • Functional ambulatory capacity test • Short Physical Performance Battery Test • Changes of body composition • Post-stroke complications
Starting date	Date of first enrolment: January 6, 2014
Contact information	Dr. Wolfram Doehner Charite Universitätsmedizin, Berlin, Germany wolfram.doehner@charite.de
Notes	

IRCT20190305042937N1

Study name	Clinical trial comparison of the effect of folic acid and vitamin D supplementation in the prevention of cerebrovascular attacks in patients referred to Shahid Beheshti Hospital in 3 months
Methods	Randomised, parallel, triple-blind
Participants	Targeted enrolment: 120 participants Inclusion criteria: • Haemorrhagic or ischaemic stroke of any severity • Over 30 years old • No previous use of supplements • Not having a history of allergy to drugs • The first episode of stroke • Having no problem swallowing • Resident of Qom province Exclusion criteria: • Pregnancy • No ability to swallow medicine
Interventions	1) oral folic acid for a period of three months at a dose of 5 mg once a day, along with vitamin D placebo 2) vitamin D in addition to routine treatment for a period of three months at a dose of 1000 IU once a day, with folic acid placebo 3) folic acid for a period of three months at a dose of 5 mg once a day and vitamin D administered at a dose of 1000 IU once a day 4) placebo control group undergoing routine treatment; 'along with the placenta two other drugs'
Outcomes	• Recurrent stroke
Starting date	July 23, 2019
Contact information	Ehsan Sharifipur Ghoum University of Medical Sciences Iran

IRCT20190305042937N1 *(Continued)*

	ehsansharifipoor@yahoo.com
Notes	Last update: August 10, 2019

NCT02347995

Study name	Resistive training combined with nutritional therapy after stroke
Methods	Randomised, parallel, double-blind
Participants	Targeted enrolment: 150 participants Inclusion criteria: • Stroke > 3 months prior • Completion of all regular post-stroke physical therapy • Adequate language and neurocognitive function to participate in testing and training and to provide informed consent • Able to walk 10 metres without human assistance Exclusion criteria: • Regular structured resistive exercise (> 2x/week) • Alcohol consumption > 3 oz liquor, 3 x 4 oz. glasses of wine, or 3 x 12 oz beers/day, by self-report • Neurological history of: a) dementia by clinical evaluation, b) severe receptive or global aphasia, which confounds testing and training, operationally defined as unable to follow 2-point commands, c) untreated major depression by clinical interview • Medical history: a) recent hospitalisation (less than 3 months prior to study entry) for severe medical disease, b) orthopaedic or chronic pain condition restricting exercise, c) pulmonary or renal failure, d) active cancer, e) untreated poorly controlled hypertension measured on at least 2 occasions (greater than 190/100), f) untreated and/or poorly controlled diabetes with fasting blood glucose of greater than 170 and HbA1c greater than 10.0, g) medications: oral steroids, h) currently pregnant • Cardiac history of: a) unstable angina, b) recent (less than 3 months prior to study entry) myocardial infarction, congestive heart failure (NYHA category II-IV); c) haemodynamically significant valvular dysfunction • Any medical condition that, in the opinion of the Investigator, might interfere with the subject's participation in the study, poses any added risk for the subject, or confounds the assessment of the subject
Interventions	• Resistive training + protein: 30 grams of whey protein after each resistance training session • Resistive training + placebo: a placebo beverage after each resistance training session Duration: 12 weeks
Outcomes	• Change in thigh muscle area • Change in muscle strength • 6-min walk distance Time frame: measured at baseline and after the 3-month intervention
Starting date	August 24, 2015
Contact information	Lynda C Robey Baltimore VA Medical Center United States

NCT02347995 *(Continued)*

	lynda.robey@va.gov
Notes	Estimated study completion date: October 1, 2023

NCT04259307

Study name	Effect of intensive nutritional support on functional recovery in subacute stroke patient
Methods	Randomised, parallel, single-blind (outcomes assessor)
Participants	Targeted enrolment: 150 participants Inclusion criteria: • 19 years and older • Acute first-ever stroke patients less than 7 days after onset • Body mass index (BMI) < 25 before comprehensive rehabilitation • Mini-Nutritional Assessment < 12 before comprehensive rehabilitation • Fugl-Meyer assessment < 85 at 7 days after stroke onset Exclusion criteria: • Transient ischaemic stroke • Progressive or unstable stroke • Pre-existing and active major neurological disease • Pre-existing and active (e.g. on chronic medication) major psychiatric disease • Advanced liver, kidney, cardiac, or pulmonary disease • A terminal medical diagnosis consistent with survival < 1 year • Diabetes mellitus, hyperlipidaemia, metabolic syndrome, or heart failure • Pregnant or lactating women • Prohibited from taking medication
Interventions	• Intensive nutrition group: standard nutritional support with additional intravenous nutrition of 500 kcal per day for 3 weeks • Control group: standard nutritional support only per day for 3 weeks
Outcomes	• Korean modified Barthel Index (K-MBI) at 6 months after onset
Starting date	January 29, 2020
Contact information	Won Hyuk Chang Samsung Medical Center Recruiting, Seoul, Korea wh.chang@samsung.com
Notes	Estimated study completion date: December 31, 2023

NCT04386525

Study name	The potential effect of omega3 supplement in fish oil on infarcted areas in the brain and improvement of neurological functions of ischemic stroke patients
Methods	Randomised, parallel, open-label

NCT04386525 *(Continued)*

Participants	Targeted enrolment: 60 participants Inclusion criteria: • 18 years to 110 years • Admitted ischaemic occlusive stroke after successful reperfusion therapy - stabilised in ICU 'or the inward' • Attack started 48 hours or less • Can be fed by nasogastric tube or by themselves • MRI imaging was taken in the first 24 hours and CT Exclusion criteria: • Haemorrhagic stroke • Non-occlusive hypoxic brain • Global cerebral ischaemia • Transient ischaemic attack • Non-scanned by MRI or CT in the first 48 hours of onset • Non-reperfused stroke patient or non-successful reperfusion therapy • Deteriorating cases and not stabilised patients • Attack exceeded 48 hours since onset • Patients not tolerant to feeding (NPO) • Unstable source of thrombi (e.g. vegetation heart valves, unstable carotid atherosclerosis, etc.) • Presence of any coagulopathy • Sickle cell anaemia • Risk for shock (e.g. septic shock, hypovolemic shock, cardiogenic shock...etc.) - time of onset not reliably known • Suspected non-stroke diagnosis • Significant concurrent medical condition • Significant pre-existing disability (will be excluded from neurological scoring assessment, not CT MRI assessment) • Liver disease
Interventions	• Omega-3 fish oil: 4 g per day of fish oil three times with meals • No Intervention Duration: 1 month
Outcomes	• Improvement of neurological symptoms and functions (severity): NIHSS • Improvement of neurological symptoms and functions (dependence) mRS Time frame: after 3 months of intervention
Starting date	1 September, 2020
Contact information	Nauf Almansour Subspecialty Consultant Neurologist And Stroke Specialist, King Fahad Medical City nalmansour.stroke@gmail.com
Notes	Recruitment status: unknown Last update posted: May 14, 2020

NCT05474105

Study name	Multi-nutrient supplementation as a therapeutic intervention in ischaemic stroke (MUST-IS)
Methods	Randomised, parallel, open-label
Participants	Targeted enrolment: 30 participants Inclusion criteria: • Age > 18 and < 80 • Acute ischaemic stroke (within 24 h of onset), including the following subtypes according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification: large-artery atherosclerosis, cardio-embolism, small-vessel occlusion, stroke of undetermined aetiology OR acute ischaemic stroke (within 24 h of onset) caused by arterial dissection • Pre-morbid (modified Rankin Scale) mRS of ≤ 2 • National Institutes of Health Stroke Scale (NIHSS) score > 4 • CT ASPECT score of ≥ 6 on presentation CT • Expected ability to provide consent • Ability to drink the ONS product within 7 days of incident stroke Exclusion criteria: • Allergies to fish oil/milk/soya • Known history of galactosaemia • Patients that develop malignant middle cerebral artery (MCA) syndrome • Current or previous haemorrhagic stroke including subarachnoid haemorrhage • Patient with nasogastric (NG) tube • Patients with dysphagia (routinely tested) who cannot drink the medical food • Known malignancy • Known pre-existing neurological diseases including multiple sclerosis, Alzheimer's disease, Parkinson's disease, previous strokes • Pregnant or breastfeeding • Inability to complete the follow-up and/or Investigators uncertainty about the ability to complete the follow-up • Chronic renal disease stage 3b and above (i.e. Glomerular filtration rate (GFR) < 44 mL/min) • Ischaemic stroke of other determined aetiology as classified by the TOAST classification (not including stroke caused by arterial dissection) • Unable to receive enteral nutrition
Interventions	• Daily active oral nutritional supplement (ONS) for 3 months + standard care: daily drink 125 mL together with meal • Standard care
Outcomes	• Quality of life • Activities of Daily Living • Nutritional status • Cognitive changes • Infection status: occurrence of pneumonia and urinary tract infections Time frame: after 3 months of intervention
Starting date	July 11, 2023
Contact information	Oliver Spooner, Dr02073777000 o.spooner@NHS.net

NCT05474105 *(Continued)*

Notes	

NCT05728229

Study name	Effects of nutrition on post stroke fatigue (NUTRE-S)
Methods	Randomised, parallel, open-label
Participants	Targeted enrolment: 24 participants Inclusion criteria: • Age greater than or equal to 5 years • Patients with ischaemic or haemorrhagic stroke outcomes documented through neuroimaging techniques (magnetic resonance or computed tomography) • Latency from an acute event between 1 and 6 months • Cognitive skills that allow you to carry out simple orders and understand the physiotherapist's instructions (assessed through the Token Test (score ≥ 26.5)) • Ability to walk independently or with little assistance • Ability to understand and sign informed consent Exclusion criteria: • Vitamin D intake greater than 3000 IU/day • Therapy with vitamin K antagonists • Conditions causing excess electrolytes in the blood • Diagnosis of metabolic mineral storage disorders (e.g. haemochromatosis, Wilson) • Dialysis patients • Systemic, neurological, cardiac pathologies that make walking risky or cause motor deficits • Oncological pathologies • Problems of an orthopaedic or postural nature • Presence of plantar ulcers • Partial or total amputation of segments of the foot • Inability to provide informed consent
Interventions	• Supplement with SiderAl® Med Nutritional supplementation with special purpose food (SiderAl® Med) • No supplement
Outcomes	• Berg Balance Scale • Short Physical Performance Battery • Motricity Index • Timed Up and Go Test • HandGrip Test • Ambulation Index • Walking handicap scale • Functional Ambulation Classification • 10 Metre Walk Test • Six-minute walk test • Modified Barthel Index • EuroQoL-5 Dimension • Frontal Assessment Battery • Stroop Colour Word Test

NCT05728229 *(Continued)*

	• Digit Cancellation Test • Trial Making Test • Dual-Energy X-ray absorptiometry
Starting date	November 7, 2022
Contact information	Silvia Giovannini Fondazione Policlinico Universitario A. Gemelli IRCCS Roma, RM, Italy, 00168
Notes	

UMIN000035365

Study name	Effects of medium-chain triglyceride on ghrelin activation, food intake, activity of daily living and muscle mass in older malnourished patients with stroke
Methods	Randomised, parallel, double blind
Participants	Targeted enrolment: 45 Inclusion criteria: • Older patients aged 70 or older undergoing convalescent rehabilitation • Malnourished: MNA-SF < 7 and BMI < 20.0 kg/m^2 • Can perform sit-up and down exercise w/o any aids Exclusion criteria: • Unconscious: JCS > II-10 • Severe cognitive decline: MMSE < 20 • Dysphagia: FILS < 3 • Judged medically inappropriate condition for participation in research
Interventions	• MCT plus protein • LCT plus protein • Protein
Outcomes	• Functional Independence Measure • Skeletal muscle mass index • Handgrip strength
Starting date	April 1, 2019
Contact information	Sayuri Shimazu Kumamoto Rehabilitation Hospital Japan
Notes	Recruitment status: pending Last update posted: March 2, 2019 Financial support: Nissin Oilio group

ALT: alanine aminotransferase
AST: aspartate aminotransferase
BI: Barthel Index
BMI: body mass index
CT: computed tomography
EAA: essential amino acids
EQ-5D: European Quality of Life-5 Dimensions
EuroQoL-5: European Quality of Life-5 Dimensions
FILS: functional oral intake scale
GFR: glomerular filtration rate
HbA1c: haemoglobin A1c
HIV: human immunodeficiency virus
K-MBI: Korean modified Barthel Index
JCS: Japan Coma Scale
LCT: long-chain triglycerides
MCA: middle cerebral artery
MCT: medium-chain triglycerides
MMSE: Mini-Mental State Examination
MNA-SF: Mini-Nutritional Assessment-Short Form
MRI: magnetic resonance imaging
mRS: modified Rankin Scale
NG: nasogastric
NIHSS: National Institute of Health Stroke scale
NPO: nothing by mouth
NYHA: New York Heart Association
ONS: oral nutritional supplement
RMA: Rivermead motor assessment
TOAST: Trial of ORG 10172 in Acute Stroke Treatment
ULN: upper limit of normal
w/o: without

DATA AND ANALYSES

Comparison 1. Oral nutritional supplements (energy and protein) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Disability (modified Rankin Scale 0 to 2, good status) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	0.97 [0.86, 1.10]
1.2 Activities of daily living (Functional Independence Measure, Motor score) at end of intervention phase	2	165	Mean Difference (IV, Random, 95% CI)	8.74 [5.93, 11.54]
1.2.1 Acute and subacute phase	1	116	Mean Difference (IV, Random, 95% CI)	7.71 [1.51, 13.91]
1.2.2 Subacute phase	1	49	Mean Difference (IV, Random, 95% CI)	9.00 [5.86, 12.14]
1.3 Subgroup analysis – type of stroke: activities of daily living	2	165	Mean Difference (IV, Random, 95% CI)	8.74 [5.93, 11.54]

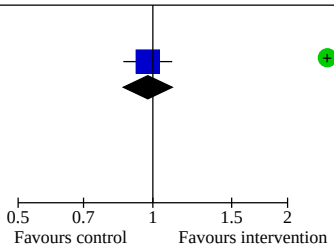
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3.1 Mixed: ischaemic and haemorrhagic stroke	1	116	Mean Difference (IV, Random, 95% CI)	7.71 [1.51, 13.91]
1.3.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	49	Mean Difference (IV, Random, 95% CI)	9.00 [5.86, 12.14]
1.4 Neurological impairment (change in NIHSS score) during intervention phase	2	190	Mean Difference (IV, Random, 95% CI)	-2.12 [-3.84, -0.39]
1.4.1 Acute phase	1	148	Mean Difference (IV, Random, 95% CI)	-3.20 [-5.02, -1.38]
1.4.2 Acute or subacute phase	1	42	Mean Difference (IV, Random, 95% CI)	-1.40 [-2.28, -0.52]
1.5 Walking capacity (2-minute walk test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.5.1 Acute and subacute	1	116	Mean Difference (IV, Fixed, 95% CI)	63.92 [29.49, 98.35]
1.6 Walking capacity (6-minute walk test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.6.1 Acute and subacute phase	1	116	Mean Difference (IV, Fixed, 95% CI)	133.27 [31.10, 235.44]
1.7 Muscle strength (grip strength) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.7.1 Subacute phase	1	49	Mean Difference (IV, Fixed, 95% CI)	4.90 [2.31, 7.49]
1.8 Nutritional status change (body weight) during intervention phase	3	205	Mean Difference (IV, Random, 95% CI)	0.90 [0.23, 1.58]
1.8.1 Acute and subacute phase	2	157	Mean Difference (IV, Random, 95% CI)	0.90 [0.22, 1.58]
1.8.2 Subacute phase	1	48	Mean Difference (IV, Random, 95% CI)	0.70 [-6.55, 7.95]
1.9 Subgroup analysis – type of stroke: nutritional status (body weight)	3	205	Mean Difference (IV, Random, 95% CI)	0.90 [0.23, 1.58]
1.9.1 Ischaemic stroke	2	89	Mean Difference (IV, Random, 95% CI)	0.86 [0.16, 1.55]
1.9.2 Mixed: ischaemic and haemorrhagic stroke	1	116	Mean Difference (IV, Random, 95% CI)	1.64 [-1.24, 4.52]
1.10 Subgroup analysis – nutritional status at baseline: nutritional status (body weight)	3	205	Mean Difference (IV, Random, 95% CI)	0.90 [0.23, 1.58]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.10.1 Inclusion criteria with malnutrition or malnutrition risk	1	116	Mean Difference (IV, Random, 95% CI)	1.64 [-1.24, 4.52]
1.10.2 No inclusion criteria with malnutrition or malnutrition risk	2	89	Mean Difference (IV, Random, 95% CI)	0.86 [0.16, 1.55]
1.11 Nutritional status (triceps skinfold thickness) at end of intervention phase	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.11.1 Acute phase	1	148	Mean Difference (IV, Random, 95% CI)	2.30 [0.92, 3.68]
1.12 All-cause mortality at follow-up	2	4065	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.14, 2.28]
1.12.1 Acute phase	2	4065	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.14, 2.28]
1.13 Subgroup analysis – type of stroke: all-cause mortality	2	4065	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.14, 2.28]
1.13.1 Mixed: intracerebral and subarachnoid haemorrhage	1	42	Odds Ratio (M-H, Random, 95% CI)	0.21 [0.04, 1.17]
1.13.2 Mixed: ischaemic stroke and intracerebral haemorrhage	1	4023	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.78, 1.14]
1.14 Subgroup analysis – nutritional status at baseline: all-cause mortality	2	4065	Odds Ratio (M-H, Random, 95% CI)	0.57 [0.14, 2.28]
1.14.1 Inclusion criteria with malnutrition or malnutrition risk	1	42	Odds Ratio (M-H, Random, 95% CI)	0.21 [0.04, 1.17]
1.14.2 No inclusion criteria with malnutrition or malnutrition risk	1	4023	Odds Ratio (M-H, Random, 95% CI)	0.94 [0.78, 1.14]
1.15 Stroke recurrence at end of intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.15.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	1.16 [0.77, 1.75]
1.16 Change in cognitive function score (Mini-Mental State Examination) during intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.16.1 Subacute phase	1	48	Mean Difference (IV, Fixed, 95% CI)	3.68 [-8.67, 16.03]
1.17 Complication (pressure sores) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.17.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.30, 1.08]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.18 Complications (infections: pneumonia, urinary tract, and septicaemias) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.18.1 Acute phase	1	42	Odds Ratio (M-H, Fixed, 95% CI)	0.68 [0.20, 2.30]
1.19 Complication (pneumonia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.19.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.88, 1.47]
1.20 Complication (urinary tract infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.20.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.72, 1.18]
1.21 Complication (hyper/hypoglycaemia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.21.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	15.60 [4.84, 50.23]
1.22 Complication (gastrointestinal haemorrhage) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.22.1 Acute phase	1	4023	Odds Ratio (M-H, Fixed, 95% CI)	1.56 [0.86, 2.82]
1.23 Complication (diarrhoea) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 1: Disability (modified Rankin Scale 0 to 2, good status) at follow-up

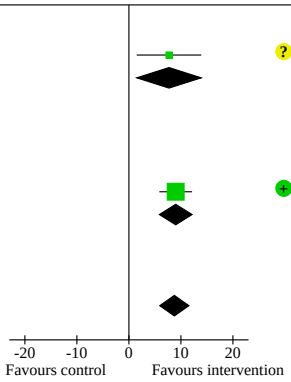
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.1.1 Acute phase						
Dennis 2005a	815	2016	824	2007	100.0%	0.97 [0.86 , 1.10]
Subtotal (95% CI)		**2016**		**2007**	**100.0%**	**0.97 [0.86 , 1.10]**
Total events:	815		824			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.41 (P = 0.68)						

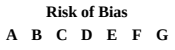


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.2. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 2: Activities of daily living (Functional Independence Measure, Motor score) at end of intervention phase

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
1.2.1 Acute and subacute phase								
Rabadi 2008	51.04	17.43	58	43.33	16.63	58	20.4%	7.71 [1.51 , 13.91]
Subtotal (95% CI)			**58**			**58**	**20.4%**	**7.71 [1.51 , 13.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.44 (P = 0.01)								
1.2.2 Subacute phase								
Yoshimura 2019	63.1	5.1	24	54.1	6.1	25	79.6%	9.00 [5.86 , 12.14]
Subtotal (95% CI)			**24**			**25**	**79.6%**	**9.00 [5.86 , 12.14]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 5.61 (P < 0.00001)								
Total (95% CI)			**82**			**83**	**100.0%**	**8.74 [5.93 , 11.54]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%								
Test for overall effect: Z = 6.11 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.13, df = 1 (P = 0.72), I² = 0%								





Risk of bias legend
(A) Random sequence generation (selection bias)
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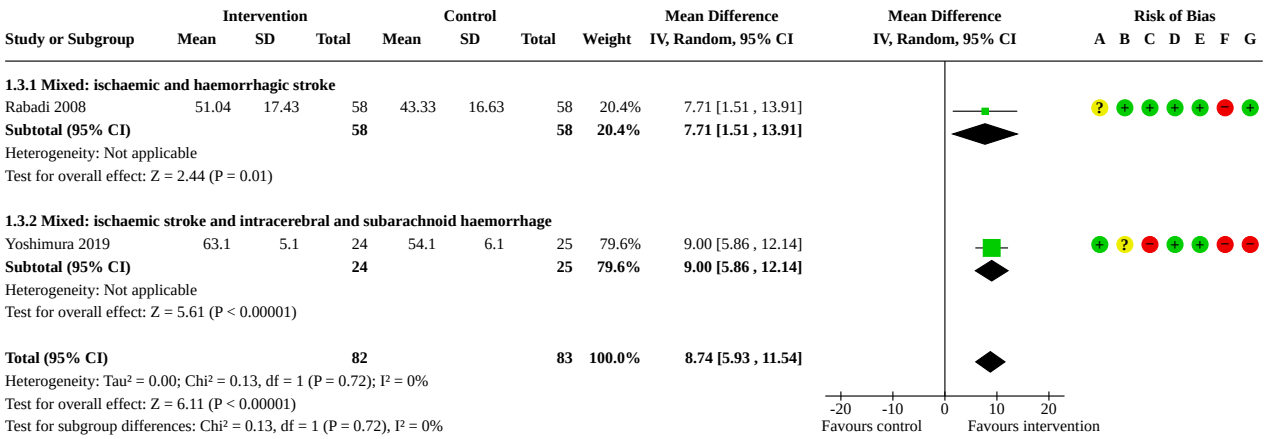
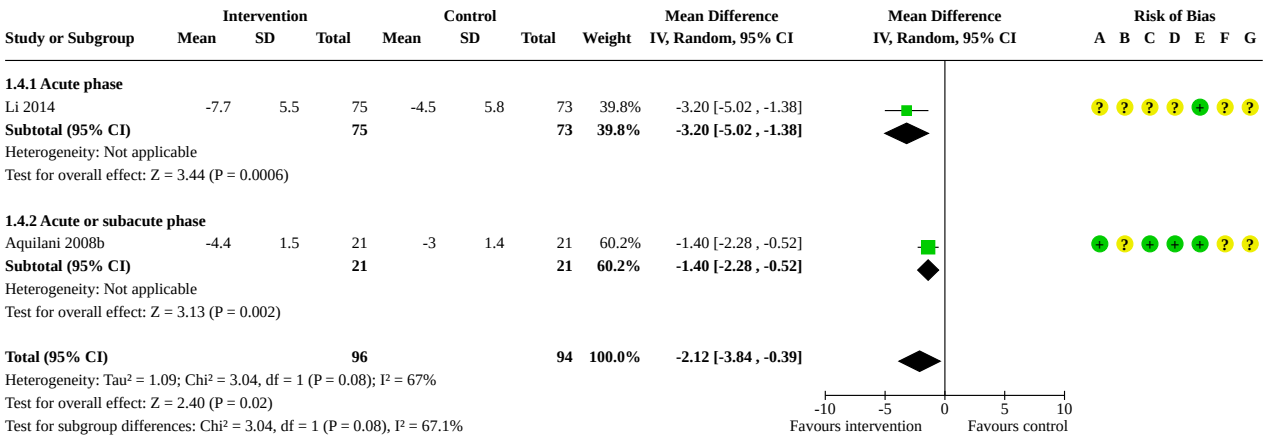
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.3. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 3: Subgroup analysis – type of stroke: activities of daily living



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

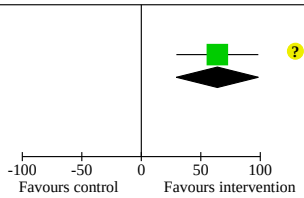
Analysis 1.4. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 4: Neurological impairment (change in NIHSS score) during intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.5. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 5: Walking capacity (2-minute walk test) at end of intervention phase

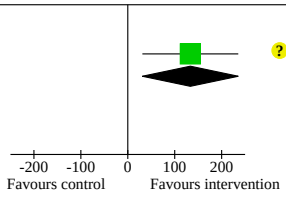
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.5.1 Acute and subacute									
Rabadi 2008	148.9	107.15	58	84.98	80.08	58	100.0%	63.92 [29.49 , 98.35]	? + + + + − +
Subtotal (95% CI)			**58**			**58**	**100.0%**	**63.92 [29.49 , 98.35]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.64 (P = 0.0003)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.6. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 6: Walking capacity (6-minute walk test) at end of intervention phase

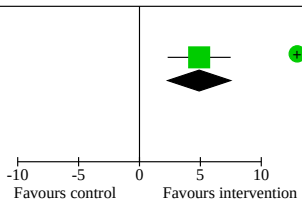
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.6.1 Acute and subacute phase									
Rabadi 2008	396.37	276.46	58	263.1	284.9	58	100.0%	133.27 [31.10 , 235.44]	? + + + + − +
Subtotal (95% CI)			**58**			**58**	**100.0%**	**133.27 [31.10 , 235.44]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.56 (P = 0.01)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.7. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 7: Muscle strength (grip strength) at end of intervention phase

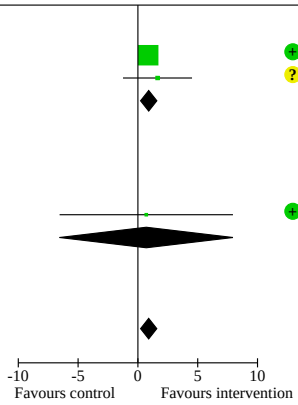
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
1.7.1 Subacute phase									
Yoshimura 2019	22.1	4.1	24	17.2	5.1	25	100.0%	4.90 [2.31 , 7.49]	+ ? − + + − −
Subtotal (95% CI)			**24**			**25**	**100.0%**	**4.90 [2.31 , 7.49]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.71 (P = 0.0002)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.8. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 8: Nutritional status change (body weight) during intervention phase

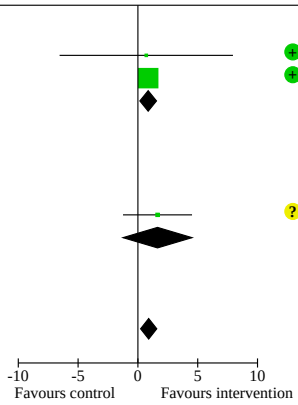
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.8.1 Acute and subacute phase									
Aquilani 2008b	0.36	0.63	20	-0.5	1.5	21	93.6%	0.86 [0.16 , 1.56]	+ ? + + + ? ?
Rabadi 2008	2.31	7.35	58	0.67	8.46	58	5.5%	1.64 [-1.24 , 4.52]	? + + + + − +
Subtotal (95% CI)			**78**			**79**	**99.1%**	**0.90 [0.22 , 1.58]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.61); I² = 0%									
Test for overall effect: Z = 2.61 (P = 0.009)									
1.8.2 Subacute phase									
Aquilani 2008a	0.4	13.2	24	-0.3	12.4	24	0.9%	0.70 [-6.55 , 7.95]	+ ? ? ? + ? −
Subtotal (95% CI)			**24**			**24**	**0.9%**	**0.70 [-6.55 , 7.95]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.19 (P = 0.85)									
Total (95% CI)			**102**			**103**	**100.0%**	**0.90 [0.23 , 1.58]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 2 (P = 0.87); I² = 0%									
Test for overall effect: Z = 2.61 (P = 0.009)									
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

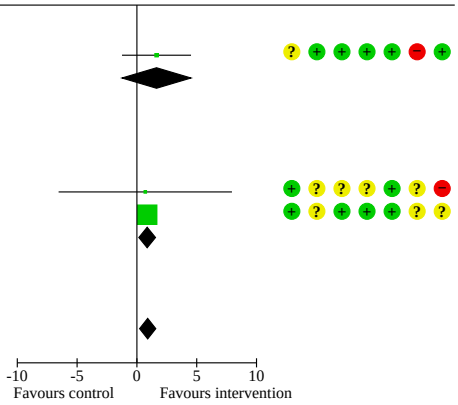
Analysis 1.9. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 9: Subgroup analysis – type of stroke: nutritional status (body weight)

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.9.1 Ischaemic stroke									
Aquilani 2008a	0.4	13.2	24	-0.3	12.4	24	0.9%	0.70 [-6.55 , 7.95]	+ ? ? ? + ? −
Aquilani 2008b	0.36	0.63	20	-0.5	1.5	21	93.6%	0.86 [0.16 , 1.56]	+ ? + + + ? ?
Subtotal (95% CI)			**44**			**45**	**94.5%**	**0.86 [0.16 , 1.55]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%									
Test for overall effect: Z = 2.42 (P = 0.02)									
1.9.2 Mixed: ischaemic and haemorrhagic stroke									
Rabadi 2008	2.31	7.35	58	0.67	8.46	58	5.5%	1.64 [-1.24 , 4.52]	? + + + + − +
Subtotal (95% CI)			**58**			**58**	**5.5%**	**1.64 [-1.24 , 4.52]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.11 (P = 0.27)									
Total (95% CI)			**102**			**103**	**100.0%**	**0.90 [0.23 , 1.58]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 2 (P = 0.87); I² = 0%									
Test for overall effect: Z = 2.61 (P = 0.009)									
Test for subgroup differences: Chi² = 0.27, df = 1 (P = 0.61), I² = 0%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

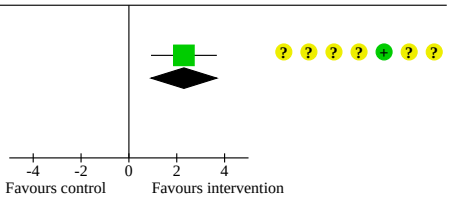
Analysis 1.10. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 10: Subgroup analysis – nutritional status at baseline: nutritional status (body weight)



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.10.1 Inclusion criteria with malnutrition or malnutrition risk									
Rabadi 2008	2.31	7.35	58	0.67	8.46	58	5.5%	1.64 [-1.24 , 4.52]	? + + + + - +
Subtotal (95% CI)			**58**			**58**	**5.5%**	**1.64 [-1.24 , 4.52]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.11 (P = 0.27)									
1.10.2 No inclusion criteria with malnutrition or malnutrition risk									
Aquilani 2008a	0.4	13.2	24	-0.3	12.4	24	0.9%	0.70 [-6.55 , 7.95]	+ ? ? ? + ? -
Aquilani 2008b	0.36	0.63	20	-0.5	1.5	21	93.6%	0.86 [0.16 , 1.56]	+ ? + + + ? ?
Subtotal (95% CI)			**44**			**45**	**94.5%**	**0.86 [0.16 , 1.55]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.97); I² = 0%									
Test for overall effect: Z = 2.42 (P = 0.02)									
Total (95% CI)			**102**			**103**	**100.0%**	**0.90 [0.23 , 1.58]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 2 (P = 0.87); I² = 0%									
Test for overall effect: Z = 2.61 (P = 0.009)									
Test for subgroup differences: Chi² = 0.27, df = 1 (P = 0.61), I² = 0%									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.11. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 11: Nutritional status (triceps skinfold thickness) at end of intervention phase



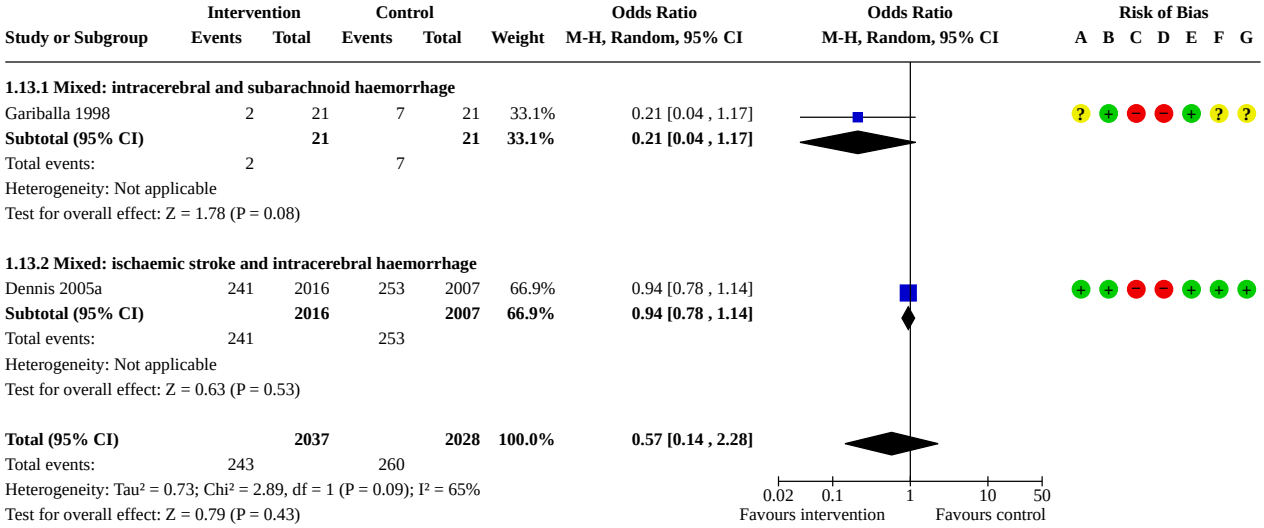
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
1.11.1 Acute phase									
Li 2014	13.5	3.9	75	11.2	4.6	73	100.0%	2.30 [0.92 , 3.68]	? ? ? ? + ? ?
Subtotal (95% CI)			**75**			**73**	**100.0%**	**2.30 [0.92 , 3.68]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.28 (P = 0.001)									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.12. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 12: All-cause mortality at follow-up

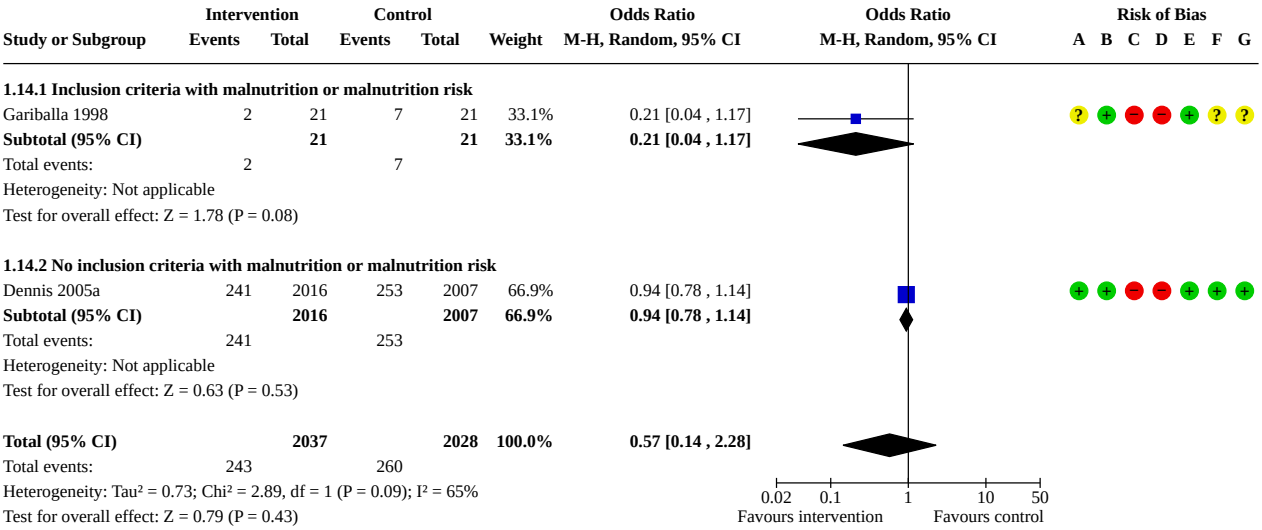
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.13. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 13: Subgroup analysis – type of stroke: all-cause mortality



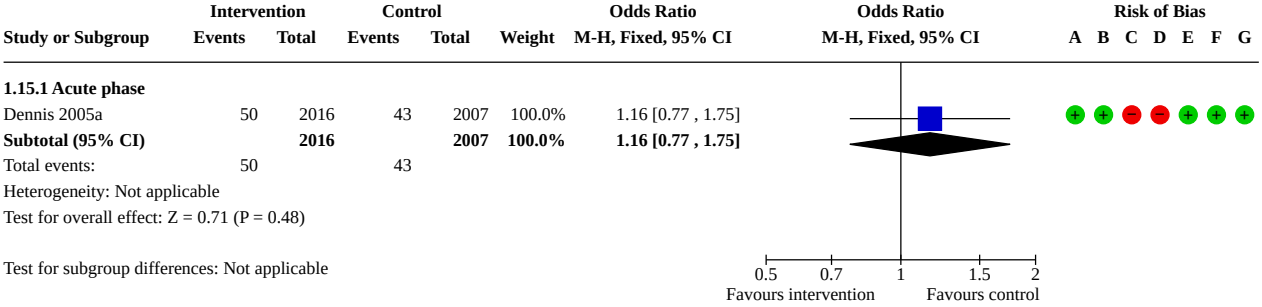
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.14. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 14: Subgroup analysis – nutritional status at baseline: all-cause mortality



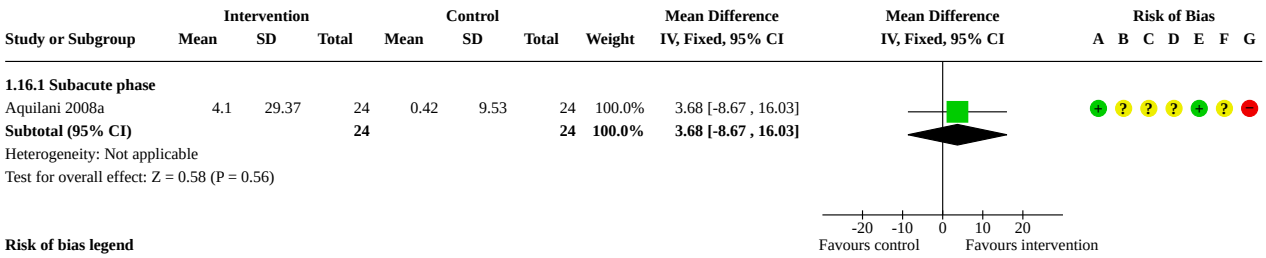
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.15. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 15: Stroke recurrence at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.16. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 16: Change in cognitive function score (Mini-Mental State Examination) during intervention phase

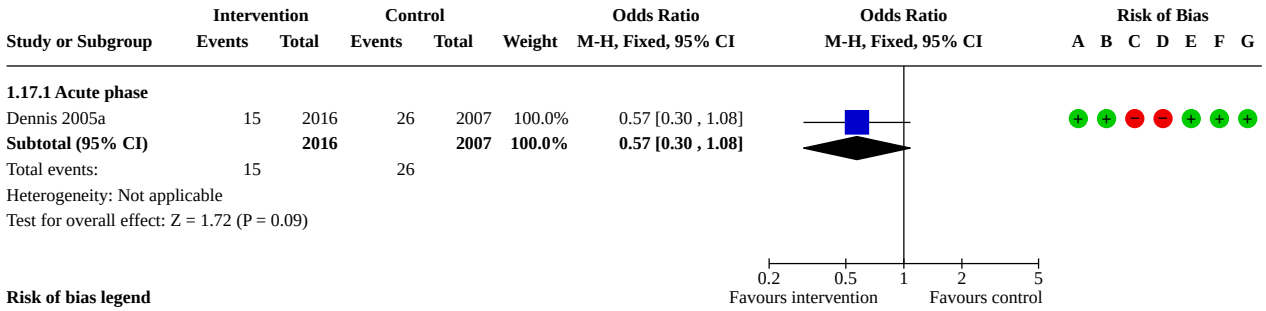


Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.16.1 Subacute phase								
Aquilani 2008a	4.1	29.37	24	0.42	9.53	24	100.0%	3.68 [-8.67 , 16.03]
Subtotal (95% CI)			**24**			**24**	**100.0%**	**3.68 [-8.67 , 16.03]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.17. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 17: Complication (pressure sores) during intervention phase



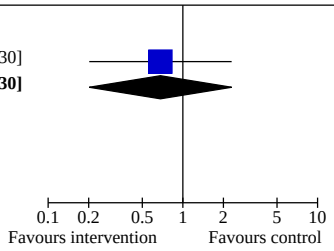
Study or Subgroup	Intervention Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.17.1 Acute phase						
Dennis 2005a	15	2016	26	2007	100.0%	0.57 [0.30 , 1.08]
Subtotal (95% CI)		**2016**		**2007**	**100.0%**	**0.57 [0.30 , 1.08]**
Total events:	15		26			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.72 (P = 0.09)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.18. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 18: Complications (infections: pneumonia, urinary tract, and septicaemias) during intervention phase

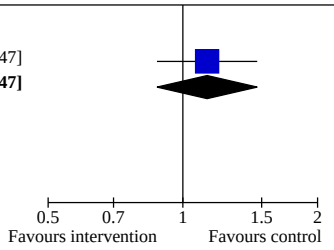
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.18.1 Acute phase						
Gariballa 1998	9	21	11	21	100.0%	0.68 [0.20 , 2.30]
Subtotal (95% CI)		**21**		**21**	**100.0%**	**0.68 [0.20 , 2.30]**
Total events:	9		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.62 (P = 0.54)						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.19. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 19: Complication (pneumonia) during intervention phase

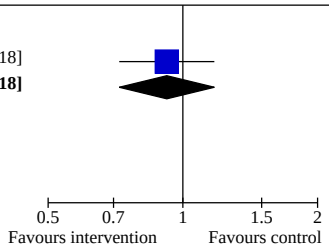
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.19.1 Acute phase						
Dennis 2005a	131	2016	116	2007	100.0%	1.13 [0.88 , 1.47]
Subtotal (95% CI)		**2016**		**2007**	**100.0%**	**1.13 [0.88 , 1.47]**
Total events:	131		116			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.95 (P = 0.34)						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.20. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 20: Complication (urinary tract infection) during intervention phase

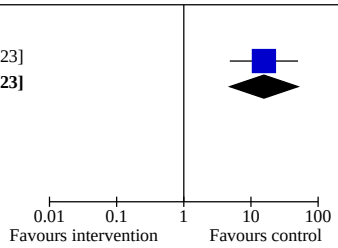
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.20.1 Acute phase						
Dennis 2005a	133	2016	143	2007	100.0%	0.92 [0.72 , 1.18]
Subtotal (95% CI)		**2016**		**2007**	**100.0%**	**0.92 [0.72 , 1.18]**
Total events:	133		143			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.21. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 21: Complication (hyper/hypoglycaemia) during intervention phase

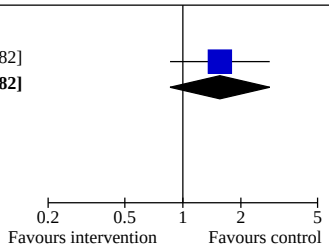
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.21.1 Acute phase						
Dennis 2005a	46	2016	3	2007	100.0%	15.60 [4.84 , 50.23]
Subtotal (95% CI)		**2016**		**2007**	**100.0%**	**15.60 [4.84 , 50.23]**
Total events:	46		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.60 (P < 0.00001)						

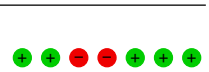


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.22. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 22: Complication (gastrointestinal haemorrhage) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.22.1 Acute phase						
Dennis 2005a	28	2016	18	2007	100.0%	1.56 [0.86 , 2.82]
Subtotal (95% CI)		**2016**		**2007**	**100.0%**	**1.56 [0.86 , 2.82]**
Total events:	28		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.46 (P = 0.15)						

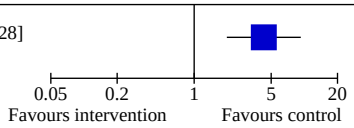




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 1.23. Comparison 1: Oral nutritional supplements (energy and protein) versus no supplements, Outcome 23: Complication (diarrhoea) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Odds Ratio M-H, Fixed, 95% CI
Dennis 2005a	34	2016	8	2007	4.29 [1.98 , 9.28]



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

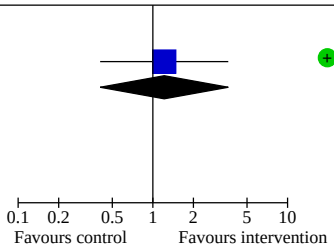
Comparison 2. Oral nutritional supplements (vitamin D) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Disability (modified Rankin Scale 0 to 2, good status) at end of intervention	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1.1 Acute phese	1	53	Odds Ratio (M-H, Fixed, 95% CI)	1.21 [0.41, 3.63]
2.2 Activities of daily living (change in Barthel Index or Functional Independence Measure) at end of intervention phase	2	140	Std. Mean Difference (IV, Random, 95% CI)	0.45 [-0.57, 1.48]
2.2.1 Acute phase	1	100	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.43, 0.36]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.2.2 Subacute phase	1	40	Std. Mean Difference (IV, Random, 95% CI)	1.01 [0.35, 1.68]
2.3 Sensitivity analysis: Activities of daily living (change in Barthel Index or Functional Independence Measure) at end of intervention phase	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.4 Subgroup analysis – type of stroke: activities of daily living (Barthel Index and Functional Independence Measure)	2	140	Std. Mean Difference (IV, Random, 95% CI)	0.45 [-0.57, 1.48]
2.4.1 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	100	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.43, 0.36]
2.4.2 Mixed: ischemic and hemorrhagic stroke	1	40	Std. Mean Difference (IV, Random, 95% CI)	1.01 [0.35, 1.68]
2.5 Nutritional status (change in calf circumference) during intervention phase	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.5.1 Acute phase	1	100	Mean Difference (IV, Random, 95% CI)	0.40 [-0.57, 1.37]
2.6 All-cause mortality at end of intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.6.1 Acute phase	1	53	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.08, 1.09]
2.7 Muscle strength (change in grip strength) during intervention phase	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.7.1 Acute phase	1	100	Mean Difference (IV, Random, 95% CI)	0.50 [-0.85, 1.85]

Analysis 2.1. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 1: Disability (modified Rankin Scale 0 to 2, good status) at end of intervention

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2.1.1 Acute phese						
Gupta 2016	11	25	11	28	100.0%	1.21 [0.41 , 3.63]
Subtotal (95% CI)		**25**		**28**	**100.0%**	**1.21 [0.41 , 3.63]**
Total events:	11		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.35 (P = 0.73)						



Risk of bias legend
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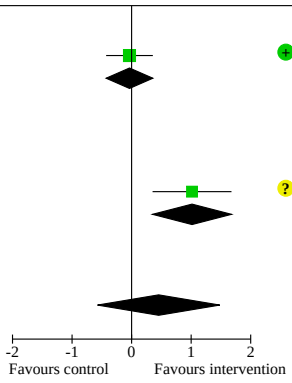
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.2. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 2: Activities of daily living (change in Barthel Index or Functional Independence Measure) at end of intervention phase

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.2.1 Acute phase								
Momosaki 2019[a]	19	14.8	50	19.5	13.1	50	53.4%	-0.04 [-0.43 , 0.36]
Subtotal (95% CI)			**50**			**50**	**53.4%**	**-0.04 [-0.43 , 0.36]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.86)								
2.2.2 Subacute phase								
Torrisi 2021[b]	36.8	20.43	20	16.64	18.47	20	46.6%	1.01 [0.35 , 1.68]
Subtotal (95% CI)			**20**			**20**	**46.6%**	**1.01 [0.35 , 1.68]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.00 (P = 0.003)								
Total (95% CI)			**70**			**70**	**100.0%**	**0.45 [-0.57 , 1.48]**
Heterogeneity: Tau² = 0.47; Chi² = 7.15, df = 1 (P = 0.008); I² = 86%								
Test for overall effect: Z = 0.87 (P = 0.39)								
Test for subgroup differences: Chi² = 7.15, df = 1 (P = 0.008), I² = 86.0%								

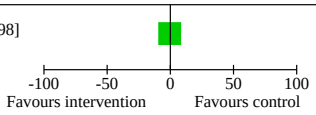


Footnotes
[a]Barthel Index
[b]Functional Independence Measure

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.3. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 3: Sensitivity analysis: Activities of daily living (change in Barthel Index or Functional Independence Measure) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Momosaki 2019	19	14.8	50	19.5	13.1	50	-0.50 [-5.98 , 4.98]	+ + + + + + +

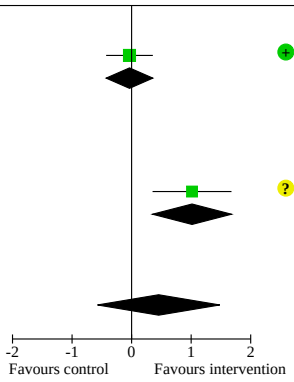


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.4. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 4: Subgroup analysis – type of stroke: activities of daily living (Barthel Index and Functional Independence Measure)

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
2.4.1 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage									
Momosaki 2019[a]	19	14.8	50	19.5	13.1	50	53.4%	-0.04 [-0.43 , 0.36]	+ + + + + + +
Subtotal (95% CI)			**50**			**50**	**53.4%**	**-0.04 [-0.43 , 0.36]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.18 (P = 0.86)									
2.4.2 Mixed: ischemic and hemorrhagic stroke									
Torrisi 2021[b]	36.8	20.43	20	16.64	18.47	20	46.6%	1.01 [0.35 , 1.68]	? ? ? ? + ? −
Subtotal (95% CI)			**20**			**20**	**46.6%**	**1.01 [0.35 , 1.68]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.00 (P = 0.003)									
Total (95% CI)			**70**			**70**	**100.0%**	**0.45 [-0.57 , 1.48]**	
Heterogeneity: Tau² = 0.47; Chi² = 7.15, df = 1 (P = 0.008); I² = 86%									
Test for overall effect: Z = 0.87 (P = 0.39)									
Test for subgroup differences: Chi² = 7.15, df = 1 (P = 0.008), I² = 86.0%									

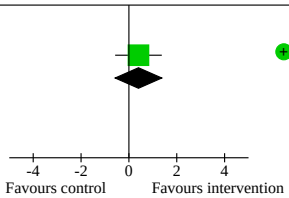


Footnotes
[a]Barthel Index
[b]Functional Independence Measure

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.5. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 5: Nutritional status (change in calf circumference) during intervention phase

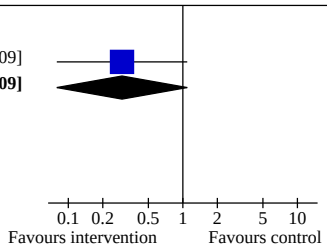
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.5.1 Acute phase								
Momosaki 2019	0.15	2.41	50	-0.25	2.56	50	100.0%	0.40 [-0.57 , 1.37]
Subtotal (95% CI)			**50**			**50**	**100.0%**	**0.40 [-0.57 , 1.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.80 (P = 0.42)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.6. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 6: All-cause mortality at end of intervention phase

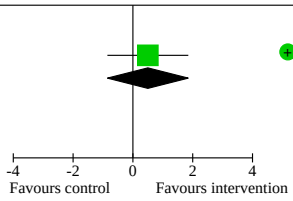
Study or Subgroup	Intervention Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2.6.1 Acute phase						
Gupta 2016	4	25	11	28	100.0%	0.29 [0.08 , 1.09]
Subtotal (95% CI)		**25**		**28**	**100.0%**	**0.29 [0.08 , 1.09]**
Total events:	4		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.83 (P = 0.07)						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 2.7. Comparison 2: Oral nutritional supplements (vitamin D) versus no supplements, Outcome 7: Muscle strength (change in grip strength) during intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2.7.1 Acute phase								
Momosaki 2019	1.3	3.4	50	0.8	3.5	50	100.0%	0.50 [-0.85 , 1.85]
Subtotal (95% CI)			**50**			**50**	**100.0%**	**0.50 [-0.85 , 1.85]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.72 (P = 0.47)								



Risk of bias legend
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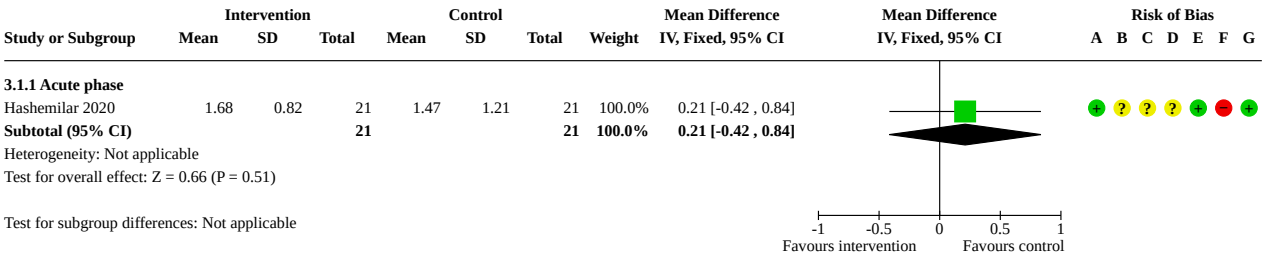
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3. Oral nutritional supplements (protein) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Disability (modified Rankin Scale) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1.1 Acute phase	1	42	Mean Difference (IV, Fixed, 95% CI)	0.21 [-0.42, 0.84]
3.2 Walking capacity (6-minute walk test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.2.1 Chronic phase	1	20	Mean Difference (IV, Fixed, 95% CI)	6.10 [-15.40, 27.60]
3.3 Nutritional status (proportion of skeletal muscle atrophy) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.4 Nutritional status (change in lean mass) during intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.4.1 Chronic phase	1	20	Mean Difference (IV, Fixed, 95% CI)	795.00 [-542.13, 2132.13]
3.5 Quality of life (short-form Neuro-QoL measurement tool, fatigue) at end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.5.1 Acute phase	1	25	Mean Difference (IV, Fixed, 95% CI)	-12.00 [-29.43, 5.43]
3.6 Quality of life (short-form Neuro-QoL measurement tool, lower extremity mobility) at end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.6.1 Acute phase	1	25	Mean Difference (IV, Fixed, 95% CI)	17.00 [1.64, 32.36]
3.7 Quality of life (short-form Neuro-QoL measurement tool, cognition) at end of follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.7.1 Acute phase	1	25	Mean Difference (IV, Fixed, 95% CI)	4.00 [-3.11, 11.11]
3.8 Physical performance (Fugl-Meyer Assessment, lower extremity function) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.8.1 Chronic group	1	20	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.36, 1.16]
3.9 Physical performance (Timed Up & Go test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.9.1 Chronic phase	1	20	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-3.97, 1.77]
3.10 Physical performance (Berg Balance Scale) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.10.1 Chronic phase	1	20	Mean Difference (IV, Fixed, 95% CI)	1.50 [0.17, 2.83]
3.11 Complication (pneumonia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.11.1 Acute phase	1	25	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 4.25]
3.12 Complication (urinary tract infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.12.1 Acute phase	1	25	Odds Ratio (M-H, Fixed, 95% CI)	0.53 [0.10, 2.98]
3.13 Neurological impairment (change in NIHSS score) during intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.13.1 Acute phase	1	42	Mean Difference (IV, Fixed, 95% CI)	-0.58 [-1.73, 0.57]

Analysis 3.1. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 1: Disability (modified Rankin Scale) at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
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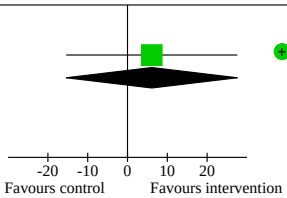
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

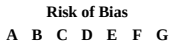
Analysis 3.2. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 2: Walking capacity (6-minute walk test) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.2.1 Chronic phase								
Cheng 2019	20.4	25.7	10	14.3	23.3	10	100.0%	6.10 [-15.40 , 27.60]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**6.10 [-15.40 , 27.60]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)

Test for subgroup differences: Not applicable





Risk of bias legend
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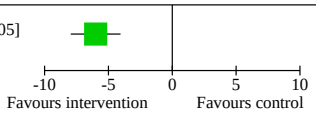
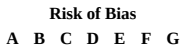
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.3. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 3: Nutritional status (proportion of skeletal muscle atrophy) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Badjatia 2021	6.5	4.1	60	12.5	6.4	58	-6.00 [-7.95 , -4.05]

Test for subgroup differences: Not applicable





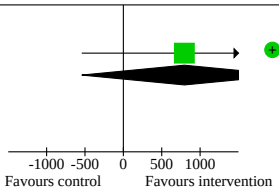
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

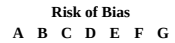
Analysis 3.4. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 4: Nutritional status (change in lean mass) during intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
3.4.1 Chronic phase								
Cheng 2019	455	1764	10	-340	1242	10	100.0%	795.00 [-542.13 , 2132.13]
Subtotal (95% CI)			**10**			**10**	**100.0%**	**795.00 [-542.13 , 2132.13]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.17 (P = 0.24)

Test for subgroup differences: Not applicable

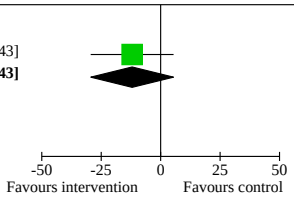




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.5. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 5: Quality of life (short-form NeuroQoL measurement tool, fatigue) at end of follow-up

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.5.1 Acute phase									
Badjatia 2021	29	15	12	41	28	13	100.0%	-12.00 [-29.43 , 5.43]	? ? ? ? + − −
Subtotal (95% CI)			**12**			**13**	**100.0%**	**-12.00 [-29.43 , 5.43]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.35 (P = 0.18)									

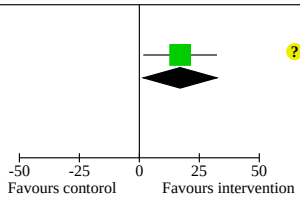


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.6. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 6: Quality of life (short-form NeuroQoL measurement tool, lower extremity mobility) at end of follow-up

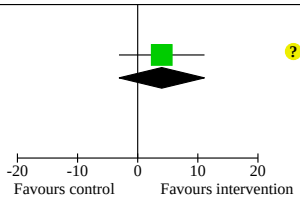
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.6.1 Acute phase									
Badjatia 2021	90	8	12	73	27	13	100.0%	17.00 [1.64 , 32.36]	? ? ? ? + − −
Subtotal (95% CI)			**12**			**13**	**100.0%**	**17.00 [1.64 , 32.36]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.17 (P = 0.03)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.7. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 7: Quality of life (short-form NeuroQoL measurement tool, cognition) at end of follow-up

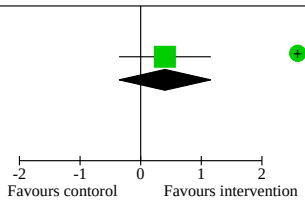
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.7.1 Acute phase									
Badjatia 2021	35	5	12	31	12	13	100.0%	4.00 [-3.11 , 11.11]	? ? ? ? + − −
Subtotal (95% CI)			**12**			**13**	**100.0%**	**4.00 [-3.11 , 11.11]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.10 (P = 0.27)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.8. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 8: Physical performance (Fugl-Meyer Assessment, lower extremity function) at end of intervention phase

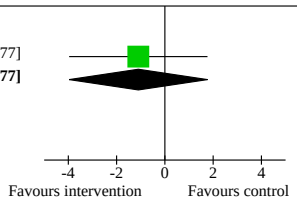
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.8.1 Chronic group									
Cheng 2019	0.6	1	10	0.2	0.7	10	100.0%	0.40 [-0.36 , 1.16]	+ + + + + + +
Subtotal (95% CI)			**10**			**10**	**100.0%**	**0.40 [-0.36 , 1.16]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.04 (P = 0.30)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.9. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 9: Physical performance (Timed Up & Go test) at end of intervention phase

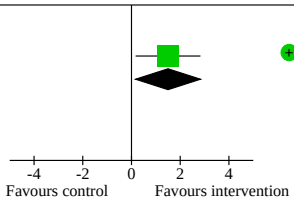
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.9.1 Chronic phase									
Cheng 2019	-1.2	3.6	10	-0.1	2.9	10	100.0%	-1.10 [-3.97 , 1.77]	+ + + + + + +
Subtotal (95% CI)			**10**			**10**	**100.0%**	**-1.10 [-3.97 , 1.77]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.75 (P = 0.45)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.10. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 10: Physical performance (Berg Balance Scale) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
3.10.1 Chronic phase									
Cheng 2019	2.1	1.9	10	0.6	1	10	100.0%	1.50 [0.17 , 2.83]	+ + + + + + +
Subtotal (95% CI)			**10**			**10**	**100.0%**	**1.50 [0.17 , 2.83]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.21 (P = 0.03)									
Test for subgroup differences: Not applicable									

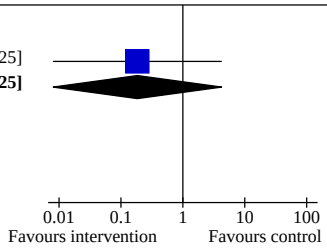


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.11. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 11: Complication (pneumonia) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
3.11.1 Acute phase							
Badjatia 2021	0	12	2	13	100.0%	0.18 [0.01 , 4.25]	? ? ? ? + − −
Subtotal (95% CI)		**12**		**13**	**100.0%**	**0.18 [0.01 , 4.25]**	
Total events:	0		2				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.06 (P = 0.29)



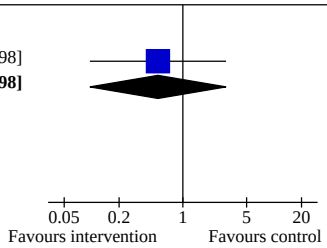
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.12. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 12: Complication (urinary tract infection) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
3.12.1 Acute phase							
Badjatia 2021	3	12	5	13	100.0%	0.53 [0.10 , 2.98]	? ? ? ? + − −
Subtotal (95% CI)		**12**		**13**	**100.0%**	**0.53 [0.10 , 2.98]**	
Total events:	3		5				

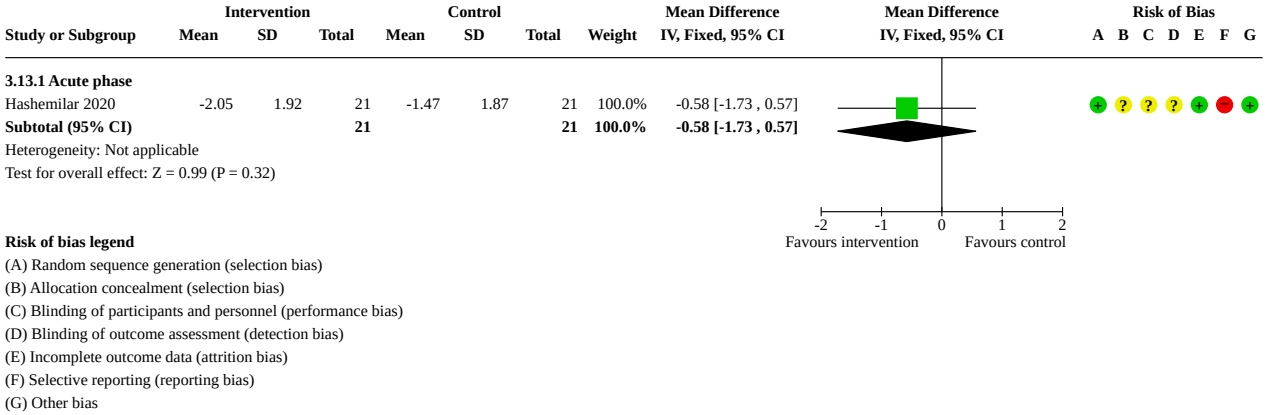
Heterogeneity: Not applicable
Test for overall effect: Z = 0.72 (P = 0.47)

Test for subgroup differences: Not applicable



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 3.13. Comparison 3: Oral nutritional supplements (protein) versus no supplements, Outcome 13: Neurological impairment (change in NIHSS score) during intervention phase



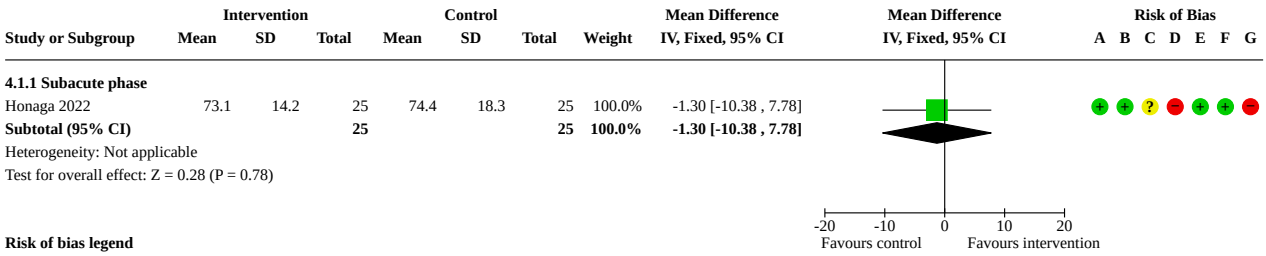
Comparison 4. Oral nutritional supplements (protein and vitamin D) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Activities of daily living (Functional Independence Measure, Motor score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-10.38, 7.78]
4.2 Gait speed (10-metre walk test) at end of intervention phase	2	65	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.21, 0.14]
4.2.1 Subacute phase	1	50	Mean Difference (IV, Random, 95% CI)	-0.09 [-0.30, 0.12]
4.2.2 Chronic phase	1	15	Mean Difference (IV, Random, 95% CI)	0.10 [-0.23, 0.43]
4.3 Walking capacity (6-minute walk test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.3.1 Chronic phase	1	15	Mean Difference (IV, Fixed, 95% CI)	46.00 [-68.51, 160.51]
4.4 Nutritional status (skeletal muscle index) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.4.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.40, 0.28]
4.5 Nutritional status (cross-sectional area of total thigh muscle area: paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.5.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-5.60 [-18.92, 7.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.6 Nutritional status (cross-sectional area of total thigh muscle area: non-paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.6.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-7.40 [-20.64, 5.84]
4.7 Nutritional status (cross-sectional area of normal thigh muscle area: paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.7.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-3.10 [-13.46, 7.26]
4.8 Nutritional status (cross-sectional area of normal thigh muscle area: non-paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.8.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-4.20 [-14.30, 5.90]
4.9 Nutritional status (cross-sectional area of thigh muscle area with fat infiltration: paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.9.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-2.50 [-6.63, 1.63]
4.10 Nutritional status (cross-sectional area of thigh muscle area with fat infiltration: non-paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.10.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-3.10 [-7.49, 1.29]
4.11 Nutritional status (body weight) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.11.1 Chronic phase	1	15	Mean Difference (IV, Fixed, 95% CI)	-2.50 [-10.75, 5.75]
4.12 Muscle strength (grip strength, paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.12.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-3.40 [-8.25, 1.45]
4.13 Muscle strength (grip strength, non-paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.13.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-5.33, 4.73]
4.14 Muscle strength (knee-extensor strength, paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.14.1 Chronic phase	1	15	Mean Difference (IV, Fixed, 95% CI)	2.80 [-7.65, 13.25]
4.15 Muscle strength (knee-extensor strength, non-paretic side) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.15.1 Chronic phase	1	15	Mean Difference (IV, Fixed, 95% CI)	4.70 [-3.96, 13.36]
4.16 Physical performance (30-second chair test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.16.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-2.30 [-6.05, 1.45]
4.17 Physical performance (Timed Up & Go test) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.17.1 Subacute phase	1	50	Mean Difference (IV, Fixed, 95% CI)	-2.30 [-6.05, 1.45]

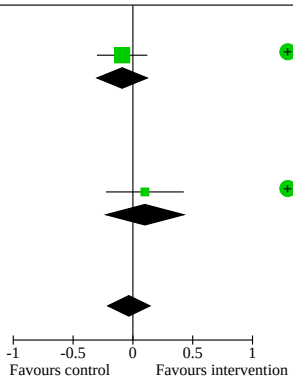
Analysis 4.1. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 1: Activities of daily living (Functional Independence Measure, Motor score) at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.2. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 2: Gait speed (10-metre walk test) at end of intervention phase

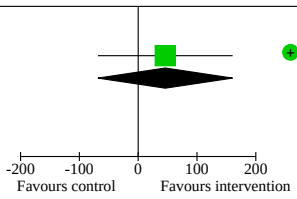
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
4.2.1 Subacute phase									
Honaga 2022	0.6	0.38	25	0.69	0.38	25	70.5%	-0.09 [-0.30 , 0.12]	+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**70.5%**	**-0.09 [-0.30 , 0.12]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.84 (P = 0.40)									
4.2.2 Chronic phase									
Sato 2022	0.95	0.31	8	0.85	0.33	7	29.5%	0.10 [-0.23 , 0.43]	+ + ? ? + + −
Subtotal (95% CI)			**8**			**7**	**29.5%**	**0.10 [-0.23 , 0.43]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.60 (P = 0.55)									
Total (95% CI)			**33**			**32**	**100.0%**	**-0.03 [-0.21 , 0.14]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.92, df = 1 (P = 0.34); I² = 0%									
Test for overall effect: Z = 0.38 (P = 0.71)									
Test for subgroup differences: Chi² = 0.92, df = 1 (P = 0.34), I² = 0%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.3. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 3: Walking capacity (6-minute walk test) at end of intervention phase

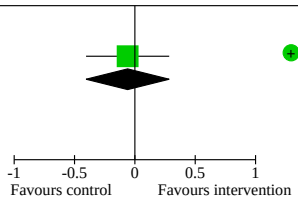
Study or Subgroup	Interventiomn Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.3.1 Chronic phase									
Sato 2022	342	108	8	296	117	7	100.0%	46.00 [-68.51 , 160.51]	+ + ? ? + + −
Subtotal (95% CI)			**8**			**7**	**100.0%**	**46.00 [-68.51 , 160.51]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.79 (P = 0.43)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.4. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 4: Nutritional status (skeletal muscle index) at end of intervention phase

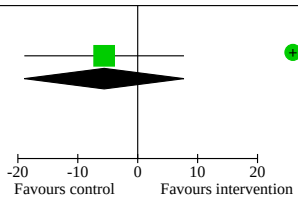
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.4.1 Subacute phase									
Honaga 2022	4.48	0.58	25	4.54	0.66	25	100.0%	-0.06 [-0.40 , 0.28]	+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-0.06 [-0.40 , 0.28]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.34 (P = 0.73)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.5. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 5: Nutritional status (cross-sectional area of total thigh muscle area: paretic side) at end of intervention phase

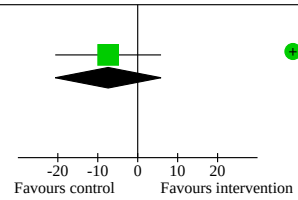
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.5.1 Subacute phase									
Honaga 2022	88.5	20.5	25	94.1	27.1	25	100.0%	-5.60 [-18.92 , 7.72]	+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-5.60 [-18.92 , 7.72]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.82 (P = 0.41)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.6. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 6: Nutritional status (cross-sectional area of total thigh muscle area: non-paretic side) at end of intervention phase

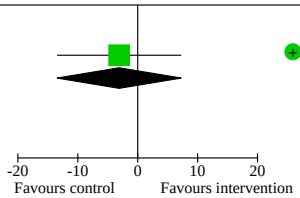
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.6.1 Subacute phase									
Honaga 2022	103.9	20.7	25	111.3	26.7	25	100.0%	-7.40 [-20.64 , 5.84]	+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-7.40 [-20.64 , 5.84]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.10 (P = 0.27)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.7. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 7: Nutritional status (cross-sectional area of normal thigh muscle area: paretic side) at end of intervention phase

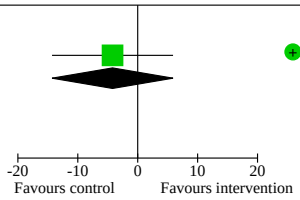
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.7.1 Subacute phase										
Honaga 2022	65.7	16.7	25	68.8	20.5	25	100.0%	-3.10 [-13.46 , 7.26]		+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-3.10 [-13.46 , 7.26]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.59 (P = 0.56)										
Test for subgroup differences: Not applicable										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.8. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 8: Nutritional status (cross-sectional area of normal thigh muscle area: non-paretic side) at end of intervention phase

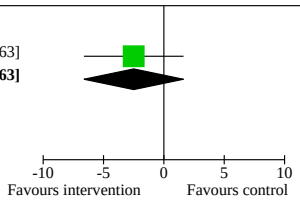
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.8.1 Subacute phase										
Honaga 2022	81.1	16.6	25	85.3	19.7	25	100.0%	-4.20 [-14.30 , 5.90]		+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-4.20 [-14.30 , 5.90]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.82 (P = 0.41)										
Test for subgroup differences: Not applicable										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.9. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 9: Nutritional status (cross-sectional area of thigh muscle area with fat infiltration: paretic side) at end of intervention phase

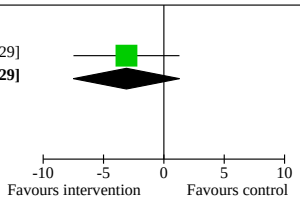
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.9.1 Subacute phase									
Honaga 2022	22.8	6.6	25	25.3	8.2	25	100.0%	-2.50 [-6.63 , 1.63]	+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-2.50 [-6.63 , 1.63]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.19 (P = 0.24)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.10. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 10: Nutritional status (cross-sectional area of thigh muscle area with fat infiltration: non-paretic side) at end of intervention phase

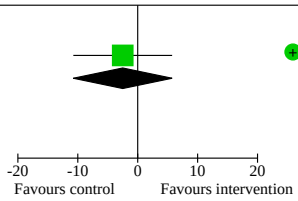
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.10.1 Subacute phase									
Honaga 2022	22.9	6.8	25	26	8.9	25	100.0%	-3.10 [-7.49 , 1.29]	+ + ? − + + −
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-3.10 [-7.49 , 1.29]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.38 (P = 0.17)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.11. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 11: Nutritional status (body weight) at end of intervention phase

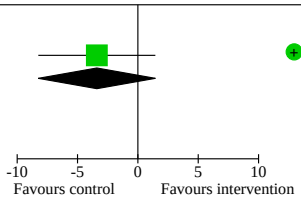
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.11.1 Chronic phase									
Sato 2022	52.9	6.2	8	55.4	9.5	7	100.0%	-2.50 [-10.75 , 5.75]	+ + ? ? + + -
Subtotal (95% CI)			**8**			**7**	**100.0%**	**-2.50 [-10.75 , 5.75]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.59 (P = 0.55)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.12. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 12: Muscle strength (grip strength, paretic side) at end of intervention phase

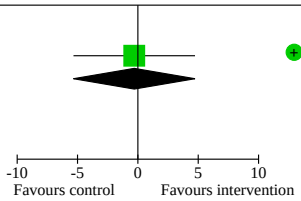
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.12.1 Subacute phase									
Honaga 2022	5.5	7.8	25	8.9	9.6	25	100.0%	-3.40 [-8.25 , 1.45]	+ + ? - + + -
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-3.40 [-8.25 , 1.45]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.37 (P = 0.17)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.13. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 13: Muscle strength (grip strength, non-paretic side) at end of intervention phase

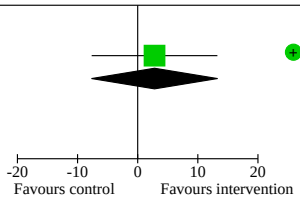
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.13.1 Subacute phase									
Honaga 2022	28.1	8.3	25	28.4	9.8	25	100.0%	-0.30 [-5.33 , 4.73]	+ + ? - + + -
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-0.30 [-5.33 , 4.73]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.12 (P = 0.91)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.14. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 14: Muscle strength (knee-extensor strength, paretic side) at end of intervention phase

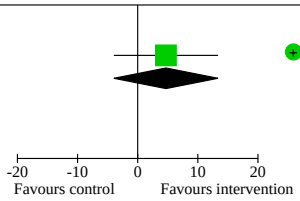
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.14.1 Chronic phase									
Sato 2022	39.6	13.8	8	36.8	5.7	7	100.0%	2.80 [-7.65 , 13.25]	+ + ? ? + + -
Subtotal (95% CI)			**8**			**7**	**100.0%**	**2.80 [-7.65 , 13.25]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.52 (P = 0.60)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.15. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 15: Muscle strength (knee-extensor strength, non-paretic side) at end of intervention phase

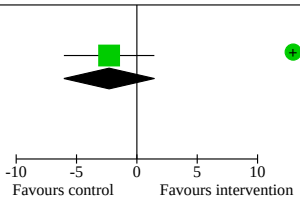
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.15.1 Chronic phase									
Sato 2022	48.9	10.6	8	44.2	6.2	7	100.0%	4.70 [-3.96 , 13.36]	+ + ? ? + + -
Subtotal (95% CI)			**8**			**7**	**100.0%**	**4.70 [-3.96 , 13.36]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.06 (P = 0.29)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

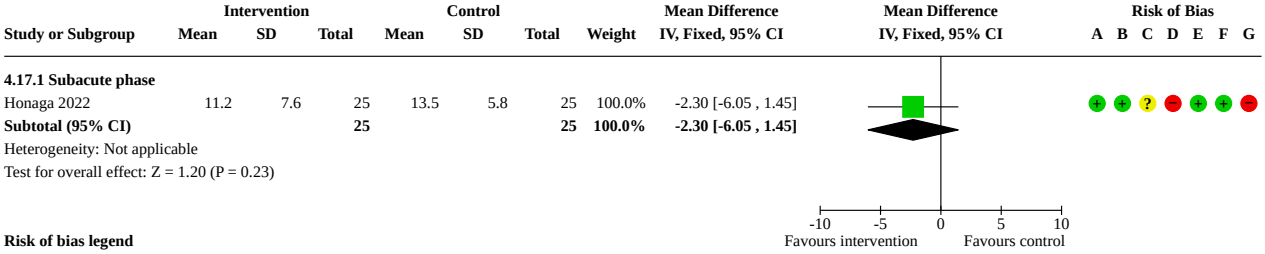
Analysis 4.16. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 16: Physical performance (30-second chair test) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
4.16.1 Subacute phase									
Honaga 2022	11.2	7.6	25	13.5	5.8	25	100.0%	-2.30 [-6.05 , 1.45]	+ + ? - + + -
Subtotal (95% CI)			**25**			**25**	**100.0%**	**-2.30 [-6.05 , 1.45]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.20 (P = 0.23)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 4.17. Comparison 4: Oral nutritional supplements (protein and vitamin D) versus no supplements, Outcome 17: Physical performance (Timed Up & Go test) at end of intervention phase

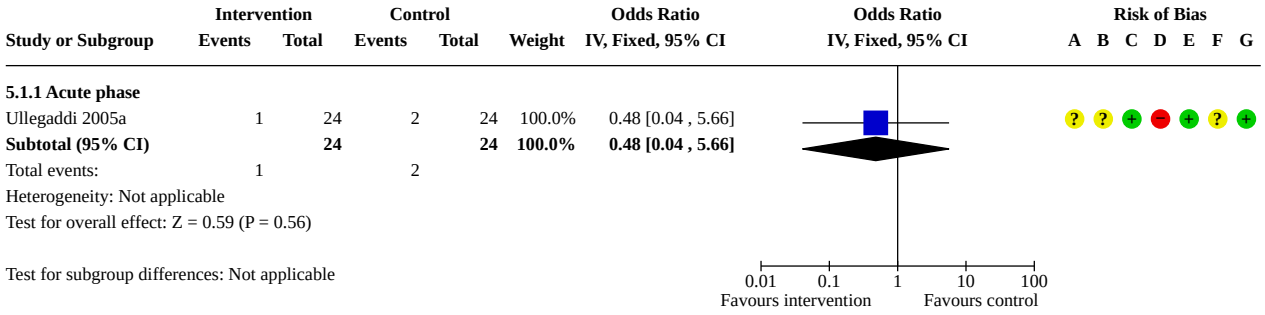


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 5. Oral nutritional supplements (vitamin C and vitamin D) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Stroke recurrence at follow-up	1		Odds Ratio (IV, Fixed, 95% CI)	Subtotals only
5.1.1 Acute phase	1	48	Odds Ratio (IV, Fixed, 95% CI)	0.48 [0.04, 5.66]

Analysis 5.1. Comparison 5: Oral nutritional supplements (vitamin C and vitamin D) versus no supplements, Outcome 1: Stroke recurrence at follow-up

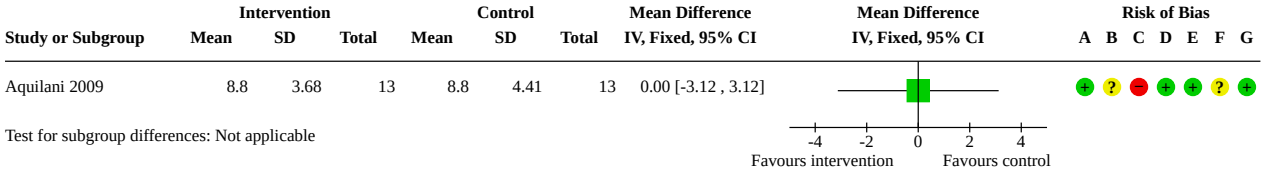


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 6. Oral nutritional supplements (zinc) versus no supplements

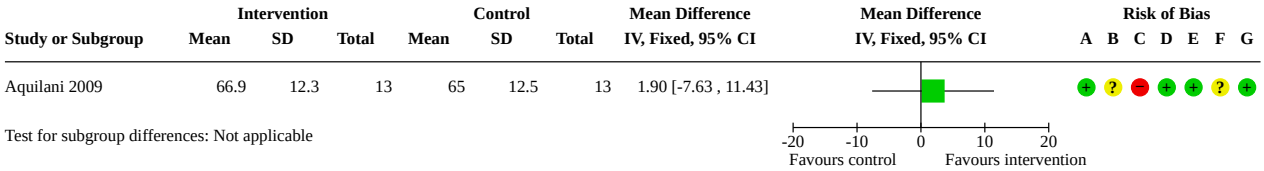
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Neurological impairment (NIHSS score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.2 Nutritional status (body weight) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Analysis 6.1. Comparison 6: Oral nutritional supplements (zinc) versus no supplements, Outcome 1: Neurological impairment (NIHSS score) at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 6.2. Comparison 6: Oral nutritional supplements (zinc) versus no supplements, Outcome 2: Nutritional status (body weight) at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

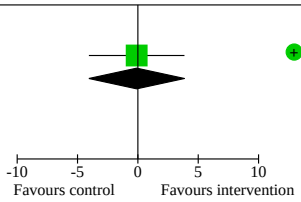
Comparison 7. Oral nutritional supplements (fatty acids) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Quality of life (SF-36, physical component scale) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1.1 Chronic phase	1	102	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-4.06, 3.86]
7.2 Quality of life (SF-36, mental component scale) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.2.1 Chronic phase	1	102	Mean Difference (IV, Fixed, 95% CI)	-1.00 [-5.10, 3.10]

Analysis 7.1. Comparison 7: Oral nutritional supplements (fatty acids) versus no supplements, Outcome 1: Quality of life (SF-36, physical component scale) at end of intervention phase

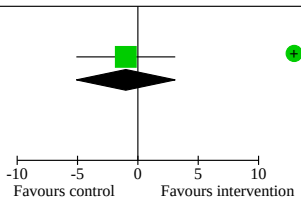
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.1.1 Chronic phase								
Poppitt 2009	44.8	10.1	51	44.9	10.3	51	100.0%	-0.10 [-4.06 , 3.86]
Subtotal (95% CI)			**51**			**51**	**100.0%**	**-0.10 [-4.06 , 3.86]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.05 (P = 0.96)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 7.2. Comparison 7: Oral nutritional supplements (fatty acids) versus no supplements, Outcome 2: Quality of life (SF-36, mental component scale) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
7.2.1 Chronic phase								
Poppitt 2009	48.6	10.3	51	49.6	10.8	51	100.0%	-1.00 [-5.10 , 3.10]
Subtotal (95% CI)			**51**			**51**	**100.0%**	**-1.00 [-5.10 , 3.10]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.48 (P = 0.63)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 8. Early enteral nutrition versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Disability: modified Rankin Scale (mRS 0 to 3, good status) at follow-up	2	1005	Odds Ratio (M-H, Random, 95% CI)	1.37 [0.76, 2.46]
8.1.1 Acute phase	2	1005	Odds Ratio (M-H, Random, 95% CI)	1.37 [0.76, 2.46]
8.2 Activities of daily living (Barthel Index score) at end of intervention phase	2	224	Mean Difference (IV, Random, 95% CI)	0.66 [-1.94, 3.26]
8.2.1 Acute phase	2	224	Mean Difference (IV, Random, 95% CI)	0.66 [-1.94, 3.26]
8.3 Subgroup analysis – type of stroke: activities of daily living (Barthel Index score)	2	224	Mean Difference (IV, Random, 95% CI)	0.66 [-1.94, 3.26]
8.3.1 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	78	Mean Difference (IV, Random, 95% CI)	-0.41 [-2.05, 1.23]
8.3.2 Mixed: ischaemic stroke and intracerebral haemorrhage	1	146	Mean Difference (IV, Random, 95% CI)	2.30 [-0.64, 5.24]
8.4 Activity of daily living (independent) at end of intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.4.1 Acute phase	1	72	Odds Ratio (M-H, Fixed, 95% CI)	1.79 [0.70, 4.60]
8.5 Neurological impairment (NIHSS score) at and of intervention phase	2	224	Mean Difference (IV, Random, 95% CI)	-1.09 [-1.84, -0.34]
8.5.1 Acute phase	2	224	Mean Difference (IV, Random, 95% CI)	-1.09 [-1.84, -0.34]
8.6 Subgroup analysis – type of stroke: neurological impairment (NIHSS)	2	224	Mean Difference (IV, Random, 95% CI)	-1.09 [-1.84, -0.34]
8.6.1 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	78	Mean Difference (IV, Random, 95% CI)	-0.51 [-2.10, 1.08]
8.6.2 Mixed: ischaemic stroke and intracerebral haemorrhage	1	146	Mean Difference (IV, Random, 95% CI)	-1.26 [-2.11, -0.41]
8.7 Neurological improvement (NIHSS score, ≥ 90% decrease) at and of intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.7.1 Acute phase	1	112	Odds Ratio (M-H, Fixed, 95% CI)	3.94 [1.72, 9.00]
8.8 Nutritional status (triceps skinfold thickness) at end of intervention phase	3	286	Mean Difference (IV, Random, 95% CI)	0.98 [0.51, 1.46]

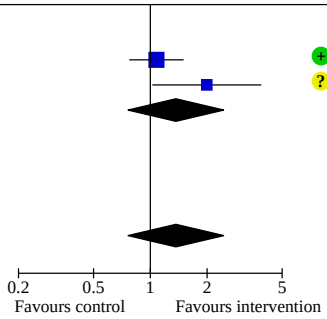
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.8.1 Acute phase	3	286	Mean Difference (IV, Random, 95% CI)	0.98 [0.51, 1.46]
8.9 Subgroup analysis – type of stroke: nutritional status (triceps skinfold thickness)	3	286	Mean Difference (IV, Random, 95% CI)	0.98 [0.51, 1.46]
8.9.1 Ischaemic stroke	1	62	Mean Difference (IV, Random, 95% CI)	1.16 [0.06, 2.26]
8.9.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	78	Mean Difference (IV, Random, 95% CI)	0.97 [0.25, 1.69]
8.9.3 Mixed: ischaemic stroke and intracerebral haemorrhage	1	146	Mean Difference (IV, Random, 95% CI)	0.91 [0.12, 1.70]
8.10 Nutritional status (arm muscular circumference) at end of intervention phase	3	286	Mean Difference (IV, Random, 95% CI)	1.45 [0.68, 2.22]
8.10.1 Acute phase	3	286	Mean Difference (IV, Random, 95% CI)	1.45 [0.68, 2.22]
8.11 Subgroup analysis – type of stroke: nutritional status (arm muscular circumference)	3	286	Mean Difference (IV, Random, 95% CI)	1.45 [0.68, 2.22]
8.11.1 Ischaemic stroke	1	62	Mean Difference (IV, Random, 95% CI)	2.46 [1.40, 3.52]
8.11.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	78	Mean Difference (IV, Random, 95% CI)	0.97 [0.25, 1.69]
8.11.3 Mixed: ischaemic stroke and intracerebral haemorrhage	1	146	Mean Difference (IV, Random, 95% CI)	1.21 [0.52, 1.90]
8.12 Swallowing function (water swallow test score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.12.1 Acute phase	1	112	Mean Difference (IV, Fixed, 95% CI)	-0.29 [-0.44, -0.14]
8.13 All-cause mortality at follow-up	3	1077	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.27, 1.07]
8.13.1 Acute phase	3	1077	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.27, 1.07]
8.14 Subgroup analysis – type of stroke: mortality	3	1077	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.27, 1.07]

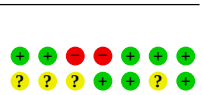
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.14.1 Mixed: ischaemic stroke and intracerebral haemorrhage	2	1005	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.25, 1.36]
8.14.2 Haemorrhagic stroke	1	72	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.09, 1.18]
8.15 Stroke recurrence at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.15.1 Acute phase	1	859	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.33, 1.25]
8.16 Complication (pneumonia) during intervention phase	4	1155	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.24]
8.16.1 Acute phase	4	1155	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.24]
8.17 Subgroup analysis – type of stroke: pneumonia	4	1155	Odds Ratio (M-H, Random, 95% CI)	0.59 [0.28, 1.24]
8.17.1 Mixed: ischaemic stroke and intracerebral haemorrhage	2	1005	Odds Ratio (M-H, Random, 95% CI)	0.95 [0.72, 1.25]
8.17.2 Haemorrhagic stroke	1	72	Odds Ratio (M-H, Random, 95% CI)	0.11 [0.03, 0.42]
8.17.3 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	78	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.31, 2.20]
8.18 Complication (urinary tract infection) during intervention phase	3	1083	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.70, 1.39]
8.18.1 Acute phase	3	1083	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.70, 1.39]
8.19 Subgroup analysis – type of stroke: urinary tract infection	3	1083	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.70, 1.39]
8.19.1 Mixed: ischaemic stroke and intracerebral haemorrhage	2	1005	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.69, 1.39]
8.19.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage	1	78	Odds Ratio (M-H, Random, 95% CI)	1.27 [0.22, 7.41]
8.20 Complication (intestinal infection) during intervention phase	2	218	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.07, 1.37]
8.20.1 Acute phase	2	218	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.07, 1.37]
8.21 Subgroup analysis – type of stroke: intestinal infection	2	218	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.07, 1.37]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.21.1 Mixed: ischaemic stroke and intracerebral haemorrhage	1	146	Odds Ratio (M-H, Random, 95% CI)	0.60 [0.20, 1.78]
8.21.2 Haemorrhagic stroke	1	72	Odds Ratio (M-H, Random, 95% CI)	0.13 [0.03, 0.66]
8.22 Complication (sepsis) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.22.1 Acute phase	1	72	Odds Ratio (M-H, Fixed, 95% CI)	0.20 [0.02, 1.91]
8.23 Complication (pressure sores) during intervention phase	2	1005	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.08, 4.76]
8.23.1 Acute phase	2	1005	Odds Ratio (M-H, Random, 95% CI)	0.63 [0.08, 4.76]
8.24 Complication (vomiting) during intervention phase	1		Odds Ratio (IV, Fixed, 95% CI)	Subtotals only
8.24.1 Acute phase	1	62	Odds Ratio (IV, Fixed, 95% CI)	0.19 [0.05, 0.79]
8.25 Complication (diarrhoea) during intervention phase	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.25.1 Acute phase	2	937	Odds Ratio (M-H, Fixed, 95% CI)	1.35 [0.67, 2.73]
8.26 Complication (gastrointestinal haemorrhage) during intervention phase	3	993	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.47, 1.33]
8.26.1 Acute phase	3	993	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.47, 1.33]
8.27 Subgroup analysis – type of stroke: gastrointestinal haemorrhage	3	993	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.47, 1.33]
8.27.1 Ischaemic stroke	1	62	Odds Ratio (M-H, Fixed, 95% CI)	0.21 [0.06, 0.73]
8.27.2 Haemorrhagic stroke	1	72	Odds Ratio (M-H, Fixed, 95% CI)	0.13 [0.03, 0.66]
8.27.3 Mixed: ischaemic or haemorrhagic stroke	1	859	Odds Ratio (M-H, Fixed, 95% CI)	2.06 [0.99, 4.30]
8.28 Complication (renal problems) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only

Analysis 8.1. Comparison 8: Early enteral nutrition versus control, Outcome 1: Disability: modified Rankin Scale (mRS 0 to 3, good status) at follow-up

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
8.1.1 Acute phase						
Dennis 2005b	90	429	85	430	61.4%	1.08 [0.77 , 1.50]
Zheng 2015	39	75	25	71	38.6%	1.99 [1.03 , 3.88]
Subtotal (95% CI)		**504**		**501**	**100.0%**	**1.37 [0.76 , 2.46]**
Total events:	129		110			
Heterogeneity: Tau² = 0.12; Chi² = 2.63, df = 1 (P = 0.10); I² = 62%						
Test for overall effect: Z = 1.04 (P = 0.30)						
Total (95% CI)		**504**		**501**	**100.0%**	**1.37 [0.76 , 2.46]**
Total events:	129		110			
Heterogeneity: Tau² = 0.12; Chi² = 2.63, df = 1 (P = 0.10); I² = 62%						
Test for overall effect: Z = 1.04 (P = 0.30)						
Test for subgroup differences: Not applicable						

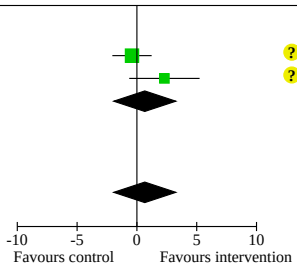


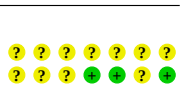


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.2. Comparison 8: Early enteral nutrition versus control, Outcome 2: Activities of daily living (Barthel Index score) at end of intervention phase

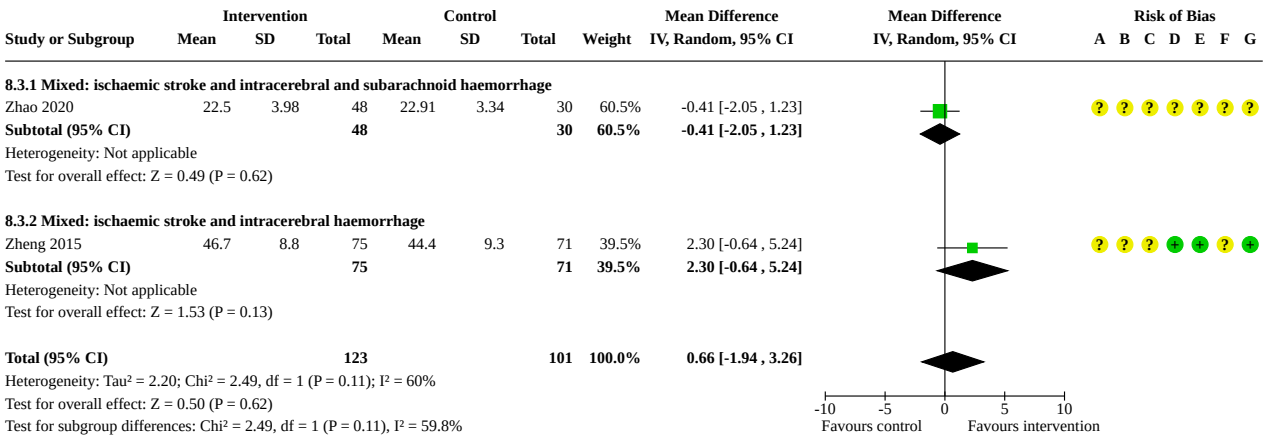
Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
8.2.1 Acute phase								
Zhao 2020	22.5	3.98	48	22.91	3.34	30	60.5%	-0.41 [-2.05 , 1.23]
Zheng 2015	46.7	8.8	75	44.4	9.3	71	39.5%	2.30 [-0.64 , 5.24]
Subtotal (95% CI)			**123**			**101**	**100.0%**	**0.66 [-1.94 , 3.26]**
Heterogeneity: Tau² = 2.20; Chi² = 2.49, df = 1 (P = 0.11); I² = 60%								
Test for overall effect: Z = 0.50 (P = 0.62)								
Total (95% CI)			**123**			**101**	**100.0%**	**0.66 [-1.94 , 3.26]**
Heterogeneity: Tau² = 2.20; Chi² = 2.49, df = 1 (P = 0.11); I² = 60%								
Test for overall effect: Z = 0.50 (P = 0.62)								
Test for subgroup differences: Not applicable								





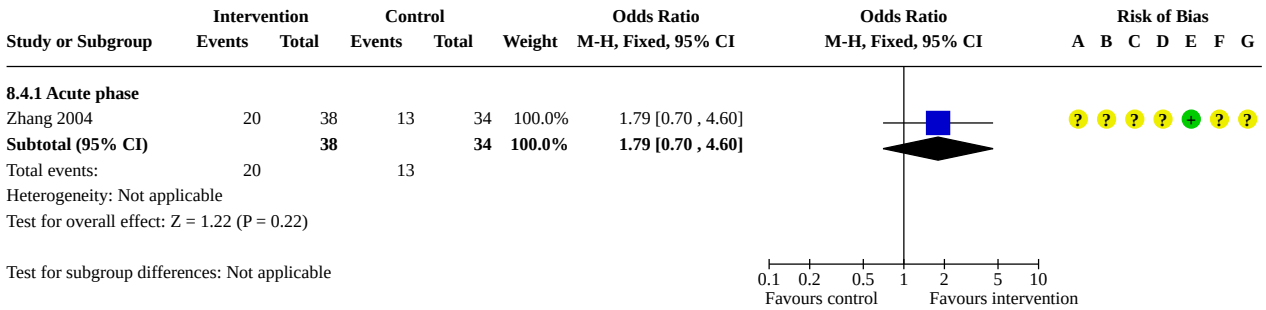
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.3. Comparison 8: Early enteral nutrition versus control, Outcome 3: Subgroup analysis – type of stroke: activities of daily living (Barthel Index score)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

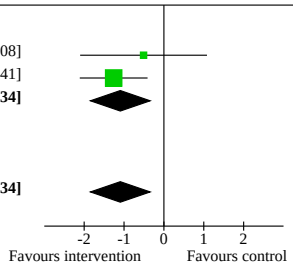
Analysis 8.4. Comparison 8: Early enteral nutrition versus control, Outcome 4: Activity of daily living (independent) at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.5. Comparison 8: Early enteral nutrition versus control, Outcome 5: Neurological impairment (NIHSS score) at and of intervention phase

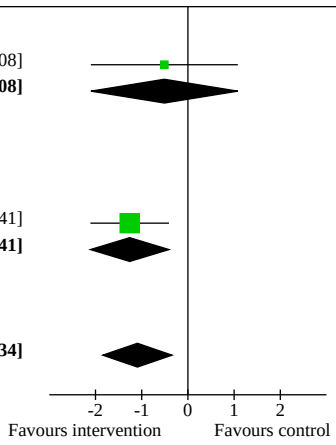
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
8.5.1 Acute phase									
Zhao 2020	12.05	3.62	48	12.56	3.4	30	22.2%	-0.51 [-2.10 , 1.08]	? ? ? ? ? ? ?
Zheng 2015	10.78	2.69	75	12.04	2.55	71	77.8%	-1.26 [-2.11 , -0.41]	? ? ? + + ? +
Subtotal (95% CI)			**123**			**101**	**100.0%**	**-1.09 [-1.84 , -0.34]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 1 (P = 0.41); I² = 0%									
Test for overall effect: Z = 2.86 (P = 0.004)									
Total (95% CI)			**123**			**101**	**100.0%**	**-1.09 [-1.84 , -0.34]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 1 (P = 0.41); I² = 0%									
Test for overall effect: Z = 2.86 (P = 0.004)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

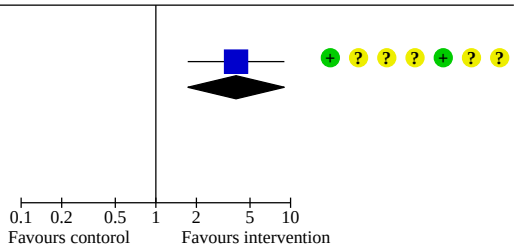
Analysis 8.6. Comparison 8: Early enteral nutrition versus control, Outcome 6: Subgroup analysis – type of stroke: neurological impairment (NIHSS)

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
8.6.1 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage								
Zhao 2020	12.05	3.62	48	12.56	3.4	30	22.2%	-0.51 [-2.10 , 1.08]
Subtotal (95% CI)			**48**			**30**	**22.2%**	**-0.51 [-2.10 , 1.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.63 (P = 0.53)								
8.6.2 Mixed: ischaemic stroke and intracerebral haemorrhage								
Zheng 2015	10.78	2.69	75	12.04	2.55	71	77.8%	-1.26 [-2.11 , -0.41]
Subtotal (95% CI)			**75**			**71**	**77.8%**	**-1.26 [-2.11 , -0.41]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.91 (P = 0.004)								
Total (95% CI)			**123**			**101**	**100.0%**	**-1.09 [-1.84 , -0.34]**
Heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 1 (P = 0.41); I² = 0%								
Test for overall effect: Z = 2.86 (P = 0.004)								
Test for subgroup differences: Chi² = 0.66, df = 1 (P = 0.41), I² = 0%								



Analysis 8.7. Comparison 8: Early enteral nutrition versus control, Outcome 7: Neurological improvement (NIHSS score, ≥ 90% decrease) at and of intervention phase

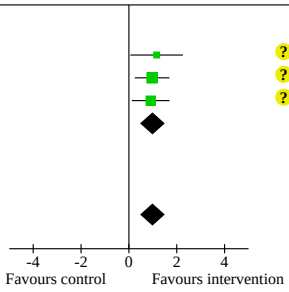
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
8.7.1 Acute phase						
Li 2016	44	56	27	56	100.0%	3.94 [1.72 , 9.00]
Subtotal (95% CI)		**56**		**56**	**100.0%**	**3.94 [1.72 , 9.00]**
Total events:	44		27			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.25 (P = 0.001)						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

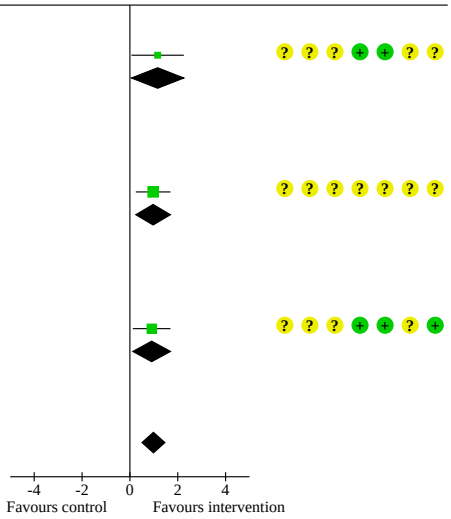
Analysis 8.8. Comparison 8: Early enteral nutrition versus control, Outcome 8: Nutritional status (triceps skinfold thickness) at end of intervention phase

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
8.8.1 Acute phase								
Ouyang 2003	13.51	2.27	31	12.35	2.13	31	19.1%	1.16 [0.06 , 2.26]
Zhao 2020	15.75	2.05	48	14.78	1.21	30	43.8%	0.97 [0.25 , 1.69]
Zheng 2015	13.69	2.33	75	12.78	2.51	71	37.1%	0.91 [0.12 , 1.70]
Subtotal (95% CI)			**154**			**132**	**100.0%**	**0.98 [0.51 , 1.46]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.93); I² = 0%								
Test for overall effect: Z = 4.03 (P < 0.0001)								
Total (95% CI)			**154**			**132**	**100.0%**	**0.98 [0.51 , 1.46]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.93); I² = 0%								
Test for overall effect: Z = 4.03 (P < 0.0001)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

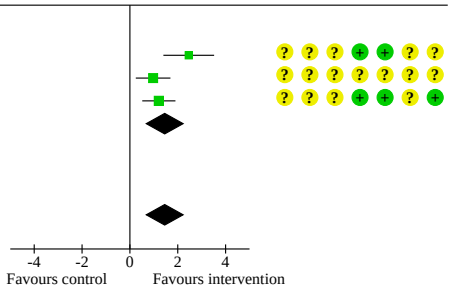
Analysis 8.9. Comparison 8: Early enteral nutrition versus control, Outcome 9: Subgroup analysis – type of stroke: nutritional status (triceps skinfold thickness)



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
8.9.1 Ischaemic stroke									
Ouyang 2003	13.51	2.27	31	12.35	2.13	31	19.1%	1.16 [0.06 , 2.26]	? ? ? + + ? ?
Subtotal (95% CI)			**31**			**31**	**19.1%**	**1.16 [0.06 , 2.26]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.07 (P = 0.04)									
8.9.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage									
Zhao 2020	15.75	2.05	48	14.78	1.21	30	43.8%	0.97 [0.25 , 1.69]	? ? ? ? ? ? ?
Subtotal (95% CI)			**48**			**30**	**43.8%**	**0.97 [0.25 , 1.69]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.63 (P = 0.009)									
8.9.3 Mixed: ischaemic stroke and intracerebral haemorrhage									
Zheng 2015	13.69	2.33	75	12.78	2.51	71	37.1%	0.91 [0.12 , 1.70]	? ? ? + + ? +
Subtotal (95% CI)			**75**			**71**	**37.1%**	**0.91 [0.12 , 1.70]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.27 (P = 0.02)									
Total (95% CI)			**154**			**132**	**100.0%**	**0.98 [0.51 , 1.46]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.93); I² = 0%									
Test for overall effect: Z = 4.03 (P < 0.0001)									
Test for subgroup differences: Chi² = 0.13, df = 2 (P = 0.93), I² = 0%									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

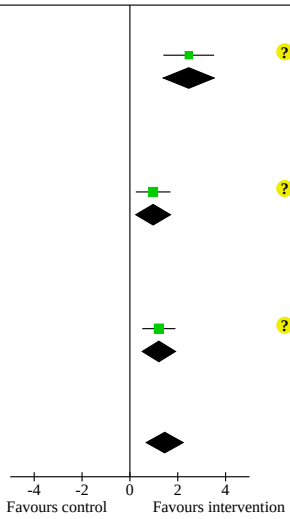
Analysis 8.10. Comparison 8: Early enteral nutrition versus control, Outcome 10: Nutritional status (arm muscular circumference) at end of intervention phase



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
8.10.1 Acute phase									
Ouyang 2003	21.35	2.43	31	18.89	1.78	31	26.5%	2.46 [1.40 , 3.52]	? ? ? + + ? ?
Zhao 2020	15.75	2.05	48	14.78	1.21	30	36.3%	0.97 [0.25 , 1.69]	? ? ? ? ? ? ?
Zheng 2015	21.32	2.29	75	20.11	1.98	71	37.2%	1.21 [0.52 , 1.90]	? ? ? + + ? +
Subtotal (95% CI)			**154**			**132**	**100.0%**	**1.45 [0.68 , 2.22]**	
Heterogeneity: Tau² = 0.29; Chi² = 5.42, df = 2 (P = 0.07); I² = 63%									
Test for overall effect: Z = 3.70 (P = 0.0002)									
Total (95% CI)			**154**			**132**	**100.0%**	**1.45 [0.68 , 2.22]**	
Heterogeneity: Tau² = 0.29; Chi² = 5.42, df = 2 (P = 0.07); I² = 63%									
Test for overall effect: Z = 3.70 (P = 0.0002)									
Test for subgroup differences: Not applicable									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

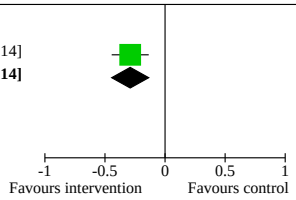
Analysis 8.11. Comparison 8: Early enteral nutrition versus control, Outcome 11: Subgroup analysis – type of stroke: nutritional status (arm muscular circumference)



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
8.11.1 Ischaemic stroke									
Ouyang 2003	21.35	2.43	31	18.89	1.78	31	26.5%	2.46 [1.40 , 3.52]	? ? ? + + ? ?
Subtotal (95% CI)			**31**			**31**	**26.5%**	**2.46 [1.40 , 3.52]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 4.55 (P < 0.00001)									
8.11.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage									
Zhao 2020	15.75	2.05	48	14.78	1.21	30	36.3%	0.97 [0.25 , 1.69]	? ? ? ? ? ? ?
Subtotal (95% CI)			**48**			**30**	**36.3%**	**0.97 [0.25 , 1.69]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.63 (P = 0.009)									
8.11.3 Mixed: ischaemic stroke and intracerebral haemorrhage									
Zheng 2015	21.32	2.29	75	20.11	1.98	71	37.2%	1.21 [0.52 , 1.90]	? ? ? + + ? +
Subtotal (95% CI)			**75**			**71**	**37.2%**	**1.21 [0.52 , 1.90]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.42 (P = 0.0006)									
Total (95% CI)			**154**			**132**	**100.0%**	**1.45 [0.68 , 2.22]**	
Heterogeneity: Tau² = 0.29; Chi² = 5.42, df = 2 (P = 0.07); I² = 63%									
Test for overall effect: Z = 3.70 (P = 0.0002)									
Test for subgroup differences: Chi² = 5.42, df = 2 (P = 0.07), I² = 63.1%									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.12. Comparison 8: Early enteral nutrition versus control, Outcome 12: Swallowing function (water swallow test score) at end of intervention phase

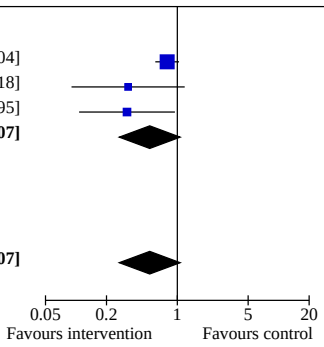


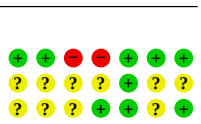
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
8.12.1 Acute phase									
Li 2016	2.25	0.34	56	2.54	0.48	56	100.0%	-0.29 [-0.44 , -0.14]	+ ? ? ? + ? ?
Subtotal (95% CI)			**56**			**56**	**100.0%**	**-0.29 [-0.44 , -0.14]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.69 (P = 0.0002)									
Test for subgroup differences: Not applicable									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.13. Comparison 8: Early enteral nutrition versus control, Outcome 13: All-cause mortality at follow-up

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
8.13.1 Acute phase						
Dennis 2005b	182	429	207	430	56.0%	0.79 [0.61 , 1.04]
Zhang 2004	4	38	9	34	19.7%	0.33 [0.09 , 1.18]
Zheng 2015	5	75	13	71	24.3%	0.32 [0.11 , 0.95]
Subtotal (95% CI)		**542**		**535**	**100.0%**	**0.53 [0.27 , 1.07]**
Total events:	191		229			
Heterogeneity: Tau² = 0.20; Chi² = 4.10, df = 2 (P = 0.13); I² = 51%						
Test for overall effect: Z = 1.78 (P = 0.08)						
Total (95% CI)		**542**		**535**	**100.0%**	**0.53 [0.27 , 1.07]**
Total events:	191		229			
Heterogeneity: Tau² = 0.20; Chi² = 4.10, df = 2 (P = 0.13); I² = 51%						
Test for overall effect: Z = 1.78 (P = 0.08)						
Test for subgroup differences: Not applicable						

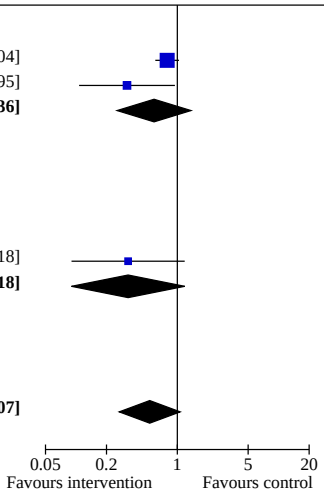


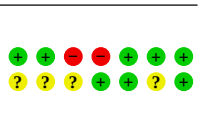


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.14. Comparison 8: Early enteral nutrition versus control, Outcome 14: Subgroup analysis – type of stroke: mortality

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
8.14.1 Mixed: ischaemic stroke and intracerebral haemorrhage						
Dennis 2005b	182	429	207	430	56.0%	0.79 [0.61 , 1.04]
Zheng 2015	5	75	13	71	24.3%	0.32 [0.11 , 0.95]
Subtotal (95% CI)		**504**		**501**	**80.3%**	**0.59 [0.25 , 1.36]**
Total events:	187		220			
Heterogeneity: Tau² = 0.25; Chi² = 2.55, df = 1 (P = 0.11); I² = 61%						
Test for overall effect: Z = 1.24 (P = 0.22)						
8.14.2 Haemorrhagic stroke						
Zhang 2004	4	38	9	34	19.7%	0.33 [0.09 , 1.18]
Subtotal (95% CI)		**38**		**34**	**19.7%**	**0.33 [0.09 , 1.18]**
Total events:	4		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.70 (P = 0.09)						
Total (95% CI)		**542**		**535**	**100.0%**	**0.53 [0.27 , 1.07]**
Total events:	191		229			
Heterogeneity: Tau² = 0.20; Chi² = 4.10, df = 2 (P = 0.13); I² = 51%						
Test for overall effect: Z = 1.78 (P = 0.08)						
Test for subgroup differences: Chi² = 0.57, df = 1 (P = 0.45), I² = 0%						

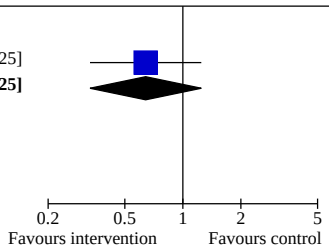


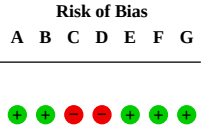


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.15. Comparison 8: Early enteral nutrition versus control, Outcome 15: Stroke recurrence at follow-up

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
8.15.1 Acute phase						
Dennis 2005b	15	429	23	430	100.0%	0.64 [0.33 , 1.25]
Subtotal (95% CI)		**429**		**430**	**100.0%**	**0.64 [0.33 , 1.25]**
Total events:	15		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.31 (P = 0.19)						

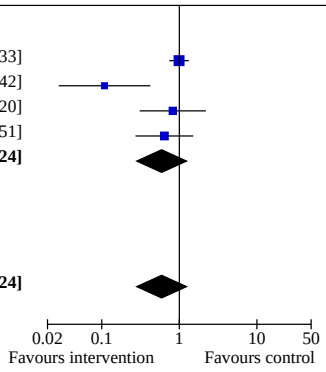


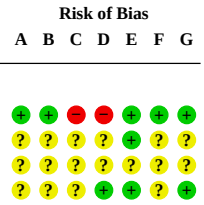


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.16. Comparison 8: Early enteral nutrition versus control, Outcome 16: Complication (pneumonia) during intervention phase

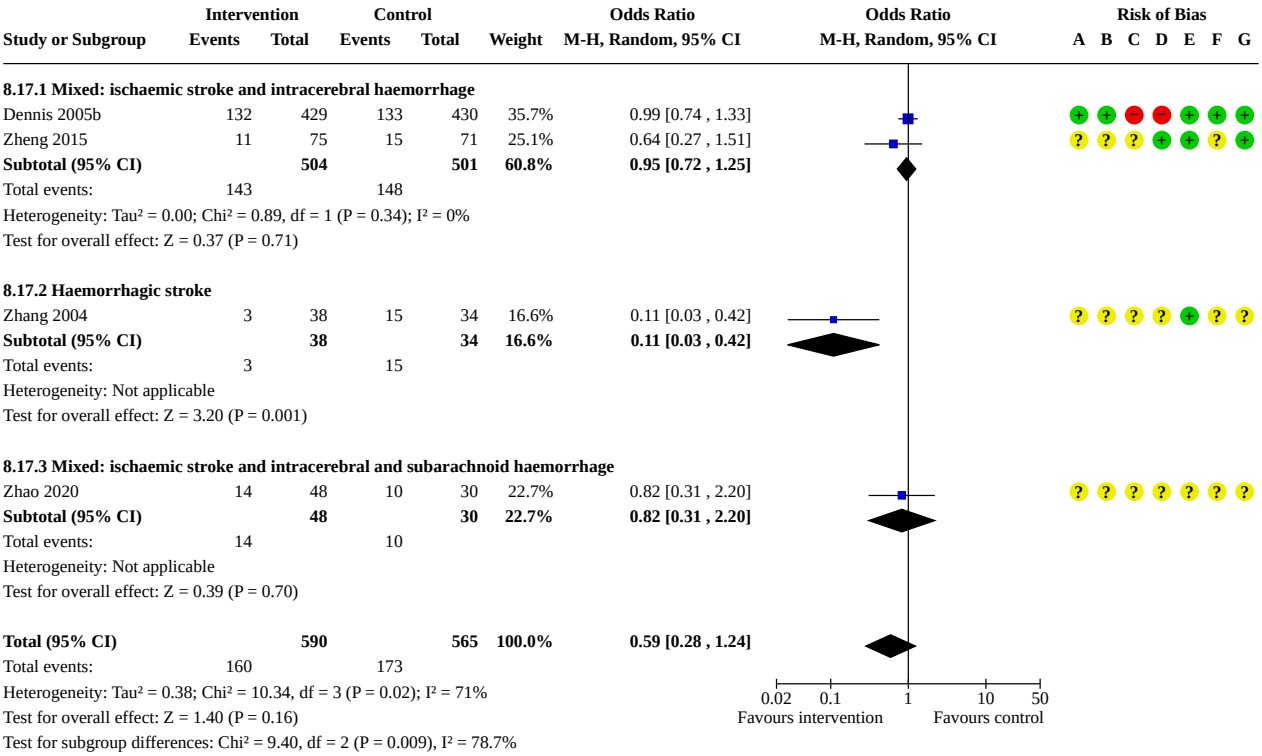
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
8.16.1 Acute phase						
Dennis 2005b	132	429	133	430	35.7%	0.99 [0.74 , 1.33]
Zhang 2004	3	38	15	34	16.6%	0.11 [0.03 , 0.42]
Zhao 2020	14	48	10	30	22.7%	0.82 [0.31 , 2.20]
Zheng 2015	11	75	15	71	25.1%	0.64 [0.27 , 1.51]
Subtotal (95% CI)		**590**		**565**	**100.0%**	**0.59 [0.28 , 1.24]**
Total events:	160		173			
Heterogeneity: Tau² = 0.38; Chi² = 10.34, df = 3 (P = 0.02); I² = 71%						
Test for overall effect: Z = 1.40 (P = 0.16)						
Total (95% CI)		**590**		**565**	**100.0%**	**0.59 [0.28 , 1.24]**
Total events:	160		173			
Heterogeneity: Tau² = 0.38; Chi² = 10.34, df = 3 (P = 0.02); I² = 71%						
Test for overall effect: Z = 1.40 (P = 0.16)						
Test for subgroup differences: Not applicable						





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.17. Comparison 8: Early enteral nutrition versus control, Outcome 17: Subgroup analysis – type of stroke: pneumonia

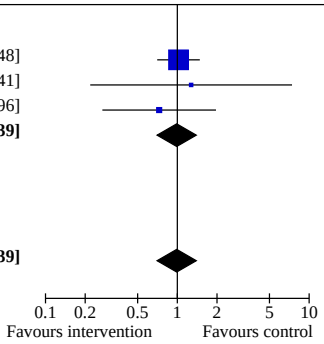


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.18. Comparison 8: Early enteral nutrition versus control, Outcome 18: Complication (urinary tract infection) during intervention phase

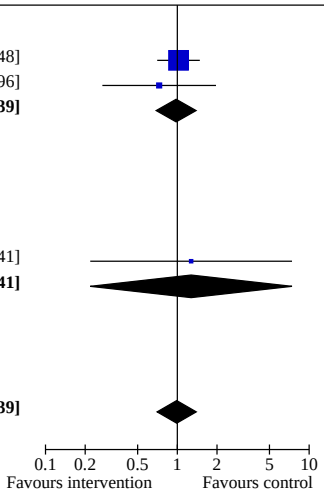
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
8.18.1 Acute phase							
Dennis 2005b	66	429	65	430	84.4%	1.02 [0.70 , 1.48]	+ + − − + + +
Zhao 2020	4	48	2	30	3.8%	1.27 [0.22 , 7.41]	? ? ? ? ? ? ?
Zheng 2015	8	75	10	71	11.9%	0.73 [0.27 , 1.96]	? ? ? + + ? +
Subtotal (95% CI)		**552**		**531**	**100.0%**	**0.99 [0.70 , 1.39]**	
Total events:	78		77				
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 2 (P = 0.79); I² = 0%							
Test for overall effect: Z = 0.06 (P = 0.95)							
Total (95% CI)		**552**		**531**	**100.0%**	**0.99 [0.70 , 1.39]**	
Total events:	78		77				
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 2 (P = 0.79); I² = 0%							
Test for overall effect: Z = 0.06 (P = 0.95)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

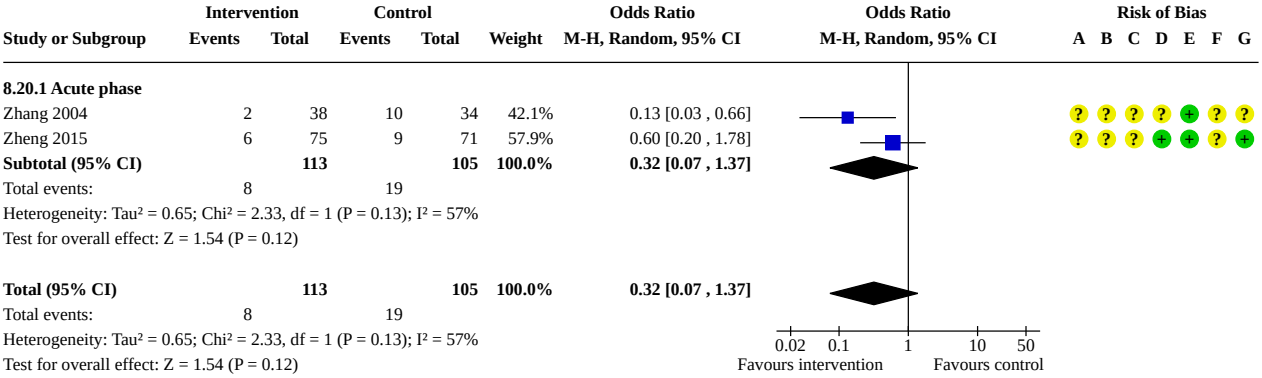
Analysis 8.19. Comparison 8: Early enteral nutrition versus control, Outcome 19: Subgroup analysis – type of stroke: urinary tract infection

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
8.19.1 Mixed: ischaemic stroke and intracerebral haemorrhage							
Dennis 2005b	66	429	65	430	84.4%	1.02 [0.70 , 1.48]	+ + − − + + +
Zheng 2015	8	75	10	71	11.9%	0.73 [0.27 , 1.96]	? ? ? + + ? +
Subtotal (95% CI)		**504**		**501**	**96.2%**	**0.98 [0.69 , 1.39]**	
Total events:	74		75				
Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 1 (P = 0.53); I² = 0%							
Test for overall effect: Z = 0.12 (P = 0.91)							
8.19.2 Mixed: ischaemic stroke and intracerebral and subarachnoid haemorrhage							
Zhao 2020	4	48	2	30	3.8%	1.27 [0.22 , 7.41]	? ? ? ? ? ? ?
Subtotal (95% CI)		**48**		**30**	**3.8%**	**1.27 [0.22 , 7.41]**	
Total events:	4		2				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.27 (P = 0.79)							
Total (95% CI)		**552**		**531**	**100.0%**	**0.99 [0.70 , 1.39]**	
Total events:	78		77				
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 2 (P = 0.79); I² = 0%							
Test for overall effect: Z = 0.06 (P = 0.95)							
Test for subgroup differences: Chi² = 0.08, df = 1 (P = 0.77), I² = 0%							



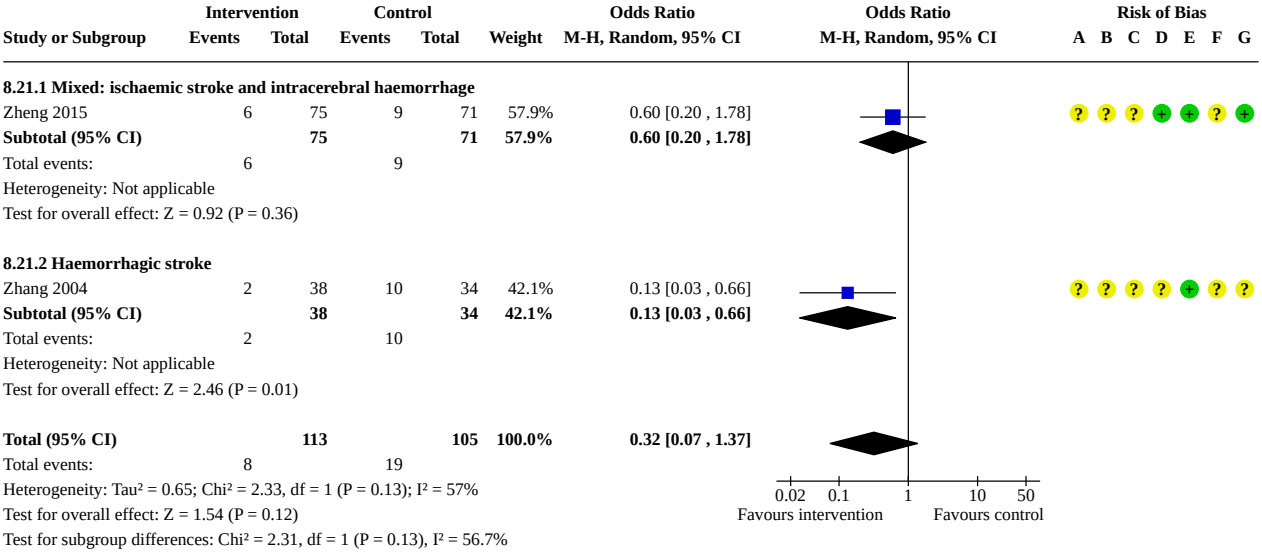
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.20. Comparison 8: Early enteral nutrition versus control, Outcome 20: Complication (intestinal infection) during intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

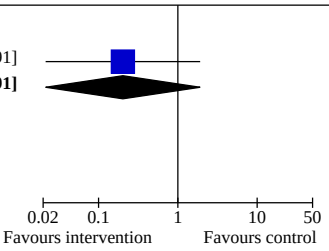
Analysis 8.21. Comparison 8: Early enteral nutrition versus control, Outcome 21: Subgroup analysis – type of stroke: intestinal infection



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.22. Comparison 8: Early enteral nutrition versus control, Outcome 22: Complication (sepsis) during intervention phase

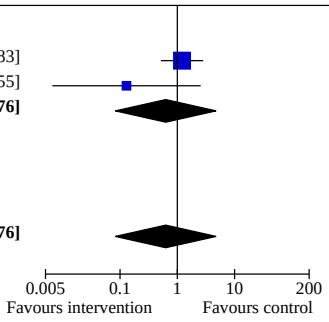
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
8.22.1 Acute phase								
Zhang 2004	1	38	4	34	100.0%	0.20 [0.02 , 1.91]		? ? ? ? + ? ?
Subtotal (95% CI)		**38**		**34**	**100.0%**	**0.20 [0.02 , 1.91]**		
Total events:	1		4					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.39 (P = 0.16)								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.23. Comparison 8: Early enteral nutrition versus control, Outcome 23: Complication (pressure sores) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
8.23.1 Acute phase								
Dennis 2005b	12	429	10	430	70.6%	1.21 [0.52 , 2.83]		+ + − − + + +
Zheng 2015	0	75	3	71	29.4%	0.13 [0.01 , 2.55]		? ? ? + + ? +
Subtotal (95% CI)		**504**		**501**	**100.0%**	**0.63 [0.08 , 4.76]**		
Total events:	12		13					
Heterogeneity: Tau² = 1.32; Chi² = 2.06, df = 1 (P = 0.15); I² = 51%								
Test for overall effect: Z = 0.45 (P = 0.65)								
Total (95% CI)		**504**		**501**	**100.0%**	**0.63 [0.08 , 4.76]**		
Total events:	12		13					
Heterogeneity: Tau² = 1.32; Chi² = 2.06, df = 1 (P = 0.15); I² = 51%								
Test for overall effect: Z = 0.45 (P = 0.65)								
Test for subgroup differences: Not applicable								



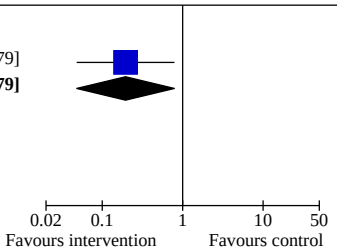
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.24. Comparison 8: Early enteral nutrition versus control, Outcome 24: Complication (vomiting) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio IV, Fixed, 95% CI
8.24.1 Acute phase						
Ouyang 2003	3	31	11	31	100.0%	0.19 [0.05 , 0.79]
Subtotal (95% CI)		**31**		**31**	**100.0%**	**0.19 [0.05 , 0.79]**
Total events:	3		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.29 (P = 0.02)

Test for subgroup differences: Not applicable



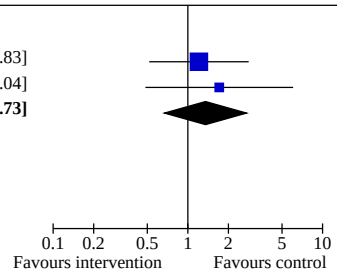
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.25. Comparison 8: Early enteral nutrition versus control, Outcome 25: Complication (diarrhoea) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
8.25.1 Acute phase						
Dennis 2005b	12	429	10	430	71.4%	1.21 [0.52 , 2.83]
Zhao 2020	10	48	4	30	28.6%	1.71 [0.48 , 6.04]
Subtotal (95% CI)		**477**		**460**	**100.0%**	**1.35 [0.67 , 2.73]**
Total events:	22		14			

Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.84 (P = 0.40)

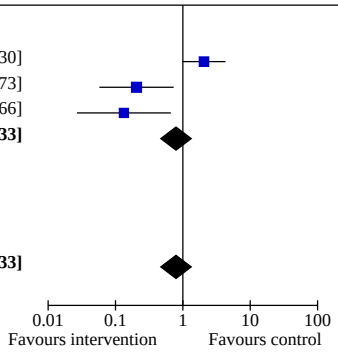
Test for subgroup differences: Not applicable

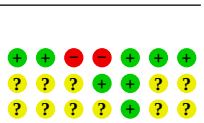


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.26. Comparison 8: Early enteral nutrition versus control, Outcome 26: Complication (gastrointestinal haemorrhage) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
8.26.1 Acute phase						
Dennis 2005b	22	429	11	430	32.8%	2.06 [0.99 , 4.30]
Ouyang 2003	4	31	13	31	35.7%	0.21 [0.06 , 0.73]
Zhang 2004	2	38	10	34	31.5%	0.13 [0.03 , 0.66]
Subtotal (95% CI)		**498**		**495**	**100.0%**	**0.79 [0.47 , 1.33]**
Total events:	28		34			
Heterogeneity: Chi² = 15.56, df = 2 (P = 0.0004); I² = 87%						
Test for overall effect: Z = 0.88 (P = 0.38)						
Total (95% CI)		**498**		**495**	**100.0%**	**0.79 [0.47 , 1.33]**
Total events:	28		34			
Heterogeneity: Chi² = 15.56, df = 2 (P = 0.0004); I² = 87%						
Test for overall effect: Z = 0.88 (P = 0.38)						
Test for subgroup differences: Not applicable						

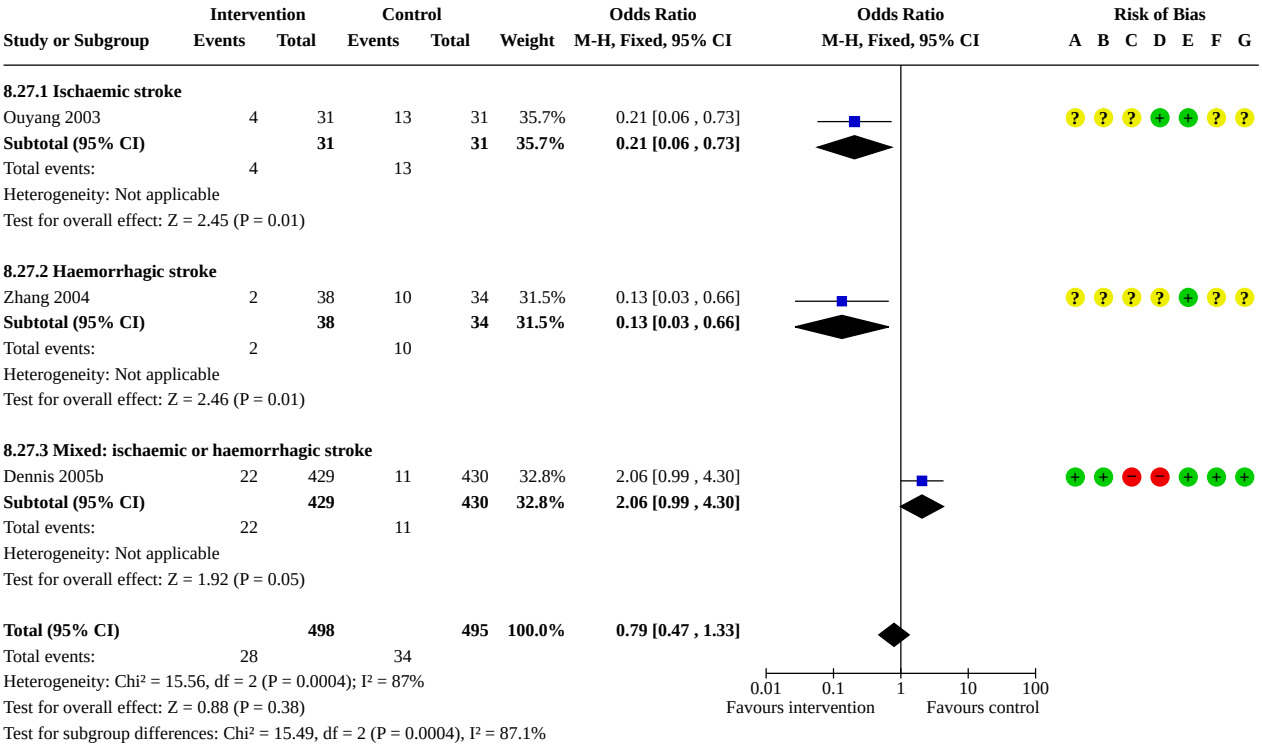




Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

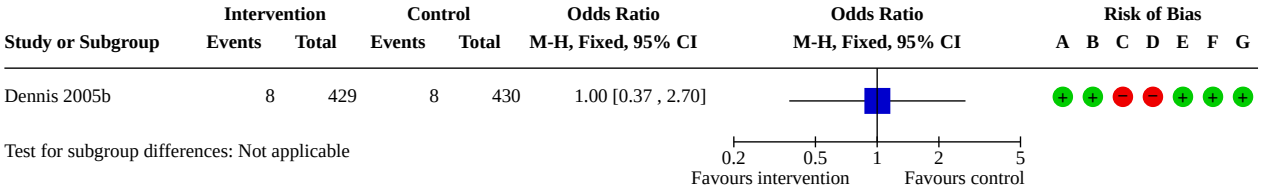
Analysis 8.27. Comparison 8: Early enteral nutrition versus control, Outcome 27: Subgroup analysis – type of stroke: gastrointestinal haemorrhage



Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
8.27.1 Ischaemic stroke						
Ouyang 2003	4	31	13	31	35.7%	0.21 [0.06 , 0.73]
Subtotal (95% CI)		**31**		**31**	**35.7%**	**0.21 [0.06 , 0.73]**
Total events:	4		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.45 (P = 0.01)						
8.27.2 Haemorrhagic stroke						
Zhang 2004	2	38	10	34	31.5%	0.13 [0.03 , 0.66]
Subtotal (95% CI)		**38**		**34**	**31.5%**	**0.13 [0.03 , 0.66]**
Total events:	2		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.46 (P = 0.01)						
8.27.3 Mixed: ischaemic or haemorrhagic stroke						
Dennis 2005b	22	429	11	430	32.8%	2.06 [0.99 , 4.30]
Subtotal (95% CI)		**429**		**430**	**32.8%**	**2.06 [0.99 , 4.30]**
Total events:	22		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.92 (P = 0.05)						
Total (95% CI)		**498**		**495**	**100.0%**	**0.79 [0.47 , 1.33]**
Total events:	28		34			
Heterogeneity: Chi² = 15.56, df = 2 (P = 0.0004); I² = 87%						
Test for overall effect: Z = 0.88 (P = 0.38)						
Test for subgroup differences: Chi² = 15.49, df = 2 (P = 0.0004), I² = 87.1%						

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 8.28. Comparison 8: Early enteral nutrition versus control, Outcome 28: Complication (renal problems) during intervention phase



Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Odds Ratio M-H, Fixed, 95% CI
Dennis 2005b	8	429	8	430	1.00 [0.37 , 2.70]
Test for subgroup differences: Not applicable					

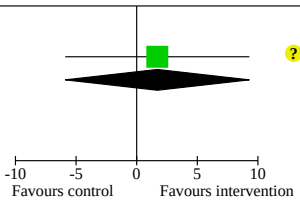
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 9. Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Nutritional status (arm muscular circumference) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1.1 Acute phase	1	54	Mean Difference (IV, Fixed, 95% CI)	1.70 [-5.89, 9.29]
9.2 Nutritional status (triceps skinfold thickness) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.2.1 Acute phase	1	54	Mean Difference (IV, Fixed, 95% CI)	1.70 [0.21, 3.19]
9.3 Complication (pneumonia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.3.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.41 [0.11, 1.59]
9.4 Complication (urinary tract infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.4.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.10, 4.17]
9.5 Complication (intestinal infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.5.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.03, 3.16]
9.6 Complication (pressure sores) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.6.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 8.24]

Analysis 9.1. Comparison 9: Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements, Outcome 1: Nutritional status (arm muscular circumference) at end of intervention phase

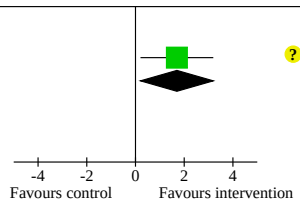
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
9.1.1 Acute phase									
Zheng 2006	22.3	2.3	27	20.6	20	27	100.0%	1.70 [-5.89 , 9.29]	? ? ? ? + ? ?
Subtotal (95% CI)			**27**			**27**	**100.0%**	**1.70 [-5.89 , 9.29]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.44 (P = 0.66)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 9.2. Comparison 9: Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements, Outcome 2: Nutritional status (triceps skinfold thickness) at end of intervention phase

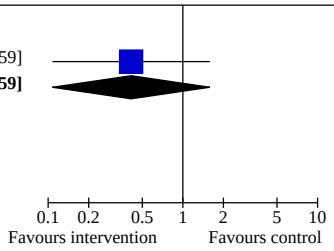
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
9.2.1 Acute phase									
Zheng 2006	13.9	2.9	27	12.2	2.7	27	100.0%	1.70 [0.21 , 3.19]	? ? ? ? + ? ?
Subtotal (95% CI)			**27**			**27**	**100.0%**	**1.70 [0.21 , 3.19]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.23 (P = 0.03)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 9.3. Comparison 9: Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements, Outcome 3: Complication (pneumonia) during intervention phase

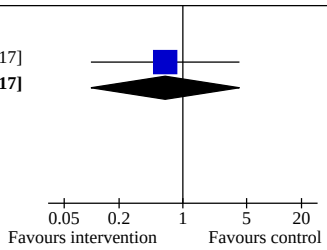
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
9.3.1 Acute phase								
Zheng 2006	4	27	8	27	100.0%	0.41 [0.11 , 1.59]		? ? ? ? + ? ?
Subtotal (95% CI)		**27**		**27**	**100.0%**	**0.41 [0.11 , 1.59]**		
Total events:	4		8					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.29 (P = 0.20)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

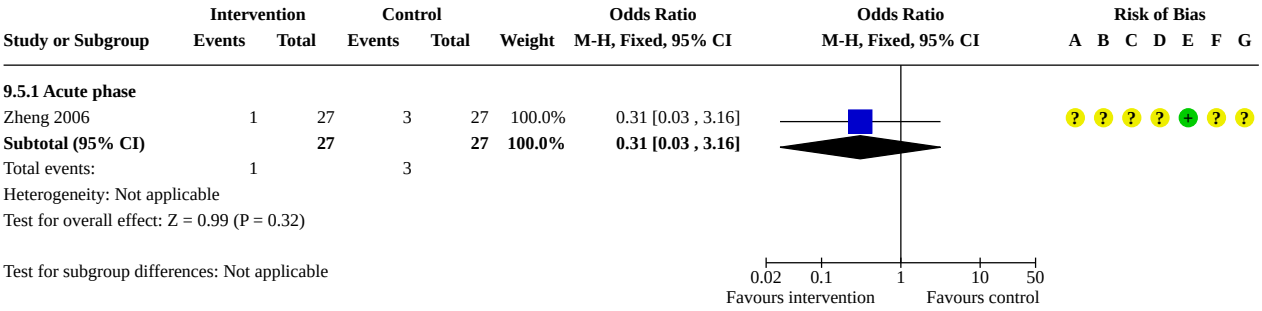
Analysis 9.4. Comparison 9: Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements, Outcome 4: Complication (urinary tract infection) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
9.4.1 Acute phase								
Zheng 2006	2	27	3	27	100.0%	0.64 [0.10 , 4.17]		? ? ? ? + ? ?
Subtotal (95% CI)		**27**		**27**	**100.0%**	**0.64 [0.10 , 4.17]**		
Total events:	2		3					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.47 (P = 0.64)								
Test for subgroup differences: Not applicable								



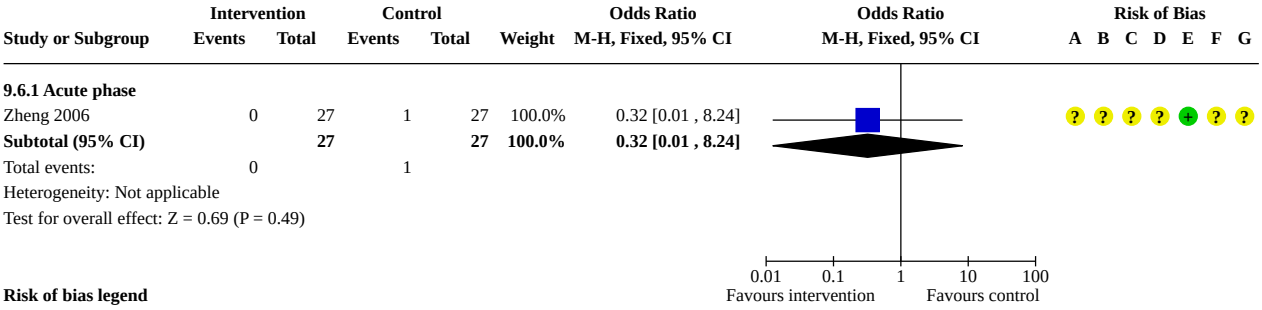
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 9.5. Comparison 9: Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements, Outcome 5: Complication (intestinal infection) during intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 9.6. Comparison 9: Enteral nutritional supplements (high energy and multi-nutrients) versus no supplements, Outcome 6: Complication (pressure sores) during intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 10. Enteral nutritional supplements (energy) versus no supplements

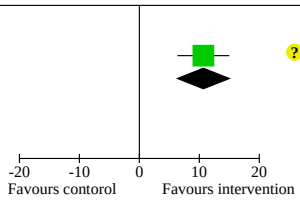
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Activity of daily living (ADL score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1.1 Acute phase	1	54	Mean Difference (IV, Fixed, 95% CI)	10.68 [6.35, 15.01]
10.2 Neurological impairment (NIHSS score) at end of intervention phase	2	134	Mean Difference (IV, Fixed, 95% CI)	-2.35 [-2.55, -2.15]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.2.1 Acute phase	2	134	Mean Difference (IV, Fixed, 95% CI)	-2.35 [-2.55, -2.15]
10.3 Subgroup analysis – type of stroke: NIHSS score	2	134	Mean Difference (IV, Random, 95% CI)	-2.35 [-2.55, -2.15]
10.3.1 Ischaemic stroke	1	80	Mean Difference (IV, Random, 95% CI)	-2.35 [-2.55, -2.15]
10.3.2 Mixed: ischaemic and haemorrhagic stroke	1	54	Mean Difference (IV, Random, 95% CI)	-2.11 [-3.64, -0.58]
10.4 Physical performance (Fugl-Meyer Assessment score) at end of intervention phase	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
10.5 Quality of life (SF-36, Physiological Function score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.6 Quality of life (SF-36, Role Function score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.7 Quality of life (SF-36, Physical Pain score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.8 Quality of life (SF-36, General Health score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.9 Quality of life (SF-36, Mental Health score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.10 Quality of life (SF-36, Energy score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.11 Quality of life (SF-36, Social Function score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.12 Quality of life (SF-36, Emotional Function score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.13 Complication (pneumonia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.13.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.40 [0.11, 1.44]
10.14 Complication (urinary tract infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.14.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.58 [0.14, 2.47]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.15 Complication (intestinal infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.15.1 Acute phase	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.78 [0.14, 4.25]

Analysis 10.1. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 1: Activity of daily living (ADL score) at end of intervention phase

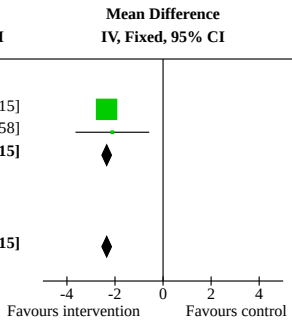
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
10.1.1 Acute phase								
Li 2008	75.92	7.75	30	65.24	8.3	24	100.0%	10.68 [6.35 , 15.01]
Subtotal (95% CI)			**30**			**24**	**100.0%**	**10.68 [6.35 , 15.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.84 (P < 0.00001)								
Test for subgroup differences: Not applicable								

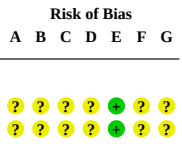


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.2. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 2: Neurological impairment (NIHSS score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
10.2.1 Acute phase								
Dang 2023	3.27	0.33	40	5.62	0.56	40	98.3%	-2.35 [-2.55 , -2.15]
Li 2008	8.14	3.22	30	10.25	2.53	24	1.7%	-2.11 [-3.64 , -0.58]
Subtotal (95% CI)			**70**			**64**	**100.0%**	**-2.35 [-2.55 , -2.15]**
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%								
Test for overall effect: Z = 23.02 (P < 0.00001)								
Total (95% CI)			**70**			**64**	**100.0%**	**-2.35 [-2.55 , -2.15]**
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%								
Test for overall effect: Z = 23.02 (P < 0.00001)								
Test for subgroup differences: Not applicable								

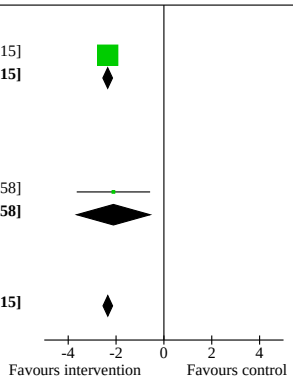




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.3. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 3: Subgroup analysis – type of stroke: NIHSS score

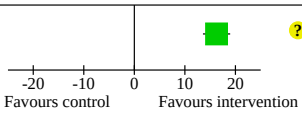
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
10.3.1 Ischaemic stroke								
Dang 2023	3.27	0.33	40	5.62	0.56	40	98.3%	-2.35 [-2.55 , -2.15]
Subtotal (95% CI)			**40**			**40**	**98.3%**	**-2.35 [-2.55 , -2.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 22.87 (P < 0.00001)								
10.3.2 Mixed: ischaemic and haemorrhagic stroke								
Li 2008	8.14	3.22	30	10.25	2.53	24	1.7%	-2.11 [-3.64 , -0.58]
Subtotal (95% CI)			**30**			**24**	**1.7%**	**-2.11 [-3.64 , -0.58]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.70 (P = 0.007)								
Total (95% CI)			**70**			**64**	**100.0%**	**-2.35 [-2.55 , -2.15]**
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%								
Test for overall effect: Z = 23.02 (P < 0.00001)								
Test for subgroup differences: Chi² = 0.09, df = 1 (P = 0.76), I² = 0%								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.4. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 4: Physical performance (Fugl-Meyer Assessment score) at end of intervention phase

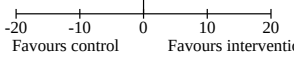
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Random, 95% CI
Dang 2023	68.85	6.87	40	52.58	5.32	40	16.27 [13.58 , 18.96]
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.5. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 5: Quality of life (SF-36, Physiological Function score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	82.71	8.26	40	70.23	7.05	40	12.48 [9.11 , 15.85]		? ? ? ? + ? ?



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.6. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 6: Quality of life (SF-36, Role Function score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	73.39	7.36	40	66.28	6.64	40	7.11 [4.04 , 10.18]		? ? ? ? + ? ?
Test for subgroup differences: Not applicable									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

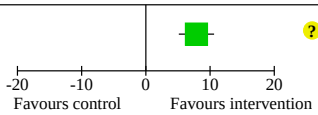
Analysis 10.7. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 7: Quality of life (SF-36, Physical Pain score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	82.69	8.29	40	70.67	7.06	40	12.02 [8.65 , 15.39]		? ? ? ? + ? ?
Test for subgroup differences: Not applicable									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.8. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 8: Quality of life (SF-36, General Health score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	66.62	6.65	40	58.74	5.86	40	7.88 [5.13 , 10.63]		? ? ? ? + ? ?

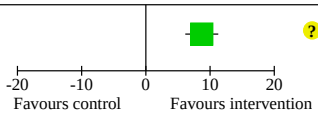


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.9. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 9: Quality of life (SF-36, Mental Health score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	62.39	6.31	40	53.68	5.37	40	8.71 [6.14 , 11.28]		? ? ? ? + ? ?

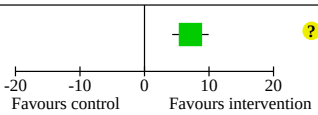


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.10. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 10: Quality of life (SF-36, Energy score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	67.87	6.78	40	60.75	6.08	40	7.12 [4.30 , 9.94]		? ? ? ? + ? ?

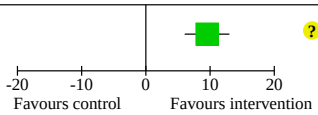


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.11. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 11: Quality of life (SF-36, Social Function score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	85.78	8.59	40	76.25	7.25	40	9.53 [6.05 , 13.01]		? ? ? ? + ? ?

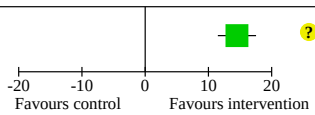


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.12. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 12: Quality of life (SF-36, Emotional Function score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Dang 2023	75.74	7.56	40	61.23	6.15	40	14.51 [11.49 , 17.53]		? ? ? ? + ? ?

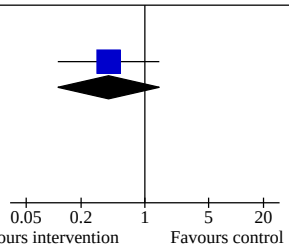


Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.13. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 13: Complication (pneumonia) during intervention phase

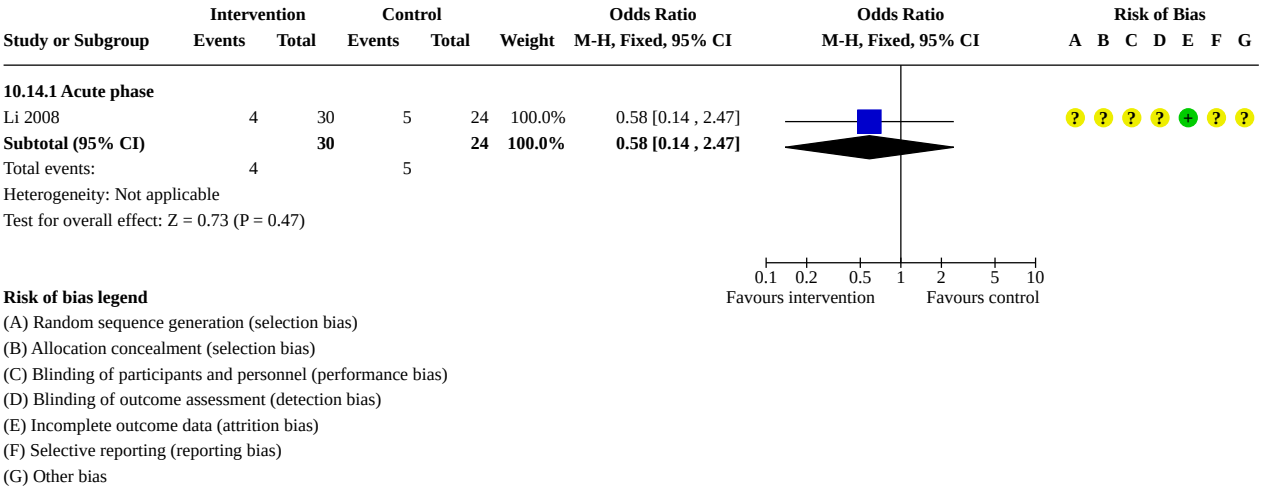
Study or Subgroup	Intervention Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
10.13.1 Acute phase								
Li 2008	5	30	8	24	100.0%	0.40 [0.11 , 1.44]		? ? ? ? + ? ?
Subtotal (95% CI)		**30**		**24**	**100.0%**	**0.40 [0.11 , 1.44]**		
Total events:	5		8					



Heterogeneity: Not applicable
Test for overall effect: Z = 1.40 (P = 0.16)

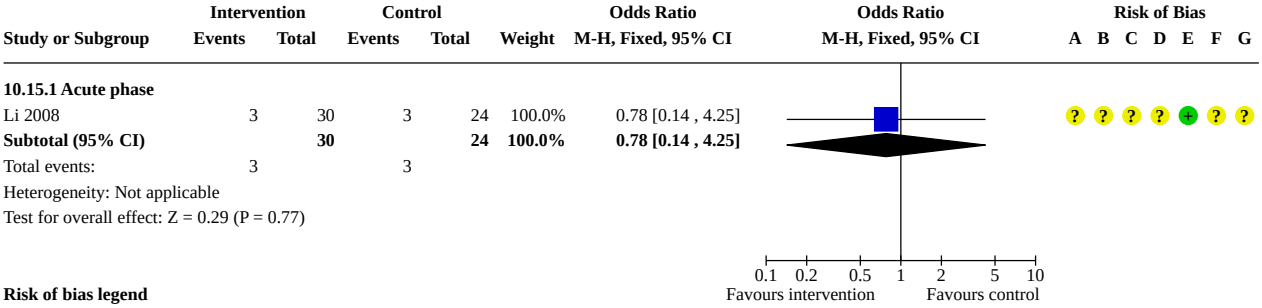
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.14. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 14: Complication (urinary tract infection) during intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 10.15. Comparison 10: Enteral nutritional supplements (energy) versus no supplements, Outcome 15: Complication (intestinal infection) during intervention phase

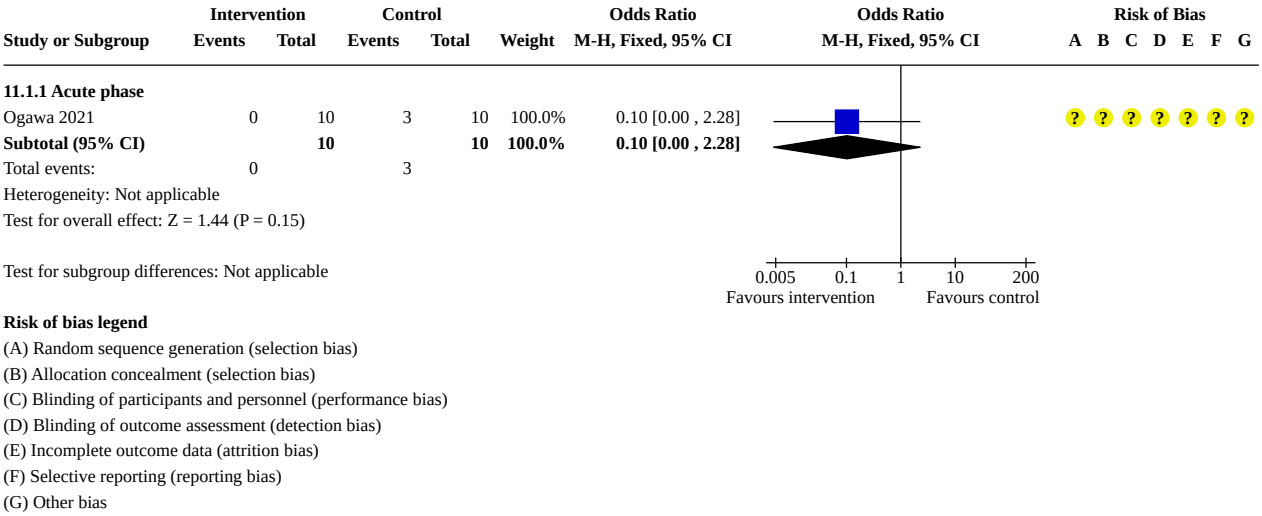


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 11. Enteral nutritional supplements (fatty acids) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 Complication (pressure sores) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1.1 Acute phase	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.10 [0.00, 2.28]

Analysis 11.1. Comparison 11: Enteral nutritional supplements (fatty acids) versus no supplements, Outcome 1: Complication (pressure sores) during intervention phase



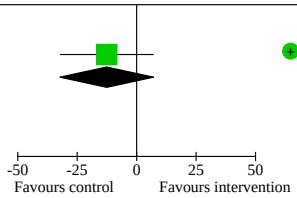
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 12. Oral or enteral nutritional supplements (essential amino acids) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Activities of daily living (Functional Independence Measure, total score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.1.1 Subacute phase	1	38	Mean Difference (IV, Fixed, 95% CI)	-12.60 [-32.33, 7.13]
12.2 Nutritional status (body weight) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.2.1 Subacute phase	1	38	Mean Difference (IV, Fixed, 95% CI)	3.80 [-2.56, 10.16]
12.3 Swallowing function (Dysphagia Outcome and Severity Scale score) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.3.1 Subacute phase	1	38	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-2.35, -0.25]
12.4 Swallowing function (improvement in Dysphagia Outcome and Severity Scale score) at end of intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
12.4.1 Subacute phase	1	42	Odds Ratio (M-H, Fixed, 95% CI)	0.62 [0.16, 2.42]

Analysis 12.1. Comparison 12: Oral or enteral nutritional supplements (essential amino acids) versus no supplements, Outcome 1: Activities of daily living (Functional Independence Measure, total score) at end of intervention phase

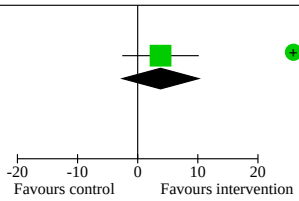
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
12.1.1 Subacute phase									
Aquilani 2014	47.4	23.9	19	60	36.8	19	100.0%	-12.60 [-32.33 , 7.13]	+ ? ? ? ? ? −
Subtotal (95% CI)			**19**			**19**	**100.0%**	**-12.60 [-32.33 , 7.13]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.25 (P = 0.21)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 12.2. Comparison 12: Oral or enteral nutritional supplements (essential amino acids) versus no supplements, Outcome 2: Nutritional status (body weight) at end of intervention phase

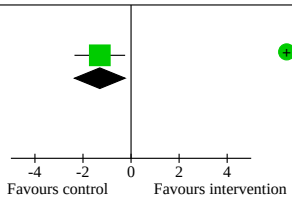
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
12.2.1 Subacute phase									
Aquilani 2014	59.7	12	19	55.9	7.5	19	100.0%	3.80 [-2.56 , 10.16]	+ ? ? ? ? ? −
Subtotal (95% CI)			**19**			**19**	**100.0%**	**3.80 [-2.56 , 10.16]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.17 (P = 0.24)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

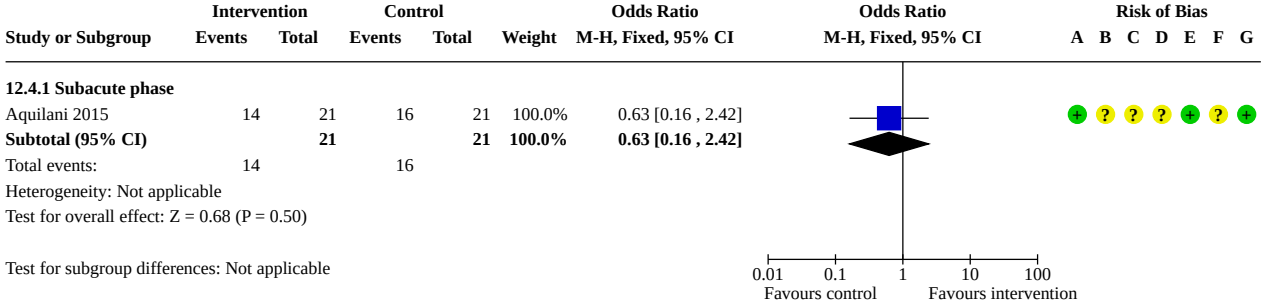
Analysis 12.3. Comparison 12: Oral or enteral nutritional supplements (essential amino acids) versus no supplements, Outcome 3: Swallowing function (Dysphagia Outcome and Severity Scale score) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
12.3.1 Subacute phase									
Aquilani 2014	2.6	1.5	19	3.9	1.8	19	100.0%	-1.30 [-2.35 , -0.25]	+ ? ? ? ? ? −
Subtotal (95% CI)			**19**			**19**	**100.0%**	**-1.30 [-2.35 , -0.25]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.42 (P = 0.02)									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 12.4. Comparison 12: Oral or enteral nutritional supplements (essential amino acids) versus no supplements, Outcome 4: Swallowing function (improvement in Dysphagia Outcome and Severity Scale score) at end of intervention phase



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 13. Oral or enteral individualised nutritional therapy versus control

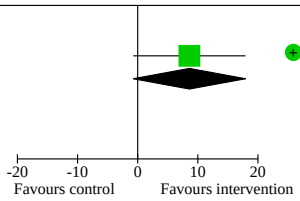
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 Activities of daily living (Functional Independence Measure, motor score) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.1.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	8.60 [-0.74, 17.94]
13.2 Nutritional status (change in body weight) during follow-up or intervention phase	2	252	Mean Difference (IV, Random, 95% CI)	1.07 [0.10, 2.04]
13.2.1 Acute phase	2	252	Mean Difference (IV, Random, 95% CI)	1.07 [0.10, 2.04]
13.3 Subgroup analysis – nutritional status at baseline: change in body weight	2	252	Mean Difference (IV, Random, 95% CI)	1.07 [0.10, 2.04]
13.3.1 Inclusion criteria with malnutrition or malnutrition risk	1	124	Mean Difference (IV, Random, 95% CI)	1.30 [1.05, 1.55]
13.3.2 No inclusion criteria with malnutrition or malnutrition risk	1	128	Mean Difference (IV, Random, 95% CI)	0.00 [-2.07, 2.07]
13.4 Nutritional status (thigh circumference, paretic side) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.4.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	2.10 [0.59, 3.61]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.5 Nutritional status (thigh circumference, non-paretic side) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.5.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	1.80 [0.12, 3.48]
13.6 Nutritional status (calf circumference, paretic side) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.6.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	1.40 [0.25, 2.55]
13.7 Nutritional status (calf circumference, non-paretic side) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.7.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	1.60 [0.38, 2.82]
13.8 Nutritional status (arm circumference, paretic side) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.8.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	1.60 [0.44, 2.76]
13.9 Nutritional status (arm circumference, non-paretic side) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.9.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	1.80 [0.63, 2.97]
13.10 Nutritional status (arm circumference, dominant or non-dominant arm) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.11 Nutritional status (arm muscular circumference) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.12 Nutritional status (triceps skinfold thickness) at end of intervention phase	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.13 Cognitive function (Functional Independence Measure, cognition score) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.13.1 Acute phase	1	128	Mean Difference (IV, Fixed, 95% CI)	2.90 [-0.49, 6.29]
13.14 Quality of life (EQ-5D questionnaire, improvement in mobility) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.14.1 Acute phase	1	170	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.37, 2.30]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.15 Quality of life (EQ-5D questionnaire, improvement in self-care) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.15.1 Acute phase	1	170	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.48, 2.64]
13.16 Quality of life (EQ-5D questionnaire, improvement in usual activities) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.16.1 Acute phase	1	170	Odds Ratio (M-H, Fixed, 95% CI)	1.79 [0.70, 4.56]
13.17 Quality of life (EQ-5D questionnaire, improvement in pain/discomfort) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.17.1 Acute phase	1	170	Odds Ratio (M-H, Fixed, 95% CI)	1.16 [0.44, 3.01]
13.18 Quality of life (EQ-5D questionnaire, improvement in anxiety/depression) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.18.1 Acute phase	1	170	Odds Ratio (M-H, Fixed, 95% CI)	0.59 [0.23, 1.51]
13.19 Muscle strength (change in grip strength) at follow-up	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.19.1 Acute phase	1	170	Mean Difference (IV, Fixed, 95% CI)	2.60 [1.30, 3.90]
13.20 All-cause mortality at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.20.1 Acute phase	1	170	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.49, 1.71]

Analysis 13.1. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 1: Activities of daily living (Functional Independence Measure, motor score) at follow-up

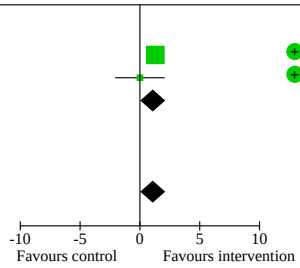
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
13.1.1 Acute phase									
Otsuki 2020	59.1	26.6	64	50.5	27.3	64	100.0%	8.60 [-0.74 , 17.94]	+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**100.0%**	**8.60 [-0.74 , 17.94]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.81 (P = 0.07)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

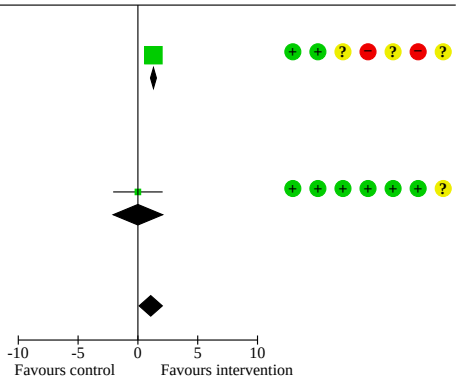
Analysis 13.2. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 2: Nutritional status (change in body weight) during follow-up or intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
13.2.1 Acute phase									
Ha 2010b	-1.4	0.7	58	-2.7	0.7	66	82.4%	1.30 [1.05 , 1.55]	+ + ? − ? − ?
Otsuki 2020	-5.4	6.4	64	-5.4	5.5	64	17.6%	0.00 [-2.07 , 2.07]	+ + + + + + ?
Subtotal (95% CI)			**122**			**130**	**100.0%**	**1.07 [0.10 , 2.04]**	
Heterogeneity: Tau² = 0.28; Chi² = 1.50, df = 1 (P = 0.22); I² = 33%									
Test for overall effect: Z = 2.17 (P = 0.03)									
Total (95% CI)			**122**			**130**	**100.0%**	**1.07 [0.10 , 2.04]**	
Heterogeneity: Tau² = 0.28; Chi² = 1.50, df = 1 (P = 0.22); I² = 33%									
Test for overall effect: Z = 2.17 (P = 0.03)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

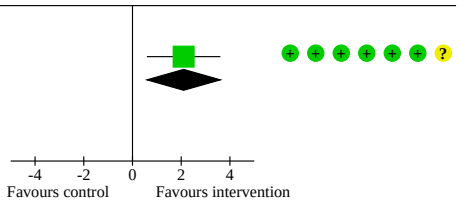
Analysis 13.3. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 3: Subgroup analysis – nutritional status at baseline: change in body weight



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
13.3.1 Inclusion criteria with malnutrition or malnutrition risk									
Ha 2010b	-1.4	0.7	58	-2.7	0.7	66	82.4%	1.30 [1.05 , 1.55]	+ + ? − ? − ?
Subtotal (95% CI)			**58**			**66**	**82.4%**	**1.30 [1.05 , 1.55]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 10.32 (P < 0.00001)									
13.3.2 No inclusion criteria with malnutrition or malnutrition risk									
Otsuki 2020	-5.4	6.4	64	-5.4	5.5	64	17.6%	0.00 [-2.07 , 2.07]	+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**17.6%**	**0.00 [-2.07 , 2.07]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.00 (P = 1.00)									
Total (95% CI)			**122**			**130**	**100.0%**	**1.07 [0.10 , 2.04]**	
Heterogeneity: Tau² = 0.28; Chi² = 1.50, df = 1 (P = 0.22); I² = 33%									
Test for overall effect: Z = 2.17 (P = 0.03)									
Test for subgroup differences: Chi² = 1.50, df = 1 (P = 0.22), I² = 33.2%									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.4. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 4: Nutritional status (thigh circumference, paretic side) at follow-up

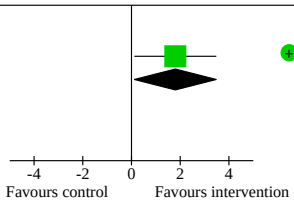


Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
13.4.1 Acute phase									
Otsuki 2020	39.4	4.2	64	37.3	4.5	64	100.0%	2.10 [0.59 , 3.61]	+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**100.0%**	**2.10 [0.59 , 3.61]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.73 (P = 0.006)									
Test for subgroup differences: Not applicable									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.5. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 5: Nutritional status (thigh circumference, non-paretic side) at follow-up

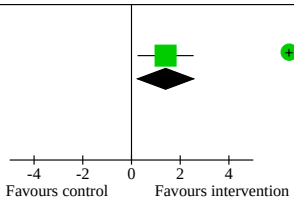
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
13.5.1 Acute phase										
Otsuki 2020	39.8	4.6	64	38	5.1	64	100.0%	1.80 [0.12 , 3.48]		+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**100.0%**	**1.80 [0.12 , 3.48]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.10 (P = 0.04)										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.6. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 6: Nutritional status (calf circumference, paretic side) at follow-up

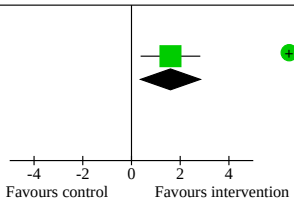
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
13.6.1 Acute phase										
Otsuki 2020	30.4	3.7	64	29	2.9	64	100.0%	1.40 [0.25 , 2.55]		+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**100.0%**	**1.40 [0.25 , 2.55]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.38 (P = 0.02)										
Test for subgroup differences: Not applicable										



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.7. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 7: Nutritional status (calf circumference, non-paretic side) at follow-up

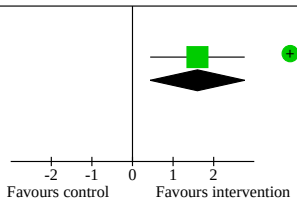
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
13.7.1 Acute phase										
Otsuki 2020	30.7	4	64	29.1	3	64	100.0%	1.60 [0.38 , 2.82]		+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**100.0%**	**1.60 [0.38 , 2.82]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.56 (P = 0.01)										
Test for subgroup differences: Not applicable										

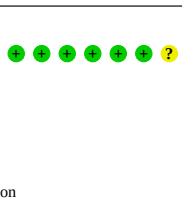


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.8. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 8: Nutritional status (arm circumference, paretic side) at follow-up

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
13.8.1 Acute phase								
Otsuki 2020	26	3.6	64	24.4	3.1	64	100.0%	1.60 [0.44 , 2.76]
Subtotal (95% CI)			**64**			**64**	**100.0%**	**1.60 [0.44 , 2.76]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.69 (P = 0.007)								
Test for subgroup differences: Not applicable								

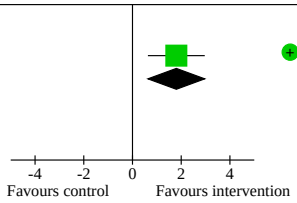




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.9. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 9: Nutritional status (arm circumference, non-paretic side) at follow-up

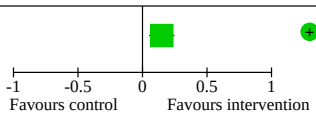
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
13.9.1 Acute phase								
Otsuki 2020	26.4	3.7	64	24.6	3	64	100.0%	1.80 [0.63 , 2.97]
Subtotal (95% CI)			**64**			**64**	**100.0%**	**1.80 [0.63 , 2.97]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.02 (P = 0.003)								
Test for subgroup differences: Not applicable								

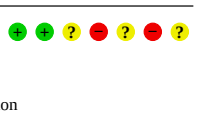


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.10. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 10: Nutritional status (arm circumference, dominant or non-dominant arm) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Ha 2010b	-0.65	0.3	58	-0.8	0.25	66	0.15 [0.05 , 0.25]

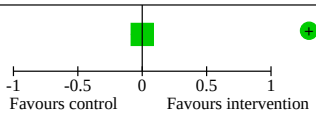




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.11. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 11: Nutritional status (arm muscular circumference) at end of intervention phase

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Ha 2010b	-0.4	0.25	58	-0.4	0.25	66	0.00 [-0.09 , 0.09]		+ + ? − ? − ?



Test for subgroup differences: Not applicable

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.12. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 12: Nutritional status (triceps skinfold thickness) at end of intervention phase

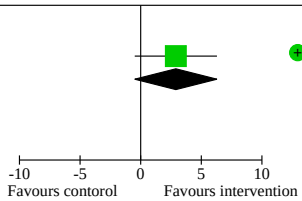
Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
Ha 2010b	-1	0.45	58	-1.25	0.45	66	0.25 [0.09 , 0.41]		+ + ? − ? − ?

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.13. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 13: Cognitive function (Functional Independence Measure, cognition score) at follow-up

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
13.13.1 Acute phase										
Otsuki 2020	23.5	8.9	64	20.6	10.6	64	100.0%	2.90 [-0.49 , 6.29]		+ + + + + + ?
Subtotal (95% CI)			**64**			**64**	**100.0%**	**2.90 [-0.49 , 6.29]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.68 (P = 0.09)



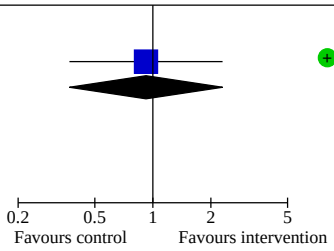
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.14. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 14: Quality of life (EQ-5D questionnaire, improvement in mobility) at follow-up

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
13.14.1 Acute phase						
Ha 2010a	10	84	11	86	100.0%	0.92 [0.37 , 2.30]
Subtotal (95% CI)		**84**		**86**	**100.0%**	**0.92 [0.37 , 2.30]**
Total events:	10		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.86)

Test for subgroup differences: Not applicable



Risk of Bias: A B C D E F G — + + ? − + + +

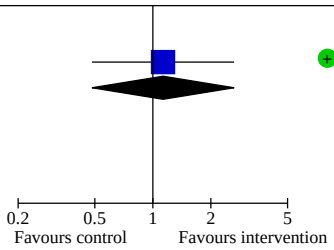
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.15. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 15: Quality of life (EQ-5D questionnaire, improvement in self-care) at follow-up

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
13.15.1 Acute phase						
Ha 2010a	13	84	12	86	100.0%	1.13 [0.48 , 2.64]
Subtotal (95% CI)		**84**		**86**	**100.0%**	**1.13 [0.48 , 2.64]**
Total events:	13		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)

Test for subgroup differences: Not applicable

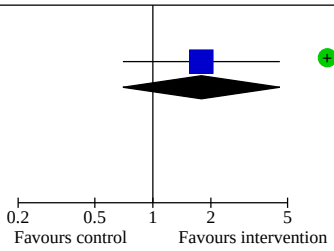


Risk of Bias: A B C D E F G — + + ? − + + +

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.16. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 16: Quality of life (EQ-5D questionnaire, improvement in usual activities) at follow-up

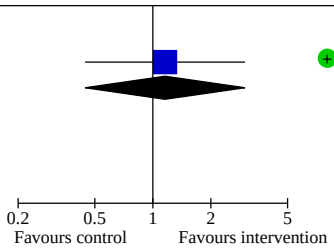
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
13.16.1 Acute phase							
Ha 2010a	13	84	8	86	100.0%	1.79 [0.70 , 4.56]	+ + ? − + + +
Subtotal (95% CI)		**84**		**86**	**100.0%**	**1.79 [0.70 , 4.56]**	
Total events:	13		8				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.21 (P = 0.23)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.17. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 17: Quality of life (EQ-5D questionnaire, improvement in pain/discomfort) at follow-up

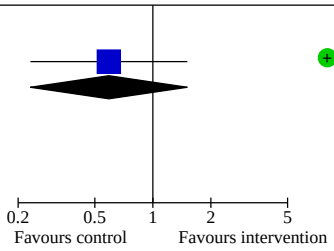
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
13.17.1 Acute phase							
Ha 2010a	10	84	9	86	100.0%	1.16 [0.44 , 3.01]	+ + ? − + + +
Subtotal (95% CI)		**84**		**86**	**100.0%**	**1.16 [0.44 , 3.01]**	
Total events:	10		9				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.30 (P = 0.77)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.18. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 18: Quality of life (EQ-5D questionnaire, improvement in anxiety/depression) at follow-up

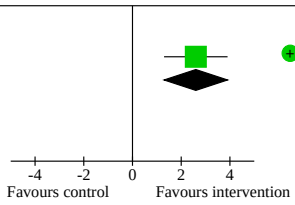
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
13.18.1 Acute phase						
Ha 2010a	8	84	13	86	100.0%	0.59 [0.23 , 1.51]
Subtotal (95% CI)		**84**		**86**	**100.0%**	**0.59 [0.23 , 1.51]**
Total events:	8		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.10 (P = 0.27)						
Test for subgroup differences: Not applicable						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

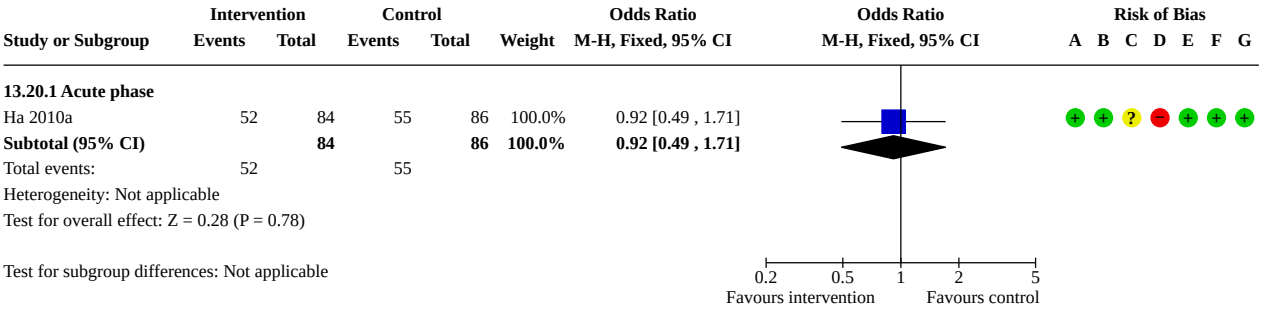
Analysis 13.19. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 19: Muscle strength (change in grip strength) at follow-up

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
13.19.1 Acute phase								
Ha 2010a	2.3	3.7	84	-0.3	4.9	86	100.0%	2.60 [1.30 , 3.90]
Subtotal (95% CI)			**84**			**86**	**100.0%**	**2.60 [1.30 , 3.90]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.91 (P < 0.0001)								
Test for subgroup differences: Not applicable								



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 13.20. Comparison 13: Oral or enteral individualised nutritional therapy versus control, Outcome 20: All-cause mortality at follow-up



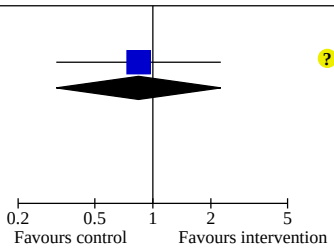
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 14. Early parenteral nutrition versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Activity of daily living (independent) at end of intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.1.1 Acute phase	1	69	Odds Ratio (M-H, Fixed, 95% CI)	0.84 [0.32, 2.25]
14.2 All-cause mortality at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.2.1 Acute phase	1	69	Odds Ratio (M-H, Fixed, 95% CI)	0.96 [0.33, 2.82]
14.3 Complication (pneumonia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.3.1 Acute phase	1	69	Odds Ratio (M-H, Fixed, 95% CI)	0.66 [0.25, 1.75]
14.4 Complication (intestinal infection) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.4.1 Acute phase	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.10 [0.39, 3.07]
14.5 Complication (sepsis) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.5.1 Acute phase	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.25 [0.31, 5.11]

Analysis 14.1. Comparison 14: Early parenteral nutrition versus control, Outcome 1: Activity of daily living (independent) at end of intervention phase

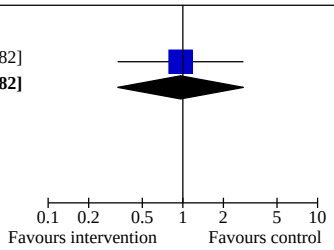
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
14.1.1 Acute phase						
Zhang 2004	12	35	13	34	100.0%	0.84 [0.32 , 2.25]
Subtotal (95% CI)		**35**		**34**	**100.0%**	**0.84 [0.32 , 2.25]**
Total events:	12		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.34 (P = 0.73)						
Test for subgroup differences: Not applicable						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 14.2. Comparison 14: Early parenteral nutrition versus control, Outcome 2: All-cause mortality at follow-up

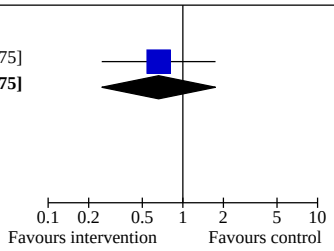
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
14.2.1 Acute phase						
Zhang 2004	9	35	9	34	100.0%	0.96 [0.33 , 2.82]
Subtotal (95% CI)		**35**		**34**	**100.0%**	**0.96 [0.33 , 2.82]**
Total events:	9		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.07 (P = 0.94)						
Test for subgroup differences: Not applicable						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 14.3. Comparison 14: Early parenteral nutrition versus control, Outcome 3: Complication (pneumonia) during intervention phase

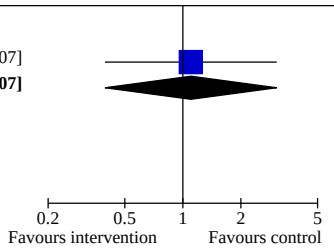
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
14.3.1 Acute phase							
Zhang 2004	12	35	15	34	100.0%	0.66 [0.25 , 1.75]	? ? ? ? + ? ?
Subtotal (95% CI)		**35**		**34**	**100.0%**	**0.66 [0.25 , 1.75]**	
Total events:	12		15				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.83 (P = 0.40)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

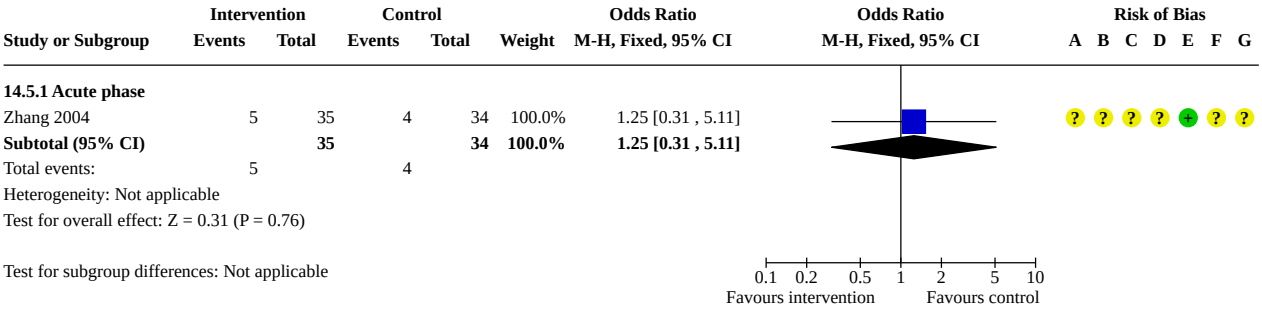
Analysis 14.4. Comparison 14: Early parenteral nutrition versus control, Outcome 4: Complication (intestinal infection) during intervention phase

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
14.4.1 Acute phase							
Zhang 2004	11	35	10	34	100.0%	1.10 [0.39 , 3.07]	? ? ? ? + ? ?
Subtotal (95% CI)		**35**		**34**	**100.0%**	**1.10 [0.39 , 3.07]**	
Total events:	11		10				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.18 (P = 0.86)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 14.5. Comparison 14: Early parenteral nutrition versus control, Outcome 5: Complication (sepsis) during intervention phase

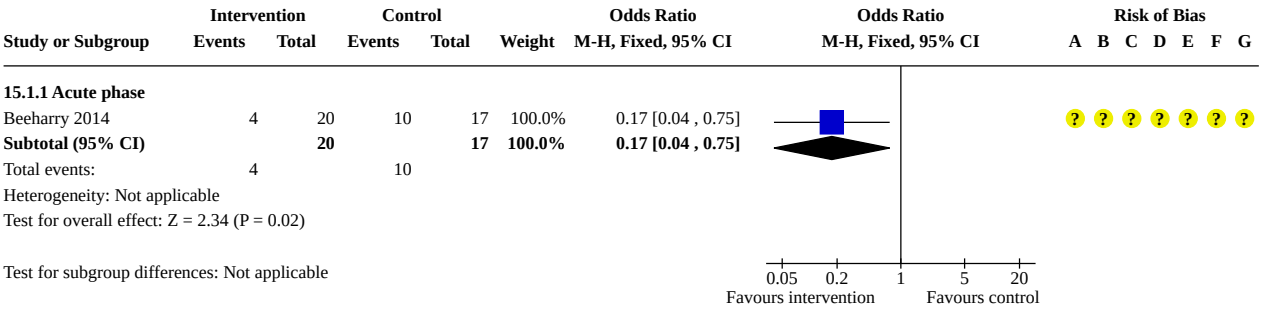


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 15. Parenteral nutritional supplements (amino acids) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.1 Nutritional status (decreased nutritional status) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
15.1.1 Acute phase	1	37	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.04, 0.75]

Analysis 15.1. Comparison 15: Parenteral nutritional supplements (amino acids) versus no supplements, Outcome 1: Nutritional status (decreased nutritional status) during intervention phase

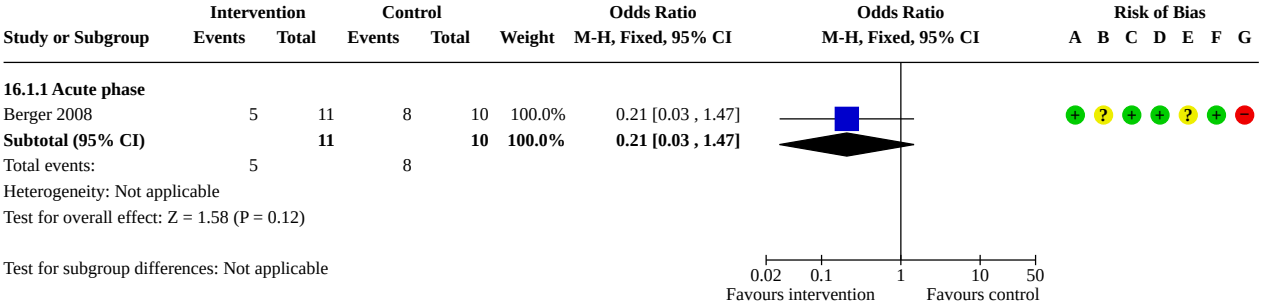


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 16. Parenteral (selenium, zinc, vitamin C, and vitamin B1) and enteral (vitamin E) supplements versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16.1 Complication (pneumonia) during intervention phase	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
16.1.1 Acute phase	1	21	Odds Ratio (M-H, Fixed, 95% CI)	0.21 [0.03, 1.47]

Analysis 16.1. Comparison 16: Parenteral (selenium, zinc, vitamin C, and vitamin B1) and enteral (vitamin E) supplements versus no supplements, Outcome 1: Complication (pneumonia) during intervention phase



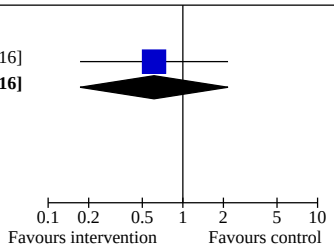
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 17. Oral and parenteral supplements (fatty acids) versus no supplements

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17.1 Disability (Glasgow Outcome Scale Extended score 1 to 4, poor status) at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
17.1.1 Acute phase	1	41	Odds Ratio (M-H, Fixed, 95% CI)	0.61 [0.17, 2.16]
17.2 Stroke recurrence at follow-up	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
17.2.1 Acute phase	1	41	Odds Ratio (M-H, Fixed, 95% CI)	0.38 [0.10, 1.45]

Analysis 17.1. Comparison 17: Oral and parenteral supplements (fatty acids) versus no supplements, Outcome 1: Disability (Glasgow Outcome Scale Extended score 1 to 4, poor status) at follow-up

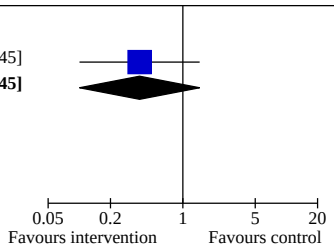
Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
17.1.1 Acute phase							
Saito 2017	7	21	9	20	100.0%	0.61 [0.17 , 2.16]	? + − − + ? +
Subtotal (95% CI)		**21**		**20**	**100.0%**	**0.61 [0.17 , 2.16]**	
Total events:	7		9				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.76 (P = 0.45)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Analysis 17.2. Comparison 17: Oral and parenteral supplements (fatty acids) versus no supplements, Outcome 2: Stroke recurrence at follow-up

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
17.2.1 Acute phase							
Saito 2017	5	21	9	20	100.0%	0.38 [0.10 , 1.45]	? + − − + ? +
Subtotal (95% CI)		**21**		**20**	**100.0%**	**0.38 [0.10 , 1.45]**	
Total events:	5		9				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.41 (P = 0.16)							
Test for subgroup differences: Not applicable							



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

ADDITIONAL TABLES

Table 1. Characteristics of included studies

Study ID	Country	n	Gender (men/ women)	Age (years)	Stroke type	Stroke phase	Inclusion criteria for malnutri-tion	Stroke severity at baseline‡
Aquilani 2008a	Italy	48	27/21	Mean age (SD): Intervention 73 (6.2) Control 71(8.5)	Not reported	Subacute	No	-
Aquilani 2008b	Italy	42	27/15	Mean age (SD): All 66.4 (11)	Ischaemic	Acute and subacute	No	Not reported
Aquilani 2009	Italy	26	17/9	Mean age (SD): Intervention 74 (8.0) Control 72 (6.5)	Ischaemic	Subacute	No	NIHSS: mean: IG: 13.5 95% CI (11.3 to 14.8), CG:12.1 (10.5 to 14.1)
Aquilani 2014	Italy	38	29/9	Mean age (SD): All 69.7 (69.7)	Ischaemic and haemor-rhagic	Subacute	No	-
Aquilani 2015	Italy	42	27/15	Mean age (SD): All 71 (9)	Ischaemic	Subacute	No	-
Badjatia 2021	USA	26	11/15	Mean age (SD): All 59 (11)	SAH	Acute	No	Hunt Hess Grade: grade 2 = 28%, grade 3 = 24%, grade 4 = 40%, grade 5 = 8%
Beeharry 2014	Russia	37	21/16	Mean age (SD): All 73.4 (6.2)	Ischaemic	Acute	No	Not reported
Berger 2008	Switzerland	21	5/16	Mean age (SD): All 54 (9)	SAH	Acute	No	Not reported
Cheng 2019	Taiwan	20	14/4*	Mean age (SD): All 58.8 (7.1)*	Ischaemic and haemor-rhagic	Chronic	No	-
Daga 1997	India	27	Not report-ed	Not reported	Ischaemic	Acute	No	Not reported
Dang 2018	China	22	Not report-ed	Not reported	Ischaemic	Subacute	No	-

Table 1. Characteristics of included studies *(Continued)*

Dang 2023	China	80	45/35	Mean age (SD): Intervention 61.02 (6.61) Control 60.52 (6.58)	Ischaemic	Acute	No	NIHSS, mean(SD): IG: 8.60 (0.87), CG: 8.57 (0.86)
Das 2021	India	12	Not reported	Not reported	Ischaemic	Acute	No	Not reported
De Aguilar-Nascimento 2011	Brazil	31	12/19	Median age (range): All 74 (65–90)	Ischaemic	Acute	No	Not reported
Dennis 2005a	15 countries	4023	2149/1874	Mean age (SD): Intervention 71 (12) Control 71 (13)	Ischaemic and haemorrhagic	Acute	No	Not reported
Dennis 2005b	15 countries	859	394/465	Mean age (SD): Intervention 76 (11) Control 76 (11)	Ischaemic and haemorrhagic	Acute	No	Not reported
Gao 2008	China	60	41/19	Mean age (SD): Intervention 63.17 (12.68) Control 67.47 (12.33)	Ischaemic and haemorrhagic	Acute	No	Not reported
Garbagnati 2009	Italy	72	47/25	Mean age (SD): All 65.3 (12.9)	Ischaemic	Subacute	No	Canadian Neurological Scale, mean (SD)§: IG1 5.5 (2.5), IG2 6.3 (1.8), IG3 5.9 (1.8), CG 5.6 (2.5)
Gariballa 1998	UK	42	21/21	Mean age (SD): Intervention 78 (10) Control 80 (7)	Cerebral, haemorrhage, and SAH	Acute	Yes	Not reported
Gupta 2016	India	53	37/16	Mean age (SD): All 60.4 (11.3)	Ischaemic	Acute	No	NIHSS, median (range): IG: 12 (3 to 25), CG: 12 (2 to 29)
Ha 2010a	Norway	170	60/64*	Mean age (SD): Intervention 78.5 (7.4) Control 79.7 (6.8)*	Ischaemic and haemorrhagic	Acute	Yes	Scandinavian Stroke Scale, median (IQR): IG: 41 (6 to 58), CG: 42 (7 to 58)

Table 1. Characteristics of included studies *(Continued)*

Ha 2010b	Norway	170	60/64*	Mean age (SD): Intervention 78.5 (7.4) Control 79.7 (6.8)*	Ischaemic and haemorrhagic	Acute	Yes	Scandinavian Stroke Scale, median (IQR): IG: 41 (6 to 58), CG: 42 (7 to 58)
Hashemilar 2020	Iran	42	34/6*	Mean age (SD): Intervention 65.73 (11.63) Control 71.90 (5.91)*	Ischaemic	Acute	No	NIHSS, mean (SD): IG: 7.36 (4.28), CG: 5.28 (4.57)
Honaga 2022	Japan	50	30/15*	Mean age (SD): Intervention 64.2 (8.9) Control 61.3 (11.5)*	Ischaemic and haemorrhagic	Subacute	No	-
Kadri 2020	Indonesia	120	53/67	Mean age (SD): vitamin A + vitamin D 65.85 (4.23) vitamin A 66.85 (4.62) vitamin D 62.65 (5.66) Control 66.35 (5.30)	Ischaemic	Acute	No	Not reported
Kang 2023	China	70	40/30	Mean age (SD): Intervention 66.84 (6.36) Control 63.69 (5.87)	Haemorrhagic	Acute	No	NIHSS was assessed but the score was not reported. It was stated as 'severe'.
Laviano 2011	Italy	20	10/10	Mean age (SD): Intervention 56.8 (8.9) Control 61.3 (12.2)	Haemorrhagic	Acute	Yes	Not reported
Li 2008	China	54	32/22	Mean age (SD): Intervention 73.3 (9.5) Control 75.4 (10.4)	Ischaemic and haemorrhagic	Acute	No	NIHSS, mean (SD): IG: 14.14 (3.55), CG: 13.78 (4.23)
Li 2014	China	148	86/62	Mean age (SD): All 64.1 (12.3)	Ischaemic and haemorrhagic	Acute	No	NIHSS, mean (SD): IG: 18.8 (3.6), CG: 19.2 (4.3)
Li 2016	China	112	73/39	Mean age (SD): All 68.5 (5.1)	Ischaemic	Acute	No	Not reported
Mohan 2015	Malaysia	70	31/39	Mean age (SD): All 74.6 (6.7)	Ischaemic	Acute	No	Not reported
Momosaki 2019	Japan	97	68/29	Mean age (SD): Intervention 67.6 (11.7) Control 65.5 (11.7)	Ischaemic, cerebral haemorrhage, and SAH	Acute	No	Not reported

Table 1. Characteristics of included studies *(Continued)*

Ogawa 2021	Japan	20	Not reported	Median: Not reported, Range: 55 to 85	Ischaemic	Acute	No	Not reported
Otsuki 2020	Japan	124	50/74	Median age (IQR): Intervention 78.5 (71 to 85) Control 80.5 (75 to 86)	Ischaemic, cerebral haemorrhage, and SAH	Acute	No	NIHSS, median (IQR): CG: 8.5 (3 to 16), IG: 8 (3 to 20)
Ouyang 2003	China	62	39/23	Mean age (SD): Intervention 64.1 (9.02) Control 62.55 (10.57)	Ischaemic	Acute	No	Not reported
Pan 2017	Taiwan	291	185/106	Mean age (SD):K salt 64.4 (9.8), K/Mg salt 64.7 (9.9), Na salt 64.8 (10.3)	Ischaemic and haemorrhagic	Acute and subacute	No	NIHSS, mean (SD)[§]: IG1 2.3 (2.5), IG2 2.2 (2.4), IG3 2.3 (2.6)
Poppitt 2009	New Zealand	102	51/51	Mean age (SD): Intervention 64 (10) Control 65 (12)	Ischaemic	Chronic	No	-
Rabadi 2008	USA	116	68/48	Mean age (SD): Intervention 75.0 (10.58) Control 73.58 (13.02)	Ischaemic and haemorrhagic	Acute and subacute	Yes	Not reported
Saito 2017	Chile	41	15/25*	Median age (SD): Intervention 48 (20 to 67) Control 53 (22 to 68)	SAH	Acute	No	World Federation of Neurosurgical Societies scale: IG: scale 1 = 40%, scale 2 = 40%, CG: scale 1 = 30%, scale 2 = 35%
Sato 2022	Italy	16	8/8	Mean age (SD): Intervention 76.1 (5.3) Control 75.6 (6.9)	Ischaemic and haemorrhagic	Chronic	No	-
Tajiri 2008	Japan	41	22/19	Mean age (SD): Intervention 78.1 (10.6) Control 77.2 (10.7)	Ischaemic and haemorrhagic	Acute	No	NIHSS, median: IG: 16.9, CG: 17.7
Toole 2004	3 countries	3680	2301/1379	Mean age (SD): Intervention 66.4 (10.8) Control 66.2 (10.8)	Ischaemic	Subacute	No	NIHSS, mean (SD): IG: 1.7 (2.0) CG: 1.7 (2.0)

Table 1. Characteristics of included studies *(Continued)*

Torrisi 2021	Italy	40	53.3%/46.7% (reported only %)	Mean age (SD): Intervention 59.20 (11.38) Control 62.07 (10.82)	Ischaemic and haemorrhagic	Subacute	No	-
Ullegaddi 2005a	UK	48	24/24	Median age (IQR): Intervention 76 (68 to 81) Control 79 (73 to 84)	Ischaemic	Acute	No	Not reported
Ullegaddi 2005b	UK	72	51/21	Median age (IQR): vitamin E + vitamin C 76 (68 to 81), vitamin B 77 (68 to 81), vitamin E + vitamin C + vitamin B 76 (66 to 82) Control 79 (73 to 84)	Ischaemic	Acute	No	Not reported
Yoshimura 2019	Japan	49	19/30*	Mean age (SD): Intervention 80.8 (7.1) Control 78.9 (6.3)*	Ischaemic, haemorrhagic, and SAH	Subacute	Yes	NIHSS at onset, median (IQR): IG: 9 (6 to 19), CG: 8 (5 to 15)
Zhang 2004	China	107	76/31	Mean age (SD): All 59.6 (13.1)	Haemorrhagic	Acute	No	Not reported
Zhang 2014	China	89	58/31	Mean age (SD): All 61.9 (5.2)	Ischaemic	Acute	No	Not reported
Zhao 2020	China	78	46/32	Mean age (SD): Intervention 64.13 (8.13) Control 65.13 (9.03)	Ischaemic and haemorrhagic	Acute	No	NIHSS, mean (SD): IG: 18.25 (3.12), CG 17.81 (3.09)
Zheng 2006	China	49	32/17	Mean age (SD): All 71.4 (6.3)	Ischaemic and haemorrhagic	Acute	No	NIHSS, mean (SD): IG: 15.5 (0.8), CG: 15.0 (0.8)
Zheng 2015	China	146	85/61	Mean age (SD): Intervention 71.4 (9.3) Control 71.8 (10.1)	Ischaemic and haemorrhagic	Acute	No	NIHSS, mean (SD): IG: 12.53 (3.32), CG: 13.21 (3.78)
Zhou 2006	China	51	29/22	Mean age (SD): All 65.69 (15.63)	Ischaemic and haemorrhagic	Acute	No	Not reported

*Number after the exclusion of dropouts and lost to follow-up

‡ For studies with acute stroke patients (because severity is basically assessed at the onset) and other studies with an assessment. The other studies were indicated with a dash. Showed stroke-specific severity assessment tools

§ See Table 2

CG: control group; **IG**: intervention group; **IQR**: interquartile range; **NIHSS**: national institutes of health stroke scale; **SAH**: subarachnoid haemorrhage; **SD**: standard deviation

Table 2. Characteristics of interventions in included studies

Study ID	Route of intervention	Type of intervention	Dose/day	Control	Length of intervention	Latest time point of assessment
Aquilani 2008a	Oral	Energy and protein	250 kcal energy, 20 g proteins	SOC (spontaneous alimentation)	21 days	21 days
Aquilani 2008b	Oral	Energy and protein	20 g proteins	SOC (spontaneous alimentation)	21 days	21 days
Aquilani 2009	Oral	Zinc	10 mg	Placebo	30 days	30 days
Aquilani 2014	Oral	Essential amino acids	8 g	Placebo	Until patients' discharge	At patients' discharge from rehabilitation (mean 42 ± SD 4 days from admission)
Aquilani 2015	Oral or enteral	Essential amino acids	8 g	Placebo	35 days	At mean 38 ± SD 1 days
Badjatia 2021	Oral	Protein + NMES	1.75 g/kg (at least 3 g leucine)	SOC (no NMES and no protein)	14 days	90 days
Beeharry 2014	Enteral and parenteral	Amino acids + energy	According to the patient's protein loss	Energy only	Not reported	During ICU stay (day not reported)
Berger 2008	Enteral and parenteral	Zinc + vitamin C + vitamin B + vitamin E	Zinc (60 to 30 mg), vitamin C (2700 to 1600 mg), vitamin B1 (305 to 102.5 mg), vitamin E (612.8 to 306.4 mg)	SOC (500 mg vitamin C)	5 days	3 months
Cheng 2019	Oral	Protein	40 g	Placebo	Mean 21.4 ± SD 1.9 days	8 weeks
Daga 1997	Oral	Vitamin E	300 mg	Placebo	15 days	6 weeks
Dang 2018	Enteral	Early enteral nutrition	Not reported	SOC (daily diet)	Not reported	4 weeks
Dang 2023	Enteral	Energy	400 mL (520 kcal) per day	SOC	Not reported	After intervention (day not reported)

Table 2. Characteristics of interventions in included studies *(Continued)*

Das 2021	Enteral	Individualised nutrition (energy, calculated by indirect calorimeter)	Individualised	SOC	Not reported	Not reported
De Aguilar-Nascimento 2011	Enteral	Protein (whey)	1.2 g/kg	Casein	5 days	During the ICU stay (day not reported)
Dennis 2005a	Oral	Energy and protein	360 mL supplements (energy 6.27 kJ/mL, protein 62.5 g/L)	SOC	Until discharge	6 months
Dennis 2005b	Enteral	Early enteral nutrition (started as soon as possibe)	No dose information	SOC (parenteral nutrition, avoided tube feeding for at least 7 days)	Not applicable	6 months
Gao 2008	Enteral	Protein	Calorie ratio protein: carbohydrate: fat: 20 : 45: 35	Diabetes-specific nutrition (calorie ratio protein: carbohydrate: fat 15 : 53: 32)	Not reported (during hospitalization)	3 months
Garbagnati 2009	Oral	1) vitamin E + vitamin C, 2) fatty acids, 3) vitamin E + vitamin C + fatty acids	Vitamin E 290 mg, vitamin C 240 mg, fatty acids 500 mg	Comparison between 3 groups	12 months	12 months
Gariballa 1998	Oral	Energy and protein	Energy 600 kcal, protein 20 g	SOC	4 weeks or until death or discharge	12 weeks
Gupta 2016	Oral	Vitamin D	60,000 IU (once a month)	SOC	6 months	6 months
Ha 2010a	Oral or enteral	Individualised nutrition (energy and protein, considered physical activity level)	Individualised	SOC	Median 12 days (during hospitalisation)	3 months
Ha 2010b	Oral or enteral	Individualised nutrition (energy and protein, considered individual nutritional intake)	Individualised	SOC	During hospitalisation (days not reported)	3 months
Hashemilar 2020	Oral	Protein	20 g	SOC	3 weeks	3 weeks
Honaga 2022	Oral	Protein + vitamin D	20 g protein, 40 µg vitamin D	Placebo	16 weeks	16 weeks
Kadri 2020	Oral	1) vitamin A 2) vitamin D	Vitamin A 50,000 IU/week, vitamin D 50,000 IU/week	Placebo	12 weeks	12 weeks

Table 2. Characteristics of interventions in included studies *(Continued)*

		3) vitamin A + vitamin D				
Kang 2023	Enteral	Early enteral nutrition	Not reported	SOC (ordinary liquid food)	14 days	14 days
Laviano 2011	Enteral or parenteral	Amino acids	Based on the patient's 20% of nitrogen requirements	SOC (isonitrogenous standard protein)	14 days	14 days
Li 2008	Enteral	Energy	20 to 30 kcal/kg/day	SOC	21 days	21 days ADL: 30 days
Li 2014	Enteral	Energy and protain	Not reported	SOC	21 days	21 days
Li 2016	Enteral	Early enteral nutrition (started within 48 hours from admission)	Gradually increased to about 2000 kcal	SOC (parenteral nutrition: amino-acid 500 mL/day)	1 month	1 month
Mohan 2015	Parenteral	Amino acids + enteral nutrition	Based patient's protein loss	SOC (enteral nutrition)	Not reported	30 days
Momosaki 2019	Oral	Vitamin D	2000 IU	Placebo	8 weeks	8 weeks
Ogawa 2021	Enteral	Fatty acid: eicosapentaenoic acid	Not reported	SOC	At least 14 days	14 days
Otsuki 2020	Oral or enteral	Individualised nutrition (energy, considered stress and physical activity level)	Individualised	SOC (only based on body weight)	During hospitalisation in an acute hospital (median 28 to 30)	At the time of discharge from the recovery hospital or at 3 months
Ouyang 2003	Enteral	Early enteral feeding (started after 48 hours from stroke onset)	Not reported	SOC (starting on day 3 to 4 after stroke)	Not applicable	28 days
Pan 2017	Oral	1) sodium 2) potassium 3) potassium + magnesium Used different types of salt	Each type of salt 1 kg/month	Comparison between 3 groups	6 months	6 months
Poppitt 2009	Oral	Fatty acid: omega-3 polyunsaturated	3 g	Placebo	12 weeks	12 weeks
Rabadi 2008	Oral	Energy and protein	720 kcal, 33 g protein	SOC (381 kcal, 15 g protein)	During hospitalisation (mean 25 to 26 days)	At discharge

Table 2. Characteristics of interventions in included studies *(Continued)*

Saito 2017	Oral and parenteral	Fatty acids	Parenteral for the first 5 days, then oral (1840 mg of EPA and 1520 mg of DHA)	SOC	60 days	90 days
Sato 2022	Oral	Protein + vitamin D	20 g protein, 40 µg vitamin D/weekday, 10 g protein, 20 µg vitamin D on Saturday	Placebo	3 weeks	3 weeks
Tajiri 2008	Enteral	1) Protein (nonessential amino acid based)-enriched nutrition 2) Amino acids (essential) and fatty acids- enriched nutrition	Based on a patient's condition	Comparison between 2 groups	10 days	Death: at discharge NIHSS: 10 days
Toole 2004	Oral	High-dose multivitamin (vitamin B group)	Pyridoxine 25 mg, cobalamin 0.4 mg, and folic acid 2.5 mg	Low-dose vitamin	2 years	2 years
Torrisi 2021	Oral	Vitamin D	2000 IU	Placebo	12 weeks	12 weeks
Ullegaddi 2005a	Oral	Vitamin C + vitamin D	Vitamin C 500 mg, vitamin D 800 IU	SOC	14 days	3 months
Ullegaddi 2005b	Oral	1) vitamin E + vitamin C 2) vitamin B 3) vitamin E + vitamin C + vitamin B	Vitamin E 800 IU, vitamin C 500 mg, vitamin B (5 mg folic acid, 5 mg vitamin B2, 50 mg vitamin B6, 0.4 mg vitamin B12)	SOC	14 days	3 months
Yoshimura 2019	Oral	Amino acids	3 g (leucine 40% enriched essential amino acids)	SOC	8 weeks	8 weeks
Zhang 2004	Enteral and parenteral	1) Early enteral nutrition 2) Early parenteral nutrition (within 48 hours after stroke onset)	Based on a patient's condition	SOC (starting enteral nutrition from 5 days from admission)	Not applicable	3 months
Zhang 2014	Enteral	High-dose protein	1.6 g/kg body weight	0.9 g or 1.2 g	14 days	14 days
Zhao 2020	Enteral	Early enteral nutrition (started within 3 days after stroke onset)	Based on a patient's condition	SOC (starting from 4 to 7 days after stroke onset)	Not applicable	4 weeks
Zheng 2006	Enteral	Energy and multi-nutrients	Based on a patient's condition	SOC (family managed enteral nutrition)	21 days	21 days
Zheng 2015	Enteral	Early enteral nutrition	Based on a patient's condition	SOC (family managed regular food)	21 days	21 days

Table 2. Characteristics of interventions in included studies *(Continued)*

						mRS: 90 days
Zhou 2006	Enteral	Protein-enriched nutrition	Calorie ratio protein: sugar:lipids = 20:45:35	SOC (calorie ratio protein:sugar:lipids = 16:45:35)	14 days	90 days

DHA: docosahexaenoic acid; **EPA:** eicosapentaenoic acid; **ICU:** intensive care unit; **mRS:** modified Rankin Scale; **NIHSS:** national institutes of health stroke scale; **NMES**: neuromuscular electrical stimulation; **SD:** standard deviation; **SOC**: standard of care

APPENDICES

Appendix 1. MEDLINE (Ovid) search strategy

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or brain ischemia/ or exp brain infarction/ or ischemic attack, transient/ or vertebrobasilar insufficiency/ or exp carotid artery diseases/ or cerebral small vessel diseases/ or stroke, lacunar/ or vertebral artery dissection/ or intracranial arterial diseases/ or cerebral arterial diseases/ or infarction, anterior cerebral artery/ or infarction, middle cerebral artery/ or infarction, posterior cerebral artery/ or intracranial arteriosclerosis/ or exp intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or intracranial hemorrhages/ or exp cerebral hemorrhage/ or intracranial hemorrhage, hypertensive/ or exp subarachnoid hemorrhage/ or stroke/ or hemorrhagic stroke/ or exp ischemic stroke/ or vasospasm, intracranial/
2. stroke rehabilitation/
3. (stroke or poststroke or post-stroke or cerebrovasc$ or (cerebr$ adj3 vasc$) or CVA$ or apoplectic or apoplex$ or (transient adj3 isch?emic adj3 attack) or tia$ or SAH or AVM or ESUS or ICH or (cerebral small vessel adj3 disease$)).tw.
4. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulat$) or lenticulostriate or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 ((blood adj5 clot$) or disease$ or damage$ or disorder$ or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct$ or anomal$)).tw.
5. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or lacunar or cortical or ocular) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$ or vasospasm or obstruct$ or vasoconstrict$)).tw.
6. ((cerebr$ or cerebell$ or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or subarachnoid $ or arachnoid$) adj3 (h?emorrhag$ or h?ematom$ or bleed$)).tw.
7. hemiplegia/ or paresis/ or exp gait disorders, neurologic/
8. (hemipleg$ or hemipar$ or paresis or paretic or hemineglect or hemi-neglect or ((unilateral or spatial or hemi?spatial or visual) adj5 neglect)).tw.
9. or/1-8
10. nutrition therapy/ or diet therapy/ or nutritional support/ or feeding methods/
11. enterostomy/ or enteral nutrition/
12. (enterostom$ or ((nutrient$ or nutrition$ or food$ or diet$ or mineral or vitamin or feed$) adj3 (parenteral or artificial or tube or enteric or enteral or enteric or intragastric or intestinal intraintestinal or method$))).tw.
13. exp dietary supplements/ or foods, specialized/ or food, formulated/ or amino acids/ or amino acids, essential/ or exp dietary proteins/ or soy milk/
14. eating/ or energy intake/ or malnutrition/
15. ((nutrient$ or nutrition$ or food$ or diet$ or mineral or vitamin or feed$ or amino or protein$) adj4 (intervention$ or treatment$ or therap$ or restrict$ or supplement$ or support$ or formulated or special$)).tw.
16. or/10-15
17. randomized controlled trial.pt.
18. controlled clinical trial.pt.
19. randomized.ab.
20. placebo.ab.
21. clinical trials as topic.sh.
22. random$.ab.
23. trial.ti.

24. or/17-23
25. exp animals/ not humans.sh.
26. 24 not 25
27. 9 and 16 and 26

Appendix 2. CENTRAL search strategy

#1 MeSH descriptor: [Cerebrovascular Disorders] this term only 1457
#2 MeSH descriptor: [Basal Ganglia Cerebrovascular Disease] explode all trees 30
#3 MeSH descriptor: [Brain Ischemia] explode all trees 3902
#4 MeSH descriptor: [Brain Infarction] this term only 116
#5 MeSH descriptor: [Brain Stem Infarctions] this term only 13
#6 MeSH descriptor: [Cerebral Infarction] this term only 1017
#7 MeSH descriptor: [Infarction, Anterior Cerebral Artery] this term only 7
#8 MeSH descriptor: [Infarction, Middle Cerebral Artery] this term only 145
#9 MeSH descriptor: [Infarction, Posterior Cerebral Artery] this term only 4
#10 MeSH descriptor: [Ischemic Attack, Transient] this term only 803
#11 MeSH descriptor: [Carotid Artery Diseases] this term only 500
#12 MeSH descriptor: [Carotid Artery Thrombosis] this term only 20
#13 MeSH descriptor: [Carotid Stenosis] this term only 675
#14 MeSH descriptor: [Cerebral Arterial Diseases] this term only 27
#15 MeSH descriptor: [Intracranial Arteriosclerosis] this term only 184
#16 MeSH descriptor: [Intracranial Arteriovenous Malformations] explode all trees 66
#17 MeSH descriptor: [Intracranial Embolism and Thrombosis] explode all trees 329
#18 MeSH descriptor: [Intracranial Hemorrhages] this term only 295
#19 MeSH descriptor: [Cerebral Hemorrhage] this term only 1026
#20 MeSH descriptor: [Cerebral Intraventricular Hemorrhage] this term only 20
#21 MeSH descriptor: [Intracranial Hemorrhage, Hypertensive] this term only 48
#22 MeSH descriptor: [Subarachnoid Hemorrhage] this term only 617
#23 MeSH descriptor: [Stroke] this term only 10022
#24 MeSH descriptor: [Hemorrhagic Stroke] this term only 13
#25 MeSH descriptor: [Ischemic Stroke] explode all trees 204
#26 MeSH descriptor: [Vasospasm, Intracranial] this term only 157
#27 MeSH descriptor: [Stroke Rehabilitation] this term only 2806
#28 (stroke or poststroke or post-stroke or cerebrovasc* or (cerebr* near/3 vasc*) or CVA* or apoplectic or apoplex* or (transient near/3 isch?emic near/3 attack) or tia* or SAH or AVM or ESUS or ICH or (cerebral small vessel near/3 disease*)):ti,ab,kw 76860
#29 ((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) near/3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) near/3 arter*)) near/3 (disease or damage* or disorder* or disturbance or dissection or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*)):ti,ab,kw 22033
#30 ((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA* or ((anterior or posterior) near/3 circulation) or basal ganglia or ((basilar or brachial or vertebr*) near/3 arter*) or space-occupying or brain ventricle* or lacunar or cortical or ocular) near/3 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi* or vasospasm or obstruct* or vasoconstrict*)):ti,ab,kw 17270
#31 ((cerebr* or cerebell* or vertebrobasil* or interhemispheric or hemispher* or intracran* or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA* or ((anterior or posterior) near/3 circulation) or basal ganglia or ((basilar or brachial or vertebr*) near/3 arter*) or space-occupying or brain ventricle* or subarachnoid* or arachnoid*) near/3 (h?emorrhag* or h?ematom* or bleed*)):ti,ab,kw 12477
#32 ((carotid or cerebr* or cerebell* or intracranial or ((basilar or brachial or vertebr*) near/3 arter*)) near/3 (aneurysm or malformation* or block* or dysplasia or disease* or bruit or injur* or narrow* or obstruct* or occlusion or constriction or presclerosis or scleros* or stenos* or atherosclero* or arteriosclero* or plaque* or thrombo* or embol* or arteriopathy)):ti,ab,kw 13343
#33 MeSH descriptor: [Hemiplegia] this term only 777
#34 MeSH descriptor: [Paresis] this term only 917
#35 MeSH descriptor: [Gait Disorders, Neurologic] explode all trees 748
#36 (hemipleg* or hemipar* or paresis or paretic or hemineglect or hemi-neglect or ((unilateral or spatial or hemi?spatial or visual) near/5 neglect)):ti,ab,kw 7458
#37 {or #1-#36} 95179
#38 MeSH descriptor: [Nutrition Therapy] this term only 206
#39 MeSH descriptor: [Diet Therapy] explode all trees 6425
#40 MeSH descriptor: [Nutritional Support] this term only 274
#41 MeSH descriptor: [Feeding Methods] this term only 60

#42 MeSH descriptor: [Enterostomy] this term only 18
#43 MeSH descriptor: [Enteral Nutrition] this term only 1965
#44 (enterostom* or ((nutrient* or nutrition* or food* or diet* or mineral or vitamin or feed*) near/3 (parenteral or artificial or tube or enteric or enteral or enteric or intragastric or intestinal or intraintestinal or method*))):ti,ab,kw 16957
#45 MeSH descriptor: [Dietary Supplements] explode all trees 13986
#46 MeSH descriptor: [Foods, Specialized] this term only 29
#47 MeSH descriptor: [Food, Formulated] this term only 794
#48 MeSH descriptor: [Amino Acids] this term only 1808
#49 MeSH descriptor: [Amino Acids, Essential] this term only 187
#50 MeSH descriptor: [Dietary Proteins] explode all trees 4353
#51 MeSH descriptor: [Soy Milk] this term only 77
#52 MeSH descriptor: [Eating] this term only 2947
#53 MeSH descriptor: [Energy Intake] this term only 5002
#54 MeSH descriptor: [Malnutrition] this term only 1233
#55 ((nutrient* or nutrition* or food* or diet* or mineral or vitamin or feed* or amino or protein*) near/4 (intervention* or treatment* or therap* or restrict* or supplement* or support* or formulated or special*)):ti,ab,kw 95552
#56 {or #38-#55} 113770
#57 #37 and #56 3825

Appendix 3. Embase (Ovid) search strategy

1. cerebrovascular disease/ or exp cerebrovascular accident/ or exp cerebrovascular malformation/ or exp basal ganglion haemorrhage/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or cerebral artery disease/ or exp carotid artery disease/ or brain atherosclerosis/ or exp stroke patient/ or stroke rehabilitation/ or occlusive cerebrovascular disease/ or basilar artery obstruction/ or exp cerebral sinus thrombosis/ or middle cerebral artery occlusion/ or vertebral artery stenosis/ or ocular ischemic syndrome/ or vertebrobasilar insufficiency/ or exp carotid artery/ or carotid artery surgery/ or carotid endarterectomy/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or (cerebr$ adj3 vasc$) or CVA$ or apoplectic or apoplex$ or (transient adj3 isch?emic adj3 attack) or tia$ or SAH or AVM or (cerebral small vessel adj3 disease)).ti,ab.
3. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulat$) or lenticulostriate or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 (disease or damage$ or disorder$ or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct$ or anomal$)).ti,ab.
4. ((cerebr$ or cerebell$ or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or subarachnoid$ or arachnoid$) adj3 (h?emorrhage or h?ematoma or bleed$ or microh?emorrhage or microbleed or (encephalorrhagia or hematencephal $))).ti,ab.
5. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or lacunar or cortical or ocular) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$ or vasospasm or obstruct$ or vasculopathy or vasoconstrict$)).ti,ab.
6. hemiparesis/ or hemiplegia/ or paresis/
7. (hemipleg$ or hemipar$ or paresis or paretic or hemineglect or hemi-neglect or ((unilateral or spatial or hemi?spatial or visual) adj5 neglect)).tw.
8. or/1-7
9. diet therapy/ or exp diet restriction/ or diet supplementation/ or mineral supplementation/ or nutritional support/ or vitamin supplementation/
10. nutrition/ or nutrient management/ or nutrition education/ or nutritional counseling/
11. supplementation/ or diet supplementation/ or mineral supplementation/ or nutritional support/ or vitamin supplementation/
12. enteric feeding/ or exp parenteral nutrition/ or exp enterostomy/ or enterostomy tube/
13. ((nutrient$ or nutrition$ or food$ or diet$ or mineral or vitamin or feed$) adj4 (intervention$ or treatment$ or therap$ or restrict$ or supplement$ or support$)).tw.
14. (enterostom$ or ((feeding or nutrition$) adj3 (parenteral or artificial or tube or enteric or enteral or enteric or intragastric or intestinal or intraintestinal or method$))).tw.
15. or/9-14
16. Randomized Controlled Trial/ or "randomized controlled trial (topic)"/
17. Randomization/
18. Controlled clinical trial/ or "controlled clinical trial (topic)"/
19. control group/ or controlled study/
20. clinical trial/ or "clinical trial (topic)"/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/
21. crossover procedure/

22. single blind procedure/ or double blind procedure/ or triple blind procedure/
23. placebo/ or placebo effect/
24. (random$ or RCT or RCTs).tw.
25. (controlled adj5 (trial$ or stud$)).tw.
26. (clinical$ adj5 trial$).tw.
27. clinical trial registration.ab.
28. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
29. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
30. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
31. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
32. (cross-over or cross over or crossover).tw.
33. (placebo$ or sham).tw.
34. trial.ti.
35. (assign$ or allocat$).tw.
36. controls.tw.
37. or/16-36
38. 8 and 15 and 37

Appendix 4. CINAHL (EBSCO) search strategy

S1 (MH "Cerebrovascular Disorders") OR (MH "Basal Ganglia Cerebrovascular Disease+") OR (MH "Carotid Artery Diseases") OR (MH "Carotid Artery Dissections") OR (MH "Carotid Artery Thrombosis") OR (MH "Carotid Stenosis") OR (MH "Cerebral Ischemia") OR (MH "Cerebral Ischemia, Transient") OR (MH "Hypoxia-Ischemia, Brain") OR (MH "Stroke, Lacunar") OR (MH "Cerebral Small Vessel Diseases") OR (MH "Intracranial Arterial Diseases") OR (MH "Cerebral Arterial Diseases") OR (MH "Cerebral Aneurysm") OR (MH "Intracranial Arteriosclerosis") OR (MH "Intracranial Embolism and Thrombosis+") OR (MH "Intracranial Hemorrhage") OR (MH "Cerebral Hemorrhage") OR (MH "Subarachnoid Hemorrhage") OR (MH "Stroke+")
S2 TI ((stroke or poststroke or post-stroke or cerebrovasc* or (cerebr* N3 vasc*) or CVA* or apoplectic or apoplex* or (transient N3 isch?emic N3 attack) or tia* or SAH or AVM or ESUS or ICH or (cerebral small vessel N3 disease*))) OR AB ((stroke or poststroke or post-stroke or cerebrovasc* or (cerebr* N3 vasc*) or CVA* or apoplectic or apoplex* or (transient N3 isch?emic N3 attack) or tia* or SAH or AVM or ESUS or ICH or (cerebral small vessel N3 disease*)))
S3 TI (((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) N3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) N3 arter*)) N3 ((blood N5 clot*) or disease* or damage* or disorder* or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*))) OR AB (((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or intracerebral or infratentorial or supratentorial or MCA* or ((anterior or posterior) N3 circulat*) or lenticulostriate or ((basilar or brachial or vertebr*) N3 arter*)) N3 ((blood N5 clot*) or disease* or damage* or disorder* or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct* or anomal*)))
S4 TI (((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA* or ((anterior or posterior) N3 circulation) or basal ganglia or ((basilar or brachial or vertebr*) N3 arter*) or space-occupying or brain ventricle* or lacunar or cortical or ocular) N3 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi* or vasospasm or obstruct* or vasoconstrict*))) OR AB (((cerebr* or cerebell* or arteriovenous or vertebrobasil* or interhemispheric or hemispher* or intracran* or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA* or ((anterior or posterior) N3 circulation) or basal ganglia or ((basilar or brachial or vertebr*) N3 arter*) or space-occupying or brain ventricle* or lacunar or cortical or ocular) N3 (isch?emi* or infarct* or thrombo* or emboli* or occlus* or hypoxi* or vasospasm or obstruct* or vasoconstrict*)))
S5 TI (((cerebr* or cerebell* or vertebrobasil* or interhemispheric or hemispher* or intracran* or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA* or ((anterior or posterior) N3 circulation) or basal ganglia or ((basilar or brachial or vertebr*) N3 arter*) or space-occupying or brain ventricle* or subarachnoid* or arachnoid*) N3 (h?emorrhag* or h?ematom* or bleed*))) OR AB (((cerebr* or cerebell* or vertebrobasil* or interhemispheric or hemispher* or intracran* or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA* or ((anterior or posterior) N3 circulation) or basal ganglia or ((basilar or brachial or vertebr*) N3 arter*) or space-occupying or brain ventricle* or subarachnoid* or arachnoid*) N3 (h?emorrhag* or h?ematom* or bleed*)))
S6 (MH "Hemiplegia")
S7 (MH "Gait Disorders, Neurologic+")
S8 TI ((hemipleg* or hemipar* or paresis or paretic or hemineglect or hemi-neglect or ((unilateral or spatial or hemi?spatial or visual) N5 neglect))) OR AB ((hemipleg* or hemipar* or paresis or paretic or hemineglect or hemi-neglect or ((unilateral or spatial or hemi?spatial or visual) N5 neglect)))
S9 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S10 (MH "Diet Therapy")
S11 (MH "Nutrition Services+")
S12 (MH "Nutritional Support") OR (MH "Dietary Supplementation") OR (MH "Enteral Nutrition") OR (MH "Home Nutritional Support")

S13 (MH "Feeding Methods")
S14 (MH "Enterostomy")
S15 TI ((enterostom* or ((nutrient* or nutrition* or food* or diet* or mineral or vitamin or feed*) N3 (parenteral or artificial or tube or enteric or enteral or enteric or intragastric or intestinal or intraintestinal or method*)))) OR AB ((enterostom* or ((nutrient* or nutrition* or food* or diet* or mineral or vitamin or feed*) N3 (parenteral or artificial or tube or enteric or enteral or enteric or intragastric or intestinal or intraintestinal or method*))))
S16 (MH "Dietary Supplements+") OR (MH "Nutrients") OR (MH "Food, Formulated") OR (MH "Amino Acids+") OR (MH "Dietary Proteins") OR (MH "Soy Milk") OR (MH "Food")
S17 (MH "Eating") OR (MH "Food Intake") OR (MH "Energy Intake") OR (MH "Diet") OR (MH "Malnutrition")
S18 TI (((nutrient* or nutrition* or food* or diet* or mineral or vitamin or feed* or amino or protein*) N4 (intervention* or treatment* or therap* or restrict* or supplement* or support* or formulated or special*))) OR AB (((nutrient* or nutrition* or food* or diet* or mineral or vitamin or feed* or amino or protein*) N4 (intervention* or treatment* or therap* or restrict* or supplement* or support* or formulated or special*)))
S19 S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18
S20 MH Random Assignment or MH Single-blind Studies or MH Double-blind Studies or MH Triple-blind Studies or MH Crossover design or MH Factorial Design
S21 TI ("multicentre study" or "multicenter study" or "multi-centre study" or "multi-center study") or AB ("multicentre study" or "multicenter study" or "multi-centre study" or "multi-center study") or SU ("multicentre study" or "multicenter study" or "multi-centre study" or "multi-center study")
S22 TI random* or AB random*
S23 AB "latin square" or TI "latin square"
S24 TI (crossover or cross-over) or AB (crossover or cross-over) or SU (crossover or cross-over)
S25 MH Placebos
S26 (AB (singl* or doubl* or trebl* or tripl*) or TI (singl* or doubl* or trebl* or tripl*)) AND (TI blind* or AB mask* or AB blind* or TI mask*)
S27 TI Placebo* or AB Placebo* or SU Placebo*
S28 MH Clinical Trials
S29 TI (Clinical AND Trial) or AB (Clinical AND Trial) or SU (Clinical AND Trial)
S30 S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29
S31 S9 AND S19 AND S30

Appendix 5. AMED (Ovid) search strategy

1. cerebrovascular disorders/ or cerebral hemorrhage/ or cerebral infarction/ or cerebral ischemia/ or cerebrovascular accident/ or stroke/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or (cerebr$ adj3 vasc$) or CVA$ or apoplectic or apoplex$ or (transient adj3 isch?emic adj3 attack) or tia$ or SAH or AVM or ESUS or ICH).tw.
3. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulat$) or lenticulostriate or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 ((blood adj5 clot$) or disease$ or damage$ or disorder$ or disturbance or dissection or lesion or syndrome or arrest or accident or lesion or vasculopathy or insult or attack or injury or insufficiency or malformation or obstruct$ or anomal$)).tw.
4. ((cerebr$ or cerebell$ or arteriovenous or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or lacunar or cortical or ocular) adj3 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$ or vasospasm or obstruct$ or vasoconstrict$)).tw.
5. ((cerebr$ or cerebell$ or vertebrobasil$ or interhemispheric or hemispher$ or intracran$ or corpus callosum or intracerebral or intracortical or intraventricular or periventricular or posterior fossa or infratentorial or supratentorial or MCA$ or ((anterior or posterior) adj3 circulation) or basal ganglia or ((basilar or brachial or vertebr$) adj3 arter$) or space-occupying or brain ventricle$ or subarachnoid $ or arachnoid$) adj3 (h?emorrhag$ or h?ematom$ or bleed$)).tw.
6. ((carotid or cerebr$ or cerebell$ or intracranial or ((basilar or brachial or vertebr$) adj3 arter$)) adj3 (aneurysm or malformation$ or block$ or dysplasia or disease$ or bruit or injur$ or narrow$ or obstruct$ or occlusion or constriction or presclerosis or scleros$ or stenos $ or atherosclero$ or arteriosclero$ or plaque$ or thrombo$ or embol$ or arteriopathy)).tw.
7. hemiplegia/
8. (hemipleg$ or hemipar$ or paresis or paretic or hemineglect).tw.
9. or/1-8
10. nutrition/ or exp diet/ or nutritional status/ or nutrition therapy/ or exp diet therapy/
11. feeding methods/ or enteral feeding/ or enterostomy/
12. (enterostom$ or ((nutrient$ or nutrition$ or food$ or diet$ or mineral or vitamin or feed$) adj3 (parenteral or artificial or tube or enteric or enteral or enteric or intragastric or intestinal or intraintestinal or method$))).tw.
13. food/ or exp amino acids/ or dietary proteins/
14. eating/ or energy metabolism/
15. ((nutrient$ or nutrition$ or food$ or diet$ or mineral or vitamin or feed$ or amino or protein$) adj4 (intervention$ or treatment$ or therap$ or restrict$ or supplement$ or support$ or formulated or special$)).tw.

16. 10 or 11 or 12 or 13 or 14 or 15
17. 9 and 16

Appendix 6. Clinical trials register searches

US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov)

(diet OR nutrition OR nutrient OR food OR feed OR enteral OR eating) AND AREA[StudyType] EXPAND[Term] COVER[FullMatch] "Interventional" AND AREA[ConditionSearch] (Brain Infarction OR Intracranial Hemorrhages OR Carotid Artery Diseases OR Brain Ischemia OR Cerebral Hemorrhage OR Cerebrovascular Disorders OR Stroke) AND AREA[StdAge] EXPAND[Term] COVER[FullMatch] ("Adult" OR "Older Adult")

World Health Organization International Clinical Trials Registry Platform (trialsearch.who.int/Default.aspx)

1. diet AND stroke OR nutrition AND stroke OR nutrient AND stroke OR food AND stroke OR feed AND stroke OR enteral AND stroke OR eating AND stroke

2. diet AND cerebrovascular OR nutrition AND cerebrovascular OR nutrient AND cerebrovascular OR food AND cerebrovascular OR feed AND cerebrovascular OR enteral AND cerebrovascular OR eating AND stroke

HISTORY

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- Substantial contributions to the conception or design of the work; the acquisition, analysis, or interpretation of data; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Author's contributions:

- Conceptualisation: KS, MN, RM, DY, EH
- Screening, data extraction, and/or assessment of risk of bias and certainty of the evidence: KS, MN, RM, EN, KM, TM, NT, EH, NS
- Data curation: KS, DY
- Analysis: KS, DY
- Supervision: DY, EH, RM, NS
- Funding acquisition: KS
- Writing original draft: KS
- Writing: reviewing and editing: all authors
- Revising it critically for important intellectual content: NS
- Guarantor: KS

DECLARATIONS OF INTEREST

- Kotomi Sakai: Published a review related to this topic in 2018 in the Journal of Nutrition, Health & Aging. Work as a researcher: Department of Research, Heisei Medical Welfare Group Research Institute. A researcher in the Division of Policy Evaluation, Department of Health Policy, Research Institute, National Center for Child Health and Development. Work as a health professional: speech-language-hearing therapist, Sakai Heisei Hospital.
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  Kotomi Sakai

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- We planned to extract outcomes that were assessed using validated tools, but we extracted all relevant outcomes regardless of the tool used and reported them in the results section (see Results).
- We extracted the outcome of neurological impairment, leg strength, and gastrointestinal haemorrhage in addition to the outcomes in the protocol (see Results)
- We planned to conduct subgroup analyses using types of nutritional therapy. However, due to heterogeneity amongst nutrients, we analysed the outcomes by types of nutritional therapy (see Results).
- We used Cochrane's Screen4Me workflow to help identify potential reports of randomised trials during the screening process (see Selection of studies).

INDEX TERMS

Medical Subject Headings (MeSH)

*Activities of Daily Living; Bias; Malnutrition [diet therapy] [prevention & control]; Nutrition Therapy [methods]; Nutritional Status; Quality of Life; *Randomized Controlled Trials as Topic; *Stroke [complications]; *Stroke Rehabilitation [methods]

MeSH check words

Humans