Supplementary Online Content

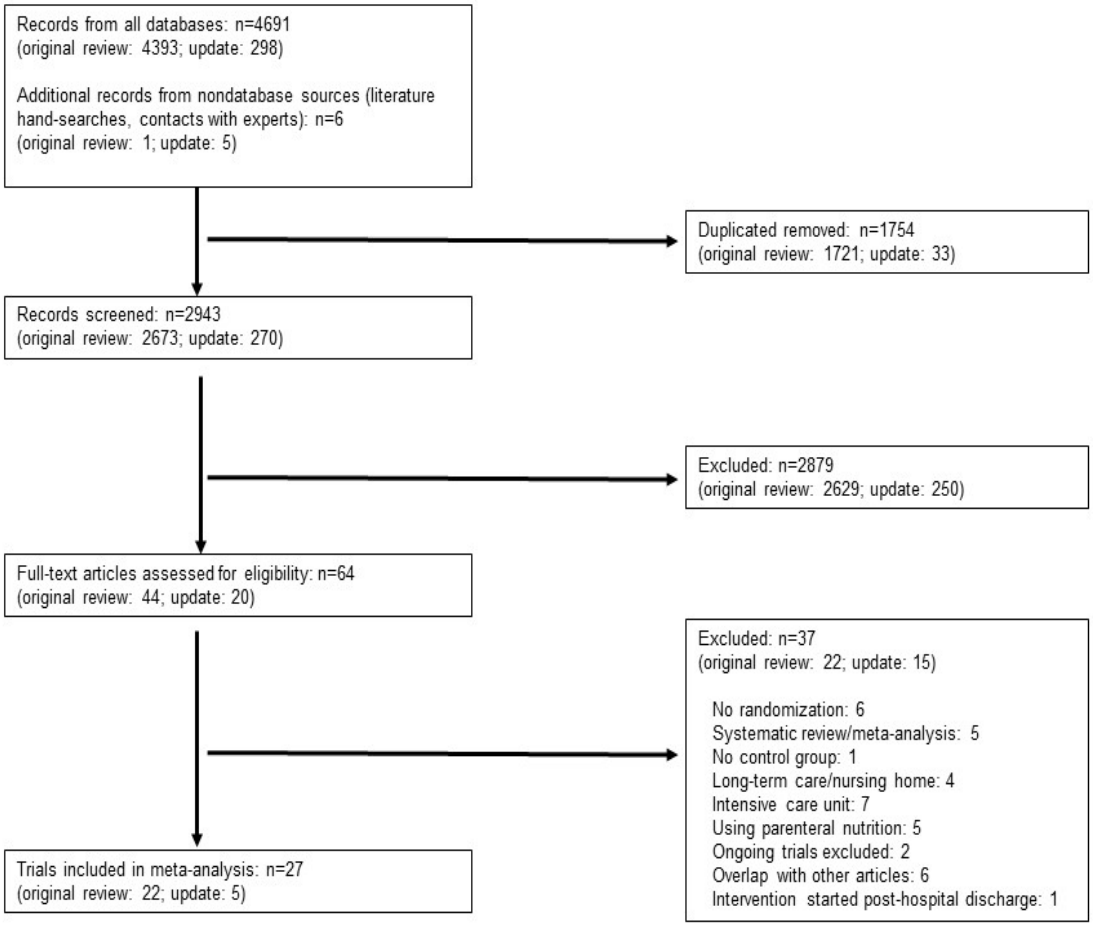
Gomes F, Baumgartner A, Bounoure L, et al. Association of nutritional support with clinical outcomes among medical inpatients who are malnourished or at nutritional risk: an updated systematic review and meta-analysis. *JAMA Netw Open.* 2019;2(11): e1915138. doi:10.1001/jamanetworkopen.2019.15138

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Search Strategy Used in MEDLINE

1. exp *PROTEIN-ENERGY MALNUTRITION/ or malnutrition.mp. or exp *MALNUTRITION/
2. maln*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
3. undern*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
4. 1 or 2 or 3
5. exp *Nutrition Therapy/ or exp *Enteral Nutrition/ or nutritional therapy.mp.
6. exp *Nutritional Support/ or nutrition support.mp.
7. (nutrition* adj3 (support or therapy)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
8. dietary advice.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
9. food fortification.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
10. oral nutrition* supplement*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
11. (enteral adj1 (nutrition or feeding)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
12. 5 or 6 or 7 or 8 or 9 or 10 or 11
13. hospital.mp. or exp *Hospitals/
14. hospital*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
15. ward*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
16. in?patient*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
17. 13 or 14 or 15 or 16
18. 4 and 12 and 17
19. limit 18 to yr="2015 - 2019"

eFigure 1. Flow Chart of Studies' Selection

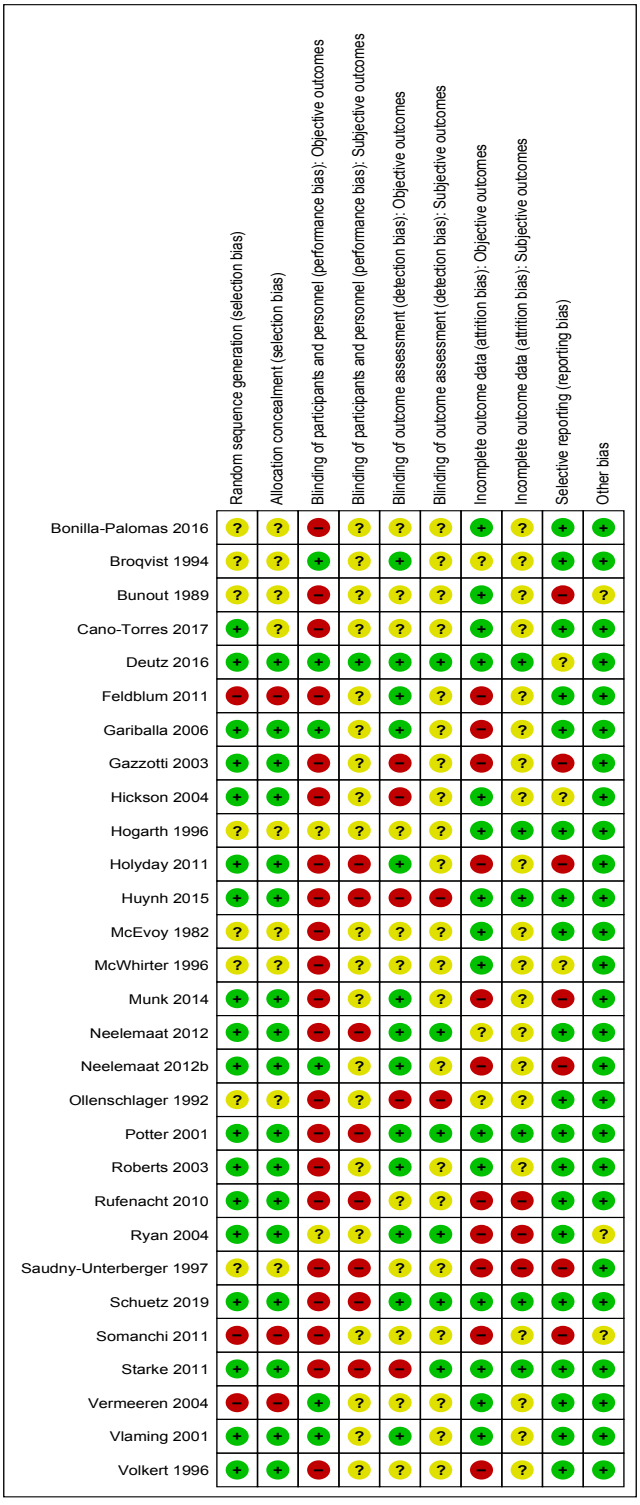


eFigure 2. Risk of Bias Overall and Stratified by Trial

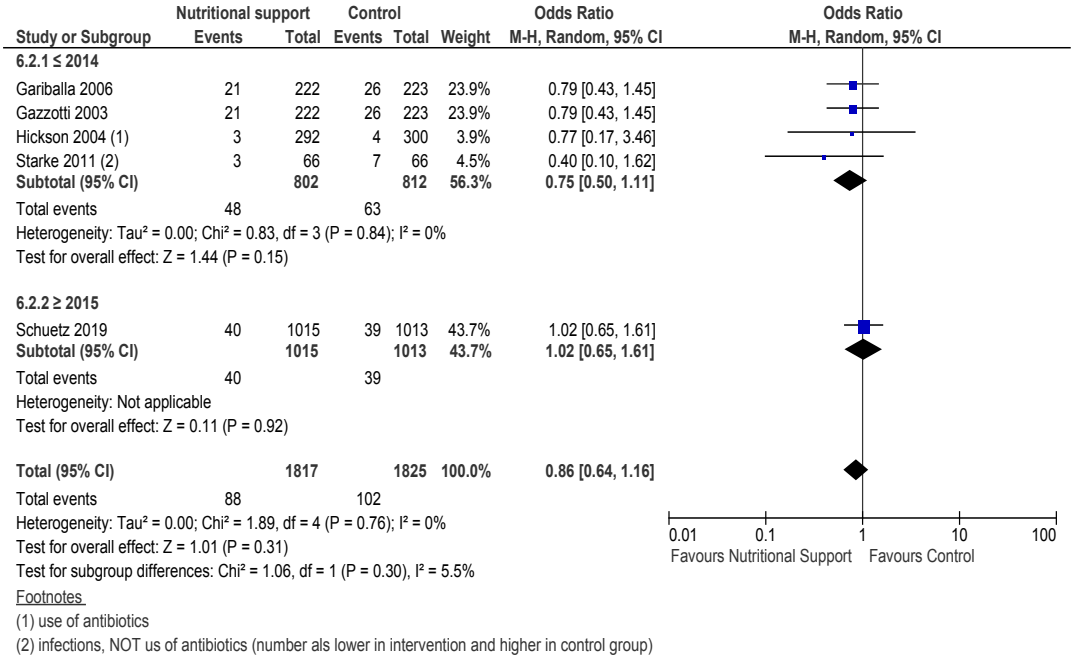
eFigure 2A. Risk of Bias Graph Overall

Review authors' judgements about each risk of bias item presented as percentages across all included studies

eFigure 2B. Risk of Bias Graph Stratified by Trial



eFigure 3. Forest Plot Comparing Nutritional Intervention vs. Control for Infection Stratified by Publication Year

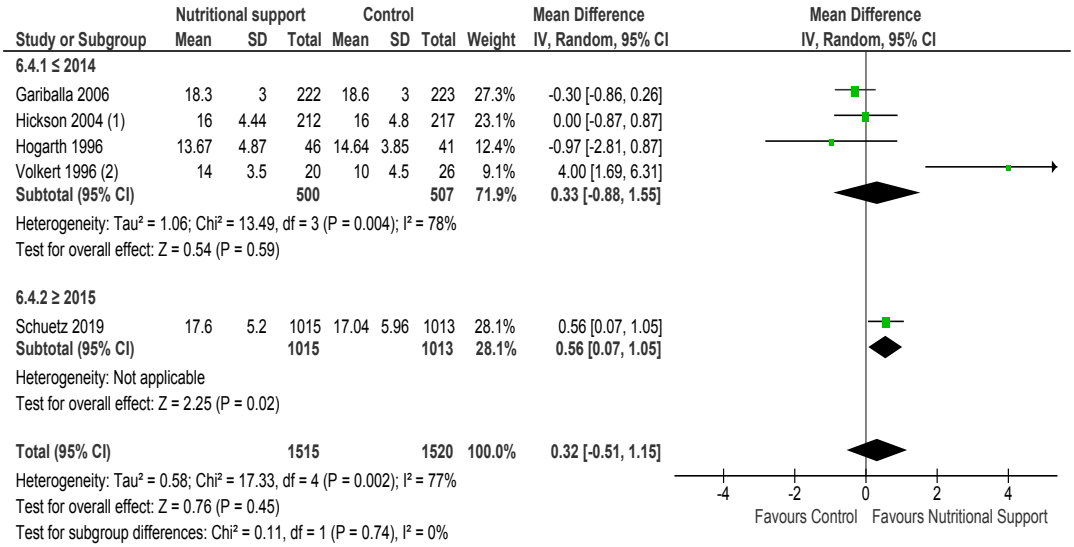


Footnotes

(1) use of antibiotics

(2) infections, NOT us of antibiotics (number als lower in intervention and higher in control group)

eFigure 4. Forest Plot Comparing Nutritional Intervention vs. Control for Functional Outcome Stratified by Publication Year

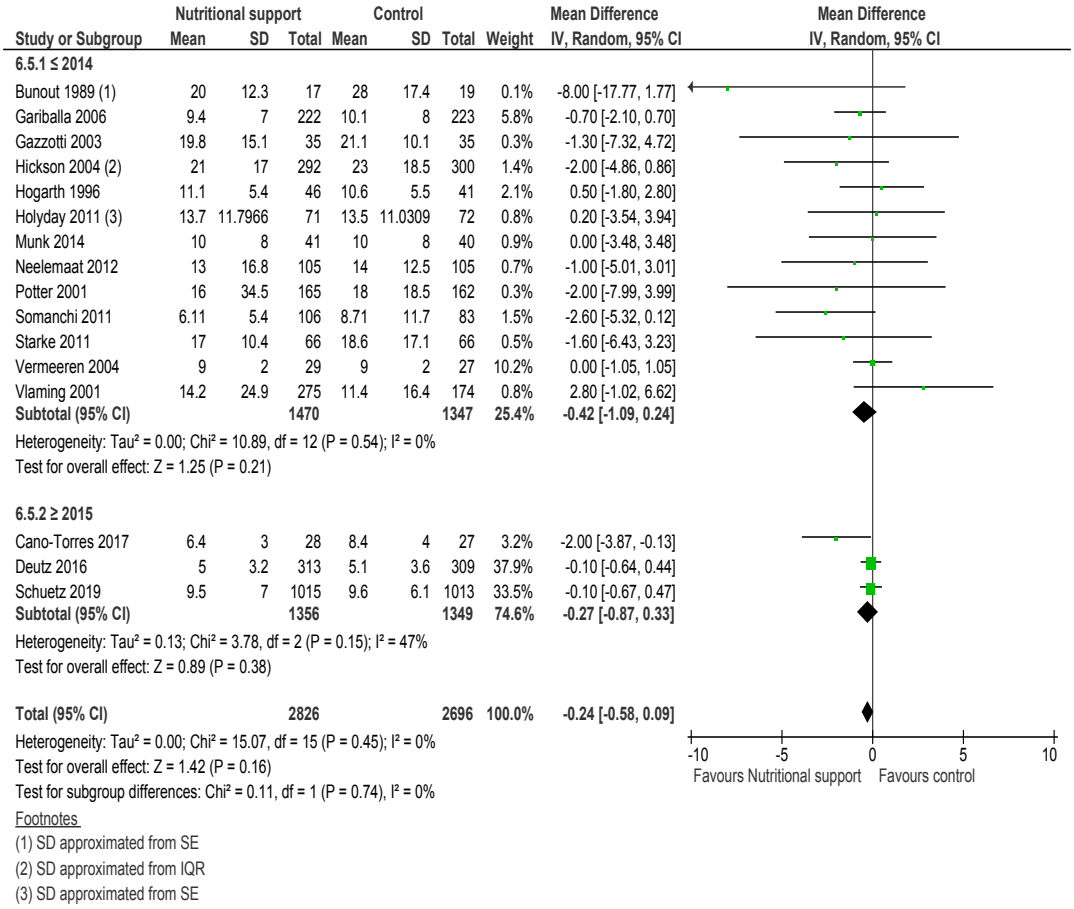


Footnotes

(1) SD approximated from interquartile range

(2) results combined for patients with good and bad compliance; mean and SD approximated; Barthel 100 scale adapted to Barthel 20 points scale

eFigure 5. Forest Plot Comparing Nutritional Intervention vs. Control for Length of Stay Stratified by Publication Year



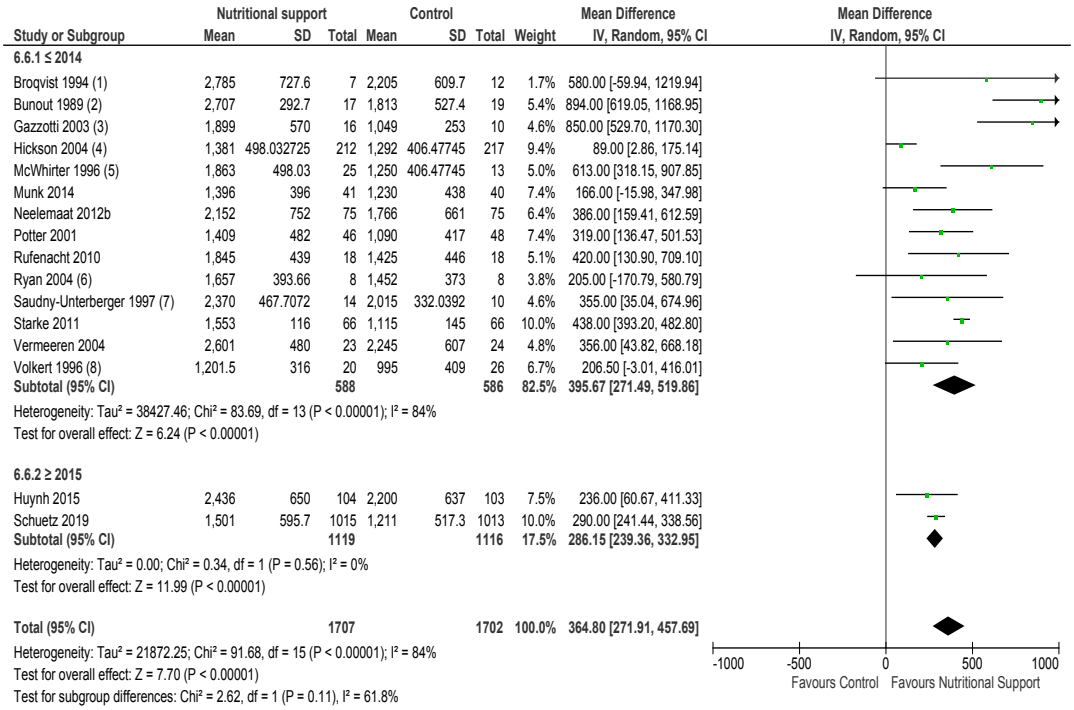
Footnotes

(1) SD approximated from SE

(2) SD approximated from IQR

(3) SD approximated from SE

eFigure 6. Forest Plot Comparing Nutritional Intervention vs. Control for Daily Energy Intake Stratified by Publication Year



Footnotes

(1) SD approximated from SEM

(2) SD approximated from SEM

(3) intervention: spontaneous intake and intake from supplements combined

(4) SD approximated from median SD other included studies

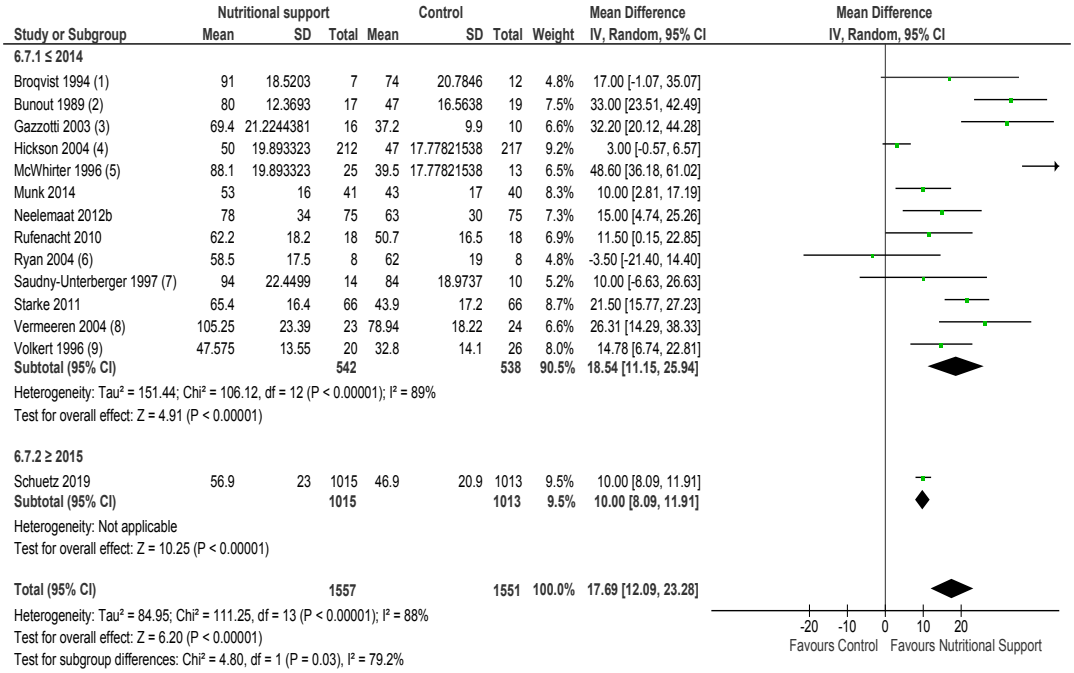
(5) second intervention group compared to 50% of control group (see also oral feeding only vs no support), SD approximated from median SD other included studies

(6) 2 intervention groups combined, cross over design, 16 patients in total, analysed with 8/8

(7) SD approximated from SEM

(8) 2 intervention groups pooled

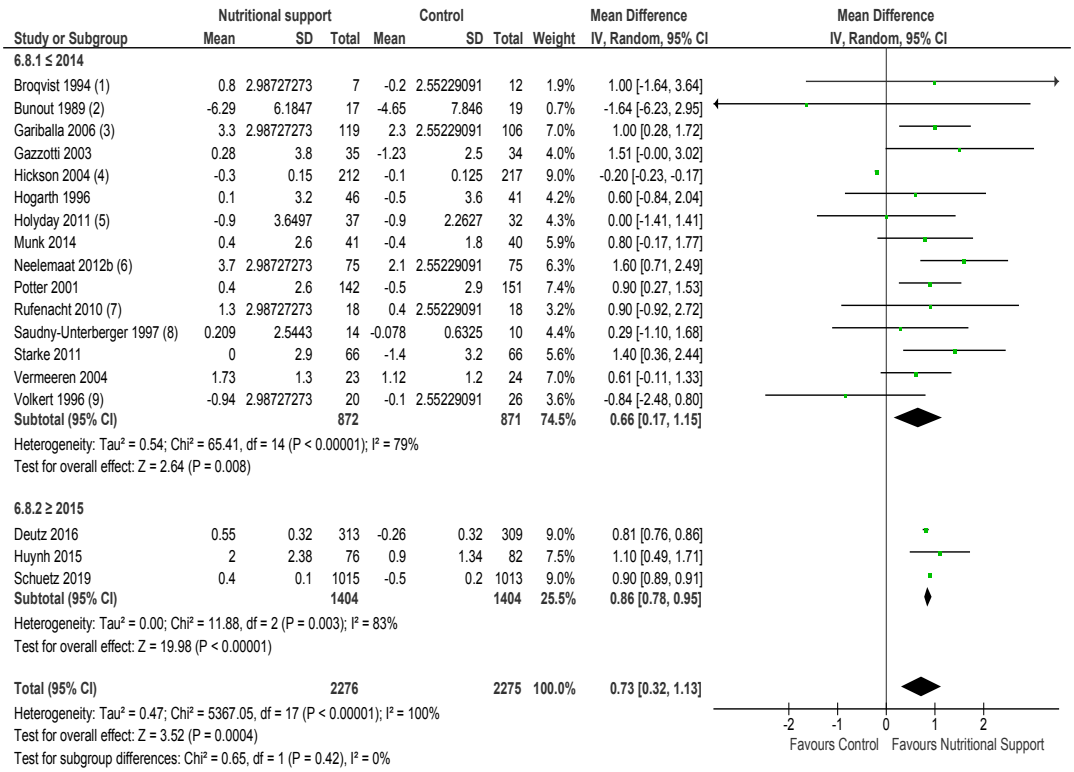
eFigure 7. Forest Plot Comparing Nutritional Intervention vs. Control for Daily Protein Intake Stratified by Publication Year



Footnotes

(1) SD approximated from SEM
(2) approximated from SEM
(3) SD intervention group combined spontaneous intake and supplement intake
(4) SD approximated from median SD other included studies
(5) second intervention group compared to 50% of control group, SD approximated from median SD other included studies
(6) 2 intervention groups pooled, cross over design, 16 patients in total, analysed with 8/8
(7) approximated from SEM
(8) protein intake approximated based on calculated body weight (from weight change)
(9) intervention: groups combined (good and bad supplement acceptance)

eFigure 8. Forest Plot Comparing Nutritional Intervention vs. Control for Weight Change Stratified by Publication Year



Footnotes

(1) SD approximated from median SD of other publications
(2) SD approximated from SEM
(3) calculated from baseline-weight and weight at follow up, SD approximated from SD other publications
(4) SD approximated from interquartile range
(5) SD approximated from SE
(6) mean calculated fromweight at baseline and follow up, SD approximated from SD other publications
(7) SD estimated from median SD of other publications
(8) SD approximated from SEM
(9) SD approximated from SD other publications

eTable. Adherence to Study Protocol

First author, and year of publication	Compliance rate (in %)		Method for measurement of energy and protein intakes		Patients achieving energy and protein targets (in %)		Reasons behind a reduced compliance or efficiency		Adherence (final judgment)	Comments to author judgement
	INTERVENTION	*CONTROL*	*INTERVENTION*	*CONTROL*	*INTERVENTION*	*CONTROL*	*INTERVENTION*	*CONTROL*		
Bonilla-Paloma 2016 (1)	NR	NR	NR Nutritional intake was only assessed at baseline	NR Nutritional intake was only assessed at baseline	NR Nutritional intake was only assessed at baseline	NR Nutritional intake was only assessed at baseline	NR	NR	Poor	
Broqvist 1994 (2)	- Meals: NR - ONS: 76.8% of total ONS offered consumed	- Meals: NR - Placebo: 89.3% of total consumed	- Meals: dietary history (questionnaires) - ONS: counting number of bottles consumed	- Meals: dietary history (questionnaires) - ONS: counting number of bottles consumed	50% of patients achieving energy target (protein: NR)	14% of patients achieving energy target (protein: NR)	NR	NR	Good	
Bunout 1989 (3)	- Meals: NR - Casein-based product: NR	- Meals: NR	- Meals: Weighing of food trays - Casein-based product: NR	- Meals: Weighing of food trays	NR	NR	NR	NR	Good	Energy intake in intervention group approximately1000 kcal/d more than in control group
Cano-Torres 2017 (4)	- adherence to diet during hospital stay: 90.1%	- adherence to diet during hospital stay: 77.7%	Adherence to dietary intake was assessed by 24-hour recording.	Adherence to dietary intake was assessed by 24-hour recording	NR Total percentage of energy intake was not available	NR Total percentage of energy intake was not available	NR	NR	Good	The dietary advice received included motivation to adhere to a diet.
Deutz 2016 (5)	- Meals: NR - ONS: mean expected intake was 73.2% in-hospital and 76.9% at 30-days post-discharge	- Meals: NR - ONS: mean expected intake was 72.7% in-hospital and 78.4% at 30-days post-dsicharge	NR	NR	NR	NR	Reasons may be dependent on appetite, other clinical variables, or on reimbursement policies	Reasons may be dependent on appetite, other clinical variables, or on reimbursement policies	Good	The greater increases in body weight and serum 25-hydroxyvitamin D concentration among the intervention patients can be considered indicative of adherence with product intake
Feldblum 2011 (6)	NR	NR	24- hour recall (data not shown for assessment by Food Frequency Questionnaire)	24- hour recall (data not shown for assessment by Food Frequency Questionnaire)	NR	NR	NR	NR	Poor	No significant differences in intake between intervention and control group
Gariballa 2006 (7)	- 69% of patients consumed 0-25% of ONS	- 68% of patients consumed 0-25% of placebo	- Meals: validated food diary - ONS: leftover supplements measured	- Meals: validated food diary - Placebo: leftover supplements measured	NR	NR	NR	NR	Poor	

	- 6% of patients consumed 26-50%of ONS - 25% of patients consumed 51-75% of ONS - 10% of patients consumed 76-100% of ONS - Meals: NR	- 6% of patients consumed 26-50% of placebo - 22% of patients consumed 51-75% 15% 76-100% of placebo - Meals: NR								
Gazzotti 2003 (8)	- Meals: NR - ONS: 88% of total ONS offered consumed	Meals: NR	Consumption of each portion of ONS and regular meals measured by direct observation and recorded as all, three quarters, half, one-quarter or none of the portion	Consumption of regular meals measured by direct observation and recorded as all, three quarters, half, one-quarter or none of the portion	NR	NR	Medical reasons rather than patients finding the supplements unpalatable	NR	Good	
Hickson 2004 (9)	NR	NR	Weighing the main meals and food records for breakfast, snacks and drinks	Weighing the main meals and food records for breakfast, snacks and drinks	NR	NR	NR	NR	Poor	Data revealed only a “trend towards higher intake in intervention group”
Hogarth 1996 (10)	Active energy group (active and placebo vitamin): 31% patients consuming > 50% of offered drinks	Placebo energy group (active and placebo vitamin): 31% patients consuming > 50% of offered drinks	- Measure of unconsumed fluid each day during admission. - Following discharge, estimation of the volume of fluid (in quarters) remaining in each bottle each day.	- Measure of unconsumed fluid each day during admission. - Following discharge, estimation of the volume of fluid (in quarters) remaining in each bottle each day.	NR	NR	Patients were unable to tolerate the large volume (750ml) of sweet, fizzy fluid that was provided.	Patients were unable to tolerate the large volume (750ml) of sweet, fizzy fluid that was provided.	Poor	
Holyday 2011 (11)	NR	NR	NR	NR	NR	NR	NR	NR	Poor	
Huynh 2015 (12)	- ONS: 90% of compliance. - 85.9% attended at least two sessions of dietary counselling over the study period	- 86.6% attended at least two sessions of dietary counselling over the study period	Dietary intakes: 24-h food recall administered by site dietitians at baseline and every 4 weeks. Compliance with ONS during hospital stay by direct observation; post-discharge compliance by monitoring the	Dietary intakes: 24-h food recall administered by site dietitians at baseline and every 4 weeks.	NR	NR	NR A number of reasons for explaining the high compliance with ONS was provided.	NR A number of reasons for explaining the high compliance with ONS was provided.	Good	

			return of empty ONS sachets							
McEvoy 1982 (13)	NR	NR	NR	NR	NR	NR	NR	NR	Good	Patients “received 2 units of ONS”, according to significant weight gain good adherence must be assumed
McWhirter 1996 (14)	- ONS group: 74% of prescription consumed - Enteral feeding group: 78% of prescription consumed	NR	- Meals: food charts completed by nursing staff - ONS and enteral feeding: documented (method NR).	Food charts completed by nursing staff	- ONS group: 71% patients achieving > 80% energy target - Enteral feeding group: 88% patients achieving > 80% energy target	4% patients achieving >80% energy target	NR	NR	Good	
Munk 2014 (15)	- Meals: NR - ONS: consumption measured (method and results NR)	- Meals: NR - ONS: consumption measured (method and results NR)	Meals and ONS: visual assessment of amount consumed and recorded in quartiles (0%, 25%, 50%, 75% and 100%) by nursing staff or patients. Daily dietary recall interviews to ensure and verify the content of patients’ dietary records	- Meals and ONS: visual assessment of amount consumed and recorded in quartiles (0%, 25%, 50%, 75% and 100%) by nursing staff or patients. Daily dietary recall interviews to ensure and verify the content of patients’ dietary records	- 76% of patients achieved >75% energy target. - 66% of patients achieved >75% protein target	- 28% of patients achieved >75% energy target. - 12% of patients achieved >75% protein target	NR	NR	Good	
Neelemaat 2012 (16)	- Adherence to oral nutritional support: 80% - Adherence to telephone counselling by dietician: 96%	NR	NR	NR	NR	NR	NR	NR	Good	
Ollenschläger 1992 (17)	NR	NR	NR	NR	NR	NR	NR	NR	Good	Severely observed patients and interventions, therefore adherence probably good
Potter 2001 (18)	NR	NR	- Percentage of supplement consumed recorded - Weighed dietary intakes of voluntary food, (ie, normal diet and snacks)	Weighed dietary intakes of voluntary food, (ie, normal diet and snacks)	NR	NR	Reduced oral intake for medical reasons rather than patients finding the supplements unpalatable.	NR	Good	Observed ONS intake, compliance was good, 50% of patients consumed a mean additional intake of 430 to 540 kcal/d, and a further 25% of patients consumed a

										mean additional intake of at least 270 kcal/d
Roberts 2003 (19)	- 52% consumed 80–100% of total sip-feed provided - 22% consumed 79–50% - 26% consumed less than 50% - Meals: NR	NR	- Counting of the number of sip feed consumed throughout hospital stay - Meal: NR	NR	48% with total energy intake ≥ minimum energy requirements	25% with total energy intake ≥ minimum energy requirements	The reason for non-compliance was generally medical, e.g. no oral intake, vomiting	NR	Good	
Rüfenacht 2010 (20)	NR	NR	Meals weighed before and after consumption	Meals weighed before and after consumption	- 94% of patients achieving >75% energy requirements - 78% of patients achieving >75% protein requirements	- 61% of patients achieving >75% energy requirements - 67% of patients achieving >75% protein requirements	NR	NR	Good	
Ryan 2004 (21)	NR	NR	Weighing of food and drinks before and after meals	Weighing of food and drinks before and after meals and adding nutrients provided by ONS (method for assessing ONS consumption NR)	NR	NR	NR	NR	Good	Energy intake was assessed over 3 consecutive days, intervention group consumed 800 kJ more/d
Saudny-Unterberger 1997 (22)	NR	NR	Food and ONS: calorie count verified by 24-h dietary recall	Food: calorie count verified by 24-h dietary recall	NR	NR	NR	NR	Good	Intervention group consumed significantly more energy/ kg body weight (39 kcal/kg/d) than did the control group
Schuetz 2019 (23)	NR	NR	Nutritional intake reassessed every 24–48 h throughout the hospital stay by the trained registered dietician based on daily food records for each patients	Nutritional intake reassessed every 24–48 h throughout the hospital stay by the trained registered dietician based on daily food records for each patients	78% reached both nutritional goals (energy and protein) during the first 10 days	48% reached both nutritional goals (energy and protein) during the first 10 days	Patient, treatment, and hospital factors (e.g., delay or refusal to start enteral or parenteral nutrition by the patient, early discharge of patients, diagnostic exams interfering with nutritional support) may have prevented full adherence to the protocol	NR	Good	The daily re-assessment by dietitians and individualized nutritional care plan is probably contributing to a good adherence in the intervention group
Somanchi 2011 (24)	NR	NR	NR	NR	NR	NR	NR	NR	Poor	

										No information therefore poor adherence assumed
Starke 2012 (25)	- Meals: all patients had at least one meal during hospitalisation which was consumed less than 75% - ONS: NR	- Meals: NR - ONS: - 40% of the patients taking less than one quarter - 9% taking 25-50% - 16% taking 50-75% - 35% taking three quarters or more.	- Meals: The consumed part of each food item was visually estimated and recorded. - Snacks, drinks and ONS: reported by ward staff	The consumed part of each food item was visually estimated and recorded	- 83% managed to reach a mean daily energy intake ≥75% threshold of their individual estimated total energy expenditure	- 30% managed to reach a mean daily energy intake ≥75% threshold of their individual estimated total energy expenditure	NR	NR	Good	
Vermeeren 2004 (26)	- Meals: NR - ONS: 98% (± 2%) of supplements provided consumed	- Meals: NR - Placebo: NR	- Meals: dietary records and use of an automated food distribution system. Verification by dietician - ONS: monitoring of proportion consumed	- Meals: dietary records and use of an automated food distribution system. Verification by dietician - Placebo: NR	NR	NR	NR	NR	Good	
Vlaming 2001 (27)	- Meals: NR - ONS: - 18% consumed <25% of sipfeeds - 19% consumed 25-49.9% of sipfeeds - 29% consumed 50-74.9% - 34% consumed >75%	- Meals: NR - Placebo: NR	Sipfeeds: drug charts	Placebo: NR	NR	NR	NR	NR	Good	
Volkert 1996 (28)	- Meals: NR - ONS: - 55% consumed regularly one per day - 45% consumed one every two days or less	- Meals: NR	- Meals: 3-day weighing records - ONS: consumption recorded daily by visits during hospitalization and every week after discharge	- Meals: 3-day weighing records	NR	NR	Anorexia or dislike	NR	Poor	

NR = Not reported; ONS = oral nutrition supplements

eReferences

1. Bonilla-Palomas JL, Gamez-Lopez AL, Castillo-Dominguez JC, Moreno-Conde M, Lopez Ibanez MC, Alhambra Exposito R, et al. Nutritional Intervention in Malnourished Hospitalized Patients with Heart Failure. Arch Med Res. 2016;47(7):535-40.
2. Broqvis M, Arnqvist H., Dahlström U, Larsson J, Nylander E, Permert J**.** Nutritional assessment and muscle energy metabolism in severe chronic congestive heart failure — effects of long-term dietary supplementation. European Heart Journal. 1994;15:1641-50.
3. Bunout D, Aicardi V, Hirsch S, Petermann M, Kelly M, Silva G, et al. Nutritional support in hospitalized patients with alcoholic liver disease. Eur J Clin Nutr. 1989;43(9):615-21.
4. Cano-Torres EA, Simental-Mendia LE, Morales-Garza LA, Ramos-Delgado JM, Reyes-Gonzalez MM, Sanchez-Nava VM, et al. Impact of Nutritional Intervention on Length of Hospital Stay and Mortality among Hospitalized Patients with Malnutrition: A Clinical Randomized Controlled Trial. J Am Coll Nutr. 2017;36(4):235-9.
5. Deutz NE, Matheson EM, Matarese LE, Luo M, Baggs GE, Nelson JL, et al. Readmission and mortality in malnourished, older, hospitalized adults treated with a specialized oral nutritional supplement: A randomized clinical trial. Clinical Nutrition. 2016;35(1):18-26.
6. Calvey H. DM, Williams R. Controlled tiral of nutritionan supplementation, with and without branched chain amino acid enrichment, in treatment of acute alcoholic hepatitis. Journal of Hepathology. 1985;1:141-51.
7. Gariballa S, Forster S, Walters S, Powers H**.** A randomized, double-blind, placebo-controlled trial of nutritional supplementation during acute illness. Am J Med. 2006;119(8):693-9.
8. Gazzotti C, Arnaud-Battandier F, Parello M, Farine S, Seidel L, Albert A, et al. Prevention of malnutrition in older people during and after hospitalisation: results from a randomised controlled clinical trial. Age Ageing. 2003;32(3):321-5.
9. Hickson M, Bulpitt C, Nunes M, Peters R, Cooke J, Nicholl C, et al. Does additional feeding support provided by health care assistants improve nutritional status and outcome in acutely ill older in-patients?—a randomised control trial. Clinical Nutrition. 2004;23(1):69-77.
10. Hogarth MB, Marshall P, Lovat LB, Palmer AJ, Frost CG, Fletcher AE, et al. Nutritional supplementation in elderly medical in-patients: a double-blind placebo-controlled trial. Age Ageing. 1996;25(6):453-7.
11. Holyday M, Daniells S, Bare M, Caplan GA, Petocz P, Bolin T**.** Malnutrition screening and early nutrition intervention in hospitalised patients in acute aged care: a randomised controlled trial. J Nutr Health Aging. 2012;16(6):562-8.
12. Huynh DT, Devitt AA, Paule CL, Reddy BR, Marathe P, Hegazi RA, et al. Effects of oral nutritional supplementation in the management of malnutrition in hospital and post-hospital discharged patients in India: a randomised, open-label, controlled trial. J Hum Nutr Diet. 2015;28(4):331-43.
13. McEvoy AW, James OF**.** The effect of a dietary supplement (Build-up) on nutritional status in hospitalized elderly patients. Hum Nutr Appl Nutr. 1982;36(5):374-6.
14. Mcwhirter JP PC**.** A Comparison Between Oral and Nasogastric Nutritional Supplements in Malnourished Patients. Nutrition. 1996;12(7-8):502-6.
15. Munk T, Beck AM, Holst M, Rosenbom E, Rasmussen HH, Nielsen MA, et al. Positive effect of protein-supplemented hospital food on protein intake in patients at nutritional risk: a randomised controlled trial. J Hum Nutr Diet. 2014;27(2):122-32.
16. Neelemaat F, Lips P, Bosmans JE, Thijs A, Seidell JC, van Bokhorst-de van der Schueren MAE**.** Short-Term Oral Nutritional Intervention with Protein and Vitamin D Decreases Falls in Malnourished Older Adults. Journal of the American Geriatrics Society. 2012;60(4):691-9.

17. Ollenschläger G TW, Konkol K, Diehl V, Roth E**.** Nutritional behaviour and quality of life during oncological polychemotherapy: results of a prospective study on the efficacy of oral nutritional therapy in patients with akute leukemia. European Jounal of Clinical Investigation. 1992;22.
18. Potter JM, Roberts MA, McColl JH, Reilly JJ**.** Protein energy supplements in unwell elderly patients--a randomized controlled trial. JPEN J Parenter Enteral Nutr. 2001;25(6):323-9.
19. Roberts M, Potter J, McColl J, Reilly J**.** Can prescription of sip-feed supplements increase energy intake in hospitalised older people with medical problems? British Journal of Nutrition. 2007;90(02):425.
20. Rufenacht U, Ruhlin M, Wegmann M, Imoberdorf R, Ballmer PE**.** Nutritional counseling improves quality of life and nutrient intake in hospitalized undernourished patients. Nutrition. 2010;26(1):53-60.
21. Ryan M, Salle A, Favreau AM, Simard G, Dumas JF, Malthiery Y, et al. Oral supplements differing in fat and carbohydrate content: effect on the appetite and food intake of undernourished elderly patients. Clin Nutr. 2004;23(4):683-9.
22. Saundy-Unterberger H. MJG, Gray-Donald K. Impact of Nutritional Support on Functional Status During an Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 1997;156:794-9.
23. Schuetz P, Fehr R, Baechli V, Geiser M, Gomes F, Kutz A, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. The Lancet. 2019;393(10188):2312-21.
24. Somanchi M, Tao X, Mullin GE**.** The facilitated early enteral and dietary management effectiveness trial in hospitalized patients with malnutrition. JPEN J Parenter Enteral Nutr. 2011;35(2):209-16.
25. Starke J, Schneider H, Alteheld B, Stehle P, Meier R**.** Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients. Clin Nutr. 2011;30(2):194-201.
26. Vermeeren MA, Wouters EF, Geraerts-Keeris AJ, Schols AM**.** Nutritional support in patients with chronic obstructive pulmonary disease during hospitalization for an acute exacerbation; a randomized controlled feasibility trial. Clin Nutr. 2004;23(5):1184-92.
27. Vlaming S, Biehler A, Hennessey EM, Jamieson CP, Chattophadhyay S, Obeid OA, et al. Should the food intake of patients admitted to acute hospital services be routinely supplemented? A randomized placebo controlled trial. Clin Nutr. 2001;20(6):517-26.
28. Volkert D, Hubsch S, Oster P, Schlierf G**.** Nutritional support and functional status in undernourished geriatric patients during hospitalization and 6-month follow-up. Aging (Milano). 1996;8(6):386-95.