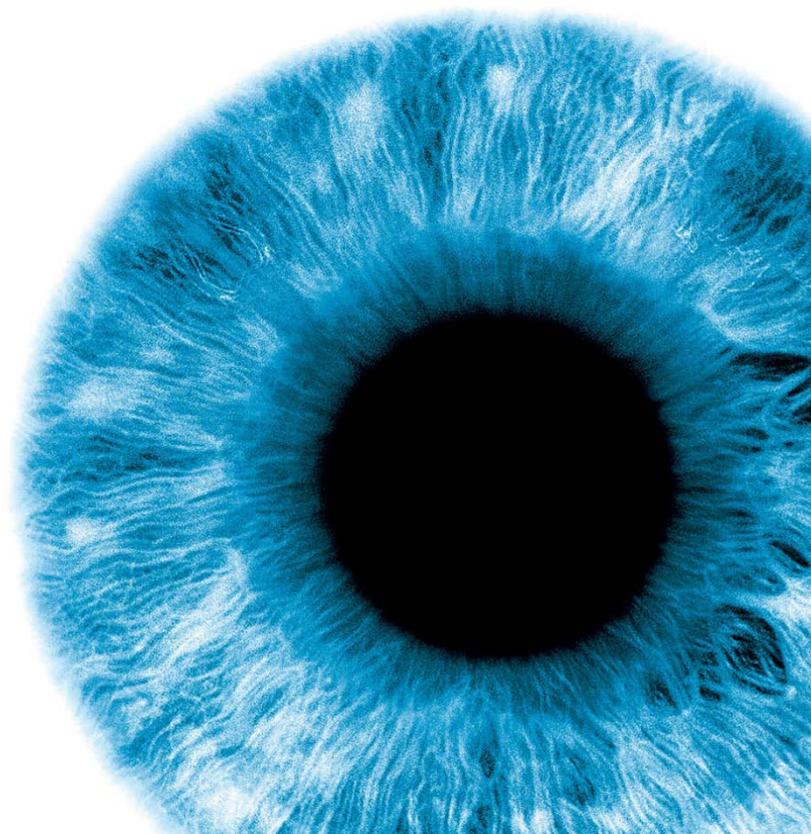


Nutrition support in adults

Evidence Update August 2013

A summary of selected new evidence relevant to NICE clinical guideline 32 'Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition' (2006)

Evidence Update 46



Evidence Updates provide a summary of selected new evidence published since the literature search was last conducted for the accredited guidance they relate to. They reduce the need for individuals, managers and commissioners to search for new evidence. Evidence Updates highlight key points from the new evidence and provide a commentary describing its strengths and weaknesses. They also indicate whether the new evidence may have a potential impact on current guidance. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline, available from the NICE Evidence Services topic page for [diet and nutrition](#).

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Introduction

This Evidence Update identifies new evidence that is relevant to, and may have a potential impact on, the following reference guidance:

- ¹ [Nutrition support in adults](#). NICE clinical guideline 32 (2006)

A search was conducted for new evidence from 8 December 2010 to 11 March 2013. A total of 491 pieces of evidence were initially identified. Following removal of duplicates and a series of automated and manual sifts, 23 items were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An [Evidence Update Advisory Group](#), comprising topic experts, reviewed the prioritised evidence and provided a commentary.

Although the process of updating NICE guidance is distinct from the process of an Evidence Update, the relevant NICE guidance development centres have been made aware of the new evidence, which will be considered when guidance is reviewed.

Other relevant NICE guidance

The focus of the Evidence Update is on the guidance stated above. However, overlap with other NICE guidance has been outlined as part of the Evidence Update process. Where relevant, this Evidence Update therefore makes reference to the following guidance:

²  [Chronic obstructive pulmonary disease](#). NICE clinical guideline 101 (2010)

²  [Stroke](#). NICE clinical guideline 68 (2008)

- ¹ [Dementia](#). NICE clinical guideline 42 (2006)

NICE Pathways

- [Nutrition support in adults](#). NICE Pathway

Quality standards

- [Nutrition support in adults](#). NICE quality standard 24

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

¹ Guidance published prior to NICE accreditation

² NICE-accredited guidance is denoted by the Accreditation Mark 

Key points

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key points for this Evidence Update. It also indicates the EUAG's opinion on whether the new evidence may have a potential impact on the current guidance listed in the introduction. For further details of the evidence behind these key points, please see the full commentaries.

The section headings used in the table below are taken from the guidance.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

Key point	Potential impact on guidance	
	Yes	No
Organisation of nutrition support in hospital and the community <ul style="list-style-type: none"> Multicomponent oral nutrition support for older people started during acute hospitalisation and continuing after discharge may reduce mortality and increase weight. It may also improve functioning (namely, ability to perform everyday activities such as climbing stairs). There is some evidence that such interventions may also be cost effective in terms of functioning. Oral nutritional supplements in older patients after hospital discharge may increase energy intake and weight, and may also be associated with a cost-effective improvement in quality of life. 		 ✓ ✓
Screening for malnutrition and the risk of malnutrition in hospital and the community <ul style="list-style-type: none"> Nutrition screening followed up with a multicomponent malnutrition care plan appears to reduce hospital stays among older malnourished patients. 		✓
What to give in hospital and the community <ul style="list-style-type: none"> Certain groups of patients commencing nutrition support (who are already identified as being at risk of refeeding syndrome using current NICE criteria) may be at even greater risk of subsequently developing refeeding syndrome, such as those with low serum magnesium, or those fed nasogastrically. Some data question current risk markers; however the lack of universally accepted criteria for a diagnosis of refeeding syndrome prevents a definitive assessment. 		✓
Oral nutrition support in hospital and the community <ul style="list-style-type: none"> Tailored, multicomponent oral nutrition support for older malnourished patients in hospital appears to improve nutritional outcomes. Dietary advice with or without oral nutritional supplements in disease-related malnutrition may improve body weight and indicators of muscle mass. 		 ✓ ✓

Key point	Potential impact on guidance	
	Yes	No
<ul style="list-style-type: none"> • Oral nutritional supplements appear to prevent weight loss after hip fracture surgery in older patients with a body mass index less than 25 kg/m², and may reduce length of hospital stay. • Oral nutrition support may improve quality of life in malnourished patients with cancer. • Oral nutritional supplements appear to improve energy and protein intake, body weight, and functional outcomes (such as peripheral muscle strength, and maximum inspiratory and expiratory pressure) in malnourished patients with stable COPD. • Immune enhancing nutrition (specialised nutrients that may help regulate response to illness and injury) may reduce postoperative complications in patients undergoing non-emergency gastrointestinal surgery. 		<ul style="list-style-type: none"> ✓ ✓ ✓ ✓
<p>Enteral tube feeding in hospital and the community</p> <ul style="list-style-type: none"> • Prophylactic percutaneous endoscopic gastrostomy in patients with advanced head and neck cancer may improve quality of life and could help to reduce weight loss. • Percutaneous endoscopic gastrostomy may be at less risk of failure (namely, failure to introduce the tube, recurrent displacement or treatment interruption) than nasogastric tubes in patients with dysphagia needing nutrition support. • Percutaneous endoscopic gastrostomy does not appear to improve survival or quality of life in advanced dementia. • Use of decision aids may reduce conflict among carers when making decisions about feeding options in advanced dementia, and may also help to ensure appropriate nutritional support and to reduce weight loss in people with dementia. • Limited data suggest that acupuncture may have benefits over standard motility drugs in treating delayed gastric emptying in critical care. 		<ul style="list-style-type: none"> ✓ ✓ ✓ ✓ ✓
<p>Areas not currently covered by NICE CG32</p> <ul style="list-style-type: none"> • Data remain insufficient for the effect of swallowing therapy, feeding, and nutritional and fluid supplementation on functional outcome and death in patients with dysphagia after stroke. There is some evidence for reduced pressure sores following nutritional supplementation in these patients. • Although the benefits of nutrition support in patients with liver disease appear to be restricted, more robust evidence is needed to confirm findings. 		<ul style="list-style-type: none"> ✓ ✓

1 Commentary on new evidence

These commentaries analyse the key references identified specifically for the Evidence Update. The commentaries focus on the 'key references' (those identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update), which are identified in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from the guidance.

1.1 Organisation of nutrition support in hospital and the community

Continuity of nutrition support between hospital and community

NICE clinical guideline 32 ([NICE CG32](#)) recommends that a specialist nutrition support nurse should work alongside nursing staff, as well as dietitians and other experts in nutrition support, to support coordination of care between the hospital and the community. However, there are no specific recommendations about the exact nature of the coordinated care.

The NICE quality standard 'Nutrition support in adults' ([NICE QS24](#)) also emphasises continuity of care:

- [Quality statement 3](#): All people who are screened for the risk of malnutrition have their screening results and nutrition support goals (if applicable) documented and communicated in writing within and between settings.

Interventions starting in hospital and continuing in the community

Three studies looked at the transition of nutrition support between hospital and community.

A randomised controlled trial (RCT; n=259) in Israel by [Feldblum et al. \(2011\)](#) studied the effects of tailored, multicomponent oral nutrition support versus usual care during and after discharge from acute hospitalisation. Patients aged 65 years and over (mean age=75 years) admitted to a general medicine department of a single hospital were screened for malnutrition. Those scoring less than 10 on the Mini Nutritional Assessment tool, or with weight loss of more than 10% in the previous 6 months, were eligible. Patients were randomised to 1 of 3 groups:

- Group 1: a hospital and community nutritional intervention (comprising visits from a research dietitian in hospital and on 3 occasions after discharge; and provision of a tailored oral nutrition support programme including treatment goals, dietary advice, food supplements, and addressing problems with food intake).
- Group 2: the same nutritional intervention as group 1, but only during their hospital stay.
- Group 3: standard hospital dietetic services.

For statistical analysis, groups 2 and 3 were combined into a single control group. The primary outcome was mortality. At 6-month follow-up:

- Mortality was significantly lower in group 1 (3/78, 3.8%) than in the control group (21/181, 11.6%; p=0.046).
- The increase in Mini Nutritional Assessment score was significantly greater in group 1 than the control group (3.01 versus 1.81, p=0.004), although this was mainly driven by an increase in score on the section of the tool involving subjective assessment by both patients and researchers.
- No significant effects of the intervention were seen on dietary intake of macronutrients, or changes from baseline in either weight, or functional, cognitive or depression status.

Limitations of the evidence included that:

- 58 (32%) patients withdrew in the control group versus 9 (11.5%) in the intervention group, which may have biased results (although the authors stated that demographic, nutritional, and functional indicators did not differ between those completing and those leaving the study)
- cognitively impaired patients were excluded, so results may not be generalisable to this group.

An RCT (n=210) in the Netherlands by [Neelemaat et al. \(2011\)](#) also studied the effect of multicomponent oral nutrition support versus control in malnourished patients aged 60 years or over (mean age=75 years) during and after hospital discharge. Patients admitted to any of several departments of a single hospital, who were identified as malnourished after screening, and were expected to stay more than 2 days, were eligible. Those with senile dementia were excluded. Patients were randomised to the intervention or control. The intervention was started in hospital and continued for 3 months after discharge, and comprised: a protein and energy enriched diet (in hospital); oral nutritional supplements (protein energy drinks); vitamin D and calcium supplements; and telephone counselling from a dietitian. Control was usual nutritional care, in which prescribed nutritional support after discharge was uncommon.

Oral nutrition support did not appear to significantly improve scores on the Functional Limitations Questionnaire (measuring problems with everyday activities such as climbing stairs; score range 0–6) or body weight. However, in a subgroup of patients not previously exposed to nutrition support or counselling, significant improvements were seen with both the functional limitations score (mean difference [MD]=−0.6, 95% confidence interval [CI] −1.2 to 0.0 [negative score represents improvement], p value not stated; n=97) and weight (MD=2.2 kg, 95% CI 0.3 to 4.2 kg, p value not stated; n=98).

In a cost-effectiveness study (based on the above RCT by Neelemaat et al. 2011) conducted by [Neelemaat et al. \(2012\)](#), a significant improvement in functional limitations score was now seen with oral nutrition support (MD=−0.72, 95% CI −1.15 to −0.28, p value not stated). The reason for the difference in results from Neelemaat et al. (2011) was likely due to a different approach to the analysis; in the 2012 paper, only patients who had died (n=25) were excluded from the primary analyses (with other missing results dealt with by ‘multiple imputation’, in which a model is used to fill in data gaps). Whereas in the 2011 paper, all patients with missing follow-up data (n=60) were excluded from the primary analysis.

The cost-effectiveness analysis produced the following results:

- The mean additional cost of the intervention was €539.
- When all other costs (mainly secondary care) were included, the difference in total costs between the groups was not significant (MD=€445, 95% CI €−2779 to 3938, p value not stated).
- Using the significant results for functional limitations in Neelemaat et al. (2012), it was determined that 1 point of extra improvement on the functional limitations scale in the intervention group cost €618 extra compared with control.
- Using a cost-effectiveness probability curve (plotting probability of cost-effectiveness against the amount society is willing to pay to gain 1 unit on the functional limitations scale), the authors calculated that if society is willing to pay €6500, there is a 95% probability that the intervention is cost effective. It was stated that in the Netherlands, an investment of less than €20,000 is considered cost effective.
- A further analysis (based on quality-adjusted life years [QALY]), suggested that the incremental cost-effectiveness ratio (namely the investment needed to gain 1 extra QALY) would be €26,962. The authors stated that based on this measure, the intervention would not be deemed cost effective in the Netherlands.

Limitations of the evidence from Neelemaat et al. (2011 and 2012) included that:

- Some elements of the multicomponent intervention (hospital diet, and vitamin and mineral supplements) were not the primary focus of [NICE CG32](#), and it is not clear which of the subcomponents may have been most responsible for the results seen.
- The significant effects seen in Neelemaat et al. (2011) were from a subgroup analysis that may have been post-hoc.
- Data were not complete for all measurements in all patients (with the most ill patients having the most missing data), and different methods of managing the missing data were used in the two articles.
- It was stated that the analysis was underpowered to detect cost differences.
- The clinical significance of the change in functional limitations score was not discussed.
- Results may not be transferable outside of the Netherlands where the trial was based.

Taken together, the evidence suggests that multicomponent oral nutrition support for older people started during acute hospitalisation and continuing after discharge may reduce mortality, increase weight and improve functioning. There is some evidence that such interventions may also be cost effective in terms of functioning. This is consistent with the need to coordinate care between hospital and community as recommended by [NICE CG32](#) and reiterated in [NICE QS24](#).

Key references

Feldblum I, German L, Castel H et al. (2011) [Individualized nutritional intervention during and after hospitalization: the nutrition intervention study clinical trial](#). *Journal of the American Geriatrics Society* 59: 10–17

Neelemaat F, Bosmans JE, Thijs A et al. (2011) [Post-discharge nutritional support in malnourished elderly individuals improves functional limitations](#). *Journal of the American Medical Directors Association* 12: 295–301

Neelemaat F, Bosmans JE, Thijs A et al. (2012) [Oral nutritional support in malnourished elderly decreases functional limitations with no extra costs](#). *Clinical Nutrition* 31: 183–90

Interventions starting after hospital discharge

Two studies looked at the effect of oral nutrition support after discharge from hospital.

A systematic review and meta-analysis by [Beck et al. \(2013\)](#) assessed the effects of oral nutrition support in medical and surgical patients aged 65 years or over after hospital discharge. Studies were included of nutrition support lasting for a minimum of 1 week, in the form of supplements, or fortification of normal food and dietary advice, aimed at improving protein and energy intake. Primary outcomes were hospital readmissions and mortality. A total of 6 RCTs (n=716) were included, of which 4 were in medical patients and 2 were in surgical patients. In all except 1 trial, patients were classified as malnourished (or at risk) following screening, and all trials used commercial oral nutritional supplements.

No significant effects of oral nutrition support were seen for:

- mortality (odds ratio [OR]=0.80, 95% CI 0.46 to 1.39, p=0.43; 4 RCTs, n=532)
- or readmissions (OR=1.07, 95% CI 0.71 to 1.61, p=0.75; 4 RCTs, n=478).

Benefits of nutrition support were seen in all trials for either energy intake or weight in compliant participants (data not provided), but these were secondary outcomes of both the review and the individual trials.

Limitations of the evidence included that:

- 2 studies compared different oral supplements with each other (as opposed to usual care) which may have diminished the effects in groups within these trials that were analysed as 'intervention' by the review
- the studies were relatively short (most ranged from 4 to 8 weeks in duration, and the authors noted that patients may continue to lose weight for several weeks after nutritional intervention)
- the review only included studies from the last 5 years, although this may increase its relevance to current practice.

An RCT and cost-effectiveness analysis (n=114) in Germany by [Norman et al. \(2011\)](#) also investigated effects of oral nutritional supplements versus control in malnourished patients (mean age=51 years). Patients discharged from a single hospital department (gastroenterology, hepatology and endocrinology) with a benign gastrointestinal disease, and classified as malnourished according to the Subjective Global Assessment, were eligible. Those with malignant disease, renal insufficiency, life expectancy less than 3 months, or younger than 18 years, were excluded.

Patients were randomised to the intervention (oral nutritional supplements plus dietary counselling), or control (dietary counselling alone), for 3 months after discharge. Patients in the intervention group were asked to take up to 3 oral supplements per day (in the form of a 200 ml protein energy drink) and to record the actual number of drinks consumed. Quality of life was measured on the 36-item Short Form General Health Survey. Health status utilities were then obtained using an algorithm to transform survey scores into values on a scale from 0 (death) to 1 (complete health). The analysis considered 2 pricing scenarios based on low and high prices of 1 supplement of €2.30 and €2.93 respectively.

Cost-effectiveness was then calculated based on the following results:

- Average consumption of supplements in the intervention group was 2.4 per day.
- Additional mean costs per patient in the supplements group for the low-cost and high-cost scenarios were €424 and €540 respectively (based only on the cost of supplements).
- Health status utilities were not significantly different between groups at baseline, but after 3 months were higher among patients receiving supplements than among those not receiving them (0.731 versus 0.671, p=0.028).
- Combining health utility data with additional costs in both the low-price and high-price scenarios gave incremental cost-effectiveness ratios (namely, cost per QALY gained with supplements) of €9497 and €12,099 respectively.

The authors therefore concluded that oral supplements were cost-effective based on a hypothetical threshold of up to €50,000 (as suggested by healthcare economists and in line with other German studies).

Limitations of the evidence included that:

- Only the costs of supplements were considered, therefore it is a partial cost analysis. Costs associated with medication, use of other healthcare resources, and indirect costs were not included. Readmissions to hospital were also not taken into account, despite evidence that fewer patients in the supplements group than the control group were readmitted (17 versus 26, p=0.029). The authors noted the possibility that including these data may have increased the cost effectiveness of supplements (a separate analysis of the data by [Nuijten and Mittendorf 2012](#) that did include hospitalisation costs found that costs of supplements were offset by reduced costs for hospitalisation).
- Only 114 of 160 randomised patients were included in the analysis (40 dropped out and 6 did not complete the quality of life questionnaire).
- Results may not be transferable outside of Germany where the trial was based.

Evidence suggests that oral nutritional supplements in older patients after hospital discharge may increase energy intake and weight, and may also be associated with a cost-effective improvement in quality of life. Supplements do not appear to improve mortality or hospital readmission rates. These data are consistent with the need to coordinate care between hospital and community as recommended by [NICE CG32](#) and reiterated in [NICE QS24](#).

It should be noted that this evidence is based on patients discharged from hospital (namely, those who had been diagnosed with malnutrition in an acute care setting). Evidence among those identified as malnourished in a primary or community care setting is lacking, and more research where interventions both start and end outside of hospital is needed.

Further advice on the use of oral nutritional supplements in community and primary care is available from the National Prescribing Centre (now the NICE Medicines and Prescribing Centre) in '[Prescribing of adult oral nutritional supplements \(ONS\): guiding principles for improving the systems and processes for ONS use](#)'.

Key references

Beck AM, Holst M, Rasmussen HH (2013) [Oral nutritional support of older \(65 years+\) medical and surgical patients after discharge from hospital: systematic review and meta-analysis of randomized controlled trials](#). *Clinical Rehabilitation* 27: 19–27

Norman K, Pirlich M, Smoliner C et al. (2011) [Cost-effectiveness of a 3-month intervention with oral nutritional supplements in disease-related malnutrition: a randomised controlled pilot study](#). *European Journal of Clinical Nutrition* 65: 735–42

Supporting reference

Nuijten M, Mittendorf T (2012) [The health economic impact of oral nutritional supplements \(ONS\) in Germany](#). *Aktuelle Ernährungsmedizin* 37: 126–33

1.2 [Screening for malnutrition and the risk of malnutrition in hospital and the community](#)

Malnutrition screening in hospital admissions among older people

[NICE CG32](#) recommends that all hospital inpatients on admission and all outpatients at their first clinic appointment should be screened for malnutrition. Screening should be repeated weekly for inpatients and when there is clinical concern for outpatients.

An RCT (n=143) in Sydney, Australia by [Holyday et al. \(2012\)](#) studied the impact of nutrition screening, followed by a malnutrition care plan or usual care, among hospitalised patients admitted to an acute geriatric ward of a single hospital. All patients (mean age=83 years) were screened using the Mini Nutritional Assessment tool, and categorised as 'malnourished', 'at risk of malnutrition', or 'well-nourished'. Patients were then assigned either to the malnutrition care plan (including education, modified meals, oral supplements and assistance with meals, which were tailored according to a clinical dietitian assessment), or to usual nutrition care (namely, the ward's clinical dietitian was not informed of the screening outcome and only saw patients if referred by other health professionals). Any patients in the usual care group who were referred to the dietitian received the same malnutrition care plan as those in the intervention group. The study was powered to assess length of hospital stay.

The mean length of hospital stay among all patients was not significantly different between groups (p=0.64). However, among the 32 malnourished patients, length of stay was significantly shorter after the intervention than after usual care (10.6 days versus 19.5 days, p=0.013).

The proportion of patients receiving specialist dietetic care was significantly greater in the intervention group:

- For malnourished patients, 100% (12/12) received dietetic support in the intervention group versus 35% (7/20) in the usual care group ($p < 0.001$).
- For patients at risk of malnourishment, 85% (40/47) received dietetic support in the intervention group versus 20% (8/40) in the usual care group ($p < 0.001$).

Based on the reductions in length of stay, the authors estimated that for a hospital admitting 500 older patients per year for acute care, the potential net saving could be \$AUD 365,000.

Limitations of the evidence included that: the care model in the trial hospital (acute admissions of older people directly to geriatric medicine) may not be used by other institutions; and non-English speaking and cognitively impaired patients were excluded, so results may not be generalisable to these groups.

The evidence suggests that nutrition screening followed up with a multicomponent malnutrition care plan appears to reduce hospital stays among older malnourished patients. This is consistent with recommendations in [NICE CG32](#) to screen all patients admitted to hospital for malnutrition.

Key reference

Holyday M, Daniells S, Bare M et al. (2012) [Malnutrition screening and early nutrition intervention in hospitalised patients in acute aged care: a randomised controlled trial](#). *Journal of Nutrition, Health & Aging* 16: 562–8

1.3 [Indications for nutrition support in hospital and the community](#)

No new key evidence was found for this section.

1.4 [What to give in hospital and the community](#)

Refeeding syndrome

[NICE CG32](#) states that people who meet the following criteria should be considered to be at high risk of developing refeeding problems.

Patient has 1 or more of the following:

- BMI less than 16 kg/m²
- unintentional weight loss greater than 15% within the last 3–6 months
- little or no nutritional intake for more than 10 days
- low levels of potassium, phosphate or magnesium prior to feeding.

Or patient has 2 or more of the following:

- BMI less than 18.5 kg/m²
- unintentional weight loss greater than 10% within the last 3–6 months
- little or no nutritional intake for more than 5 days
- a history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.

Two studies recently examined refeeding syndrome.

A prospective cohort study in the UK (n=243) by [Rio et al. \(2013\)](#) assessed the incidence of, and risk factors for, refeeding syndrome among patients starting enteral or parenteral nutrition support in a single hospital. The study was powered based on reported prevalence of refeeding syndrome. Energy requirements for each patient were based on basal metabolic rate and stress-related factors. The hospital's nutrition policy for those at risk of refeeding

syndrome was hypocaloric feeding of 800 kcal/day or 50% of estimated adult energy needs. The criteria for determining risk of refeeding syndrome were those set out by the NICE guideline (as listed above). A set of 3 criteria were used to confirm refeeding syndrome, all of which were required for a diagnosis:

- severely low concentrations of potassium (<2.5 mmol/litre), phosphate (<0.32 mmol/litre) and magnesium (<0.5 mmol/litre)
- peripheral oedema or acute circulatory fluid overload
- disturbance to organ function including respiratory or cardiac failure and pulmonary oedema.

Serum electrolytes were recorded at baseline then every 3rd day for a maximum of 15 days (recording was stopped if nutrition support was withdrawn). Patients or the next of kin were asked about dietary intake in the 10 days before entry to the study to highlight instances of poor nutritional intake. Most patients (87%) were enterally fed.

A total of 133 patients had 1 or more risk factors for refeeding syndrome, and 6% (15/243) of patients on day 3 had serum phosphate <0.5 mmol/litre (which the authors noted was higher than reports of 0.2–2% in the adult hospital population, possibly due to recruitment from high dependency and intensive care units). The authors stated that based on the diagnostic criteria for refeeding syndrome applied in this study, the risk factors listed in [NICE CG32](#) were weak predictors, with only baseline low-serum magnesium an independent predictor ($p=0.021$). In total, 3 participants were diagnosed with refeeding syndrome following nutrition support: 2 who were dependent on alcohol, and 1 who had Crohn's disease and partial resection of the colon. All 3 patients had been identified as at risk of refeeding syndrome and therefore received hypocaloric feeding in line with hospital policy, but this failed to prevent the syndrome. The 3 patients were also all given intravenous glucose infusion, which the authors stated may have contributed to the development of the syndrome. No deaths were caused directly by refeeding syndrome.

Limitations of the evidence included that:

- although the study used clearly defined and standardised criteria to diagnose refeeding syndrome, these criteria were stricter than those used by some other studies (such as Zeki et al. 2011 discussed below, which only considered phosphate)
- the results may not be generalisable to other patient groups such as those receiving oral nutrition support
- only 3/243 participants developed refeeding syndrome so statistical analyses were limited
- only half of the 484 patients eligible for the study were recruited, mainly because of consent not being given (potentially explained by confusion, cognitive impairment or communication problems in severely ill patients), which may have introduced bias.

A retrospective audit of patient records ($n=321$) by [Zeki et al. \(2011\)](#) examined the overall and comparative incidence of refeeding syndrome in patients starting on parenteral or nasogastric nutrition support in a single UK hospital. Secondary aims included assessing the predictive ability of NICE criteria for indicating risk of refeeding syndrome. It was noted that the term 'refeeding syndrome' is often used, but in this study the outcome measured was defined as 'refeeding hypophosphataemia' (namely, a fall in serum phosphate from a normal level of 0.74–1.52 mmol/litre before feeding to <0.6 mmol/litre within a week of starting the initial feed). Patients with low phosphate levels before feeding began were excluded.

In total, 92 of 321 patients were deemed at risk of refeeding hypophosphataemia according to NICE criteria. Hypophosphataemia then went on to develop in:

- 25% (23/92) of the at-risk patients versus 11% (26/229) of those not identified as at-risk ($p=0.003$).

- 33% (18/54) of the at-risk patients who were fed nasogastrically versus 13% (5/38) of those at risk and fed parenterally (p=0.03).

The NICE criteria for defining risk of refeeding syndrome had a sensitivity and specificity of 0.76 and 0.50 respectively for nasogastric feeding, and 0.73 and 0.38 respectively for parenteral feeding, when hypophosphataemia (serum phosphate <0.6 mmol/litre) was used as the 'reference standard'. Refeeding hypophosphataemia was not associated with death within 7 days (p=0.73).

Limitations of the evidence included that:

- It was a retrospective, single-site study, and patients were not randomly selected.
- The mean age of patients fed nasogastrically was 70 years versus 54 years in those fed parenterally (p value not provided), although this difference may reflect heterogeneity in the type of patients typically fed by these 2 methods (for example, younger patients receiving parenteral nutrition perioperatively).
- Hypophosphataemia was the only marker used for refeeding syndrome, which although usually present, may often have other causes ([Hoffmann et al. 2008](#)). The specificity of hypophosphataemia alone in diagnosing refeeding syndrome may therefore be questionable. It was also noted that this trial used a fall in phosphate levels to below an absolute value, whereas a percentage drop may have been more sensitive.
- Use of differing cut-off values for electrolytes such as phosphate in diagnosing refeeding syndrome between trials makes comparing results difficult.

Taken together, evidence suggests that certain patients commencing nutrition support (who are already identified as being at risk of refeeding syndrome using current criteria in [NICE CG32](#)) may be at even greater risk of subsequently developing refeeding syndrome, such as those with low serum magnesium, or those fed nasogastrically. Although this is broadly consistent with [NICE CG32](#), some data question the validity or lack of specificity of some risk markers set out by NICE. However, the lack of universally accepted criteria for a diagnosis of refeeding syndrome prevents a definitive assessment of the predictive ability of risk factors, therefore this evidence is unlikely to have an impact on [NICE CG32](#). Further research is needed.

Key references

Rio A, Whelan K, Goff L et al. (2013) [Occurrence of refeeding syndrome in adults started on artificial nutrition support: prospective cohort study](#). *BMJ Open* 3: e002173

Zeki S, Culkin A, Gabe SM et al. (2011) [Refeeding hypophosphataemia is more common in enteral than parenteral feeding in adult in patients](#). *Clinical Nutrition* 30: 365–8

Supporting reference

Hoffmann M, Zemlin AE, Meyer WP et al. (2008) [Hypophosphataemia at a large academic hospital in South Africa](#). *Journal of Clinical Pathology* 61: 1104–7

1.5 [Monitoring of nutrition support in hospital and the community](#)

No new key evidence was found for this section.

1.6 [Oral nutrition support in hospital and the community](#)

Oral nutrition support

[NICE CG32](#) recommends that 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. The guideline states that oral nutrition support includes any of the following methods to improve nutritional intake: fortified food with protein, carbohydrate and/or

fat, plus minerals and vitamins; snacks; oral nutritional supplements; altered meal patterns; the provision of dietary advice.

Tailored oral nutrition support

An RCT (n=132) in Switzerland by [Starke et al. \(2011\)](#) examined tailored nutritional care versus standard care for malnourished patients in hospital. All patients consecutively admitted to the general medical ward of a single hospital were screened using the Nutritional Risk Screening-2002 tool and those scoring 3 or more were eligible for the study. Patients were excluded if they had a terminal condition, were expected to stay less than 5 days in hospital, or were on starvation, parenteral nutrition or dialysis. Patients were randomised to tailored nutritional care (mean age=70 years) or standard care (mean age=75 years; p=0.091 for difference). Tailored care included detailed assessment, individual food supply, fortified meals, snacks, and oral supplements. Standard care included oral supplements and nutrition therapy prescribed only as part of routine ward care. Primary outcomes were average daily energy and protein intake.

Compared with standard care, patients receiving tailored nutritional care had a higher mean daily intake of both energy (1553 kcal versus 1115 kcal, p<0.001) and protein (65.4 g versus 43.9 g, p<0.001). Patients who received tailored care also retained more body weight (p=0.008), had better scores on the physical component summary of the Short Form-36 quality of life scale (p=0.033), and had fewer hospital readmissions after 6 months (p=0.027). There was no significant difference in mortality between groups.

Limitations of the evidence included that although non-significant, an age difference of 5 years (in favour of the intervention group), particularly among older people, could have influenced results. Equally, a baseline difference in the disease component of the Nutritional Risk Screening-2002 score in favour of the intervention group was close to significance (p=0.057) and may have affected outcomes.

The evidence suggests that tailored, multicomponent oral nutrition support for older malnourished patients in hospital appears to improve nutritional outcomes, consistent with recommendations in [NICE CG32](#).

Key reference

[Starke J, Schneider H, Alteheld B et al. \(2011\) Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients. Clinical Nutrition 30: 194–201](#)

Dietary advice with or without oral nutritional supplements

A Cochrane review by [Baldwin and Weekes \(2011\)](#) examined the impact of dietary advice with and without the addition of oral supplements in disease-related malnutrition. Studies of patients with, or at risk of, disease-related malnutrition in any setting were included. Studies in pregnant women, people with eating disorders, or conditions of food insufficiency, were excluded. A total of 45 RCTs and quasi-RCTs (n=3186) were included, which examined:

- dietary advice versus no advice (12 trials)
- dietary advice versus oral nutritional supplements (8 trials)
- dietary advice versus dietary advice plus oral nutritional supplements (16 trials)
- dietary advice plus supplements (if needed) versus no advice and no supplements (14 trials); some studies compared more than 1 intervention.

Primary outcomes were mortality, morbidity, and measures of nutritional status (such as weight change). Mortality and morbidity did not differ significantly between any of the comparison groups tested.

Significant improvements in body weight were seen with:

- Dietary advice versus no advice, both for interventions longer than 12 months (MD=3.75 kg, 95% CI 0.97 to 6.53 kg, p=0.0081; 1 trial, n=92), and for interventions of all lengths up to 12 months (MD=1.47 kg, 95% CI 0.32 to 2.61 kg, p=0.012; 9 trials, n=733). However, the authors noted that the effect size was influenced by 1 quasi-randomised trial with a high risk of bias.
- Dietary advice plus nutritional supplements (if needed) versus no advice (MD=2.20 kg, 95% CI 1.16 to 3.25 kg, p=0.000038; 9 trials, n=454).

Significant increases in mid-arm muscle circumference were also seen with:

- Dietary advice versus no advice (MD=0.81 cm, 95% CI 0.31 to 1.31 cm, p=0.0015; 2 trials, n=130).
- Dietary advice plus nutritional supplements versus dietary advice alone (MD=0.89 cm, 95% CI 0.43 to 1.35 cm, p=0.00016; 3 trials, n=492).

Limitations of the evidence included that:

- apart from mortality, the pooled effects were based on trials with statistical and clinical heterogeneity
- the included trials were mostly of outpatients with a mean age over 65 years which may limit transferability of results to other groups
- most studies did not report details of the dietary interventions, or of the experience and training of dietitians giving the advice
- the quality of the evidence base was assessed as low to moderate.

The evidence suggests that dietary advice with or without oral nutritional supplements in disease-related malnutrition may improve body weight and indicators of muscle mass. This is consistent with recommendations for oral nutrition support (incorporating oral supplements and dietary advice) in [NICE CG32](#).

Key reference

Baldwin C, Weekes CE (2011) [Dietary advice with or without oral nutritional supplements for disease-related malnutrition in adults](#). Cochrane Database of Systematic Reviews issue 9: CD002008

Oral nutrition support in older patients with hip fracture

An RCT (n=126) in Hong Kong by [Myint et al. \(2013\)](#) investigated oral nutritional supplements versus usual care in patients aged over 60 years (mean age=81) transferred to a rehabilitation department after surgery for low-impact osteoporotic fracture of the proximal femur. All patients were screened for eligibility for nutritional support. Exclusion criteria were: needing to be tube fed; an unstable medical condition; body mass index of 25 or over; malignancy; contraindication to a high-protein diet; and cognitive impairment or communication problems. Patients were randomised to standard hospital diet plus oral supplements, or hospital diet alone. The oral supplement comprised 240 ml twice daily of an oral nutritional supplement drink of the patient's choice (18–24 g protein and 500 kcal energy per day) and was continued for 28 days or until discharge. Both groups received vitamin D and calcium supplements, and concurrent rehabilitation therapy.

Reductions in the primary outcome of body mass index were significantly less in the oral supplements group than in the control group at both discharge (0.25 kg/m² versus 0.72 kg/m²) and at 4-week follow-up (0.03 kg/m² versus 0.49 kg/m², p=0.012 for between-group difference). No significant differences in rates of change were seen for other primary outcomes (serum albumin, or scores on the Functional Independence Measure and the Elderly Mobility Scale). A secondary outcome of length of stay in the rehabilitation ward was 3.8 days less in the oral supplements group (p=0.04).

Limitations of the evidence included that: decisions about discharge were made mainly by non-blinded members of staff who were not study investigators (although decisions were made as part of a multidisciplinary case conference to help ensure objectivity); and because mean length of stay was different between groups, the length of exposure to intervention and control treatments (and also rehabilitation therapy) differed.

The evidence suggests that oral nutritional supplements appear to prevent weight loss after hip fracture surgery in older patients with a body mass index less than 25 kg/m², and may reduce length of hospital stay. This is consistent with recommendations in [NICE CG32](#) to screen patients for malnourishment and if necessary provide oral nutrition support which may include oral supplements.

Key reference

[Myint MW, Wu J, Wong E et al. \(2013\) Clinical benefits of oral nutritional supplementation for elderly hip fracture patients: a single blind randomised controlled trial. Age and Ageing 42: 39–45](#)

Oral nutrition support in cancer

A systematic review and meta-analysis by [Baldwin et al. \(2012\)](#) examined oral nutritional interventions in malnourished patients (or those at risk) receiving active or palliative treatment for cancer at any site and of any stage. A total of 13 RCTs (n=1414) were included, which compared: dietary advice with routine care (6 trials), oral nutritional supplements with routine care (3 trials), and dietary advice plus supplements if needed with routine care (7 trials). Four studies included more than 1 intervention. Types of cancers treated were leukaemia, lymphoma, gastrointestinal, gynaecological, bladder, lung, breast, head and neck. Therapies varied between studies and included adjuvant, neoadjuvant, and primary treatment with both chemotherapy and radiotherapy. Primary outcomes were mortality and quality of life.

Oral nutritional support was associated with the following outcomes versus usual care:

- No effect on mortality (relative risk [RR]=1.06, 95% CI 0.92 to 1.22, p=0.43; 11 RCTs, n=1240).
- Benefits for some aspects of quality of life (based on mean difference from baseline in scores on the European Organization for Research and Treatment of Cancer 30-item questionnaire): emotional functioning (MD=5.2, p=0.02), dyspnoea (MD=-2.9, p<0.001), loss of appetite (MD=-2.35, p=0.03), and global quality of life (MD=5.5, p=0.02). Results were based on meta-analyses of 3 RCTs, with heterogeneous comparisons excluded.
- Improvements in weight (MD=1.86 kg, 95% CI 0.25 to 3.47 kg, p=0.02; 8 RCTs, n=710) and energy intake (MD=432 kcal/day, 95% CI 172 to 693 kcal, p=0.001; 4 RCTs, n=383). However, after removing the main causes of heterogeneity, these differences were no longer statistically significant.

Limitations of the evidence included that:

- studies were assessed as low to moderate quality
- studies were heterogeneous for types and treatments of cancer, type of nutrition intervention, and nutrition status of patients, meaning that sizes of observed effects may be uncertain, and findings are more difficult to extrapolate
- quality of life data used in the analyses were all collected by unblinded assessors which may have introduced bias, and the clinical significance of changes observed in quality of life scores are uncertain (interpretation may have been assisted by the reporting of percentage changes).

Evidence suggests that oral nutrition support may improve quality of life in malnourished patients with cancer, consistent with recommendations in [NICE CG32](#).

Key reference

[Baldwin C, Spiro A, Ahern R et al. \(2012\) Oral nutritional interventions in malnourished patients with cancer: a systematic review and meta-analysis. Journal of the National Cancer Institute 104: 371–85](#)

Oral nutrition support in chronic obstructive pulmonary disease (COPD)

Alongside the recommendations in [NICE CG32](#) for general oral nutrition support, 'Chronic obstructive pulmonary disease' ([NICE CG101](#)) recommends that if the body mass index is low, patients with COPD should be given nutritional supplements to increase their total calorific intake and be encouraged to take exercise to augment the effects of nutritional supplementation.

Three systematic reviews recently assessed nutrition support (mainly in the form of oral nutritional supplements) in COPD.

A systematic review and meta-analysis by [Collins et al. \(2012\)](#) assessed nutritional support (including food strategies, dietary advice, oral nutritional supplements, or enteral tube feeding, which provided all or a proportion of daily nutritional requirements) in patients with stable COPD. Studies of parenteral nutrition were excluded. A total of 13 RCTs were included (11 of oral nutritional supplements, 1 of dietary advice, and 1 of enteral tube feeding; n=439). Of these, 8 trials were in outpatients, 3 were in inpatients, and 2 covered both settings. In most studies, the majority of patients were malnourished.

Nutritional support was associated with significantly greater increases from baseline in:

- Total protein intake (MD=14.8 g, standard deviation [SD] 3.6 g, p<0.001; 2 RCTs, n=115).
- Total energy intake (MD=236 kcal, SD 71 kcal, p<0.001; 5 RCTs, n=196).
- Body weight (MD=1.94 kg, SD 0.26 kg, p<0.001; 11 RCTs, n=308), which the authors noted was close to the level of weight gain (≥ 2 kg) that may be associated with functional and clinical benefits.
- Grip strength (MD=5.3%, SD 2.7%, p<0.05; 4 studies, n=156), which the authors noted was a mild to moderate increase, but may produce clinical or functional benefits in patients close to the threshold of disability.

A further systematic review and meta-analysis by [Collins et al. \(2013\)](#) investigated nutritional support in patients with stable COPD, but focused on functional capacity and quality of life outcomes. The review used the same methodology and inclusion/exclusion criteria as Collins et al. (2012) discussed above, and included the same studies except for 1 trial (n=20) of oral nutritional supplements that did not assess relevant outcomes.

Nutritional support was associated with significant improvements versus control in the following outcomes:

- Changes in inspiratory muscle strength (maximal inspiratory mouth pressure: MD=4.04 cm H₂O, standard error [SE] 1.86 cm H₂O, p=0.03; 5 RCTs, n=177) and expiratory muscle strength (maximal expiratory mouth pressure: MD=13.06 cm H₂O, SE 5.81 cm H₂O, p=0.025; 4 RCTs, n=106), which were also associated with weight gains of 2.2 kg and 3.1 kg respectively (p<0.001).
- Changes in hand grip strength (standardised MD=0.57 kg, SE 0.22 kg, p=0.009; 4 RCTs, n=156), which was also associated with weight gain of 2.1 kg (p=0.001).
- Quality of life, and exercise tolerance walking tests (benefits were seen in 3 of 5 trials and 4 of 7 trials respectively that assessed these outcomes, but meta-analysis was not possible).

No improvements were seen in respiratory function (forced expiratory volume in 1 second, lung capacity, or blood gases).

Limitations common to both of the reviews by Collins et al. included that:

- most studies were assessed as poor quality on the Jadad scoring system
- a lack of reported data among the included studies meant that the effect of inflammation on nutrition status and response to nutrition support could not be examined

- most studies were of oral supplements therefore conclusions about other forms of nutrition support were limited
- the clinical significance of statistical improvements in outcomes not directly relevant to patients' wellbeing can be difficult to establish (but the authors noted that weight gains of more than 2 kg are of a level that may be associated with functional and clinical benefits).

A Cochrane review by [Ferreira et al. \(2012\)](#) also assessed nutrition support (including oral, enteral, or parenteral nutrition with any caloric supplement over more than 2 weeks) in patients with stable COPD. A total of 17 RCTs were included (15 of oral nutritional supplements, 1 of dietary advice, 1 of enteral tube feeding; n=632). Of these, 13 trials were in outpatients and 4 included an inpatient component. In most studies, the majority of patients were malnourished. All studies included in the 2 reviews by Collins et al. discussed above were also included in the Cochrane review. The primary outcomes were anthropometric measures and functional exercise.

Nutritional support was associated with significantly greater increases from baseline in:

- Body weight (MD=1.62 kg, 95% CI 1.27 to 1.96 kg, p<0.00001; 14 RCTs, n=511), with a greater increase seen among malnourished patients (MD=1.73 kg, p<0.00001; 11 RCTs, n=324).
- Fat-free mass/fat-free mass index (standardised MD=0.57; 95% CI 0.04 to 1.09, p=0.03; 6 RCTs, n=287), which was larger for malnourished patients (standardised MD=1.08, p<0.00001; 3 RCTs, n=125).
- 6-minute walk distance (MD=39.96 m, 95% CI 22.66 to 57.26 m, p<0.00001; 5 RCTs, n=140).

Limitations of the evidence included that: the evidence base was assessed as moderate quality for weight gain and fat/fat-free mass, but low quality for other outcomes; and data for changes in body weight from baseline had to be imputed in 5 of the 14 RCTs meta-analysed for this outcome (although an analysis removing these 5 studies did not substantially alter the effect size).

It should also be noted that the previous version of this Cochrane review from 2008 concluded that 'nutritional support had no significant effect on anthropometric measures, lung function or exercise capacity in patients with stable COPD.' The substantially different conclusions of the 2012 review may have been driven by the inclusion of 3 new trials, which contributed to several of the significant results detailed above. These 3 trials included additional interventions in the nutrition support arm that did not feature in the control arms, such as exercise programmes, and immune enhancing nutrition (namely, formulations of specialised nutrients such as arginine and omega-3 fatty acids that may help regulate response to illness and injury). All of the trials included in the 2008 Cochrane review, and the 2 reviews by Collins et al., did not feature these additional interventions. Therefore, the significant effects observed in the 2012 Cochrane review may not be due entirely to nutrition support.

The evidence suggests that oral nutritional supplements appear to improve energy and protein intake, body weight, and functional outcomes (such as peripheral muscle strength, and maximum inspiratory and expiratory pressure) in malnourished patients with stable COPD. This is consistent with the general oral nutrition support recommendations in [NICE CG32](#). The evidence is also consistent with the recommendation in [NICE CG101](#) to give nutritional supplements to patients with COPD and a low body mass index (but it should be noted that the evidence for this recommendation was listed as grade D in [the full version of NICE CG101](#), whereas the evidence base now appears to be more robust).

Key references

Collins PF, Stratton RJ, Elia M (2012) [Nutritional support in chronic obstructive pulmonary disease: a systematic review and meta-analysis](#). *American Journal of Clinical Nutrition* 95: 1385–95

Collins PF, Elia M, Stratton RJ (2013) [Nutritional support and functional capacity in chronic obstructive pulmonary disease: a systematic review and meta-analysis](#). *Respirology* 18: 616–29

Ferreira IM, Brooks D, White J et al. (2012) [Nutritional supplementation for stable chronic obstructive pulmonary disease](#). *Cochrane Database of Systematic Reviews* issue 12: CD000998

Surgical patients

[NICE CG32](#) recommends that perioperative oral nutrition support should be considered for surgical patients who can swallow safely and are malnourished. Surgical patients who are malnourished, have inadequate or unsafe oral intake and a functional, accessible gastrointestinal tract, and are due to undergo major abdominal procedures, should be considered for preoperative enteral tube feeding. Healthcare professionals should also consider supplementary perioperative parenteral nutrition in malnourished surgical patients who have inadequate or unsafe oral and/or enteral nutritional intake, and a non-functional, inaccessible or perforated (leaking) gastrointestinal tract.

A Cochrane review by [Burden et al. \(2012\)](#) assessed preoperative nutritional support in patients undergoing non-emergency gastrointestinal surgery. Nutrition support by any route, using any formulation or dietary modification, over any time during the period from 3 months up to 24 hours before surgery, was eligible. Trials of a single nutrient or immune enhancing agent were excluded. A total of 13 RCTs (n=1192) were included, assessing parenteral nutrition (3 trials), standard enteral nutrition (2 trials), standard oral supplements (3 trials) and immune enhancing nutrition (including formulations of arginine, omega 3, and RNA; 7 trials). Two of the trials assessed more than one intervention. It should be noted that immune enhancing feeds were outside the scope of [NICE CG32](#).

All trials of parenteral nutrition administered nutrition for 10 days preoperatively, however administration of oral supplements and immune enhancing nutrition varied between studies (though 6 of the 7 trials of immune enhancing nutrition, and all trials of oral nutrition, used the same respective supplements). Only 4 studies specifically recruited malnourished patients; in the remainder, a proportion of, or none of, the participants were malnourished. Primary outcomes were postoperative complications and length of hospital stay.

Postoperative complications were significantly reduced with:

- immune enhancing nutrition (RR=0.67, 95% CI 0.53 to 0.84, p=0.0006; 6 RCTs, n=548, many of whom were not malnourished)
- parenteral nutrition (RR=0.64, 95% CI 0.46 to 0.87, p=0.005; 3 RCTs, n=260, most of whom were malnourished).

Meta-analyses of 2 trials of enteral nutrition and 3 trials of standard oral supplements (in predominantly well-nourished patients) did not indicate any significant effect on the primary outcomes.

Limitations of the evidence included that:

- most included patients were not malnourished, however this may provide useful information about the potential importance of perioperative nutrition support even for those who are well nourished
- it was noted that the 3 trials of parenteral nutrition were all published at least 10 years ago (1 trial 30 years ago), and the authors stated that recent developments with intravenous nutrition support meant that this result was likely of academic relevance only
- it was also stated that perioperative surgical management has changed in the last decade (such as the introduction of the 'Enhanced Recovery After Surgery' protocol), which may reduce the relevance of older studies generally
- most trials involved malignant disease therefore results may not be generalisable to surgery for other conditions.

The evidence suggests that immune enhancing nutrition may reduce postoperative complications in patients (many of whom were not malnourished) undergoing non-emergency gastrointestinal surgery. However, limitations of the evidence, combined with some potential issues of adverse reactions to immune enhancing supplements in critical care populations noted by the authors, mean that this finding is unlikely to affect [NICE CG32](#). However, further research into the effects of perioperative nutrition support across the spectrum of nutritional status, not just malnourished patients, may be useful.

Key reference

Burden S, Todd C, Hill J et al. (2012) [Pre-operative nutrition support in patients undergoing gastrointestinal surgery](#). Cochrane Database of Systematic Reviews issue 11: CD008879

1.7 [Enteral tube feeding in hospital and the community](#)

Prophylactic percutaneous endoscopic gastrostomy in head and neck cancer

[NICE CG32](#) recommends that people in general medical, surgical and intensive care wards who are malnourished or at risk of malnutrition, and have inadequate or unsafe oral intake, and a functional, accessible gastrointestinal tract, should be fed via a tube into the stomach unless there is upper gastrointestinal dysfunction. It also states that gastrostomy feeding should be considered in people likely to need long-term (4 weeks or more) enteral tube feeding.

An RCT (n=134) in Sweden by [Silander et al. \(2012\)](#) assessed the effects of prophylactic percutaneous endoscopic gastrostomy versus usual care in patients with advanced head and neck cancer. Patients with newly diagnosed and untreated pharyngeal or oral cancer, or malignant neck nodes with unknown primary in stage III or IV, were eligible. Exclusion criteria were: treatment with palliative intent; inability to answer questionnaires; or unsuitability for gastrostomy because of previous abdominal surgery. Patients were randomised to the intervention (individual nutritional counselling with tube feeding if oral intake was inadequate, indicated by >1 kg weight loss) or to usual clinical practice (including nutritional advice and enteral feeding when necessary).

Tube feeding provided 30 kcal energy and 1.2–1.5 g protein/kg body weight/day, with the addition of energy and protein-rich supplements when needed. In terms of cancer treatment, pharyngeal tumours were usually treated with chemotherapy and radiotherapy (with surgery as salvage), and oral cancer and malignant lymph nodes with unknown primary tumour were mostly treated with surgery and postoperative radiotherapy. All patients were assessed at baseline and at 1, 2, 3, 6, 12 and 24 months.

In the prophylactic gastrostomy group, enteral feeding commenced a mean of 23 days earlier than in the control group (p=0.0001), and continued for a mean of 177 days versus 122 days in the control group (p<0.0001).

At 6 months, benefits were seen with prophylactic versus control treatment for:

- Some aspects of quality of life (as measured by the European Organization for Research and Treatment of Cancer 30-item Questionnaire): physical functioning (p=0.02), role functioning (p=0.05), cognitive functioning (p=0.008), Global Health Status (p=0.02), and fatigue (p=0.01). These differences were not significant at 12 or 24 months.
- Percentage body weight lost (among only those patients who had lost weight), which was less in the intervention group (11.4%) than the control group (13.6%, p=0.03). However, absolute weight loss in all patients was not significantly different between groups at 6, 12 or 24 months.

- The number of malnourished patients, which was approximately 10% more in the control group throughout the 1st year of follow-up (the authors noted that this was not statistically significant but may be of clinical importance).

The authors stated that most complications at the gastrostomy site were mild. However, 1 patient with advanced hypopharyngeal cancer (excluded from analysis because of death before the start of treatment 6 days after gastrostomy surgery) developed peritonitis followed by general organ failure after tube dislodgement.

Limitations of the evidence included that:

- one third of eligible patients declined participation, which may have led to bias (reasons included not wanting to undergo gastrostomy in the absence of current feeding problems, or inability to make decisions about joining the trial if they had just received their cancer diagnosis)
- both groups had access to nutritional advice from the same dietitians, which may have lessened the differences in outcomes observed between the groups.

There is some evidence to suggest that prophylactic percutaneous endoscopic gastrostomy in patients with advanced head and neck cancer may improve quality of life and could help to reduce weight loss. Although [NICE CG32](#) does not directly recommend prophylactic gastrostomy, it is often performed in practice among this patient group, and evidence from the study is broadly consistent with recommendations to consider gastrostomy in people likely to need long-term enteral tube feeding. These data are therefore unlikely to have an impact on the guideline.

Key reference

Silander E, Nyman J, Bove M et al. (2012) [Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer—a randomized study](#). *Head & Neck* 34: 1–9

Percutaneous endoscopic gastrostomy versus nasogastric tube feeding in dysphagia

[NICE CG32](#) recommends that in the acute setting, for example following stroke, people unable to swallow safely or take sufficient energy and nutrients orally should have an initial 2–4 week trial of nasogastric enteral tube feeding. Healthcare professionals with relevant skills and training in the diagnosis, assessment and management of swallowing disorders should assess the prognosis and options for future nutrition support. The guideline also recommends that gastrostomy feeding should be considered in people likely to need long-term (4 weeks or more) enteral tube feeding.

A Cochrane review by [Gomes et al. \(2012\)](#) compared percutaneous endoscopic gastrostomy with nasogastric tube feeding in patients with dysphagia and indications for nutrition support. A total of 9 RCTs (n=686) were included. The primary outcome was intervention failure (defined as failure to introduce the tube, recurrent displacement, or treatment interruption).

Fewer intervention failures were observed with gastrostomy (19/156, 12%) than with nasogastric tubes (63/158, 40%), corresponding to a lower failure risk in favour of gastrostomy (RR=0.24, 95% CI 0.08 to 0.76, p=0.01; 7 RCTs, n=314). No significant differences in mortality (p=0.84; 8 RCTs, n=584) or complications (p=0.93; 5 RCTs, n=503) were observed between groups.

Limitations of the evidence included that:

- the primary outcome of intervention failure combined cases of failure to place the tube with cases where the tube had to be replaced after it had been introduced; separate analysis of these subgroups may have been useful
- 4 of the studies were assessed as high risk of bias, and the number of participants was small in most studies

- almost half of the studies did not report methods of sequencing or allocation concealment, and there were also issues of unpublished or high rates of loss during follow up.

The evidence suggests that percutaneous endoscopic gastrostomy may be at less risk of failure (namely, failure to introduce the tube, recurrent displacement or treatment interruption) than nasogastric tubes in patients with dysphagia needing nutrition support. This is broadly consistent with recommendations in [NICE CG32](#) for a short-term trial of a nasogastric tube, with gastrostomy for longer term enteral feeding.

Key reference

Gomes CA Jr, Lustosa SA, Matos D et al. (2012) [Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances](#). Cochrane Database of Systematic Reviews issue 3: CD008096

Nutrition support in dementia

Managing dysphagia in dementia

[NICE CG32](#) recommends that 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. Additionally, 'Dementia' ([NICE CG42](#)) recommends that health and social care staff should encourage people with dementia to eat and drink by mouth for as long as possible. Specialist assessment and advice concerning swallowing and feeding in dementia should be available. Dietary advice may also be beneficial. Nutritional support, including artificial (tube) feeding, should be considered if dysphagia is thought to be a transient phenomenon, but artificial feeding should not generally be used in people with severe dementia for whom dysphagia or disinclination to eat is a manifestation of disease severity.

A systematic review by [Alagiakrishnan et al. \(2013\)](#) looked at patterns, diagnosis and management of dysphagia across different types of dementia. A total of 19 studies (n=12,904) were included, comprising 8 cohort studies, 3 RCTs, 3 case-controlled studies, 2 surveys, 2 observational studies and 1 case series. Heterogeneity of design, methodology, assessments and primary outcomes between the studies prevented meta-analysis.

Dysphagia prevalence varied from 13 to 57% across the included studies. The review assessed a wide range of diagnostic methods (clinical swallow evaluation, videofluoroscopic swallow studies, and fibre optic endoscopic evaluation of swallowing) and management methods (changes to diet and posture, oral rehabilitation, tube or enteral feeding, and drug treatments). The authors concluded that there was limited evidence for most of these methods, but stated that in advanced dementia, percutaneous endoscopic gastrostomy did not seem to benefit survival, quality of life, or reduction in aspiration.

Limitations of the evidence included that: many studies had methodological issues, such as heterogeneity between the intervention and control groups for some key characteristics, or not assessing risk of bias; and blinding was not possible for some management strategies such as insertion of tubes or dietary modification.

The evidence suggests that percutaneous endoscopic gastrostomy does not appear to improve survival or quality of life in advanced dementia, which is consistent with recommendations in both [NICE CG32](#) and [NICE CG42](#) to feed orally for as long as possible. Further research is needed to address the lack of evidence for the diagnosis and management of dysphagia in people with dementia.

Key reference

Alagiakrishnan K, Bhanji RA, Kurian M (2013) [Evaluation and management of oropharyngeal dysphagia in different types of dementia: a systematic review](#). Archives of Gerontology and Geriatrics 56: 1–9

Decision-making for feeding options in advanced dementia

[NICE CG32](#) recommends that healthcare professionals should ensure that people having nutrition support, and their carers, are kept fully informed about their treatment. They should also have access to appropriate information and be given the opportunity to discuss diagnosis and treatment options. Additionally, 'Dementia' ([NICE CG42](#)) recommends that specialist assessment and advice concerning swallowing and feeding in dementia should be available, and dietary advice may also be beneficial. [NICE CG42](#) also recommends that trainers developing educational programmes for health and social care staff working with older people should consider the following elements:

- Applying the principles of person-centred care when working with people with dementia and their carers.
- The importance of and use of communication skills for working with people with dementia and their carers.

A cluster RCT across 24 nursing homes in the USA by [Hanson et al. \(2011\)](#) assessed decision aids in decision-making about feeding options in advanced dementia compared with usual treatment. Nursing home residents aged 65 years or over, and scoring 5 to 6 (namely, severe or very severe impairment) on the Cognitive Performance Scale in the Minimum Data Set, were assessed for trial eligibility. Those with advanced dementia (confirmed by chart diagnosis and dementia severity of 6 to 7 on the Global Deterioration Scale) and evidence of poor intake (fewer than 75% of meals in the previous 14 days), dysphagia or weight loss, were invited to participate. Exclusion criteria were: a feeding tube or contraindication to tube feeding; enrolment in a hospice; or diuretic weight loss. A total of 256 residents (mean age=85 years) and their surrogate decision makers (a carer such as a family member) were enrolled. Nursing homes were randomised in matched pairs to intervention or control.

In the intervention group, carers were given a structured decision aid with information about: dementia; feeding options and outcomes; the pros and cons of feeding tubes and assisted oral feeding; feeding for comfort near the end of life; and the role of the carer in decision-making. Carers in the control group received usual treatment, namely information from healthcare providers. The primary outcome was decisional conflict among carers at 3 months, measured by the Decisional Conflict Scale (score range 1–5, based on responses to 16 questions about decisions made around feeding options).

After 3 months, the mean decisional conflict score was significantly lower among carers using the decision aid than those who received usual care (1.65 versus 1.97, $p<0.001$). Decisional conflict within both groups of carers had reduced from baseline by 3 months, but a significantly lower reduction was seen in the decision aid group than the control group (-0.60 versus -0.13 , $p<0.001$). Among residents in the intervention group, dysphagia diets were more common at 3 months (89% versus 76%, $p=0.04$), and at 9 months weight loss was less common (6% versus 16%, $p=0.01$). Few residents in either group had a feeding tube at 9 months (1 in the intervention group and 3 in the control group, $p=0.34$).

Limitations of the evidence included that:

- Low rates of tube feeding in the control group may suggest changes in behaviour of healthcare staff in control nursing homes through awareness of the trial.
- Randomisation of nursing homes rather than individuals prevented double blinding, and could have introduced site-effect bias.
- Varying knowledge and practice around decision-making between individual clinicians could have influenced outcomes.
- Although the effects were statistically significant, it was noted that this may not translate into clinical significance.

The evidence suggests that use of decision aids may reduce conflict among carers when making decisions about feeding options in advanced dementia, and may also help to ensure appropriate nutritional support and to reduce weight loss in people with dementia. This is consistent with recommendations about information provision and communication in [NICE CG32](#) and [NICE CG42](#).

Key reference

Hanson LC, Carey TS, Caprio AJ et al. (2011) [Improving decision-making for feeding options in advanced dementia: a randomized, controlled trial](#). *Journal of the American Geriatrics Society* 59: 2009–16

Motility agents

[NICE CG32](#) recommends that for people in intensive care with delayed gastric emptying who are not tolerating enteral tube feeding, a motility agent should be considered, unless there is a pharmacological cause that can be rectified or suspicion of gastrointestinal obstruction. It does not include recommendations about non-drug treatments for improving motility.

A single-blind RCT (n=30) in Germany by [Pfab et al. \(2011\)](#) assessed the effect of acupuncture versus standard motility drug treatment on delayed gastric emptying among neurosurgical patients in critical care. Mechanically ventilated patients aged 18–75 years with cerebral aneurysm, haemorrhage or traumatic injury, and with delayed gastric emptying (defined as gastric reflux of at least 500 ml per 24 hours measured on 2 consecutive days after surgery) were included. Exclusion criteria were:

- recent abdominal surgery or trauma, suspected bowel obstruction or perforation, history of gastrectomy, or pancreatitis
- administration of motility drugs (metoclopramide, cisapride, or erythromycin) within the previous 24 hours, or known allergy to these drugs or a macrolide antibiotic
- administration of drugs known to interact with erythromycin.

Patients were randomised to either electrical stimulation of an acupuncture point on each forearm several times per day, or intravenous metoclopramide 10–20 mg every 8 hours. In both groups, therapy continued for 6 days, or until feeding tolerance was achieved (defined as 2 consecutive days with a gastric residual volume less than 200 ml per day and no vomiting). All patients received enteral nutrition via nasogastric tube, started as early as possible with a dose of 250 ml/day, increasing to 1000 ml/day on day 4. Patients also received parenteral nutrition aiming for a daily intake of 25 kcal/kg body weight.

After 5 days of treatment, there was no significant difference between feeding tolerance in the acupuncture group (12/15; 80%) and the drug treatment group (9/15; 60%; p value not stated). However, among the acupuncture group:

- Mean gastric residual volume decreased significantly from 970 ml to 346 ml (p=0.003) on treatment day 1, versus an increase from 903 ml to 1040 ml (p=0.015) with drug treatment.
- Mean enteral feeding balance (defined as volume of enteral feeding minus gastric residual volume) showed a significant increase (p=0.001 to 0.003) on every day of treatment. Whereas with drug therapy, a significantly increased feeding balance was seen only on treatment day 6 (p=0.044).

Limitations of the evidence included that:

- the study involved only 30 participants, and did not include those scheduled for intra-abdominal surgery (who may be at more risk of delayed gastric emptying)
- patients were unconscious, therefore informed consent was waived (although this may have reduced any placebo effects associated with acupuncture)

- the actual volume of enteral feed administered in the treatment groups, which may have influenced feeding balance values, was not compared
- the single-blinded design may have introduced bias.

Limited data suggest that acupuncture may have benefits over standard motility drugs in treating delayed gastric emptying in critical care. However, limitations of the evidence mean that it is unlikely to have an impact on [NICE CG32](#) and further research is needed.

Key reference

Pfab F, Winhard M, Nowak-Machen M et al. (2011) [Acupuncture in critically ill patients improves delayed gastric emptying: a randomized controlled trial](#). *Anesthesia & Analgesia* 112: 150–5

1.8 [Parenteral nutrition in hospital and the community](#)

No new key evidence was found for this section.

1.9 [Supporting patients in the community](#)

No new key evidence was found for this section.

Areas not currently covered by NICE CG32

Nutrition support in specific conditions

Most recommendations in [NICE CG32](#) are not specific to particular patient groups. Studies of nutrition support in specific conditions have been discussed above, where possible, in the section of the guideline most relevant to the intervention type assessed. However, the 2 following Cochrane reviews examined a wider range of interventions within specific conditions, and therefore were not aligned to any particular section of the guideline (and in the case of stroke, covered by other guidelines).

Nutrition support in stroke

Alongside general recommendations for nutrition support in [NICE CG32](#), ‘Stroke’ ([NICE CG68](#)) recommends that on admission, people with acute stroke should have their swallowing screened by an appropriately trained healthcare professional before being given any oral food, fluid or medication. If the admission screen indicates problems with swallowing, the person should have a specialist assessment of swallowing, preferably within 24 hours of admission and not more than 72 hours afterwards. It also recommends that people with acute stroke who are unable to take adequate nutrition and fluids orally should:

- receive tube feeding with a nasogastric tube within 24 hours of admission
- be considered for a nasal bridle tube or gastrostomy if they are unable to tolerate a nasogastric tube
- be referred to an appropriately trained healthcare professional for detailed nutritional assessment, individualised advice and monitoring.

A Cochrane review by [Geeganage et al. \(2012\)](#) investigated interventions for dysphagia and nutrition support in patients with acute and subacute (within 6 months from onset) stroke. A total of 33 RCTS (n=6779) were identified, covering several types of swallowing therapies and nutrition support.

For the primary outcome of death, or dependency or disability (defined as a Barthel Index of 0–55 or Rankin score of 3 to 5), there was no effect of acupuncture, drug therapy, physical stimulation, electrical stimulation (transcranial, neuromuscular, or pharyngeal), transcranial magnetic stimulation, percutaneous endoscopic gastrostomy, nasogastric tube, timing of feeding, or nutritional or fluid supplementation.

Other results for secondary outcomes included:

- Benefits of percutaneous endoscopic gastrostomy over nasogastric tube in terms of fewer treatment failures (OR=0.09, 95% CI 0.01 to 0.51, p=0.007; 3 RCTs, n=72)
- Reduced pressure sores with nutritional supplementation (OR=0.56, 95% CI 0.32 to 0.96, p=0.03; 2 RCTs, n=4125).

Limitations of the evidence included that:

- no studies reported food intake using calories or feed volume, which may have been useful to assess transitions from non-oral to oral feeding
- many studies were excluded from the analysis, often because they compared 2 active treatments rather than including a control or placebo arm, or did not report clinical outcomes of interest
- acupuncture methods varied between trials and data from these studies was extracted from Chinese translations
- the analyses did not consider acute and subacute stroke separately.

The authors concluded that data remain insufficient for the effect of swallowing therapy, feeding, and nutritional and fluid supplementation on functional outcome and death in patients with dysphagia after stroke, and the evidence is unlikely to have an impact on [NICE CG68](#). The evidence for reduced pressure sores is broadly consistent with recommendations for general nutrition support in [NICE CG32](#).

Key reference

Geeganage C, Beavan J, Ellender S et al. (2012) [Interventions for dysphagia and nutritional support in acute and subacute stroke](#). *Cochrane Database of Systematic Reviews* issue 10: CD000323

Nutrition support in liver disease

[NICE CG32](#) does not contain recommendations specific to patients with liver disease.

A Cochrane review by [Koretz et al. \(2012\)](#) assessed the effects of parenteral, enteral and oral nutrition support (provided for at least 5 days) in patients with underlying liver disease. Trials of transplanted patients were not generally included, except for those of perioperative nutrition support (in which only the period during and 30 days after transplant surgery was considered). A total of 37 RCTs (n=2145) were included, of which 9 were of parenteral, 9 were of enteral, and 19 were of oral nutrition support. The nutrition status of patients was not clear. Primary outcomes were mortality, hepatic morbidity, health-related quality of life, and adverse events. Patients were analysed according to the type of nutrition received, and whether they were treated for medical or surgical disorders.

The authors observed that most analyses did not show any significant differences. Some of the significant effects seen for primary outcomes were:

- In surgical patients, parenteral nutrition was associated with a reduced incidence of postoperative ascites (RR=0.65, 95% CI 0.48 to 0.87, p=0.0039; 2 RCTs, n=188). However, this result was from a fixed-effect model; in a random-effects model (which may be more valid given the heterogeneity between trials), the result was no longer significant (p=0.07).
- In medical patients, oral nutritional supplements were associated with a reduced occurrence of ascites (RR=0.58, 95% CI 0.38 to 0.87, p=0.0083; 4 RCTs, n=368), and improved resolution of hepatic encephalopathy (RR=3.75, 95% CI 1.15 to 12.18, p=0.028; 2 trials, n=53). It should be noted that the result for encephalopathy was from a fixed-effect model; in a random-effects model (which may be more valid given the heterogeneity between trials), the result was no longer significant (p=0.7).

The authors also noted that subgroup analyses (of alcoholic hepatitis, cirrhosis, and hepatocellular carcinoma) and exploratory analyses (for example, combining medical and surgical trials for each intervention) did not provide much additional insight.

Limitations of the evidence included that: only 1 trial was assessed as being at low risk of bias; analyses for many of the outcomes were based on small numbers of trials and patients; and it was not clear whether patients were malnourished.

Although evidence suggests that the benefits of nutrition support in patients with liver disease appear to be restricted, limitations of current data prevent firm conclusions and more robust evidence is needed to confirm findings.

Key reference

Koretz RL, Avenell A, Lipman TO (2012) [Nutritional support for liver disease](#). *Cochrane Database of Systematic Reviews* issue 5: CD008344

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Organisation of nutrition support in hospital and the community

- [Oral nutritional support of older \(65 years+\) medical and surgical patients after discharge from hospital](#)

Oral nutrition support in hospital and the community

- [Dietary advice with or without oral nutritional supplements for disease-related malnutrition in adults](#)
- [Oral nutritional interventions in malnourished patients with cancer for survival](#)
- [Nutritional supplementation for stable chronic obstructive pulmonary disease](#)
- [Pre-operative nutrition support in patients undergoing gastrointestinal surgery](#)

Enteral tube feeding in hospital and the community

- [Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances](#)
- [Interventions for dysphagia and nutritional support in acute and subacute stroke](#)
- [Critically ill patients with delayed gastric emptying - is acupuncture effective?](#)

Areas not currently covered by NICE guidance

- [Nutritional support for liver disease](#)

Further evidence uncertainties for nutrition support can be found in the [UK DUETs database](#) and in the [NICE research recommendations database](#).

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- [Nutrition support in adults](#). NICE clinical guideline 32 (2006)

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 8 December 2010 (the end of the search period for the [latest review](#) of the need to update NICE clinical guideline 32) to 11 March 2013:

- AMED (Allied and Complementary Medicine Database)
- BNI (British Nursing Index)
- CDSR (Cochrane Database of Systematic Reviews)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- EMBASE (Excerpta Medica database)
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-Process
- NHS EED (Economic Evaluation Database)

Table 1 provides details of the MEDLINE search strategy used (based on the search strategy for the reference guidance), which was adapted to search the other databases listed above. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network [search filters for RCTs and systematic reviews](#).

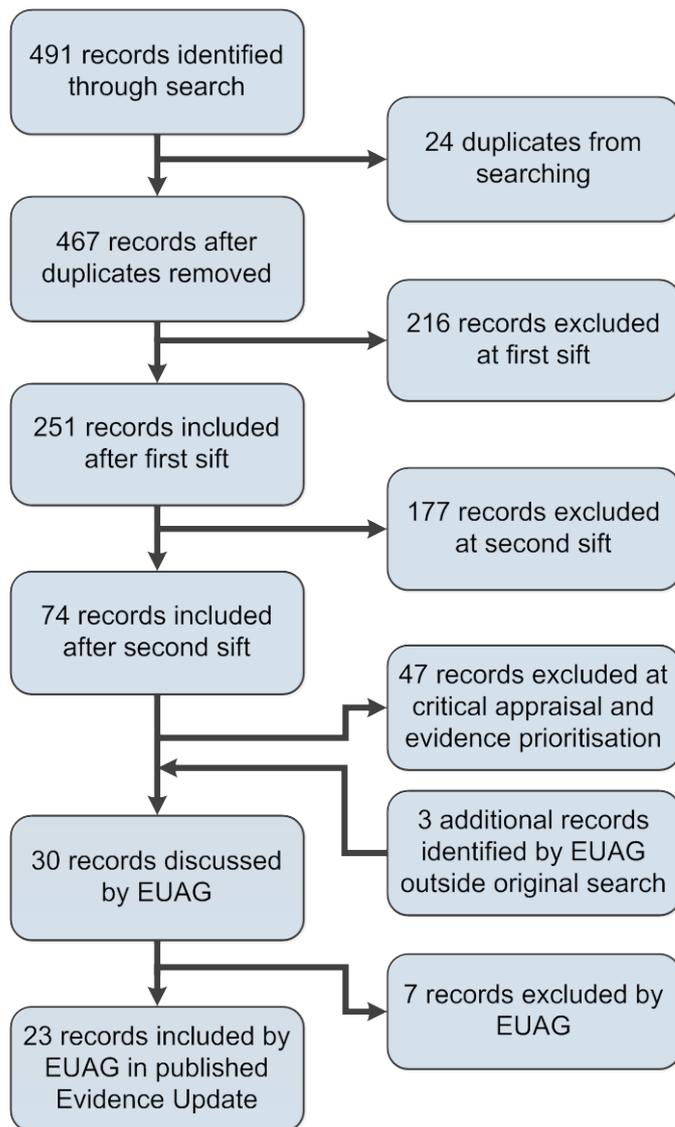
Additionally, 2 studies (Collins et al. 2013, Rio et al. 2013) were identified outside of the literature search. Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

There is more information about [how NICE Evidence Updates are developed](#) on the NICE Evidence Services website.

Table 1 MEDLINE search strategy (adapted for individual databases)

1	Nutrition disorders/		
2	exp Malnutrition/		
3	Wasting Syndrome/		
4	Thinness/		
5	Emaciation/		
6	Cachexia/		
7	Deglutition disorders/		
8	Weight loss/		
9	(malnutrition or malnourish\$ or nutrition disorder? or undernutrition or undernourish\$ or cachexia or cachectic).tw.	17	(nutrition\$ support\$ or metabolic support\$ or hyperaliment\$ or hyperaliment\$).tw.
10	(deglutition or dysphagi\$ or swallowing).tw.	18	((oral or orally or sip or bottle) adj2 (feed\$ or nutrition\$ or nourish\$)).tw.
11	(underweight or under-weight or wasting syndrome? or emaciat\$).tw.	19	((enteral or enteric) adj2 (nutrition\$ or feed\$)).tw.
12	weight loss.tw.	20	Duodenostomy/ or Gastrostomy/ or Jejunostomy/
13	or/1-12	21	(gastrostom\$ or jejunostom\$ or gastrojejunostom\$).tw.
14	exp Feeding Methods/	22	((duoden\$ or gastro\$ or gastric or nas??gastric or nas??-gastric or nas??jejun\$ or nas??duoden\$ or nas??-duoden\$ or jejun\$ or tube?) adj2 (nutrition\$ or feed\$)).tw.
15	Intubation, Gastrointestinal/	23	((parenteral\$ or intravenous\$) adj2 (feed\$ or nutrition\$)).tw.
16	Nutrition Assessment/	24	(diet\$ adj2 therap\$).tw.
		25	or/14-24
		26	(or/1-7) and dh.fs.
		27	13 and 25
		28	or/26-27

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

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