NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of Clinical Guideline (CG 32) – Nutrition support for adults Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition

1. Background information

Guideline issue date: February 2006
5 year review: 2011
National Collaborating Centre: NCGC

2. Consideration of the evidence

Literature search

From initial intelligence gathering and a high-level randomised control trial (RCT) search (run from the cut off point of the original guideline in 2006, to 2nd February 2011), 193 studies were identified relating to the original guideline recommendations. Of these, 122 were not relevant to the scope and 71 studies were related to the following 4 clinical areas within the guideline and one new clinical area:

- *Parenteral Nutrition*
- *Enteral Nutrition*
- *Oral Nutrition*
- *Nutritional support team*
- *New Clinical Area: Immunonutrition*

Four areas were developed in the original guideline that related to the clinical areas above (there were no Clinical Questions within the original scope). Qualitative feedback from other NICE departments and the views expressed by the Guideline Development Group (GDG) are also reported. The results of the searches are summarised in Table 1 below. All references identified through intelligence gathering, a high-level RCT search and those derived from the GDG can be viewed in Appendix 1.

Clinical area 1: Parenteral nutrition		
Specific clinical area	**Summary of evidence**	**Relevance to guideline recommendations**
Parenteral vs enteral nutrition (section 10.4) 10.5.1 Parenteral nutrition for surgical or critical care patients If intestinal tolerance persistently limits enteral tube feeding in surgical or critical care patients, parenteral nutrition should be used to supplement or replace enteral tube feeding. 10.4.6. Cost-effectiveness evidence As with our other reviews of the use of PN in different circumstances,	Through the high level RCT search 5 studies[1-5] relevant to the clinical area were identified. • One study in trauma patients looked at partial parenteral vs enteral nutrition and found that the parenteral nutrition group received more protein and calories and had higher albumin and transferrin concentrations[1,3,4] • There are two trial based economic evaluations[2,5] which favoured enteral over parenteral nutrition in terms of cost, without finding differences in clinical outcomes. This evidence supports the existing recommendation. The identified evidence does not change the direction of current guideline recommendations.	No new evidence was identified which would change the direction of current guideline recommendations.

evaluation of costeffectiveness studies was limited by the fact that they do not apply to the usage of PN within UK clinical settings [....] Nevertheless, it is very likely that ETF is cheaper than PN and Table 23 indicates the relative size of the hospital cost savings.		
Clinical area 2: Enteral nutrition		
Specific clinical area	**Summary of evidence**	**Relevance to guideline recommendations**
Early enteral feeding vs late enteral feeding 9.1.4. Mode of delivery 9.4.8.The studies on early post-operative ETF compared to standard practice of nil by mouth until return of GI function, do not support the use of early ETF although most did not focus on very malnourished patients who might benefit from	Through the high level RCT search 12 studies [5-16] were identified relevant to the clinical area were identified. • One study addressed immediate optimum flow rate vs incremental optimum flow rate for enteral feeding, and found that the immediate flow-rate group had significantly more calories and higher residual gastric volums than the incremental flow rate[6] • Three studies were identified that are of note for nutrition in intensive care units. One study looked at the timing of enteral nutrition (early vs late enteral nutrition)	No new evidence was identified which would change the direction of current guideline recommendations. No new evidence was identified which would change the

this approach 9.6.2.5 Feeding patients with a nasogastric tube is usually as effective as a post-pyloric tube (nasoduodenal/nasojejunal) for delivering nutrients to patients (especially to patients on intensive care). 9.9.1. People with dysphagia <u>Enteral vs parenteral nutrition</u> *9.5.1 Indications for enteral tube feeding* Enteral tube feeding should not be given to people unless they are malnourished or at risk of malnutrition and have; inadequate or unsafe oral intake and a functional, accessible gastrointestinal tract, or they are taking part in a clinical trial. *Enteral nutrition support for surgical patients:*	and found that delayed feeding resulted in a longer stay in ICU [13],another study found that early enteral feeding after Gastrointestinal surgery resulted in higher transferring levels and a quicker return of bowel sounds, but resulted in more episodes of diarhhoea and stomach cramps [15]. • One study assessed the effect of tube placement on ICU patients (post pyloric vs nasogastric)[14] and found that there was no difference between groups with respect to length of hospital stay and number of ventilator days, but the nasogastric group had better outcomes with regards to nutritional status (increased calorie intake and reached target feed in a shorter time). • A UK cost utility analysis[16] was identified that looked at the setting of enteral nutrition in patients with cerebrovascular accident, and found in favour of enteral nutrition being undertaken in the home rather than in nursing homes. This evidence is not sufficient to alter the current guideline. • Five studies were identified that may affect guidance with regards to enteral vs parenteral nutrition in various clinical settings including patients who had undergone GI surgery and patients with severe acute panceratitis[5,7,9-11] ; one found that enteral nutrition resulted in a bigger decline in quality of life than	direction of current guideline recommendations. No new evidence was identified which would change the direction of current guideline recommendations

General surgical patients should not have enteral tube feeding within 48 hours post-surgery unless they are malnourished or at risk of malnutrition and have; inadequate or unsafe oral intake and a functional, accessible gastrointestinal tract.	parenteral nutrition, yet parenteral nutrition resulted in more complications[9], another study found greater patient satisfaction with enteral nutrition[5] and another study found decreased mortality in enteral nutrition[11,] One study found that motilin and cholecystokinin were increased in the enteral nutrition group, and that they had improve electrogastrography post-operatively [10] • One study looked at enteral nutiriton vs parenteral+ enteral nutrition in patients undergoing pancreoduodectomy and found that there was no difference between groups with regards to mortality, but enteral group had a higher discontinuation of feeding, and the enteral + parenteral group had a longer duration of feed and had their line maintained for longer [12] • One study looked at early enteral nutrition vs early natural nutrition [8] in pancreoduodectomy patients, and found that early enteral nutrition received more energy in the first 5 dats post-operatively than the early natural nutrition group, there were also more complications in the early natural nutrition group The identified evidence does not change the direction of current recommendations.	
Clinical area 3: Oral nutrition		
Specific clinical area	**Summary of evidence**	**Relevance to guideline recommendations**

	Through the high level RCT search 13 studies[17-29] were identified relevant to the clinical area were identified.	
<u>Oral vs Standard care</u> *8.5.1* Indications for oral nutrition support . Healthcare professionals should consider oral nutrition support to improve nutritional intake for people who can swallow safely and are malnourished or at risk of malnutrition	• Several studies, comparing oral nutritional supplements with either standard care or dietary counselling generally show that giving oral nutritional supplements improves various outcomes such as weight gain, quality of life and decreased postoperative complications[17-20,22,25,27-29] One of these studies includes a trial based economic evaluation[27]. These studies strengthen the recommendation for oral nutritional supplementation with various care settings, especially within the community.	No new evidence was identified which would change the direction of current guideline recommendations.
	• One study looked at oral nutritional supplements (ONS) vs standard care and identified that for ONS to be effective, more than one meal should be enhanced [21]	No new evidence was identified which would change the direction of current guideline recommendations.
<u>Early oral vs delayed oral</u> 8.7. Healthcare professionals should consider giving post-abdominal surgery patients who can swallow safely, and in whom there are no specific concerns about gut function or integrity, some oral intake within 24 hours of surgery. The	• One study found that early oral nutrition compared to traditional oral feeding resulted in a shorter length of hospital stay [23], however the evidence is not sufficient to merit a change in the guidance at this time	
	• One study was identified that provides evidence for nutritional care in dementia[24]	

patient should be monitored carefully for any signs of nausea or vomiting.	The evidence is not conclusive to warrant inclusion in the update of the guideline at this time.	
Clinical area 4: Nutrition support teams		
Specific clinical area	**Summary of evidence**	**Relevance to guideline recommendations**
Nutrition support *3.7.* As expected for studies relating to service interventions, those identified by our review were of limited quality in terms of the scientific rigour of their design and all were small and heterogeneous. Nevertheless, the evidence suggests that NSTs decrease complications and costs through reductions in unnecessary treatments and prevention of complications *3.8.* Healthcare professionals should ensure that all	Through the high level RCT search five studies were identified [30-34] relevant to the clinical area were identified. • Two studies identified were related to nutrition support [30,31]. One study compared individualised nutrition to routine care in patients who had had stroke and found increased quality of life and better maintenance of weight in the intervention group, but no difference in length of hospital stay [30]. The other study assessed the timing of nutritional support in patients undergoing treatment for cancer, it was found that individuals undergoing nutritional support before treatment had worse outcomes overall [31] . These studies support current recommendations on general standards of nutritional care. • Three studies analysed nutritional counselling vs standard care and found that energy intake, protein intake and quality of life were generally improved in the groups that received nutritional counselling[32-34]One study also reported	No new evidence was identified which would change the direction of current guideline recommendations.

people who need nutrition support receive coordinated care from a multidisciplinary team	decreased mortality in the group receiving nutritional counselling[32] The identified evidence does not change the current guideline recommendations.	
New clinical area: Immunonutrition		
Specific clinical area	**Summary of evidence**	**Relevance to guideline recommendations**
Parenteral nutrition (section 10.4)	Through the high level RCT search 35 studies were identified relevant to the clinical area were identified [35-69] • Six studies were found that were related to the area of immunonutrition in a varied patient population (GI cancer, severe acute pancreatitis and critically ill patients): Three studies analysed the effect of varying quantities of omega 3 and fish oils in TPN [35-37], two studies addressed the effect of varying lipid composition of TPN[39,40], and one study looked at the effects of varying the amino acid content of TPN[41]. The largest study (166 patients in an intensive care setting) found no difference between groups with respect to inflammatory markers[35.] Other, smaller studies found that the intervention reduced the concentration of inflammatory markers[37], and had beneficial effects on serum lipid profiles[40] and reduced postoperative morbidity[41]. Two studies could potentially inform health economic considerations of this new topic once	No sufficient conclusive evidence was identified which would merit inclusion of immunonutrition into the guideline.

Parenteral nutrition (section 10.4)	conclusive clinical evidence is available [38,70]. • Ten studies were found that specifically looked at immunonutrition with regards to parenteral nutrition with glutamine vs standard parenteral nutrition [59,61-69.] These studies were relatively small (all less than 75 patients) and undertaken on a variety of patient populations, including surgical and trauma patients and patients undergoing stem cell transplantation. Studies involving patients undergoing stem cell transplants found a higher C- reactive protein[59] and increased survival [62] in the intervention group. • One study assessing immunonutrition in chronic obstructive pulmonary disease found the intervention group had a significantly higher CD3 concentration and a decreased TNFα [67]. One study assessing immunonutrition in gastrointestinal surgery found that there was not a significant difference between the control and intervention groups- both groups showed decreases in albumin, CRP, lymphocyte count, T cell and CD8 count after surgery[69]. Studies also showed improved survival [62], incidence of specific infections [63,] and decreased intolerance to feeding [71.]	
Enteral Nutrition (Section 9.2)	• Identified eleven studies pertaining to the area of immunonutrition. Studies	

Oral Nutrition (section 8.2)	involved looking at imunonutrition vs standard enteral nutrition [42,42,42,44-52,60.] One study looked at immunoenhanced enteral nutrition vs standard parenteral nutrition. Immunonutrition refers to the addition of substances such as arginine, eicosapentoic acid (EPA) and gammalinoleic acid (GLA) to the nutrition. In the majority of studies patients receiving immunonutrition tend to have better outcomes with regards to inflammatory markers, mortality, ventilator and ICU free days[7,42-49,50,51,60]. • There were seven studies pertaining to the area of immunonutrition[52,55 52-58]. These included studies comparing oral nutritional supplements with substances such as arginine, zinc, testosterone, polyunsaturated omega-3 and oligosaccharides with standard oral nutrition. The majority of studies looked at an elderly population in the community or nursing home facilities[52,56,57], one study looked at stroke patients[54], and one looked at patients with gastrointestinal tumours[55]. Some studies showed a trend towards decrease in hospital admissions, decreased length of stay, and decreased mortality[52-54] . One study specifically looked at antibody titres with respect to a population at risk from influenza; the usefulness of this study is restricted as it addresses a very specific and indirect population [56.] Two studies looked at biochemical indices, one study found a beneficial reduction in TNFα mRNA and IL6 mRNA in the intervention group [57,] and another study found that biochemical markers indicated a decrease	

Oral Nutrition (section 8.2)	in immune suppression in patients receiving immunonutrition intervention[58.] All of the studies listed here are of limited relevance as they were all carried out on relatively small populations (all less than 100 patients) and the results are inconclusive. No sufficient conclusive evidence was identified which would merit inclusion of immunonutrition into the guideline at this stage.	

Research currently in progress

The GDG members identified an ongoing trial with an unknown publication date, which addresses optimal timing and nutrient content of parenteral nutrition.

In conclusion, no newly identified conclusive and consistent evidence contradicts current guideline recommendations in the original guideline.

Guideline Development Group opinion

A questionnaire was distributed to Guideline Development Group (GDG) members to consult them on the need for an update of the guideline. Five GDG member responses were received, including the GDG chair.

- The GDG chair pointed out that the use of specialized immunonutrition has become more common throughout published trials. This topic was not included in the original guideline scope. However, the GDG chair considered that given that this is still emergent data, it would be appropriate to await further evidence at the next 3 year review for update.
- Two GDG members highlighted that since publication of the guideline more literature has become available on the benefit of total parenteral nutrition (TPN) in relation to specific conditions. One GDG member stated that there is now more evidence on early enteral feeding post surgery and oral nutrition supplements since publication of the guidance. However, the identified evidence in the high level RCT search does not change the direction of current guideline recommendations. In addition, this GDG member pointed out that there is some literature comparing enteral and parenteral nutrition in acute pancreatitis. Again, the identified evidence in the high level RCT search does not have an impact on the current recommendations.
- One GDG member stated that pre operative enteral nutrition is not usually recommended, although it is recommended in the guideline. No evidence was found during the high level RCT search that would contradict this and no other member raised this issue
- One GDG member suggested that refeeding elements of the guidance need to be revisited and rewritten to prevent overly cautious approaches to feeding which in itself can hold risks. Particularly regarding the need for clinicians to start refeeding slowly, then build levels up quite swiftly to prevent starvation. However, no evidence was found during the high level RCT search and no other member raised this issue.

- One GDG member was concerned about the harm caused by misplaced nasogastric feeding tubes in adults, which has also been a subject of a recent NPSA safety warning[1]. The main causal factor leading to harm was misinterpretation of x-rays, therefore the safety alert incorporated specific steps for healthcare professionals to follow during nasogastric tube insertion. However, no evidence was found during the high level RCT search and no other member raised this issue.
- One GDG member felt that revised guidance could improve recommendations in relation to nutritional care in a primary care setting which currently has mixed standards. However, no evidence was found during the high level RCT search and no other member raised this issue.
- One GDG member highlighted that there have been a number of initiatives within quality, innovation, productivity and prevention (QUIPP) that relate directly to this guideline. There are also new recommendations from the Care Quality Commission (CQC) and British Association for Parenteral and Enteral Nutrition (BAPEN) with which the updated NICE recommendations should align with. However, no further evidence was found during the high level RCT search to support this alignment and no other member raised this issue.

The majority of the views of the GDG members to the nutrition support guideline supported a decision not to warrant an update of the guideline.

Implementation and post publication feedback

In total, 51 enquiries were received from post-publication feedback, most of which were routine. Key themes emerging from post-publication feedback included enquiries relating to clarification of whether the line used for TPN needs to be a virgin line or a dedicated line. Guidance on feeding via syringe into the mouth rather than via percutaneous endoscopic gastrostomy (PEG) or intravenously, was requested. In addition, there was some confusion as to whether food should be syringed or pumped in during gastrostomy feeding. More clarity was also sought when a administering a PEG feed to a dehydrated person and whether timings should be altered in this population to prevent adverse reactions.

[1] The NPSA safety Warning is detailed in the following press release: http://www.npsa.nhs.uk/corporate/news/reducing-the-harm-caused-by-misplaced-nasogastric-feeding-tubes-in-adults-children-and-infants/

No new evidence was identified through post publication enquiries or implementation feedback that would indicate a need to update the guideline.

Relationship to other NICE guidance

The following NICE guidance is related to **CG32: Nutrition Support**

Guidance	**Review date**
PH 11: Guidance for midwives, health visitors, pharmacists and other primary care services to improve the nutrition of pregnant and breastfeeding mothers and children in low income households, 2008	Expected review date: TBC
PH 27: Dietary interventions and physical activity interventions for weight management before, during and after pregnancy (2010).	Expected review date: TBC
CG 02: Infection control, prevention of healthcare associated infection in primary and community care, 2007	An update of this guideline is currently scheduled for publication, 2011.
CG 63: Diabetes in pregnancy management of diabetes and its complications from preconception to the postnatal period, 2008	Reissued July 2008 Consultation on review proposal with stakeholders: 07 March 2011 - 20 March 2011
CG 66: Type 2 diabetes: the management of type 2 diabetes (update), 2010	A decision for review to be made July 2011.
CG 39: Anaemia management in people with chronic kidney disease (CKD) (2006).	An update issue in February 2011 (CG114).
CG 43: Obesity guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children, 2010	Expected review date: November 2011
CG 68: Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA) (2008).	Review decision date: July 2011
IPG 232: Serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children. (2007).	Expected Review date: TBC
CG73: Chronic Kidney Disease - National clinical guideline for early identification and management in adults in primary and secondary care, 2008	This guidance is currently being reviewed. Expected publication date: February 2011

CG 84: Management of acute diarrhoea and vomiting due to gastoenteritis in children under 5 (2009)	Review decision date: April 2012
TA142: Erythropoetin (alpha and beta) and darbepoetin for the treatment of cancer-treatment induced anaemia (2008).	Review date: February 2011
CG 09: Eating disorders: core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders, 2010	Not currently scheduled for consideration for an update
Identification and management of overweight and obese children in primary care and education, including advice to parents and carers	Public Health Guideline In progress (expected January 2013)
Preventing obesity using a 'whole-system' approach at local and community level	Public Health Guideline In progress (expected March 2012)
The management of hip fracture in adults	For Publication**: June 2011**
The Management Crohn's Disease	For Publication: December 2012
Identification and weight management of overweight or obese children: community based interventions	Public Health Guideline In progress

Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation.

Conclusion

Through the process immunonutrition was identified as an emerging topic for inclusion in the scope, however it was felt that this area is not significant on its own to merit an update and will be reviewed again in 3 years. There are no factors described above which would invalidate or change the direction of the current recommendations. The nutrition support guideline should not be updated at this time.

3. Review recommendation

The guideline should not be updated at this time. The guideline will be reviewed again according to current processes.

National Clinical Guidelines Centre

May 2011

Appendix I

Reference List

1 Arefian NM, Teymourian H, Radpay B. Effect of partial parenteral versus enteral nutritional therapy on serum indices in multiple trauma patients. Tanaffos 2007;6:37-41.

2 Ryu J. Clinical outcomes comparing parenteral and nasogastric tube nutrition after laryngeal and pharyngeal cancer surgery. Dysphagia 2009 Dec;24:378-86.

3 Wang Q, Liu ZS, Qian Q, et al. Treatment of upper gastrointestinal fistula and leakage with personal stage nutrition support. World Journal of Gastroenterology 2008 Aug 28;14:5073-7.

4 Wu XM JKWHLGZ. Total enteral nutrition in prevention of pancreatic necrotic infection in severe acute pancreatitis. Pancreas 2010 Mar;39:248-51.

5 Joos AK PP. Enteral vs parenteral nutrition in reconstructive anal surgery--a prospective-randomized trial. Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland 2008 Jul;10:605-9.

6 Desachy A. Initial efficacy and tolerability of early enteral nutrition with immediate or gradual introduction in intubated patients. Intensive Care Medicine 2008 Jun;34:1054-9.

7 Doley RP YTWJK. Enteral nutrition in severe acute pancreatitis. JOP : Journal of the pancreas 2009;10:157-62.

8 Grizas S G. A comparison of the effectiveness of the early enteral and natural nutrition after pancreatoduodenectomy. Medicina (Kaunas, Lithuania) 2008;44:678-86.

9 Hyltander A. Supportive nutrition on recovery of metabolism, nutritional state, health-related quality of life, and exercise capacity after major surgery: a randomized study. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2005 May;3:466-74.

10 Kang WM YJZ. Effects of enteral and parenteral nutrition on gastroenteric hormones and gastric motility after subtotal gastrectomy. Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih / Chinese Academy of Medical Sciences 2008 Jun;23:113-6.

11 Lam NN TNKC. Early enteral feeding for burned patients--an effective method which should be encouraged in developing countries. Burns : journal of the International Society for Burn Injuries 2008 Mar;34:192-6.

12 Nagata S F. Comparison of enteral nutrition with combined enteral and parenteral nutrition in post-pancreaticoduodenectomy patients: a pilot study. Nutrition Journal 2009;Vol.8, pp.24, 2009.

13 Nguyen NQ FRBLB. The impact of delaying enteral feeding on gastric emptying, plasma cholecystokinin, and peptide YY concentrations in critically ill patients. Critical Care Medicine 2008 May;36:1469-74.

14 Vaithiswaran V. Effect of early enteral feeding after upper gastrointestinal surgery. Tropical gastroenterology : official journal of the Digestive Diseases Foundation 2008 Apr;29:91-4.

15 White H. A randomised controlled comparison of early post-pyloric versus early gastric feeding to meet nutritional targets in ventilated intensive care patients. Critical Care (London, England) 2009;13:R187, 2009.

16 Elia M, Stratton RJ. A cost-utility analysis in patients receiving enteral tube feeding at home and in nursing homes. Clinical nutrition (Edinburgh, Scotland) 27[3], 416-423. 1-6-2008.

17 Beck AM DK. Multifaceted nutritional intervention among nursing-home residents has a positive influence on nutrition and function. Nutrition (Burbank, Los Angeles County, Calif 2008 Nov;24:1073-80.

18 Beck AM, Damkjaer K, rbye LW. Physical and social functional abilities seem to be maintained by a multifaceted randomized controlled nutritional intervention among old (>65 years) Danish nursing home residents. Archives of Gerontology & Geriatrics 2010 May;50:351-5.

19 Botella-Carretero JI, Iglesias B, Balsa JA, et al. Effects of oral nutritional supplements in normally nourished or mildly undernourished geriatric patients after surgery for hip fracture: a randomized clinical trial. Jpen: Journal of Parenteral & Enteral Nutrition 2008 Mar;32:120-8.

20 Botella-Carretero JI, Iglesias B, Balsa JA, et al. Perioperative oral nutritional supplements in normally or mildly undernourished geriatric patients submitted

to surgery for hip fracture: a randomized clinical trial. Clinical Nutrition 2010 Oct;29:574-9.

21 Castellanos VH, Marra MV, Johnson P. Enhancement of Select Foods at Breakfast and Lunch Increases Energy Intakes of Nursing Home Residents with Low Meal Intakes. Journal of the American Dietetic Association 2009;109:445-51.

22 McMurdo ME, Price RJ, Shields M, et al. Should oral nutritional supplementation be given to undernourished older people upon hospital discharge? A controlled trial. Journal of the American Geriatrics Society 2009 Dec;57:2239-45.

23 Minig L, Biffi R, Zanagnolo V, et al. Early oral versus "traditional" postoperative feeding in gynecologic oncology patients undergoing intestinal resection: a randomized controlled trial. Annals of Surgical Oncology 2009 Jun;16:1660-8.

24 Navratilova M, Jarkovsky J, Ceskova E, et al. Alzheimer disease: Malnutrition and nutritional support. Clinical and Experimental Pharmacology and Physiology 2007;34:S11-S13.

25 Norman K, Kirchner H, Freudenreich M, et al. Three month intervention with protein and energy rich supplements improve muscle function and quality of life in malnourished patients with non-neoplastic gastrointestinal disease--a randomized controlled trial. Clinical Nutrition 2008 Feb;27:48-56.

26 Ravasco P. Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. Head & neck 2005 Aug;27:659-68.

27 Simmons SF ZX. Cost-effectiveness of nutrition interventions in nursing home residents: a pilot intervention. The journal of nutrition, health & aging 2010;14:367-72.

28 van Anholt RD, Sobotka L, Meijer EP, et al. Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in non-malnourished patients. Nutrition 2010 Sep;26:867-72.

29 Wouters-Wesseling W. Early nutritional supplementation immediately after diagnosis of infectious disease improves body weight in psychogeriatric nursing home residents. Aging clinical and experimental research 2006 Feb;18:70-4.

30 Ha L, Hauge T, Spenning AB, et al. 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 Oct;29:567-73.

31 Rabinovitch R. Impact of nutrition support on treatment outcome in patients with locally advanced head and neck squamous cell cancer treated with definitive radiotherapy: a secondary analysis of RTOG trial 90-03. Head & neck 2006 Apr;28:287-96.

32 Duncan DG, Beck SJ, Hood K, et al. Using dietetic assistants to improve the outcome of hip fracture: A randomised controlled trial of nutritional support in an acute trauma ward. Age and Ageing 2006;35:148-53.

33 fenacht U, hlin M, Wegmann M, et al. Nutritional counseling improves quality of life and nutrient intake in hospitalized undernourished patients. Nutrition 2010 Jan;26:53-60.

34 Isenring EA BJC. Nutrition support using the American Dietetic Association medical nutrition therapy protocol for radiation oncology patients improves dietary intake compared with standard practice. Journal of the American Dietetic Association 2007 Mar;107:404-12.

35 Friesecke S L. Fish oil supplementation in the parenteral nutrition of critically ill medical patients: a randomised controlled trial. Intensive Care Medicine 2008 Aug;34:1411-20.

36 Wang X. Omega-3 fatty acids-supplemented parenteral nutrition decreases hyperinflammatory response and attenuates systemic disease sequelae in severe acute pancreatitis: a randomized and controlled study. JPEN 2008 May;Journal of parenteral and enteral nutrition. 32:236-41.

37 Wang X. Fish oil-supplemented parenteral nutrition in severe acute pancreatitis patients and effects on immune function and infectious risk: a randomized controlled trial. Inflammation 2009 Oct;32:304-9.

38 Jiang ZM WDWXWJZZGZWSHSJ. Randomized clinical trial of intravenous soybean oil alone versus soybean oil plus fish oil emulsion after gastrointestinal cancer surgery. The British journal of surgery 2010 Jun;97:804-9.

39 Piper SN RKB. Hepatocellular integrity in patients requiring parenteral nutrition: comparison of structured MCT/LCT vs. a standard MCT/LCT emulsion and a LCT emulsion. European journal of anaesthesiology 2008 Jul;25:557-65.

40 Puiggros C. Evolution of lipid profile, liver function, and pattern of plasma fatty acids according to the type of lipid emulsion administered in parenteral nutrition

in the early postoperative period after digestive surgery. JPEN 2009 Sep;Journal of parenteral and enteral nutrition. 33:501-12.

41 Sun LC, Shih YL, Lu CY, et al. Randomized, controlled study of branched chain amino acid-enriched total parenteral nutrition in malnourished patients with gastrointestinal cancer undergoing surgery. American Surgeon 2008 Mar;74:237-42.

42 Casas-Rodera P, mez-Candela C, tez S, et al. Immunoenhanced enteral nutrition formulas in head and neck cancer surgery: a prospective, randomized clinical trial. Nutricion Hospitalaria 2008 Mar;23:105-10.

43 Celik JB GK. The role of immunonutrition in gynecologic oncologic surgery. European journal of gynaecological oncology 2009;30:418-21.

44 Klek S K. Standard and immunomodulating enteral nutrition in patients after extended gastrointestinal surgery--a prospective, randomized, controlled clinical trial. Clinical nutrition (Edinburgh, Scotland) 2008 Aug;27:504-12.

45 Pontes-Arruda A. Effects of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in mechanically ventilated patients with severe sepsis and septic shock. Critical Care Medicine 2006 Sep;34:2325-33.

46 Qin HL ZJTDCWFXHXJY. Effect of Lactobacillus plantarum enteral feeding on the gut permeability and septic complications in the patients with acute pancreatitis. European Journal of Clinical Nutrition 2008 Jul;62:923-30.

47 Ryan AM RJH. Enteral nutrition enriched with eicosapentaenoic acid (EPA) preserves lean body mass following esophageal cancer surgery: results of a double-blinded randomized controlled trial. Annals of Surgery 2009 Mar;249:355-63.

48 Slotwinski R, Olszewski WL, Lech G, et al. Immunonutrition after major pancreatic surgery. Central-European Journal of Immunology 2008;33:67-73.

49 Theilla M, Singer P, Cohen J, et al. A diet enriched in eicosapentanoic acid, gamma-linolenic acid and antioxidants in the prevention of new pressure ulcer formation in critically ill patients with acute lung injury: A randomized, prospective, controlled study. Clinical Nutrition 2007;26:752-7.

50 van Stijn MF BPRML-MGTJD. Antioxidant-enriched enteral nutrition and immuno-inflammatory response after major gastrointestinal tract surgery. The British journal of nutrition 2010 Feb;103:314-8.

51 van Stijn MF L-MGBPSPT. Antioxidant enriched enteral nutrition and oxidative stress after major gastrointestinal tract surgery. World journal of gastroenterology : WJG 2008 Dec;14:6960-9.

52 Cereda E G. Disease-specific, versus standard, nutritional support for the treatment of pressure ulcers in institutionalized older adults: a randomized controlled trial. Journal of the American Geriatrics Society 2009 Aug;57:1395-402.

53 Chapman IM, Visvanathan R, Hammond AJ, et al. Effect of testosterone and a nutritional supplement, alone and in combination, on hospital admissions in undernourished older men and women. American Journal of Clinical Nutrition 2009 Mar;89:880-9.

54 Garbagnati F, Cairella G, De MA, et al. Is antioxidant and n-3 supplementation able to improve functional status in poststroke patients? Results from the Nutristroke Trial. Cerebrovascular Diseases 2009;27:375-83.

55 Gunerhan Y. Effect of preoperative immunonutrition and other nutrition models on cellular immune parameters. World journal of gastroenterology : WJG 2009 Jan;15:467-72.

56 Langkamp-Henken B. Nutritional formula improved immune profiles of seniors living in nursing homes. Journal of the American Geriatrics Society 2006 Dec;54:1861-70.

57 Schiffrin EJ, Thomas DR, Kumar VB, et al. Systemic inflammatory markers in older persons: the effect of oral nutritional supplementation with prebiotics. Journal of Nutrition, Health & Aging 2007 Nov;11:475-9.

58 Sorensen D. Perioperative immunonutrition in head and neck cancer. The Laryngoscope 2009 Jul;119:1358-64.

59 Blijlevens NM DJNASADB. A randomised, double-blinded, placebo-controlled, pilot study of parenteral glutamine for allogeneic stem cell transplant patients. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 2005 Oct;13:790-6.

60 Buijs N, van Bokhorst-de van der Schueren MA, Langius JA, et al. Perioperative arginine-supplemented nutrition in malnourished patients with head and neck cancer improves long-term survival. American Journal of Clinical Nutrition 2010 Nov;92:1151-6.

61 Culkin A. A double-blind, randomized, controlled crossover trial of glutamine supplementation in home parenteral nutrition. European Journal of Clinical Nutrition 2008 May;62:575-83.

62 da Gama Torres HO VEdCAGESMAAAWLFSABH. Efficacy of glutamine-supplemented parenteral nutrition on short-term survival following allo-SCT: a randomized study. Bone marrow transplantation 2008 Jun;41:1021-7.

63 Estivariz CF GDL. Efficacy of parenteral nutrition supplemented with glutamine dipeptide to decrease hospital infections in critically ill surgical patients. JPEN 2008 Jul;Journal of parenteral and enteral nutrition. 32:389-402.

64 Fan YP YJKWZ. Effects of glutamine supplementation on patients undergoing abdominal surgery. Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih / Chinese Academy of Medical Sciences 2009 Mar;24:55-9.

65 Jo S CSHJKEMMCDSJCJKY. Missing effect of glutamine supplementation on the surgical outcome after pancreaticoduodenectomy for periampullary tumors: a prospective, randomized, double-blind, controlled clinical trial. World Journal of Surgery 2006 Nov;30:1974-82.

66 Luo M. Depletion of plasma antioxidants in surgical intensive care unit patients requiring parenteral feeding: effects of parenteral nutrition with or without alanyl-glutamine dipeptide supplementation. Nutrition (Burbank, Los Angeles County, Calif 2008 Jan;24:37-44.

67 Luo Y, Xu WG, Dong HJ, et al. Glutamine for immunomodification and metabolic support in patients with chronic obstructive pulmonary disease. Chinese Journal of Clinical Rehabilitation 2005;9:234-6.

68 Tang ZF LYL. Glutamine and recombinant human growth hormone protect intestinal barrier function following portal hypertension surgery. World journal of gastroenterology : WJG 2007 Apr;13:2223-8.

69 Yeh CN LHLYCKHTJYCM. The role of parenteral glutamine supplement for surgical patient perioperatively: result of a single center, prospective and controlled study. Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie 2008 Nov;393:849-55.

70 Klek S K. The impact of immunostimulating nutrition on infectious complications after upper gastrointestinal surgery: a prospective, randomized, clinical trial. Annals of Surgery 2008 Aug;248:212-20.

71 McQuiggan M. Enteral glutamine during active shock resuscitation is safe and enhances tolerance of enteral feeding. JPEN 2008 Jan;Journal of parenteral and enteral nutrition. 32:28-35.