

# National Institute for Health and Care Excellence

## Surveillance programme

### Surveillance proposal consultation document

#### Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition NICE guideline CG32 – 2017 surveillance review

### Background information

Guideline issue date: February 2006

8-year surveillance review: no update

5-year surveillance review: no update

2-year surveillance review: no update

### Surveillance proposal for consultation

We propose to not update the NICE guideline on [nutrition support for adults](#) at this time.

We propose to transfer the guideline to the [static list](#) because:

- No evidence was identified that would impact on the current guidance and no major ongoing studies or research have been identified as due to be published in the near future (that is, within the next 3 to 5 years).

During surveillance editorial or factual corrections were identified. Details are included in [appendix A](#): summary of evidence from surveillance.

## ***Reason for the proposal***

### **Assessing the evidence**

We found 80 relevant studies in a search for randomised controlled trials and systematic reviews published between 23 September 2013 and 18 October 2016. We also included 7 relevant studies from a total of 43 identified by members of the guideline committee who originally worked on this guideline.

We also considered evidence identified in previous surveillance 2, 5 and 8 years after publication of the guideline. This included 132 studies identified by search.

From all sources, we considered 219 studies to be relevant to the guideline.

Areas where evidence is consistent with current recommendations were:

- Organisation of nutrition support in hospital and the community: cost savings of implementing NICE guidance; nutrition support teams/continuity of nutrition support between hospital and the community; interface of CG32 and policy.
- Indications for nutrition support in hospital and the community.
- What to give in hospital and the community: permissive enteral underfeeding in critically ill patients.
- Oral nutrition support in hospital and the community: oral nutritional supplements; oral nutrition support in surgical patients; enriched food.
- Enteral tube feeding in hospital and the community: enteral versus parenteral nutrition support; enteral nutrition support in surgical patients; percutaneous endoscopic gastrostomy versus nasogastric tube feeding in dysphagia; enteral nutrition versus usual care.
- Parenteral nutrition in hospital and the community: permissive parenteral underfeeding.
- Supporting patients in the community: home parenteral nutrition education; working in partnership with patients, families, and carers.

We also identified areas where evidence was inconsistent with, or not covered by, current recommendations, but the evidence was not considered to impact on the guideline at this time:

- Organisation of nutrition support in hospital and the community: nutritional counselling; supportive/mealtime interventions.
- Screening for malnutrition and the risk of malnutrition in hospital and the community: use of tools other than the Malnutrition Universal Screening Tool (MUST).
- What to give in hospital and the community: managing established refeeding syndrome; tight calorie control.
- Oral nutrition support in hospital and the community: oral nutritional supplements plus exercise in older people with sarcopenia [Note: This evidence will be logged for consideration in surveillance of other NICE guidelines in public health and social care]; oral nutrition support in injured patients.
- Enteral tube feeding in hospital and the community: post-pyloric feeding; specialised enteral product in patients with hip fracture; percutaneous radiological gastrostomy; jejunostomy.
- Parenteral nutrition in hospital and the community: intensive insulin therapy in patients with traumatic brain injury on parenteral nutrition.
- Supporting patients in the community: nutritional interventions involving home visits for older people living in the community [Note: This evidence will be logged for consideration in surveillance of other NICE guidelines in public health and social care].

We asked topic experts whether this evidence would affect current recommendations. Generally, the topic experts agreed that the new evidence would not impact recommendations in these areas.

We found evidence on immunonutrition and satiety hormone suppression, which were not covered in the guideline. This evidence was considered to be insufficiently conclusive to add new recommendations in these areas at this time. Evidence on nutrition support in specific conditions was also found that

was not covered in the guideline. However, evidence was broadly aligned with the general recommendations on nutrition support.

We did not find any evidence related to monitoring of nutrition support in hospital and the community.

Additionally, we identified no major ongoing studies or research due to be published in the next 3 to 5 years.

### **Equalities**

No equalities issues were identified during the surveillance process.

### **Overall proposed decision**

After considering all the evidence and views of topic experts, we propose to not update this guideline, and place the guideline on the static list.

### ***Further information***

See [appendix A](#): summary of evidence from surveillance below for further information.

For details of the process and update decisions that are available, see [ensuring that published guidelines are current and accurate](#) in developing NICE guidelines: the manual.

# Appendix A: summary of evidence from surveillance

## 2017 surveillance – [Nutrition support for adults](#) (2006) NICE guideline CG32

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### Summary of evidence from surveillance

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

##### Recommendations in this section of the guideline

- 1.1.1 All healthcare professionals who are directly involved in patient care should receive education and training, relevant to their post, on the importance of providing adequate nutrition.  
Education and training should cover:
- nutritional needs and indications for nutrition support
  - options for nutrition support (oral, enteral and parenteral)
  - ethical and legal concepts
  - potential risks and benefits
  - when and where to seek expert advice.
- 1.1.2 Healthcare professionals should ensure that care provides:
- food and fluid of adequate quantity and quality in an environment conducive to eating
  - appropriate support, for example, modified eating aids, for people who can potentially chew and swallow but are unable to feed themselves.
- 1.1.3 Healthcare professionals should ensure that all people who need nutrition support receive coordinated care from a multidisciplinary team.<sup>[2]</sup>
- 1.1.4 All acute hospital trusts should have a multidisciplinary nutrition support team which may include: doctors (for example gastroenterologists, gastrointestinal surgeons, intensivists or others with a specific interest in nutrition support), dietitians, a specialist nutrition nurse, other nurses, pharmacists, biochemistry and microbiology laboratory support staff, and other allied healthcare professionals (for example, speech and language therapists).
- 1.1.5 All hospital trusts should have a nutrition steering committee working within the clinical governance framework.
- 1.1.6 Members of the nutrition steering committee should be drawn from trust management, and include senior representation from medical staff, catering, nursing, dietetics, pharmacy and other healthcare professionals as appropriate, for example, speech and language therapists.
- 1.1.7 All acute hospital trusts should employ at least one specialist nutrition support nurse.
- 1.1.8 The specialist nutrition support nurse should work alongside nursing staff, as well as dietitians and other experts in nutrition support, to:
- minimise complications related to enteral tube feeding and parenteral nutrition
  - ensure optimal ward-based training of nurses

- ensure adherence to nutrition support protocols
- support coordination of care between the hospital and the community.

[2] The composition of this team may differ according to setting and local arrangements.

## Surveillance decision

This section of the guideline should not be updated.

### *The cost of malnutrition in England and potential cost savings of implementing NICE guidance*

#### **2-year surveillance summary**

Update not required after review of evidence.

#### **5-year surveillance summary**

No relevant evidence was identified.

#### **Evidence Update 2013**

No relevant evidence was identified.

#### **8-year surveillance summary**

No relevant evidence was identified.

#### **2017 surveillance summary**

Topic experts identified a costing report<sup>1</sup> which (a) examined the cost of disease-related malnutrition in England, and (b) performed a budget impact analysis of implementing the NICE clinical guidelines/quality standard on nutritional support in adults.

##### *a) The cost of malnutrition in England in 2011–12*

The public health and social care expenditure associated with malnutrition in adults and children in England in 2011–12, identified using the ‘Malnutrition Universal Screening Tool’ (‘MUST’), was estimated to be £19.6 billion, or about 15% of the total expenditure on health and social care. Most of this expenditure was due to healthcare rather than social care, and secondary rather than primary healthcare provision involving adults, predominantly older adults, rather than children. This pattern reflects the general distribution of the total expenditure on health and social care of all subjects in England. The large contribution of institutionalised care to total costs was not only due to the high cost of institutionalisation, but also the high point prevalence of malnutrition in hospitals and care homes. However, since more than 90% of the malnutrition originates and exists outside these institutions, preventive measures should be undertaken in the community to reduce the clinical economic

burden of malnutrition. Given the large estimated annual cost of malnutrition (£19.6 billion), small fractional cost savings translate to large absolute savings (e.g. 1% cost saving corresponds to £196 million). Effective recognition and treatment of malnutrition and continuity of care within and between care settings are of key importance to achieving such goals.

##### *b) Budget (cost) impact analysis involving implementation of the NICE clinical guidelines (CG32)/quality standard (QS24)*

Improvements in current nutritional care associated with fuller implementation of the NICE guideline/quality standard (identification of malnutrition and use of nutritional support in adults) not only result in better quality of care but also in a net cost saving. The investment necessary to implement better nutritional care is more than counteracted by the returns (the cost savings). When the clinical guidelines/standard was applied to 85% of subjects with high risk of malnutrition in the population of malnourished adults targeted by the NICE guidelines/quality standard there was an overall net cost saving of £63.2–76.9 million (£119.20–145.09 thousand per 100,000 of the general population) depending on the type of nutritional support and the care setting(s). When they were applied to 85% of adults with medium and high risk of malnutrition according to ‘MUST’ the net cost saving was estimated to be £172.2–229.2 million in England or £324.8–432.3 thousand per 100,000 of the general population. These estimates exceeded those reported by NICE (£71,800 per 100,000 general population), which ranked the cost saving as the third highest relative to those associated with the implementation of other NICE clinical guidelines. The above net cost savings, mostly due to appropriate use of oral nutritional supplements, represent only 0.4–3.3% of the total annual healthcare cost of disease-related malnutrition in adults, which amounted to £14.4 billion. However, the costing

models involved only a proportion of patients with malnutrition presenting to healthcare workers (that targeted by the NICE guideline/quality standard), and only a fraction of this proportion received improved nutritional care. In addition, the large total cost of disease-related malnutrition included the cost of disease, much of which is not reversed by nutritional support alone. The net cost saving was found to increase when the prevalence of malnutrition was high, when hospital admission rates were high, and when the gap between current care and desirable care was large. Rapid and reliable methods for nutritional screening were also found to produce a more favourable budget impact. To improve the robustness of the costing model, future research should aim to establish an evidence base on healthcare use and cost of other forms of nutritional support for which little data exist (e.g. dietary advice, dietary modification and food fortification), and to further extend the evidence base on the effects of prescribable oral nutritional supplements on resource use in different care settings.

#### Topic expert feedback

Topic experts noted that costs will have changed over time, and that the cost of

malnutrition has significantly increased. Several topic experts highlighted the recent costing document<sup>1</sup> which is described above.

#### Impact statement

The 2017 surveillance identified a cost report which stated that:

- Malnutrition, with and without associated disease, is a common clinical, public health and economic problem, with an estimated cost of £19.6 billion in England in 2011–12.
- Interventions to combat malnutrition in the small proportion of malnourished patients targeted by the NICE clinical guidelines/quality standard on nutritional support in adults save rather than cost money. The estimated net cost saving of £172.2–229.2 million is due to reduced healthcare use.

This evidence supports the need for CG32, and the need for its continuing implementation.

New evidence is unlikely to change guideline recommendations.

#### *Nutrition support teams / continuity of nutrition support between hospital and the community*

##### 2-year surveillance summary

Update not required after review of evidence.

##### 5-year surveillance summary

###### *In hospital*

Two studies identified were related to nutrition support teams<sup>2,3</sup>.

One study<sup>2</sup> 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.

The other study<sup>3</sup> 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.

#### Evidence Update 2013

##### *Continuity between hospital and the community*

Five studies<sup>4-8</sup> relating to continuity of nutrition support between the hospital and the community were identified. Findings were consistent with recommendations on the need to coordinate care between hospital and community.

##### 8-year surveillance summary

###### *In hospital and in the community*

Three studies<sup>9-11</sup> on organisation of nutrition support in the hospital and the community were identified. Findings were in line with guideline recommendations.

##### 2017 surveillance summary

###### *In the community*

A single-blind, parallel-group, multicentre RCT<sup>12</sup> (n=328 older adults from 7 primary health care centres) examined a multifactorial assessment and targeted multidisciplinary intervention versus control (details of control not specified in abstract). From 2-year intention-to-treat analysis, for the primary

outcome of Mini Nutritional Assessment, the intervention had no significant effect in the whole study population, nor in people with nutritional risk. Cognitive impairment was an independent factor strongly associated with a decline in nutritional status.

A cluster RCT<sup>13</sup> (n=95 participants from 3 home-care and 3 nursing-home settings) examined the use of trained nutrition coordinators plus multidisciplinary nutrition support versus control (nutrition coordinators alone). The multidisciplinary nutrition support focused on treatment of potentially modifiable nutritional risk factors identified with the Eating Validation Scheme tool, by involving the physiotherapist, registered dietitian, and occupational therapist, as relevant and independent of the municipality's ordinary assessment and referral system. After 11 weeks, quality of life, 30-seconds chair stand and oral care were all significantly better with the multidisciplinary intervention than control. Mortality did not differ significantly between groups.

#### *In hospital*

An RCT<sup>14</sup> (n=50 patients with oesophageal cancer undergoing concurrent chemoradiotherapy) examined management of nutritional status by a nutrition support team versus supervision by radiotherapy practitioners (control). At the end of chemoradiotherapy, nutritional status (evidenced by prealbumin, transferrin, and albumin parameters) was significantly better, and complications (including bone marrow suppression and infections), were significantly lower with a nutrition support team than control. In addition, only 1 patient in the nutrition support team group did not complete radiotherapy versus 6 patients in the control group, though numbers did not differ significantly. Furthermore, the average length of stay was significantly lower with a nutrition support team, though in-patient cost was not significantly different.

A cluster RCT<sup>15</sup> examined a multidisciplinary nutritional intervention (nutrition screening, provision of oral nutritional supplements, and flagging patients for feeding assistance) across control (n=135) and intervention (n=240) time periods in a metropolitan hospital. In week 1, significantly more intervention patients had a completed MUST assessment and a feeding assistance referral, but weight loss did not differ significantly between control and intervention

wards. Multivariable analysis of week 1 data found no relationship between weight loss outcomes and the treatment, the ward or time period.

#### **Topic expert feedback**

##### *8-year surveillance*

One guideline committee member commented that there are inequalities in the provision of nutrition support in non-hospital settings and that these are not well addressed in the current guideline.

##### *2017 surveillance*

Topic experts noted that like in America, our nutrition teams are focused in acute settings and asked if the guidance can provide more direction for community settings. The structure of the NHS is changing, more care is transferring from acute to community. Clarity on how nutrition steering groups can be developed in community settings, or even span from the community into the acute services would be novel and probably effective.

There were reflections on the role of clinical commissioning groups and how they could motivate the development of nutrition steering committees in the community. If the nutrition guidelines were initiated in the community and followed the patient into the acute (where necessary) what benefits would it have for the patient and their overall outcome? No evidence was provided for this, but an opportunity to explore this possibility with community based teams would be valuable.

It was further noted that the guidance does not make reference to the need to engage the whole system e.g. commissioners, public health, social care, and third sector.

A topic expert also noted that despite clear recommendations, many acute trusts do not have a functioning nutrition support team.

#### **Impact statement**

At 8-year surveillance, it was concluded that findings of studies up to this timepoint for nutrition support teams, and the need for continuity of care between hospital and the community, were in line with guideline recommendations. Feedback from the guideline committee was also deemed unlikely to impact on the guideline recommendations.

The 2017 surveillance found that multidisciplinary interventions had positive effects on quality of life, muscle strength, oral care, maintaining nutrition status, and reducing

complications and length of stay. There was some evidence that the interventions did not appear to affect nutritional status or weight loss. However the evidence was largely aligned with recommendations in CG32 that all people who need nutrition support receive coordinated care from a multidisciplinary team, and all acute hospital trusts should have a multidisciplinary nutrition support team.

Experts commented that many hospitals do not have a functioning nutrition support team,

however this is likely to reflect implementation issues, therefore no impact on CG32 is expected.

No evidence for was found for community-based nutrition steering committees, therefore despite expert comments on the potential benefits, no impact is anticipated.

New evidence is unlikely to change guideline recommendations.

## *Nutritional counselling*

### **2-year surveillance summary**

Update not required after review of evidence.

### **5-year surveillance summary**

Three studies<sup>16-18</sup> analysed nutritional counselling versus standard care and found that energy intake, protein intake and quality of life were generally improved in the groups that received nutritional counselling. One study<sup>16</sup> also reported decreased mortality in the group receiving nutritional counselling.

### **Evidence Update 2013**

No relevant evidence was identified.

### **8-year surveillance summary**

No relevant evidence was identified.

### **2017 surveillance summary**

A multicentre open-label RCT<sup>19</sup> (n=341 older patients at risk of malnutrition, mean age 78 years, treated with chemotherapy for solid tumour – most frequently colon [22%] and pancreas [17%]) examined dietary counselling versus control (usual care). Counselling aimed to achieve an energy intake of 30 kCal/kg body weight/day and 1.2 g protein/kg/day, by face-to-face discussion targeting the main nutritional symptoms. Interviews were performed 6 times during the chemotherapy sessions for 3 to 6 months, and follow-up was 2 years. Both groups increased their dietary intake, but to a significantly larger extent with dietary counselling. At the second visit, the energy and protein target was achieved in numerically more patients than controls (significance not reported in the abstract). The primary outcome of deaths during the first year was not significantly different between groups. Nor were any differences seen in nutritional status changes and response to chemotherapy.

An RCT<sup>20</sup> (n=61 outpatients in radiotherapy and/or chemotherapy for gynaecological, gastric, or oesophageal cancer) examined individual nutritional counselling. Patients were stratified by diagnoses and randomly assigned to 2 groups. The basic regimen, applied to both groups, included measurement of body weight, 24-hour dietary recall interview, micronutrient status and quality of life. In addition the intervention group received intensive, individual dietary counselling 1 hour per week and, if the patient accepted, a daily oral nutritional supplement containing 2531 kJ, 33.8 g protein and 2.2 g eicosapentaenoic acid. At the end of the treatment period, compared with control, significantly fewer patients had lost weight following nutritional counselling, and the fulfilment of estimated energy requirements was significantly better during treatment. A significant positive effect was also observed with counselling on the fulfilment of protein requirement, both during the treatment period and at follow-up.

An RCT<sup>21</sup> (n=58 outpatients with cancer and with or at risk of malnourishment) examined individual nutritional therapy (including counselling by a dietitian, food fortification, and oral nutritional supplements if required) versus standard care. After 3 months, the nutritional intervention led to a significantly higher average energy and protein intake, however was not associated with improvements in nutritional status, physical functioning, or quality of life.

An RCT<sup>22</sup> (n=144 treatment-naive outpatients with systemic immunoglobulin light-chain amyloidosis) examined nutritional counselling versus control (usual care). Patients in the nutritional counselling group maintained a stable body weight, whereas control patients had a significant decrease. However, the

difference in weight between groups was not significant. Counselling led to significantly more satisfactory energy intake (>75% of estimated requirements) and a significant increase in the mental component summary of quality of life (Short form-36) at 12 months, which was restored to a mean score of 53 (above healthy population norms). Counselling was also associated with significantly better survival.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

At 5-year surveillance, it was concluded that findings of studies up to this timepoint would not warrant a change in current guideline recommendations.

The 2017 surveillance found that nutritional counselling in patients with cancer and amyloidosis led to increased intake and better weight maintenance, but outcomes were mixed for quality of life and survival, and no effects were seen on nutritional status, physical functioning, treatment-related side effects or micronutrient deficiencies.

These mixed outcomes mean the evidence is unlikely to affect CG32, which does not specifically recommend nutritional counselling, though its recommendations do align with the principles of counselling. For example, it states that hospital multidisciplinary nutrition support teams may include dietitians and specialist nutrition nurses. It also recommends that people having nutrition support, and their carers, are kept fully informed about their treatment, and have access to appropriate information and be given the opportunity to discuss diagnosis and treatment options, and that healthcare professionals should review the indications, route, risks, benefits and goals of nutrition support at regular intervals.

A footnote to a recommendation further notes that 'Oral nutrition support includes any of the following methods to improve nutritional intake: [...] the provision of dietary advice.'

New evidence is unlikely to change guideline recommendations.

### *Supportive / mealtime interventions*

#### **2-year surveillance summary**

Update not required after review of evidence.

#### **5-year surveillance summary**

No relevant evidence was identified.

#### **Evidence Update 2013**

No relevant evidence was identified.

#### **8-year surveillance summary**

No relevant evidence was identified.

#### **2017 surveillance summary**

Topic experts identified a Cochrane review<sup>23</sup> of 41 RCTs (n=10,681) assessing the effects of supportive interventions (such as serving meals in a dining room environment or the use of assistants to feed patients) for enhancing dietary intake in malnourished or nutritionally at-risk adults. Trials were grouped according to similar interventions: changes to organisation of nutritional care (13 RCTs; n=3456), modification of meal profile or pattern (12 RCTs; n=649), additional supplementation of meals (10 RCTs; n=6022), changes to the feeding environment (5 RCTs; n=351 participants), and home meal delivery

systems (1 RCT; n=203). Follow-up ranged from 'duration of hospital stay' to 12 months. Risk of heterogeneity among trials was judged to be high as trials were in populations with different clinical backgrounds, in different healthcare settings and involved interventions that varied considerably. Meta-analyses could therefore only be conducted for some outcome measures. Supportive interventions significantly benefited all-cause mortality (12 RCTs, n=6683; moderate-quality evidence) and led to an overall significant improvement in weight gain (17 RCTs, n=2024; moderate-quality evidence) but did not significantly affect hospitalisation (5 RCTs, n=667; very low-quality evidence). Risk ratio for number of participants with any medical complication ranged from 1.42 in favour of control compared with 0.59 in favour of supportive interventions (very low-quality evidence). Only 5 RCTs (n=4451) investigated health-related quality of life showing no substantial differences between intervention and comparator. Information on patient satisfaction was unreliable. Only 3 trials (n=4108; very low-quality evidence) reported on adverse events, describing intolerance to the supplement (diarrhoea, vomiting;

5/34 participants) and discontinuation of oral nutritional supplements because of refusal or dislike of taste (567/2017 participants). Of the 27 trials investigating nutritional intake, most found no marked differences in energy intake between intervention and comparators. Only 3 trials (n=1152) reported some data on economic costs but did not use accepted health economic methods (very low-quality evidence).

Topic experts also identified a systematic review and meta-analysis<sup>24</sup> of 37 studies (n=not reported in the abstract) examining the effectiveness of mealtime interventions (namely, those that aimed to change/improve mealtime routine, practice, experience or environment) for elderly people living in residential care. Inadequate reporting in over half of the articles limited data quality appraisal. Mealtime interventions were categorised into 5 types: changes to food service, food improvement, dining environment alteration, staff training and feeding assistance. Meta-analysis found no significant effect on body weight of changes to food service, food improvement interventions, or alterations to dining environment. Although observational studies found positive effects on food/caloric intake across all intervention types, meta-analyses of randomised studies showed no significant effects on food/caloric intake in food improvement studies. There was no significant effect on daily energy intakes within dining environment studies.

A crossover RCT<sup>25</sup> (n=19 women aged >65 years with a poor appetite) examined the effect of increased variety of foods within a cooked meal. Two cooked meals of similar weight and energy density (except starch) were served under standardised conditions on 2 weekdays: a test meal consisting of 3 different varieties of vegetables, meat or fish, and starch components, and a control meal without variety. Participants ate ad libitum. Average intake in energy was significantly higher with the varied than the control meal. Total meal intake in grams was also significantly higher for the varied meal but protein intake in grams was not. This was consistent for all meal components except starch and within each component 3 varieties were consumed equally.

### **Topic expert feedback**

#### *2017 surveillance*

Topic experts noted that the guideline recommended that nutritional support is

indicated in people who are malnourished or at risk of malnutrition. The majority of evidence for this recommendation came from studies of oral nutritional interventions. The recommendation lacks detail about the specific nutritional interventions. There are several recent systematic reviews<sup>23,24</sup> that have examined what has been termed 'mealtime interventions' or supportive care interventions which could add to the detail of the guideline.

Topic experts noted that areas of interest were improvement in patient dietary intake and experience with presentation of food (improved dining environment, quality/colour of plates and utensils), and identification of 'at risk' patients and focusing of interventions e.g. 'Red trays'.

### **Impact statement**

The 2017 surveillance found evidence for a lower risk of all-cause mortality for supportive interventions, though the Cochrane review authors noted this all came from hospital-based trials and they stated that more research is needed to confirm this effect. Additionally no details on the nature of the interventions leading to this effect was provided in the abstract. The Cochrane authors further noted there is very low-quality evidence regarding adverse effects; therefore whilst some of these interventions are advocated at a national level clinicians should recognise the lack of clear evidence to support their role.

The evidence across the 2 identified reviews showed mixed outcomes of supportive interventions on weight gain. When split out by intervention type in the second review, no significant effect on body weight was seen for changes to food service, food improvement interventions, or alterations to dining environment.

The RCT suggested that increasing meal variety may increase energy intake in older adults with a poor appetite, however there were only 19 participants and although intake increased, no physical or clinical benefits were reported. Further evidence may therefore be needed for this specific intervention.

CG32 recommends that care provides food and fluid of adequate quantity and quality in an environment conducive to eating. Additionally, a footnote to a recommendation in the oral nutrition section of the guideline further notes that 'Oral nutrition support includes any of the following methods to improve nutritional intake:

[...] altered meal patterns; the provision of dietary advice.'

Although topic experts highlighted mealtime/supportive interventions as a potential consideration, the lack of detail around the nature of interventions leading to benefits for mortality in the Cochrane review,

and the mixed evidence for effect on weight, mean that the evidence identified is unlikely to affect current recommendations.

New evidence is unlikely to change guideline recommendations.

### *Interface of CG32 and policy*

#### **2-year surveillance summary**

Update not required after review of evidence.

#### **5-year surveillance summary**

No relevant evidence was identified.

#### **Evidence Update 2013**

No relevant evidence was identified.

#### **8-year surveillance summary**

No relevant evidence was identified.

#### **2017 surveillance summary**

No relevant evidence was identified.

#### **Topic expert feedback**

##### *2017 surveillance*

Topic experts noted that the guideline works with relevant policies (Equality Act 2010, Health and Social Care Act 2012, Care Act 2014) but could be more explicit for example:

[Health and Social Care Act 2008 \(Regulated Activities\) Regulations 2014: Regulation 14](#)

'The intention of this regulation is to make sure that people who use services have adequate nutrition and hydration to sustain life and good health and reduce the risks of malnutrition and dehydration while they receive care and treatment.

'To meet this regulation, where it is part of their role, providers must make sure that people have enough to eat and drink to meet their nutrition and hydration needs and receive the support they need to do so.

'People must have their nutritional needs assessed and food must be provided to meet those needs. This includes where people are prescribed nutritional supplements and/or parenteral nutrition. People's preferences, religious and cultural backgrounds must be taken into account when providing food and drink.

'Care Quality Commission (CQC) can prosecute for a breach of this regulation or a breach of part of the regulation if a failure to

meet the regulation results in avoidable harm to a person using the service or a person using the service is exposed to significant risk of harm. In these instances, CQC can move directly to prosecution without first serving a warning notice. Additionally, CQC may also take any other regulatory action. See the offences section for more detail.

'CQC must refuse registration if providers cannot satisfy us that they can and will continue to comply with this regulation.'

#### **Impact statement**

Although expert feedback queried if recommendations could be more explicit regarding alignment with policy, the following recommendations in CG32 already state that:

- Education and training of healthcare professionals should cover (among other things) ethical and legal concepts
- Care provides food and fluid of adequate quantity and quality in an environment conducive to eating
- All hospital inpatients on admission and all outpatients at their first clinic appointment should be screened.
- Healthcare professionals involved in starting or stopping nutrition support should: obtain consent from the patient if he or she is competent; act in the patient's best interest if he or she is not competent to give consent
- 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

No impact is therefore currently expected.

New evidence is unlikely to change guideline recommendations.

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## Screening for malnutrition and the risk of malnutrition in hospital and the community

### Recommendations in this section of the guideline

- 1.2.1 Screening for malnutrition and the risk of malnutrition should be carried out by healthcare professionals with appropriate skills and training.
- 1.2.2 All hospital inpatients on admission and all outpatients at their first clinic appointment should be screened. Screening should be repeated weekly for inpatients and when there is clinical concern for outpatients.
- 1.2.3 Hospital departments who identify groups of patients with low risk of malnutrition may opt out of screening these groups. Opt-out decisions should follow an explicit process via the local clinical governance structure involving experts in nutrition support.
- 1.2.4 People in care homes should be screened on admission and when there is clinical concern.<sup>[3]</sup>
- 1.2.5 Screening should take place on initial registration at general practice surgeries and when there is clinical concern<sup>[3]</sup>. Screening should also be considered at other opportunities (for example, health checks, flu injections).
- 1.2.6 Screening should assess body mass index (BMI)<sup>[4]</sup> and percentage unintentional weight loss and should also consider the time over which nutrient intake has been unintentionally reduced and/or the likelihood of future impaired nutrient intake. The Malnutrition Universal Screening Tool (MUST), for example, may be used to do this.

[3] Clinical concern includes, for example, unintentional weight loss, fragile skin, poor wound healing, apathy, wasted muscles, poor appetite, altered taste sensation, impaired swallowing, altered bowel habit, loose fitting clothes or prolonged intercurrent illness.

[4] BMI is weight (kg)/height (m<sup>2</sup>) (weight in kilograms divided by height in metres squared)

### Surveillance decision

This section of the guideline should not be updated.

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### Malnutrition screening

#### 2-year surveillance summary

Update not required after review of evidence.

#### 5-year surveillance summary

No relevant evidence was identified.

#### Evidence Update 2013

One study on malnutrition screening in hospital admissions among older people was identified<sup>26</sup>. The study findings were consistent with the recommendation in the guideline to screen all patients admitted to hospital for malnutrition.

#### 8-year surveillance summary

Eight studies on screening for malnutrition and the risk of malnutrition in hospital and the community were identified<sup>27-34</sup>. Findings of studies were broadly in line with guideline recommendations.

### 2017 surveillance summary

A pilot RCT<sup>35</sup> (n=703 older adults presenting to an emergency department) examined malnutrition screening and compared 2 service delivery models of nutritional support. The intervention group received dietetic assessment, nutrition intervention and follow-up in addition to regular support from community hospital interface programme nursing staff, whereas controls received regular treatment from the community hospital interface programme only. Of 703 patients screened, 84 (12%) were identified at malnutrition risk, of whom 24 consented to the intervention study, with 88% (21/24) confirmed to be malnourished. The authors stated that clinically important but not statistically significant differences were found over the 12-week trial, with the intervention having numerical but not

statistical benefits for weight gain, quality of life, depression and hospital admissions.

An RCT<sup>36</sup> (n=258 patients with oesophageal cancer) examined role of nutritional status and interventions in patients randomly allocated to definitive chemoradiotherapy with or without cetuximab. Nutritional Risk Index scores were calculated; a score <100 identified patients at risk of malnutrition. At baseline, Nutritional Risk Index <100 strongly significantly predicted reduced overall survival. Nutritional interventions (either dietary advice, oral supplements, or enteral feeding/tube placement) significantly improved survival if provided at baseline, but not if provided later in the treatment course. Cetuximab patients receiving enteral feeding/tube placement had significantly worse survival compared with controls.

A blinded RCT<sup>37</sup> (n=404 patients aged ≥70 years admitted to the internal, surgical and orthopaedic wards of University Hospital Graz, Austria) aimed to validate the Graz Malnutrition Screening (GMS) tool against Nutritional Risk Screening (NRS) and Mini Nutritional Assessment-short form (MNA-sf). The GMS tool was developed for the purpose of malnutrition risk screening in a large hospital setting involving different departments. Patients were screened in a blinded manner by different raters. According to GMS, 31.9% or 28.5% of the admitted patients were categorised as at 'risk of malnutrition' (depending on the rater). According to the reference standard of NRS, 24.5% of the patients suffered from malnutrition. Pearson's r values of 0.78 compared with the NRS and 0.84 compared with the MNA showed strong positive correlations. Results for the GMS of accuracy (0.85), sensitivity (0.94), specificity (0.77), positive predictive value (0.76) and negative predictive value (0.95) were also very high. Cohen's kappa for internal consistency of the GMS was 0.82.

### **Topic expert feedback**

#### *2017 surveillance*

Topic experts noted the key issue continues to be appropriate use of malnutrition screening tools and identification of patients at risk. This continues to be problematic for both acute and

community services (especially for elderly patients).

Topic experts also highlighted the [MUST self-screening tool](#) aimed at patients/population launched by BAPEN 2015, and that the concept of self-screening for malnutrition could be a valuable addition to CG32.

They further stated it could be of benefit to consider the advantage or otherwise of possible alternative methods to assess malnutrition, for example, by the use of fat-free mass index.

### **Impact statement**

The 8-year surveillance concluded that findings of studies up to this timepoint were consistent with guideline recommendations

The 2017 surveillance found a trial of screening in an emergency department followed up with a nutritional intervention in which clinically important but not statistically significant differences in outcomes were seen. A second trial found that baseline risk of malnutrition predicted reduced overall survival after chemotherapy, and nutritional interventions improved survival if provided at baseline, but not later. This evidence is consistent with CG32 that all hospital inpatients on admission and all outpatients at their first clinic appointment should be screened, and that nutrition support should be considered in people with, or at risk of, malnutrition.

A third trial suggested that GMS may be a valid and reliable instrument for the detection of malnutrition in adult patients in acute-care hospitals, though this data was from Austria and ideally the tool should be further validated in the UK before any impact on CG32 (which recommends assessment with MUST) can be considered.

Topic experts highlighted self-screening (such as the MUST self-screening tool) and fat-free mass index, however no evidence was identified for their use in assessment and screening of malnutrition, therefore no impact on CG32 is currently expected.

New evidence is unlikely to change guideline recommendations.

## Indications for nutrition support in hospital and the community

### Recommendations in this section of the guideline

- 1.3.1 Nutrition support should be considered in people who are malnourished, as defined by any of the following:
- a BMI of less than 18.5 kg/m<sup>2</sup>
  - unintentional weight loss greater than 10% within the last 3–6 months
  - a BMI of less than 20 kg/m<sup>2</sup> and unintentional weight loss greater than 5% within the last 3–6 months.
- 1.3.2 Nutrition support should be considered in people at risk of malnutrition who, as defined by any of the following:
- have eaten little or nothing for more than 5 days and/or are likely to eat little or nothing for the next 5 days or longer
  - have a poor absorptive capacity, and/or have high nutrient losses and/or have increased nutritional needs from causes such as catabolism.
- 1.3.3 Healthcare professionals should consider using oral, enteral or parenteral nutrition support, alone or in combination, for people who are either malnourished or at risk of malnutrition, as defined in 1.3.1 and 1.3.2. Potential swallowing problems should be taken into account.
- 1.3.4 Healthcare professionals involved in starting or stopping nutrition support should:
- obtain consent from the patient if he or she is competent
  - act in the patient's best interest if he or she is not competent to give consent
  - be aware that the provision of nutrition support is not always appropriate. Decisions on withholding or withdrawing of nutrition support require a consideration of both ethical and legal principles (both at common law and statute including the Human Rights Act 1998).  
When such decisions are being made guidance issued by the General Medical Council<sup>[5]</sup> and the Department of Health<sup>[6]</sup> should be followed.
- 1.3.5 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.

[5] Withholding and withdrawing life prolonging treatments: good practice in decision making. [General Medical Council](#).

[6] Reference guide to consent for examination or treatment (2001) [Department of Health](#).

### Surveillance decision

This section of the guideline should not be updated.

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#### *Miscellaneous nutrition support strategies*

##### **2-year surveillance summary**

Update not required after review of evidence.

##### **5-year surveillance summary**

No relevant evidence was identified.

##### **Evidence Update 2013**

No relevant evidence was identified.

##### **8-year surveillance summary**

No relevant evidence was identified.

#### **2017 surveillance summary**

A systematic review and meta-analysis<sup>38</sup> of 22 RCTs (n=3736) examined nutritional support (including counselling and oral and enteral feeding) in medical inpatients with malnutrition or at risk for malnutrition. Heterogeneity across RCTs was high, with overall low study quality and mostly unclear risk of bias. Intervention group patients significantly increased their weight, caloric, and protein intake compared with control group patients. No significant

differences between intervention and control were found for mortality (primary outcome), hospital-acquired infections, functional outcome, or length of hospital stay. Nonelective readmissions were significantly decreased by the intervention.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

The new evidence suggests that in medical inpatients, nutritional support increases caloric

and protein intake and body weight. Although little effect on clinical outcomes was found, the overall low study quality, the lack of detail on individual intervention types, and the benefits seen for weight and intake, mean that the evidence is unlikely to affect recommendations in CG32 that nutrition support should be considered in people who are malnourished, or at risk of malnutrition.

New evidence is unlikely to change guideline recommendations.

*Gluten-free diet*

**2-year surveillance summary**

Update not required after review of evidence.

**5-year surveillance summary**

No relevant evidence was identified.

**Evidence Update 2013**

No relevant evidence was identified.

**8-year surveillance summary**

No relevant evidence was identified.

**2017 surveillance summary**

No relevant evidence was identified.

**Topic expert feedback**

A topic expert noted that many commissioners are starting to stop making gluten-free food available on prescription, and the NICE guideline does not address this issue. However, nutritional support for patients with coeliac disease is not a completely separate issue, as some will be malnourished and vulnerable and need to have appropriate support. This support will on the whole not come from a separate pathway. It will be the same hospital or community services delivering it.

**Impact statement**

Topic experts raised the issue of nutritional support for patients with coeliac disease. CG32 does not make any specific recommendations (such as nutritional formulations containing gluten) that would exclude patients with coeliac disease. Additionally, the guideline states that healthcare professionals involved in starting or stopping nutrition support should: obtain consent from the patient if he or she is competent and act in the patient's best interest if he or she is not competent to give consent. Healthcare professionals should also 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. No impact on the guideline is anticipated.

New evidence is unlikely to change guideline recommendations.

*What to give in hospital and the community*

**Recommendations in this section of the guideline**

1.4.1 Healthcare professionals who are skilled and trained in nutritional requirements and methods of nutrition support should ensure that the total nutrient intake<sup>[7]</sup> of people prescribed nutrition support accounts for:

- energy, protein, fluid, electrolyte, mineral, micronutrients<sup>[8]</sup> and fibre needs
- activity levels and the underlying clinical condition – for example, catabolism, pyrexia

- gastrointestinal tolerance, potential metabolic instability and risk of refeeding problems
  - the likely duration of nutrition support.
- 1.4.2 For people who are not severely ill or injured, nor at risk of refeeding syndrome, the suggested nutritional prescription for total intake<sup>[7]</sup> should provide all of the following:
- 25–35 kcal/kg/day total energy (including that derived from protein<sup>[9],[10]</sup>)
  - 0.8–1.5 g protein (0.13–0.24 g nitrogen)/kg/day
  - 30–35 ml fluid/kg (with allowance for extra losses from drains and fistulae, for example, and extra input from other sources – for example, intravenous drugs)
  - adequate electrolytes, minerals, micronutrients (allowing for any pre-existing deficits, excessive losses or increased demands) and fibre if appropriate.
- 1.4.3 The prescription should be reviewed according to the person's progress, and care should be taken when:
- using food fortification which tends to supplement energy and/or protein without adequate micronutrients and minerals
  - using feeds and supplements that meet full energy and nitrogen needs, as they may not provide adequate micronutrients and minerals when only used in a supplementary role
  - using pre-mixed parenteral nutrition bags that have not had tailored additions from pharmacy.
- 1.4.4 Nutrition support should be cautiously introduced in seriously ill or injured people requiring enteral tube feeding or parenteral nutrition. It should be started at no more than 50% of the estimated target energy and protein needs. It should be built up to meet full needs over the first 24–48 hours according to metabolic and gastrointestinal tolerance. Full requirements of fluid, electrolytes, vitamins and minerals should be provided from the outset of feeding.
- 1.4.5 People who have eaten little or nothing for more than 5 days should have nutrition support introduced at no more than 50% of requirements for the first 2 days, before increasing feed rates to meet full needs if clinical and biochemical monitoring reveals no refeeding problems.
- 1.4.6 People who meet the criteria in Box should be considered to be at high risk of developing refeeding problems.

**Box 1 Criteria for determining people at high risk of developing refeeding problems**

<p><b>Patient has one or more of the following:</b></p> <ul style="list-style-type: none"> <li>• BMI less than 16 kg/m<sup>2</sup></li> <li>• unintentional weight loss greater than 15% within the last 3–6 months</li> <li>• little or no nutritional intake for more than 10 days</li> <li>• low levels of potassium, phosphate or magnesium prior to feeding.</li> </ul>
<p><b>Or patient has two or more of the following:</b></p> <ul style="list-style-type: none"> <li>• BMI less than 18.5 kg/m<sup>2</sup></li> <li>• unintentional weight loss greater than 10% within the last 3–6 months</li> <li>• little or no nutritional intake for more than 5 days</li> <li>• a history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.</li> </ul>

- 1.4.7 People at high risk of developing refeeding problems (Box 1) should be cared for by healthcare professionals who are appropriately skilled and trained and have expert knowledge of nutritional requirements and nutrition support.
- 1.4.8 The prescription for people at high risk of developing refeeding problems should consider:
- starting nutrition support at a maximum of 10 kcal/kg/day, increasing levels slowly to meet or exceed full needs by 4–7 days

- using only 5 kcal/kg/day in extreme cases (for example, BMI less than 14 kg/m<sup>2</sup> or negligible intake for more than 15 days) and monitoring cardiac rhythm continually in these people and any others who already have or develop any cardiac arrhythmias
- restoring circulatory volume and monitoring fluid balance and overall clinical status closely
- providing immediately before and during the first 10 days of feeding: oral thiamin 200–300 mg daily, vitamin B co strong 1 or 2 tablets, three times a day (or full dose daily intravenous vitamin B preparation, if necessary) and a balanced multivitamin/trace element supplement once daily
- providing oral, enteral or intravenous supplements of potassium (likely requirement 2–4 mmol/kg/day), phosphate (likely requirement 0.3–0.6 mmol/kg/day) and magnesium (likely requirement 0.2 mmol/kg/day intravenous, 0.4 mmol/kg/day oral) unless pre-feeding plasma levels are high. Pre-feeding correction of low plasma levels is unnecessary.

[7] Total intake includes intake from any food, oral fluid, oral nutritional supplements, enteral and/or parenteral nutrition support and intravenous fluid.

[8] The term 'micronutrient' is used throughout to include all essential vitamins and trace elements.

[9] This level may need to be lower in people who are overweight, BMI >25.

[10] When using parenteral nutrition it is often necessary to adjust total energy values listed on the manufacturer's information which may not include protein energy values.

## Surveillance decision

This section of the guideline should not be updated.

### Refeeding problems

#### 2-year surveillance summary

Update not required after review of evidence.

#### 5-year surveillance summary

No relevant evidence was identified.

#### Evidence Update 2013

Two observational UK studies<sup>39,40</sup> on the incidence of and risk factors for refeeding syndrome were identified. In both studies, the risk of refeeding syndrome was determined using the criteria set out in this guideline. One study<sup>39</sup> concluded that starvation and baseline low-serum magnesium concentration were independent predictors for refeeding syndrome.

The other study<sup>40</sup>, using hypophosphataemia as the 'reference standard', found that 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.

#### 8-year surveillance summary

No relevant evidence was identified.

#### 2017 surveillance summary

Topic experts identified a parallel-group, multicentre, single-blind RCT<sup>41</sup> (n=339 adult critically ill patients from 13 intensive care units)

examining caloric restriction in refeeding syndrome. Patients who developed refeeding syndrome within 72 hours of commencing nutritional support in the intensive care unit were enrolled and allocated to receive caloric restriction or continued standard nutritional support. Randomisation was stratified by enrolment serum phosphate concentration (greater or less than 0.32 mmol/litre) and BMI (greater or less than 18 kg/m<sup>2</sup>). The primary outcome of mean number of days alive after intensive care unit discharge (a composite outcome based on intensive care unit length of stay, overall survival time, and mortality) with 60 day follow-up was not significantly different between groups. However, caloric restriction improved individual components of the primary outcome: significantly more patients were alive at day 60 and overall survival time was increased.

#### Topic expert feedback

##### 8-year surveillance

One guideline committee member highlighted that there has been considerable debate about the safety of the refeeding recommendations in the guideline and that this needs to be revisited and rewritten to prevent overly cautious approaches to feeding which in itself can hold risks.

### 2017 surveillance

Topic experts noted there is some evidence<sup>41</sup> of how to deal with provision in the early stages of feeding in a study on calorie restriction with respect to refeeding syndrome in critically ill patients.

#### Impact statement

The Evidence Update 2013 concluded that taken together, the evidence is broadly consistent with the guideline, and although the findings of the studies question the validity or lack of specificity of some risk markers set out by NICE, the lack of universally accepted criteria for a diagnosis of refeeding syndrome prevents a definitive assessment. Hence this evidence is unlikely to have an impact on NICE CG32; further research is therefore needed.

At 8-year surveillance, no new evidence was found that would change the direction of current guideline recommendations; feedback from the guideline committee was also deemed

unlikely to impact on the guideline recommendations at this time.

The 2017 surveillance found evidence highlighted by topic experts that caloric restriction can improve survival in critically ill adults who develop refeeding syndrome. CG32 makes recommendations about cautiously introducing nutrition support in people at high risk of developing refeeding problems, and in seriously ill or injured people. However it does not make specific recommendations for managing established refeeding syndrome. This study therefore raises the possibility of a new question in the guideline to look at this area, though it should be noted that the evidence was from a single trial and results may need to be confirmed by further studies. No impact on the guideline is currently expected.

New evidence is unlikely to change guideline recommendations.

### *Permissive enteral underfeeding in critically ill patients*

#### 2-year surveillance summary

No relevant evidence was identified.

#### 5-year surveillance summary

No relevant evidence was identified.

#### Evidence Update 2013

No relevant evidence was identified.

#### 8-year surveillance summary

No relevant evidence was identified.

#### 2017 surveillance summary

##### *Energy underfeeding*

A multicentre RCT<sup>42</sup> (n=894 critically ill adults across 7 centres with a medical, surgical, or trauma admission category) examined permissive underfeeding (40 to 60% of calculated caloric requirements) versus standard enteral feeding (70 to 100% caloric requirements) for up to 14 days while maintaining a similar protein intake in the 2 groups. Almost all patients in both groups were on mechanical ventilation. During the intervention period, calories received and percentage of caloric requirement achieved was significantly lower in the permissive-underfeeding group than the standard-feeding group. Protein intake was similar in both

groups. The primary outcome of 90-day mortality was not significantly different between groups. No serious adverse events were reported; there were no significant between-group differences with respect to feeding intolerance, diarrhoea, infections acquired in the intensive care unit, or length of stay in the intensive care unit or hospital.

Topic experts identified a post-hoc analysis<sup>43</sup> of the above RCT<sup>42</sup> examining the effect of different baseline nutritional risk in permissive underfeeding versus standard feeding. Nutritional risk was categorised by the modified Nutrition Risk in Critically Ill (NUTRIC) score, (high nutritional risk score 5–9, low nutritional risk score 0–4). Additional analyses were performed by categorising patients by BMI, prealbumin, transferrin, phosphate, urinary urea nitrogen and nitrogen balance. Based on the NUTRIC score, 42% of all enrolled patients were high nutritional risk and 58% were low nutritional risk. There was no significant association between feeding strategy and mortality in either of the nutritional risk categories. Findings were similar in analyses using other definitions, except prealbumin. The association of permissive underfeeding versus standard feeding and 90-day mortality differed when patients were categorised by baseline

prealbumin level, with higher risk associated with higher baseline prealbumin.

A systematic review and meta-analysis<sup>44</sup> of 4 RCTs (n=not reported in the abstract) compared underfeeding and full feeding in acutely critically ill patients. There was no significant difference in the primary outcome of overall mortality between the underfeeding and full-feeding groups. Analysis of the underfeeding subgroup fed >33.3% of the standard caloric requirement indicated that overall mortality was significantly lower than in the full-feeding group. In contrast, no difference in overall mortality was found between the underfeeding subgroup fed <33.3% of the standard caloric requirement and the full-feeding group. The length of stay in hospital and the intensive care unit did not differ between the 2 groups. Moreover, no differences in other secondary clinical outcomes (duration of mechanical ventilation, incidence of pneumonia, *Clostridium difficile* colitis, other infectious complications, and gastrointestinal intolerance) were noted.

A systematic review and meta-analysis<sup>45</sup> of 6 RCTs (n=2517; mean age and BMI were 53 years and 29 kg/m<sup>2</sup>) examined hypocaloric versus normocaloric feeding in patients in the intensive care unit. Two studies compared normocaloric feeding (77% of goal) with trophic feeding (20% of goal), while 4 studies compared normocaloric feeding (72% of goal) with permissive underfeeding (49% of goal). Overall, there was no significant difference between groups in the risk of infectious complications, hospital mortality, or length of stay in the intensive care unit. Ventilator-free days were reported in 3 studies with no significant difference between the normocaloric and intentional hypocaloric groups (data not pooled).

An RCT<sup>46</sup> (n=100 critically ill patients, mean age 66 years, requiring artificial nutrition for at least 72 hours within 24 hours of admission to the intensive care unit) examined hypocaloric (given 50% of daily energy expenditure) versus normocaloric (given 100% of daily energy expenditure) feeding in the first 7 days in the intensive care unit. The mean daily caloric supply was significantly higher in the normocaloric than the hypocaloric group (19.7 versus 11.3 kcal/kg). For the primary outcome, nosocomial infections were detected significantly more frequently in the hypocaloric group than the normocaloric group. Insulin

demand was significantly higher and gastrointestinal intolerance more frequent in the normocaloric than the hypocaloric group. Mortality rates in the intensive care unit and hospital did not differ significantly between groups.

An RCT<sup>47</sup> (n=83 critically ill patients in a surgical intensive care unit) examined hypocaloric (50% of standard daily caloric requirement of 25–30 kcal/kg/day) versus eucaloric (standard daily caloric requirement) nutritional support via enteral tube feeds or parenteral nutrition, with an equal protein allocation in each group (1.5 g/kg/day). There were no significant differences between groups in the mean number of infections per patient, percentage of patients acquiring infection, mean length of stay in the intensive care unit or hospital, mean glucose concentration at 06:00 am, or number of mortalities. Further analyses revealed no differences when analysed by sex, admission diagnosis, site of infection, or causative organism.

#### *Energy and protein underfeeding*

A double-blind RCT<sup>48</sup> (n=80 critically ill patients) examined hyperproteic hypocaloric nutrition (15 kcal/kg with 1.7 g/kg protein) versus isocaloric enteral nutrition (25 kcal/kg with 20% of the calories as protein; control). All patients completed follow-up of at least 4 days. The total amount of calories delivered was similarly low in both groups (12 kcal/kg in hyperproteic hypocaloric group versus 14 kcal/kg with control), but protein delivery was significantly higher in the hyperproteic hypocaloric group. For the primary outcome, the hyperproteic hypocaloric group showed a significant improvement in sequential organ failure assessment score at 48 hours versus control. Less hyperglycemic episodes per day were seen with hyperproteic hypocaloric than control feeding.

A systematic review and meta-analysis<sup>49</sup> of 8 RCTs (n=1895) examined the effect of varying calorie and protein administration in critically ill adult patients. There was no significant difference between low-energy and high-energy groups in mortality (primary outcome), infection, or risk of gastrointestinal intolerance. In subgroup analysis, the low-energy subgroup, fed 33.3 to 66.6% of goal energy, had significantly lower mortality than the high-energy group. The improvements in mortality and gastrointestinal intolerance were absent when calorie intake was >66.6% of goal

energy in the low-energy group. High-energy intake combined with high-protein intake significantly reduced infections; however, when daily protein intake was similar in both groups, a high-energy intake did not decrease infections. No statistical differences were observed in other secondary outcomes (pneumonia, hospital and intensive care unit lengths of stay, and mechanical ventilation days).

### **Topic expert feedback**

#### *2017 surveillance*

Topic experts noted that suitable provision of energy, protein or fluid to severely ill or injured patients is a common topic of debate in clinical practice, and highlighted a recent article on the appropriate level of enteral feeding in critically ill patients<sup>42</sup>.

Topic experts noted there are lots of critical care nutrition support papers, including many publications (for example<sup>43</sup>) on permissive underfeeding and the rationale for this in critically ill patients and post-surgery. In particular the reduction in mitochondrial function with inflammation and the resultant ability to utilise substrate.

### **Impact statement**

#### *Energy*

The majority of the new evidence (both individual trials and meta-analyses) found no differences between hypocaloric and normocaloric feeding in critically ill patients on outcomes including mortality, infections, length of stay, ventilator-free days, feeding/gastrointestinal intolerance, or diarrhoea. There was some evidence that hypocaloric feeding was associated with more nosocomial infections and less insulin demand and gastrointestinal intolerance, but this was a single small study. Subgroup analyses

suggested that compared to normal calorie intake, mortality was lower after feeding 33.3–66.6% of standard caloric requirement, but did not differ after feeding <33.3% or >66.6% of standard caloric requirement.

Although the evidence suggests that caloric underfeeding may have no benefits over normal calorie intake in critically ill patients, the subanalysis that a calorie intake of 33.3–66.6% of normal may reduce mortality aligns with the recommendation in CG32 that nutrition support should be cautiously introduced in seriously ill or injured people requiring enteral tube feeding or parenteral nutrition. It should be started at no more than 50% of the estimated target energy and protein needs.

#### *Protein*

A single trial found that high-protein low-calorie nutrition therapy in critically ill patients could be associated with a decrease in multiple organ failure and hyperglycaemia, and a meta-analysis found that a high-protein high-energy intake may decrease infection, but when protein intake was similar in both groups, a high-energy intake did not decrease infections. There is therefore still some uncertainty around appropriate protein levels, particularly the suitable level of energy to accompany it, and the evidence is therefore currently unlikely to affect the recommendation in CG32 that nutrition support should be cautiously introduced in seriously ill or injured people requiring enteral tube feeding or parenteral nutrition. It should be started at no more than 50% of the estimated target energy and protein needs.

New evidence is unlikely to change guideline recommendations.

### *Tight calorie control*

#### **2-year surveillance summary**

Update not required after review of evidence.

#### **5-year surveillance summary**

No relevant evidence was identified.

#### **Evidence Update 2013**

No relevant evidence was identified.

#### **8-year surveillance summary**

No relevant evidence was identified.

#### **2017 surveillance summary**

An unblinded RCT<sup>50</sup> (n=50 older patients with hip fracture) examined tight calorie control (energy goal determined by repeated resting energy expenditure measurements using indirect calorimetry) versus control. Oral nutritional supplements were started 24 hours after surgery and the amount adjusted to make up the difference between energy received from hospital food and measured energy expenditure. The intervention group received

significantly higher daily energy intake than controls. This was associated with a significantly less negative cumulative energy balance. A significant negative correlation was found between the cumulative energy balance and total complication rate as well as for length of hospital stay.

**Topic expert feedback**

No topic expert feedback was relevant to this evidence.

**Impact statement**

The new evidence suggests that nutrition support guided by repeated measurements of resting energy expenditure improved outcomes in older patients following surgery for hip

fractures. This is broadly in line with the recommendation in CG32 that the total nutrient intake of people prescribed nutrition support accounts for (among other things) activity levels and the underlying clinical condition. Although the guideline does not specify using calorimetry to inform decisions on level of nutrition support, the trial was only in 50 patients with hip fracture and further evidence in other populations may be needed to confirm findings before any specific impact on the guideline could be considered.

New evidence is unlikely to change guideline recommendations.

*Building up feeding when nutrition support has been commenced at below target levels*

**2-year surveillance summary**

Update not required after review of evidence.

**5-year surveillance summary**

No relevant evidence was identified.

**Evidence Update 2013**

No relevant evidence was identified.

**8-year surveillance summary**

No relevant evidence was identified.

**2017 surveillance summary**

No relevant evidence was identified.

**Topic expert feedback**

A topic expert stated that people may be leaving feeding at low rates for longer than is suggested in CG32, or may be following other guidelines/recommendations instead of CG32.

**Impact statement**

CG32 states that when feeding is commenced at lower than normal levels, it should be built up over time according to circumstances:

1.4.4 Nutrition support should be cautiously introduced in seriously ill or injured people requiring enteral tube feeding or parenteral nutrition. It should be started at no more than 50% of the estimated target energy and protein

needs. It should be built up to meet full needs over the first 24–48 hours according to metabolic and gastrointestinal tolerance. Full requirements of fluid, electrolytes, vitamins and minerals should be provided from the outset of feeding.

1.4.5 People who have eaten little or nothing for more than 5 days should have nutrition support introduced at no more than 50% of requirements for the first 2 days, before increasing feed rates to meet full needs if clinical and biochemical monitoring reveals no refeeding problems.

1.4.8 The prescription for people at high risk of developing refeeding problems should consider: starting nutrition support at a maximum of 10 kcal/kg/day, increasing levels slowly to meet or exceed full needs by 4–7 days.

Although experts suggested that the guidance for building up feeding levels may not be being followed, no evidence was provided in support of this. As CG32 already states the recommended strategies for building up levels, the issue is likely to relate to implementation therefore no impact on CG153 is anticipated.

New evidence is unlikely to change guideline recommendations.

## Monitoring of nutrition support in hospital and the community

### Recommendations in this section of the guideline

- 1.5.1 Healthcare professionals should review the indications, route, risks, benefits and goals of nutrition support at regular intervals. The time between reviews depends on the patient, care setting and duration of nutrition support. Intervals may increase as the patient is stabilised on nutrition support.
- 1.5.2 People having nutrition support in hospital should be monitored by healthcare professionals with the relevant skills and training in nutritional monitoring.
- 1.5.3 Healthcare professionals should refer to the protocols for nutritional, anthropometric and clinical monitoring, shown in Table 1, when monitoring people having nutrition support in hospital.
- 1.5.4 Healthcare professionals should refer to the protocols for laboratory monitoring, shown in Table 2, when monitoring people having nutrition support in hospital. Table 2 is particularly relevant to parenteral nutrition. It could also be selectively applied when enteral or oral nutrition support is used, particularly for people who are metabolically unstable or at risk of refeeding syndrome. The frequency and extent of the observations given may need to be adapted in acutely ill or metabolically unstable people.
- 1.5.5 People having parenteral nutrition in the community need regular assessment and monitoring. This should be carried out by home care specialists and by experienced hospital teams (initially at least weekly), using observations marked \* in Table 1. In addition, they should be reviewed at a specialist hospital clinic every 3–6 months. Monitoring should be more frequent during the early months of home parenteral nutrition, or if there is a change in clinical condition, when the full range of tests in Tables 1 and 2 should be performed. Some of the clinical observations may be checked by patients or carers.
- 1.5.6 People having oral nutrition support and/or enteral tube feeding in the community should be monitored by healthcare professionals with the relevant skills and training in nutritional monitoring. This group of people should be monitored every 3–6 months or more frequently if there is any change in their clinical condition. A limited number of observations and tests from Table 1 should be performed. Some of the clinical observations may be checked by patients or carers. If clinical progress is satisfactory, laboratory tests are rarely needed.
- 1.5.7 If long-term nutrition support is needed patients and carers should be trained to recognise and respond to adverse changes in both their well-being and in the management of their nutritional delivery system.

**Table 1 Protocol for nutritional, anthropometric and clinical monitoring of nutrition support**

<b>Parameter</b>	<b>Frequency</b>	<b>Rationale</b>
<b>Nutritional</b>		
Nutrient intake from oral, enteral or parenteral nutrition (including any change in conditions that are affecting food intake)	Daily initially, reducing to twice weekly when stable	To ensure that patient is receiving nutrients to meet requirements and that current method of feeding is still the most appropriate. To allow alteration of intake as indicated
Actual volume of feed delivered*	Daily initially, reducing to twice weekly when stable	To ensure that patient is receiving correct volume of feed. To allow troubleshooting
Fluid balance charts (enteral and parenteral)	Daily initially, reducing to twice weekly when stable	To ensure patient is not becoming over/under hydrated
<b>Anthropometric</b>		
Weight*	Daily if concerns regarding fluid balance, otherwise weekly reducing to monthly	To assess ongoing nutritional status, determine whether nutritional goals are being achieved and take into account both body fat and muscle
BMI*	Start of feeding and then monthly	
Mid-arm circumference*	Monthly, if weight cannot be obtained or is difficult to interpret	
Triceps skinfold thickness	Monthly, if weight cannot be obtained or is difficult to interpret	
<b>GI function</b>		
Nausea/vomiting*	Daily initially, reducing to twice weekly	To ensure tolerance of feed
Diarrhoea*	Daily initially, reducing to twice weekly	To rule out any other causes of diarrhoea and then assess tolerance of feeds
Constipation*	Daily initially, reducing to twice weekly	To rule out other causes of constipation and then assess tolerance of feeds
Abdominal distension	As necessary	Assess tolerance of feed

<b>Enteral tube – nasally inserted</b>		
Gastric tube position (pH less than or equal to 5.5 using pH paper – or noting position of markers on tube once initial position has been confirmed)	Before each feed begins	To ensure tube in correct position
Nasal erosion	Daily	To ensure tolerance of tube
Fixation (is it secure?)	Daily	To help prevent tube becoming dislodged
Is tube in working order (all pieces intact, tube not blocked/kinked)?	Daily	To ensure tube is in working order
<b>Gastrostomy or jejunostomy</b>		
Stoma site	Daily	To ensure site not infected/red, no signs of gastric leakage
Tube position (length at external fixation)	Daily	To ensure tube has not migrated from/into stomach and external over granulation
Tube insertion and rotation (gastrostomy without jejunal extension only)	Weekly	Prevent internal overgranulation/prevention of buried bumper syndrome
Balloon water volume (balloon retained gastrostomies only)	Weekly	To prevent tube falling out
Jejunostomy tube position by noting position of external markers	Daily	Confirmation of position
<b>Parenteral nutrition</b>		
Catheter entry site*	Daily	Signs of infection/inflammation
Skin over position of catheter tip (peripherally fed people)*	Daily	Signs of thrombophlebitis
<b>Clinical condition</b>		
General condition*	Daily	To ensure that patient is tolerating feed and that feeding and route continue to be appropriate

Temperature/blood pressure	Daily initially, then as needed	Sign of infection/fluid balance
Drug therapy*	Daily initially, reducing to monthly when stable	Appropriate preparation of drug (to reduce incidence of tube blockage). To prevent/reduce drug nutrient interactions
<b>Long-/short-term goals</b>		
Are goals being met?*	Daily initially, reducing to twice weekly and then progressively to 3–6 monthly, unless clinical condition changes	To ensure that feeding is appropriate to overall care of patient
Are goals still appropriate?*	Daily initially, reducing to twice weekly and then progressively to 3–6 monthly, unless clinical condition changes	To ensure that feeding is appropriate to overall care of patient
People at home having parenteral nutrition should be monitored using observations marked *.		

**Table 2 Protocol for laboratory monitoring of nutrition support**

Parameter	Frequency	Rationale	Interpretation
Sodium, potassium, urea, creatinine	Baseline Daily until stable Then 1 or 2 times a week	Assessment of renal function, fluid status, and Na and K status	Interpret with knowledge of fluid balance and medication Urinary sodium may be helpful in complex cases with gastrointestinal fluid loss
Glucose	Baseline 1 or 2 times a day (or more if needed) until stable Then weekly	Glucose intolerance is common	Good glycaemic control is necessary
Magnesium, phosphate	Baseline Daily if risk of refeeding syndrome Three times a week until stable Then weekly	Depletion is common and under recognised	Low concentrations indicate poor status

Liver function tests including International Normalised Ratio (INR)	Baseline Twice weekly until stable Then weekly	Abnormalities common during parenteral nutrition	Complex. May be due to sepsis, other disease or nutritional intake
Calcium, albumin	Baseline Then weekly	Hypocalcaemia or hypercalcaemia may occur	Correct measured serum calcium concentration for albumin Hypocalcaemia may be secondary to Mg deficiency Low albumin reflects disease not protein status
C-reactive protein	Baseline Then 2 or 3 times a week until stable	Assists interpretation of protein, trace element and vitamin results	To assess the presence of an acute phase reaction (APR). The trend of results is important
Zinc, copper	Baseline Then every 2–4 weeks, depending on results	Deficiency common, especially when increased losses	People most at risk when anabolic APR causes Zn decrease and Cu increase
Selenium <sup>a</sup>	Baseline if risk of depletion Further testing dependent on baseline	Se deficiency likely in severe illness and sepsis, or long-term nutrition support	APR causes Se decrease Long-term status better assessed by glutathione peroxidase
Full blood count and MCV	Baseline 1 or 2 times a week until stable Then weekly	Anaemia due to iron or folate deficiency is common	Effects of sepsis may be important
Iron, ferritin	Baseline Then every 3–6 months	Iron deficiency common in long-term parenteral nutrition	Iron status difficult if APR (Fe decrease, ferritin increase)
Folate, B12	Baseline Then every 2–4 weeks	Iron deficiency is common	Serum folate/B12 sufficient, with full blood count
Manganese <sup>b</sup>	Every 3–6 months if on home parenteral nutrition	Excess provision to be avoided, more likely if liver disease	Red blood cell or whole blood better measure of excess than plasma

25-OH Vit D <sup>b</sup>	6 monthly if on long-term support	Low if housebound	Requires normal kidney function for effect
Bone densitometry <sup>b</sup>	On starting home parenteral nutrition Then every 2 years	Metabolic bone disease diagnosis	Together with lab tests for metabolic bone disease
<p><sup>a</sup> These tests are needed primarily for people having parenteral nutrition in the community.</p> <p><sup>b</sup> These tests are rarely needed for people having enteral tube feeding (in hospital or in the community), unless there is cause for concern.</p>			

### Surveillance decision

No new information was identified at any surveillance review.

This section of the guideline should not be updated.

## Oral nutrition support in hospital and the community

### Recommendations in this section of the guideline

- 1.6.1 People who present with any obvious or less obvious indicators of dysphagia listed in Box should be referred to healthcare professionals with relevant skills and training in the diagnosis, assessment and management of swallowing disorders.

#### Box 2 Indicators of dysphagia

Obvious indicators of dysphagia	Less obvious indicators of dysphagia
Difficult, painful chewing or swallowing	Change in respiration pattern
Regurgitation of undigested food	Unexplained temperature spikes
Difficulty controlling food or liquid in the mouth	Wet voice quality
Drooling	Tongue fasciculation (may be indicative of motor neurone disease)
Hoarse voice	Xerostomia
Coughing or choking before, during or after swallowing	Heartburn
Globus sensation	Change in eating habits – for example, eating slowly or avoiding social occasions
Nasal regurgitation	Frequent throat clearing
Feeling of obstruction	Recurrent chest infections
Unintentional weight loss – for example, in people with dementia	Atypical chest pain

- 1.6.2 Healthcare professionals should recognise that people with acute and chronic neurological conditions and those who have undergone surgery or radiotherapy to the upper aerodigestive tract are at high risk of developing dysphagia.

- 1.6.3 When managing people with dysphagia, healthcare professionals with relevant skills and training in the diagnosis, assessment and management of swallowing disorders should consider:

- the risks and benefits of modified oral nutrition support and/or enteral tube feeding

- the factors listed in Box.

**Box 3 Factors to be considered before modification of nutrition support and hydration in people with dysphagia**

Recurrent chest infections  
 Mobility  
 Dependency on others for assistance to eat  
 Perceived palatability and appearance of food or drink  
 Level of alertness  
 Compromised physiology  
 Poor oral hygiene  
 Compromised medical status  
 Metabolic and nutritional requirements  
 Vulnerability (for example, immunocompromised)  
 Comorbidities

- 1.6.4 People with dysphagia should have a drug review to ascertain if the current drug formulation, route and timing of administration remains appropriate and is without contraindications for the feeding regimen or swallowing process.
- 1.6.5 Healthcare professionals with relevant skills and training in the diagnosis, assessment and management of swallowing disorders should regularly monitor and reassess people with dysphagia who are having modified food and liquid until they are stable.

**Indications**

- 1.6.6 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 as defined in 1.3.1 and 1.3.2, respectively.<sup>[11]</sup>
- 1.6.7 Healthcare professionals should ensure that the overall nutrient intake of oral nutrition support offered contains a balanced mixture of protein, energy, fibre, electrolytes, vitamins and minerals.
- 1.6.8 If there is concern about the adequacy of micronutrient intake, a complete oral multivitamin and mineral supplement providing the reference nutrient intake for all vitamins and trace elements should be considered by healthcare professionals with the relevant skills and training in nutrition support who are able to determine the nutritional adequacy of a patient's dietary intake.
- 1.6.9 Oral nutrition support should be stopped when the patient is established on adequate oral intake from normal food.

**Surgical patients**

- 1.6.10 Peri-operative oral nutrition support should be considered for surgical patients who can swallow safely and are malnourished as defined in 1.3.1.
- 1.6.11 Healthcare professionals should consider giving post-caesarean or gynaecological surgical patients who can swallow safely, some oral intake within 24 hours of surgery.
- 1.6.12 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 patient should be monitored carefully for any signs of nausea or vomiting.

[11] 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.

**Surveillance decision**

This section of the guideline should not be updated.

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*Oral nutrition support – evidence identified prior to current 2017 surveillance review*

**2-year surveillance summary**

Update not required after review of evidence.

**5-year surveillance summary**

Thirteen studies<sup>51-63</sup> relevant to the clinical area were identified.

Several studies, comparing oral nutritional supplements with either standard care or dietary counselling generally showed that giving oral nutritional supplements improves various outcomes such as weight gain, quality of life and decreased postoperative complications<sup>51-54,56,59,61-63</sup>. One of these studies included a trial-based economic evaluation<sup>61</sup>. These studies strengthen the recommendation for oral nutritional supplementation with various care settings, especially within the community.

One study looked at oral nutritional supplements versus standard care and identified that for oral nutritional supplements to be effective, more than one meal should be enhanced<sup>55</sup>.

One study found that early oral nutrition compared to traditional oral feeding resulted in a shorter length of hospital stay<sup>57</sup>, however the evidence was not deemed sufficient to merit a change in the guidance.

One study was identified that provided evidence for nutritional care in dementia<sup>58</sup>.

**Evidence Update 2013**

Eight studies<sup>64-71</sup> relating to oral nutrition support in hospital and the community were

identified. Findings of studies were broadly consistent with guideline recommendations.

**8-year surveillance summary**

Twelve studies<sup>72-83</sup> of oral nutrition support in hospital and the community were identified. Findings of studies were broadly consistent with guideline recommendations.

**2017 surveillance summary**

See sections below where the evidence is categorised by sub-topic.

**Topic expert feedback**

*8-year surveillance*

One guideline committee member commented that that new recommendations on the use of oral nutrition supplements in the community where practice is highly variable could be made.

**Impact statement**

At 8-year surveillance, no new evidence was identified which would change the direction of current guideline recommendations. Feedback from the guideline committee was deemed unlikely to impact on the guideline recommendations at this time.

The evidence from the 2017 surveillance has been examined according to sub-topic and is presented, along with any decisions on impact on the guideline, in the sections below.

New evidence is unlikely to change guideline recommendations.

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*Oral nutritional supplements plus exercise in older people with sarcopenia*

**2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Oral nutrition support – evidence identified prior to current 2017 surveillance review' above for details.

**2017 surveillance summary**

A double-blind RCT<sup>84</sup> (n=130 older people with sarcopenia; mean age 80 years) examined nutritional supplements (whey protein 22 g, essential amino acids 10.9 g, including 4 g leucine, and vitamin D 2.5 mg [100 IU]) versus

placebo supplement. All participants had concurrent regular, controlled physical activity. After 12 weeks, compared with placebo, supplements significantly increased fat-free mass, relative skeletal muscle mass, android distribution of fat (i.e. around the trunk and upper body), handgrip strength, standardised summary scores for physical components, activities of daily living, mini nutritional assessment, and insulin-like growth factor I, and lowered C-reactive protein.

An RCT<sup>85</sup> (n=39 older inpatients with decreased skeletal muscle mass in a hospital convalescence rehabilitation unit) examined

resistance training plus nutritional supplementation versus resistance training alone (control). Training and supplementation were conducted from admission to discharge (2–6 months). Significant treatment effects in the training plus supplementation group compared to control were seen for calf circumference (primary outcome), arm circumference, activities of daily living (Barthel Index score), and serum albumin level.

### Topic expert feedback

#### 2017 surveillance

Topic experts noted a lack of emphasis in the guideline on frailty sarcopenia and nutrition especially in the older adult population. They also noted the role of adequate protein intake spread throughout the day on muscle function, especially in the elderly. They further queried the role of sarcopenia in post-illness rehabilitation.

#### Impact statement

The 2017 surveillance found that nutritional supplementation in conjunction with

exercise/resistance training was found to improve fat-free mass, skeletal muscle mass, distribution of fat around the trunk and upper body, handgrip strength, physical health, activities of daily living, mini nutritional assessment, and calf circumference and arm circumference.

Although CG32 recommends oral nutritional supplements, their use alongside physical activity interventions to manage sarcopenia in older people is not specifically discussed. Given comments from topic experts on the lack of emphasis in CG32 on sarcopenia, guidance in this area may therefore be needed. However, sarcopenia is a normal part of ageing and is out of scope of CG32. This evidence will be logged for consideration in surveillance of other NICE guidelines in public health and social care.

New evidence is unlikely to change guideline recommendations.

## Oral nutritional supplements

### 2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update

See 'Oral nutrition support – evidence identified prior to current 2017 surveillance review' above for details.

#### 2017 surveillance summary

A systematic review and meta-analysis<sup>86</sup> of 10 studies (n=not reported in abstract) examined oral nutrition interventions (such as oral nutritional supplements, foodservice interventions, clinical care processes, and enhanced eating environments) to prevent and treat malnutrition in patients admitted for rehabilitation. Outcome data were combined narratively and by meta-analyses. Compared to meals alone, oral nutritional supplements significantly improved energy and protein intake, with some evidence for improvements in anthropometry and length of stay. There was little evidence that speciality supplements were beneficial compared to standard versions. Meta-analyses demonstrated significantly greater energy and protein intake with energy dense meals. Opposing results were reported in studies investigating enhanced clinical care processes.

A multicenter, placebo-controlled, double-blind RCT<sup>87</sup> (n=652 malnourished patients >65 years hospitalised for congestive heart failure, acute myocardial infarction, pneumonia, or chronic obstructive pulmonary disease) examined standard care plus 2 servings/day of either a specialised high-protein oral nutritional supplement containing beta-hydroxy-beta-methylbutyrate (HP-HMB) or a placebo supplement. The primary composite endpoint of 90-day post-discharge incidence of death or non-elective readmission was similar between groups. No between-group differences were observed for 90-day readmission rate, but 90-day mortality was significantly lower with HP-HMB than placebo. The number-needed-to-treat to prevent 1 death was 20.3. Compared with placebo, HP-HMB resulted in significantly improved odds of better nutritional status (measured by Subjective Global Assessment class) at day 90, and an increase in body weight at day 30. Length of stay and activities of daily living were similar between treatments.

A systematic review<sup>88</sup> examined the cost and cost effectiveness of standard (non-disease specific) oral nutritional supplements in community and care home settings. A total of 19 publications with and without a hospital component were identified: 9 full text papers,

9 abstracts, and 1 report with retrospective analyses of 6 RCTs. From these publications a total of 31 cost and 4 cost-effectiveness analyses were identified. Most were retrospective analyses based on clinical data from RCTs. Most comparisons involved oral nutritional supplements versus no supplements. Oral nutritional supplements were significantly cost saving compared to control when used for <3 months (median saving 9.2%; 9 studies/economic models) and when used for >3 months (median saving 5%; 5 studies). In RCTs, oral nutritional supplements accounted for less than 5% of the total costs and the investment in the community produced a cost saving in hospital. Meta-analysis indicated that oral nutritional supplements reduced hospitalisation significantly (9 comparisons) and mortality non-significantly (8 comparisons). Many clinically relevant outcomes favouring oral nutritional supplements were reported: improved quality of life, reduced infections, reduced minor post-operative complications, reduced falls, and functional limitations (significance not reported in the abstract). Of the cost-effectiveness analyses involving quality adjusted life years or functional limitations, most favoured the oral nutritional supplements group (significance not reported in the abstract). The care home studies (4 cost analyses; 2 cost-effectiveness analyses) had differing aims, designs and conclusions.

A systematic review<sup>89</sup> examined the cost and cost effectiveness of using standard (non-disease specific) oral nutritional supplements in the hospital setting. Nine publications comprising 4 full text papers, 2 abstracts and 3 reports, one of which contained 11 cost analyses of controlled cohort studies, were identified. Most of these were based on retrospective analyses of RCTs designed to assess clinically relevant outcomes. The sample sizes of patients with surgical, orthopaedic and medical problems and combinations of these varied from 40 to 1.16 million. Of 14 cost analyses comparing oral nutritional supplements with no oral nutritional supplements (or routine care), 12 favoured oral nutritional supplements, and among those with quantitative data (12 studies) the mean cost saving was 12% (significance not reported in the abstract). A meta-analysis of 5 abdominal surgical studies in the UK showed a significant mean net cost saving of \$746 per patient. Meta-analyses also showed that cost

savings were typically associated with significantly improved outcomes of reduced mortality (5 studies), reduced complications (7 studies) and reduced length of hospital stay (5 surgical studies) corresponding to a reduction in hospital stay. Two studies also found oral nutritional supplements to be cost effective, one by avoiding development of pressure ulcers and releasing hospital beds, and the other by gaining quality adjusted life years.

An open-label, multicentre RCT<sup>90</sup> (n=212 malnourished patients in hospital or post-hospital) examined oral nutritional supplements plus dietary counselling versus dietary counselling (control) alone in 9 private and 4 public hospitals. Two servings (460 ml) of oral nutritional supplements were prescribed daily, providing 432 kcal, 16 g of protein and 28 micronutrients. At week 12, oral nutritional supplements led to significant improvements in the primary outcome of weight gain versus control. Other significant improvements over control were seen for increases in BMI and energy intake per day. There were no differences in biochemical parameters and modified Subjective Global Assessment score between groups. Additionally, patients on oral nutritional supplements who were more functionally impaired at baseline had significantly greater weight gain and improved handgrip strength scores than controls.

An RCT<sup>91</sup> (n=87 nursing home residents, average age 87 years, with or at risk of malnutrition) examined oral nutritional supplements (2 x 125 ml per day; 2.4 kcal/ml) for 12 weeks versus usual care (control). Compliance with oral nutritional supplements was high in 36% and low in 29% of residents. Body weight change was significantly higher with high compliance than low compliance, and significantly correlated with compliance in the oral nutritional supplements group. Significant differences and correlations were also identified for BMI, upper-arm circumference and Mini Nutritional Assessment–Short Form. High compliance was more often observed in residents with malnutrition and chewing difficulties than in those without these conditions (significance not reported in the abstract). Low compliance was significantly more prevalent in residents who were immobile, depressed or had gastrointestinal complaints.

An RCT<sup>92</sup> (n=50 well-nourished patients undergoing high-nutritional-risk conditioning chemotherapy and autologous stem-cell transplantation) examined early nutrition support (commenced when oral intake was less than 80% of estimated requirements) versus usual care (commenced when oral intake was less than 50% of estimated requirements). On secondary analysis, after exclusion of a single extreme outlier, both groups demonstrated significant weight loss over time. Weight loss at time of discharge was significantly less with early nutrition support than usual care, but the difference did not persist 6 months after discharge. In practice, an early start to nutrition support was difficult because of patient resistance and physician preference, with 8 patients (33%) in the control group and 4 (15%) in the intervention group not commencing nutrition support according to the study protocol. No significant differences between the groups were found for other outcomes.

An RCT<sup>93</sup> (n=104 malnourished care home residents; mean age 89 years) examined oral nutritional supplements versus dietary advice (control). In an intention-to-treat analysis after 12 weeks, quality of life assessed using EuroQol (EQ-5D) (adjusted for baseline quality of life, malnutrition risk, type of care received [nursing or residential]) was significantly higher with oral nutritional supplements than dietary advice. Total energy, protein and the majority of micronutrient intakes were significantly greater in the oral nutritional supplements group.

A crossover RCT<sup>94</sup> (n=28 residents from 5 care homes, aged 65 or over with or at risk of malnutrition) examined the effect of energy-dense oral nutritional supplements (oleic and linoleic acid emulsion enriched with protein and micronutrients; 30 ml 3 times daily for 6 weeks). The intervention periods combined resulted in significantly increased energy intake, weight gain, improved appetite, relative reduction of saturated fatty acids and increase in polyunsaturated fatty acids, increased apolipoprotein A, and reduced serum fibrinogen.

An RCT<sup>95</sup> (n=234 malnourished inpatients; mean age 71 years, median length of stay 10 days) examined whether providing a higher frequency of oral nutritional supplements at a higher frequency during medication rounds would improve intake of supplements. Patients were randomised to oral nutritional

supplements (300 kcal and 12 g protein per 125 ml serving) in 1 of 3 different schemes. Intervention group 1: 125 ml of supplements twice per day during medication rounds at 12 and 17 o'clock. Intervention group 2: 62 ml of supplements 4 times a day during medication rounds at 8, 12, 17 and 20 o'clock. Usual care (control): 125 ml of supplements twice per day in between meals. Follow-up was performed until discharge or until supplements were no longer needed, with a maximum follow-up period of 30 days. For the primary outcome of percentage of patients consuming at least 75% of the prescribed volume of supplements, no significant differences were observed between intervention group 1 and control. However, the percentage of patients consuming at least 75% of prescribed supplements was significantly higher in intervention group 2, with a mean increased intake of 35 ml (84 kcal) per day. The median time supplements were taken for was 5 days (range 1–17).

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

The 2017 surveillance found evidence that oral nutritional supplements appear to improve energy and protein intake, weight, BMI, nutritional status, quality of life, and mortality. Two reviews found that oral nutritional supplements in the community and in hospital appear to be cost saving and cost effective.

This evidence appears to be consistent with current recommendations in CG32 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 oral nutritional supplements.

CG32 does not make recommendations on specialised supplements. A single trial found that a specialised high-protein oral nutritional supplement containing beta-hydroxy-beta-methylbutyrate had no benefit for a composite endpoint of 90-day post-discharge incidence of death or non-elective readmission, and a review found there was little evidence that speciality supplements were beneficial compared to standard versions. This evidence is therefore unlikely to affect the guideline.

There was evidence from a single trial that a higher frequency of a lower volume of supplements during medication rounds increased the compliance of patients taking the supplements. However the trial did not measure any physical or clinical outcomes, and

the evidence is therefore currently unlikely to affect the guideline.

New evidence is unlikely to change guideline recommendations.

### *Oral nutrition support in surgical / injured patients*

#### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Oral nutrition support – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

An RCT<sup>96</sup> (n=295 patients undergoing emergency abdominal surgery) examined early oral feeding (a soft diet within 24 hours after surgery) versus usual postoperative care (a liquid diet commenced upon passage of flatus or stool and then advanced to soft food). No significant difference between groups was seen for the primary endpoint of complication rate. There was a significantly higher rate of vomiting with early oral feeding than usual care, with no differences in nasogastric tube reinsertion. Early oral feeding led to significantly proportionally lower food intake for the first 3 meals than with usual care patients. A postoperative survey revealed significantly more hunger in the usual care group. There were no differences in postoperative ileus or length of hospital stay.

An RCT<sup>97</sup> (n=55 patients undergoing elective colorectal resection surgery) examined a standard postoperative diet plus low-volume high-calorie oral supplements (6 x 60 ml supplements/day [60 ml=200 kcal + 4 g protein]) versus a standard postoperative diet alone (control). There was no significant difference in median preoperative and postoperative handgrip strengths at discharge in either group. The total median daily calorie intake was significantly higher with supplements than control. There was no difference in median number of days to first bowel movement. The median length of hospital stay was significantly shorter with supplements than control.

An open-label, multicentre RCT<sup>98</sup> (n=112 patients with gastric cancer in 8 hospitals) examined an oral elemental diet

(Elemental, comprising amino acids, very little fat, vitamins, trace elements, and dextrin) versus control. The intervention group received 300 kcal of elemental diet plus regular diet for 6–8 weeks after surgery, starting from the day the patient started a soft rice or equivalent diet after surgery, while the control group received regular diet alone. The mean treatment compliance rate in the elemental diet group was 69%. The percentage of body weight loss was significantly less with the elemental diet than control, which was also the case for patients who underwent total gastrectomy. In multivariate analysis, elemental diet, surgery type, and preoperative performance status were independently associated with percentage of body weight loss. No significant differences were observed in the other clinical variables.

A double-blind RCT<sup>99</sup> (n=30 patients with severe thermal burns of more than 20% of total body surface area on the first day in the intensive care unit) examined early and adequate nutrition support with commercially prepared solution via oral or tube feeding versus normal hospital liquid and chow diet, ad libitum (control). The caloric requirement for these patients was calculated according to the Harris-Benedict formula. There was a significant improvement in sequential organ failure assessment score between day 2 and day 9 with nutrition support but not with control. Mean length of stay in hospital was shorter with nutrition support than control (significance not reported in the abstract).

#### **Topic expert feedback**

##### *2017 surveillance*

Topic experts noted the importance of 'prehabilitation' prior to surgery, which includes diet.

#### **Impact statement**

The 2017 surveillance found that early oral feeding within 24 hours caused no additional complications after emergency abdominal surgery, though it led to more vomiting and less hunger. This is consistent with CG32 to

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 patient should be monitored carefully for any signs of nausea or vomiting.

Evidence was also found that oral supplements after gastrointestinal surgery are associated with significantly better calorie intake, reduced postoperative hospital stay, and reduced postoperative weight loss, which is consistent with CG32 to consider peri-operative oral nutrition support for surgical patients who can swallow safely and are malnourished.

CG32 does not make any specific recommendations about nutrition support after burn injury. Although evidence was found that nutritional support in patients with severe burn

can improve sequential organ failure assessment score, this was from 1 trial of 30 patients, and further evidence is needed to confirm findings. The evidence is broadly aligned with CG32 to consider oral nutrition support to improve nutritional intake for people who can swallow safely and are malnourished or at risk of malnutrition.

Topic experts noted the importance of 'prehabilitation' prior to surgery, which includes diet. However no evidence was found on this therefore no impact on CG32 is currently expected, which already recommends considering peri-operative oral nutrition support for surgical patients who can swallow safely and are malnourished.

New evidence is unlikely to change guideline recommendations.

### *Enriched food*

#### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Oral nutrition support – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

A single-blind RCT<sup>100</sup> (n=84 hospitalised patients at nutritional risk from oncology, orthopaedics and urology departments) examined protein-supplemented hospital food versus standard hospital menu (control). For the primary outcome, the number of patients reaching >75% of their energy requirements did not differ significantly between groups, but significantly more patients on supplemented food than control reached >75% of their protein requirements. The number needed to treat for achieving >75% of protein requirements was 3. Supplemented food led to a significantly higher mean intake of energy and protein when adjusted for body weight. Body weight, handgrip strength and length of hospital stay did not differ between groups.

A multicentre RCT<sup>101</sup> (n=175 malnourished older adults from 7 nursing homes; mean age 86 years) examined a standard nursing home diet plus solid oral nutritional supplements (high-protein and high-energy cookies with the texture adapted to edentulous patients; 8 cookies daily – 11.5 g protein, 244 kcal)

versus standard diet alone (control). For the primary outcome, average weight after 6 weeks had increased more with the supplemented cookies than control. Improved weight gain versus control significantly persisted at 1 month and 3 months after the end of the supplementation period. A significant reduction in diarrhoea was also seen with supplements. Subgroup analysis confirmed the positive significant impact of supplementation alone on weight increase, appetite increase and pressure ulcers reduction.

A single-blind RCT<sup>102</sup> (n=47 older patients acutely admitted to hospital) examined ad libitum protein-enriched bread (6.9 g protein/serving) and drinking yoghurt (20 g protein/serving) versus non-enriched bread (3.8 g protein/serving) and yoghurt (7.5 g protein/serving) (control) as part of daily meals. The products were almost isocaloric. Over 3 days, absolute daily protein intake was significantly higher with enriched foods than control. Mean protein intake (g/kg/day) was also significantly higher with enriched food and significantly more patients reached the minimum requirement of 1.2g/kg/day than control. Bread and drinking yoghurt contributed almost equally to the increased intake of protein in the intervention group.

A multicentre RCT<sup>103</sup> (n=68 malnourished residents aged 70–99 years from 8 nursing homes) compared 3 groups: 1) usual breakfast

plus enriched brioche (65 g portion with 12.8 g protein and 180 kcal); 2) usual breakfast plus oral nutritional supplements (200 ml liquid with 14 g protein and 200 kcal); 3) usual breakfast alone. The intervention lasted 12 weeks. The brioche group had significantly higher total energy intakes at days 30 and 90 compared with the supplement and control groups. At the end of the study, significantly more participants in the brioche group had reached the recommended minimum level of protein of 0.8 g/kg/day compared with the supplement and control groups. In addition, between day 0 and day 90 in the brioche group, blood levels of vitamins B2, B6, B9, B12 and D had increased significantly and plasma homocysteine had decreased significantly.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

The 2017 surveillance found that among older patients and/or those with, or at risk of, malnutrition, enriched food increased protein and energy intake and weight. Benefits were also seen for appetite, diarrhoea, and pressure ulcers. This evidence is consistent with CG32 to 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 can include fortified food with protein, carbohydrate and/or fat, plus minerals and vitamins, and snacks.

New evidence is unlikely to change guideline recommendations.

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

### Recommendations in this section of the guideline

In this guideline, enteral tube feeding refers to the delivery of a nutritionally complete feed (as specified in section 1.4) via a tube into the stomach, duodenum or jejunum.

#### Indications

- 1.7.1 Healthcare professionals should consider enteral tube feeding in people who are malnourished or at risk of malnutrition as defined in 1.3.1 and 1.3.2, respectively, and have:
- inadequate or unsafe oral intake, and
  - a functional, accessible gastrointestinal tract.
- 1.7.2 Enteral tube feeding should not be given to people unless they meet the criteria in 1.7.1, or they are taking part in a clinical trial.
- 1.7.3 Enteral tube feeding should be stopped when the patient is established on adequate oral intake.

#### Surgical patients

- 1.7.4 Surgical patients who are: malnourished, as defined in 1.3.1, and meet the criteria in 1.7.1, and are due to undergo major abdominal procedures, should be considered for pre-operative enteral tube feeding.
- 1.7.5 General surgical patients should not have enteral tube feeding within 48 hours post-surgery unless they meet the criteria in 1.7.1.

#### Route of access

- 1.7.6 People in general medical, surgical and intensive care wards who meet the criteria in 1.7.1 should be fed via a tube into the stomach unless there is upper gastrointestinal dysfunction.
- 1.7.7 People who meet the criteria in 1.7.1, with upper gastrointestinal dysfunction (or an inaccessible upper gastrointestinal tract) should be considered for post-pyloric (duodenal or jejunal) feeding.
- 1.7.8 Gastrostomy feeding should be considered in people likely to need long-term (4 weeks or more) enteral tube feeding.

- 1.7.9 Percutaneous endoscopic gastrostomy (PEG) tubes which have been placed without apparent complications can be used for enteral tube feeding 4 hours after insertion.

### People with dysphagia

- 1.7.10 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.

### Mode of delivery

- 1.7.11 For people being fed into the stomach, bolus or continuous methods should be considered, taking into account patient preference, convenience and drug administration.
- 1.7.12 For people in intensive care, nasogastric tube feeding should usually be delivered continuously over 16–24 hours daily. If insulin administration is needed it is safe and more practical to administer feeding continuously over 24 hours.

### Motility agents

- 1.7.13 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.
- 1.7.14 People in other acute care settings who have delayed gastric emptying and are not tolerating enteral tube feeding should also be offered a motility agent unless there is a pharmacological cause that can be rectified or suspicion of gastrointestinal obstruction.
- 1.7.15 If delayed gastric emptying is severely limiting feeding into the stomach, despite the use of motility agents, post-pyloric enteral tube feeding and/or parenteral nutrition should be considered.

### Management of tubes

- 1.7.16 People requiring enteral tube feeding should have their tube inserted by healthcare professionals with the relevant skills and training.
- 1.7.17 The position of all nasogastric tubes should be confirmed after placement and before each use by aspiration and pH graded paper (with X-ray if necessary) as per the advice from the National Patient Safety Agency (NPSA 2005). Local protocols should address the clinical criteria that permit enteral tube feeding. These criteria include how to proceed when the ability to make repeat checks of the tube position is limited by the inability to aspirate the tube, or the checking of pH is invalid because of gastric acid suppression.
- 1.7.18 The initial placement of post-pyloric tubes should be confirmed with an abdominal X-ray (unless placed radiologically). Agreed protocols setting out the necessary clinical checks need to be in place before this procedure is carried out.

## Surveillance decision

This section of the guideline should not be updated.

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### *Enteral nutrition support – evidence identified prior to current 2017 surveillance review*

#### **2-year surveillance summary**

Update not required after review of evidence.

#### **5-year surveillance summary**

Sixteen studies<sup>104-119</sup> 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 volumes than the incremental flow rate<sup>105</sup>.

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) and found that delayed feeding resulted in a longer stay in ICU<sup>114</sup>, 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 diarrhoea and stomach cramps<sup>116</sup>.

One study assessed the effect of tube placement on intensive care unit patients (post pyloric versus nasogastric)<sup>117</sup> 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<sup>107</sup> 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 with regards to enteral versus parenteral nutrition in various clinical settings including patients who had undergone gastrointestinal surgery and patients with severe acute pancreatitis<sup>106,109-112</sup>; one found that enteral nutrition resulted in a bigger decline in quality of life than parenteral nutrition, yet parenteral nutrition resulted in more complications<sup>109</sup>, another study found greater patient satisfaction with enteral nutrition<sup>110</sup> and another study found decreased mortality in enteral nutrition<sup>112</sup>. One study found that motilin and cholecystokinin were increased in the enteral nutrition group, and that they had improve electrogastrography post-operatively<sup>111</sup>.

One study looked at enteral nutrition vs parenteral + enteral nutrition in patients undergoing pancreoduodectomy and found that there was no difference between groups with regards to mortality, but the 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<sup>113</sup>.

One study looked at early enteral nutrition versus early natural nutrition in pancreoduodectomy patients<sup>108</sup>, and found that early enteral nutrition received more energy in the first 5 days post-operatively than the early natural nutrition group, there were also more complications in the early natural nutrition group.

One study<sup>118</sup> found that in upper gastrointestinal fistula and leakage, a total

parenteral nutrition stage, followed by a parental + enteral nutrition stage, and finally a total enteral nutrition stage is better than a surgical operation plus total parenteral nutrition.

One study<sup>119</sup> found that enteral nutrition is better than total parenteral nutrition in the prevention of pancreatic necrotic infection in severe acute pancreatitis.

One study in trauma patients looked at partial parenteral versus enteral nutrition and found that the parenteral nutrition group received more protein and calories and had higher albumin and transferrin concentrations<sup>104</sup>.

There are two trial-based economic evaluations<sup>110,115</sup> which favoured enteral over parenteral nutrition in terms of cost, without finding differences in clinical outcomes. This evidence supports the existing recommendation.

### **Evidence Update 2013**

Five studies<sup>120-124</sup> relating to enteral tube feeding in hospital and the community were identified.

The key point from one of the studies<sup>123</sup> was that acupuncture may have benefits over standard motility drugs in treating delayed gastric emptying in critical care. However, this was a very small (30 participants), single-blinded trial, and the Evidence Update contended that limitations of the evidence mean that it is unlikely to have an impact on CG32 and further research is needed.

### **8-year surveillance summary**

Three studies<sup>125-127</sup> on enteral tube feeding were identified; findings of studies were broadly consistent with guideline recommendations.

It was also noted that there was a large ongoing multicentre UK RCT (the NIHR HTA-sponsored [CALORIE trial](#)) expected to report in December 2015, and it would be appropriate to wait for the publication of the results of the trial to look at this again

### **2017 surveillance summary**

See sections below where the evidence is categorised by sub-topic.

### **Topic expert feedback**

#### *8-year surveillance*

One guideline committee member pointed out that there has been further guidance around nasogastric feeding tube safety.

## Impact statement

At 8-year surveillance, no new evidence was identified which would change the direction of current guideline recommendations. It was noted that it would be appropriate to await the results of a large ongoing UK multi-centre study (the CALORIE trial) that is due for completion in December 2015.

[Note: The results of the CALORIE trial have now been published and are summarised in the below section in this document: 'Enteral tube feeding in hospital and the community: Enteral versus parenteral nutrition support']

The point around safety of nasogastric tube feeding raised by a guideline committee member was also raised at the last review in 2011; it was addressed as follows: '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 National Patient Safety Association safety warning. 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'.

The evidence from the 2017 surveillance has been examined according to sub-topic and is presented, along with any decisions on impact on the guideline, in the sections below.

New evidence is unlikely to change guideline recommendations.

## Post-pyloric feeding

### 2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update

#### 5-year surveillance review

An RCT<sup>117</sup> (n=104) compared early post-pyloric versus early gastric feeding to meet nutritional targets in ventilated intensive care patients. This RCT was included in the Cochrane review<sup>128</sup> which is discussed below.

#### 2017 surveillance summary

A Cochrane review<sup>128</sup> of 14 RCTs (n=1109) evaluated the effectiveness and safety of post-pyloric feeding versus gastric feeding for critically ill adults who require enteral tube feeding. Primary outcomes were pneumonia, mortality, percentage of total nutrition delivered, and time required to achieve the full nutritional target. From the meta-analyses, post-pyloric feeding was significantly associated with low rates of pneumonia compared with gastric tube feeding (moderate quality evidence). There was a significant increase in the percentage of total nutrient delivered to the patient by post-pyloric feeding (low-quality evidence). There were no differences in duration of mechanical ventilation or in mortality (moderate quality evidence). Intensive care unit length of stay was similar between the 2 groups. The effect on the time required to achieve the full nutrition target was uncertain (very low-quality evidence). There was no increase in the rate of complications during insertion or maintenance of the tube in the post-pyloric group (low quality

evidence). Risk of bias was generally low in most studies, and review authors expressed concern regarding lack of blinding of the caregiver in most trials.

A Cochrane review<sup>129</sup> of 4 RCTs (n=204) examined the prokinetic agent metoclopramide for post-pyloric placement of naso-enteral feeding tubes in adults needing enteral nutrition. The included trials compared metoclopramide with placebo (2 trials) or with no intervention (2 trials). Metoclopramide was investigated at doses of 10 mg (2 trials) and 20 mg (2 trials). There was no significant difference between metoclopramide versus placebo or no intervention administered to promote tube placement. Metoclopramide doses of 10 mg and 20 mg were equally ineffective in facilitating post-pyloric intubation when compared with placebo or no intervention.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

The 5-year surveillance found an RCT which was considered by the Cochrane review, and its impact is therefore discussed as part of the Cochrane review below.

The 2017 surveillance found a Cochrane review suggesting that in critically ill adults who require enteral tube feeding, post-pyloric feeding was associated with less pneumonia (moderate quality evidence) and an increased

amount of nutrition delivered with no increase in complications (low quality evidence), but did not affect other outcomes such as duration of mechanical ventilation, mortality and length of stay. When the guideline was originally developed, it was noted in the full guideline that clinical studies failed to show any clear advantage in feeding post-pylorically. It was further noted that the gastric route is usually technically simpler and in most circumstances achieves similar nutrient delivery with similar risks. The authors of the current Cochrane review agreed with the technical issues, noting that the placement of the post-pyloric tube can present challenges; the procedure is technically difficult, requiring expertise and sophisticated radiological or endoscopic assistance.

This new evidence does not fully align with the recommendation in CG32 (which was based on guideline committee consensus) that people who meet the criteria for enteral feeding, with upper gastrointestinal dysfunction (or an

inaccessible upper gastrointestinal tract) should be considered for post-pyloric (duodenal or jejunal) feeding. Although the evidence suggests a wider group than just those with gastrointestinal issues may benefit from post-pyloric feeding, the benefits seen for pneumonia were not seen in the other outcomes such as duration of mechanical ventilation, mortality and length of stay. Given the Cochrane authors' comments about the technical difficulties, the evidence is therefore currently unlikely to have an impact on CG32.

A second review found by the 2017 surveillance showed that metoclopramide did not assist post-pyloric placement of feeding tubes. This evidence is unlikely to affect the guideline which does not discuss the use of metoclopramide for tube placement.

New evidence is unlikely to change guideline recommendations.

### *Enteral versus parenteral nutrition support*

#### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Enteral tube feeding – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

A multicentre parallel-group RCT<sup>130</sup> (CALORIES trial, National Institute for Health Research Health Technology Assessment; n=2400 critically ill patients from critical care units in 33 NHS hospitals in England) compared the clinical and cost-effectiveness of 5 days of early nutritional support via parenteral versus enteral route. For the first primary outcome, there was no significant difference in all-cause mortality at 30 days between patients assigned to the parenteral route and the enteral route. For the second primary outcome, cost-effectiveness measured by incremental net benefit at 1 year for the parenteral versus the enteral route was negative (–£1320, 95% CI –£3709 to £1069). The probability that the parenteral route is more cost-effective is <20%. Significantly fewer patients in the parenteral than the enteral group experienced episodes of hypoglycaemia and vomiting. There were no significant differences in the

15 other secondary outcomes and no significant interactions with pre-specified subgroups.

A systematic review and meta-analysis<sup>131</sup> of 36 RCTs (n=not reported in the abstract) examined enteral and parenteral nutrition in cancer patients. Studies were included if over half of the patient population had cancer. Parenteral nutrition resulted in significantly more infection than enteral nutrition. There was no difference between the groups for any other endpoints (nutrition support complications, major complications or mortality).

An RCT<sup>132</sup> (n=120 patients with burn-induced invasive fungal infection) examined early enteral nutrition versus parenteral nutrition for 14 days. As the treatment progressed, the levels of serum transferrin, albumin and total protein of the enteral group were significantly higher than those of the parenteral group, while the levels of serum endotoxin and D-lactic acid were significantly lower in the enteral group. After treatment, the expression levels of IL-6 and TNF-alpha were decreased in the enteral group, which were significantly different from those of the parenteral group. During treatment, the incidence rates of complications such as abdominal distension, diarrhoea, sepsis, nausea, vomiting and gastric retention

were similar. The mean wound surface healing time was significantly shorter in the enteral than the parenteral group.

An RCT<sup>133</sup> (n=50 patients who underwent thoroscopic oesophagectomy for oesophageal cancer) examined enteral versus parenteral nutrition. The rate of weight loss at postoperative day 14 was significantly lower in the enteral than parenteral group. Prealbumin levels at postoperative day 10 did not differ significantly between groups. However, incidence of postoperative pneumonia was higher in the parenteral than the enteral group (significance not reported in the abstract).

An RCT<sup>134</sup> (n=9 patients) examined enteral (nasogastric) versus parenteral nutrition support after allogeneic haematopoietic progenitor cell transplantation. Patients with severe gastro-intestinal toxicity, including severe mucositis, were excluded from randomisation. If patients did not tolerate the type of feeding given they were swapped to the alternate route. All patients randomised to enteral nutrition required changing to parenteral nutrition due to gastro-intestinal intolerance. None of the patients receiving parenteral nutrition required changing to enteral nutrition.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

The 2017 surveillance found that comparisons of enteral with parenteral nutrition support showed no differences in mortality or complications, but that enteral nutrition was cheaper, and associated with less infection, a shorter wound healing time, and lower rate of weight loss. Enteral nutrition was however associated with more episodes of hypoglycaemia and vomiting.

Overall, the results seem consistent with CG32 to offer early nutrition support via the enteral route if there is inadequate or unsafe oral intake, and parental support where there is inadequate or unsafe oral and/or enteral nutritional intake.

A single very small trial of patients who had undergone allogeneic haematopoietic progenitor cell transplantation found that due to the significant gastrointestinal toxicity, enteral nutrition was not feasible to commence when oral intake became inadequate. This evidence is also consistent with the recommendation to offer early nutrition support via the enteral route if there is inadequate or unsafe oral intake, and parental support where there is inadequate or unsafe oral and/or enteral nutritional intake.

New evidence is unlikely to change guideline recommendations.

### *Enteral nutrition support in surgical patients*

#### 2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update

See 'Enteral tube feeding – evidence identified prior to current 2017 surveillance review' above for details.

#### 2017 surveillance summary

A systematic review and meta-analysis<sup>135</sup> of 15 RCTs (n=3831) examined nutritional support in perioperative malnourished patients. Most trials were of enteral nutrition. Compared with control, nutrition support was significantly more effective in decreasing the incidence of infectious and non-infectious complications, and shortening the length of hospital stay. Moreover, the incidence of infectious complications in the immune nutrition group was significantly lower than that in the standard nutrition group. However, hospital costs and

postoperative mortality between nutrition support and control were not significantly different.

A multicentre RCT<sup>136</sup> (n=109 malnourished patients from 5 sites requiring surgery for suspected advanced epithelial ovarian cancer) examined early enteral feeding (intraoperative nasojejunal tube placement and enteral feeding until adequate oral intake could be maintained) versus standard postoperative diet as tolerated (control). No significant difference was found in the primary outcome of quality life between the groups at either 6 weeks postoperatively or 30 days after the third cycle of chemotherapy. There was a trend towards better nutritional status in patients who received the intervention but the differences did not reach statistical significance except for the intention-to-treat analysis at 7 days postoperatively.

An RCT<sup>137</sup> (n=75 older female patients with a hip fracture admitted to orthopaedic clinics)

examined postoperative nutrition with either a specialised enteral product (3 g calcium beta-hydroxy-beta-methylbutyrate, 1000 IU vitamin D, 36 g protein) or standard postoperative nutrition. Specialised supplements demonstrated significant benefits over control in terms of shorter wound-healing time, number of patients mobile on days 15 and 30, and muscle strength on day 30.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

The 2017 surveillance found a review comprising mainly studies of enteral nutrition suggesting that perioperative nutritional support in malnourished patients decreased the incidence of infectious and non-infectious complications, shortened length of hospital stay, and reduced the incidence of infectious

complications. A single trial with smaller numbers than the review found no difference in quality of life. Overall the evidence is broadly aligned with CG32 to consider enteral tube feeding in people who are malnourished or at risk of malnutrition and have: inadequate or unsafe oral intake, and a functional, accessible gastrointestinal tract.

A further single trial of a specialised enteral product in patients with hip fracture demonstrated significant benefits over control in terms of shorter wound-healing time, mobility and muscle strength. However further evidence may be needed before any specific impact on CG32 (which does not discuss specific enteral formulations) can be considered.

New evidence is unlikely to change guideline recommendations.

### *Percutaneous endoscopic gastrostomy (PEG) versus nasogastric tube (NGT) feeding in dysphagia*

#### 2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update

See 'Enteral tube feeding – evidence identified prior to current 2017 surveillance review' above for details.

#### 2017 surveillance summary

A Cochrane review<sup>138</sup> of 11 RCTs (n=735) examined PEG versus NGT feeding for adults with swallowing disturbances or dysphagia and indications for nutritional support, with any underlying diseases. Meta-analysis indicated that the primary outcome of intervention failure (e.g. feeding interruption, blocking or leakage of the tube, no adherence to treatment) occurred significantly less with PEG than NGT (8 RCTs, n=408, low quality evidence). There was no statistically significant difference between the groups for meta-analyses of the secondary outcomes of mortality (9 RCTs, n=644 participants, very low quality evidence), overall reports of any adverse event at any follow-up time point (6 RCTs, n=597, moderate quality evidence), specific adverse events including pneumonia (aspiration) (7 RCTs, n=645, low quality evidence), or for the meta-analyses of the secondary outcome of nutritional status including weight change from baseline, and mid-arm circumference at

endpoint, although there was evidence in favour of PEG for meta-analyses of mid-arm circumference change from baseline (2 RCTs, n=115 participants), and levels of serum albumin were higher in the PEG group (n=107). For meta-analyses of the secondary outcomes of time on enteral nutrition, there was no statistically significant difference (2 RCTs, n=119). For meta-analyses of quality of life measures (EuroQol) outcomes in 2 studies with 133 participants, for inconvenience, discomfort, altered body image, and social activities, the intervention significantly favoured PEG. However, there were no significant differences between the groups for pain, ease of learning to use, or the secondary outcome of length of hospital stay (2 RCTs, n=381).

A systematic review and meta-analysis<sup>139</sup> of 9 studies including 2 RCTs (n=847) examined PEG versus NGT feeding in older individuals with non-stroke dysphagia. Pooled analysis indicated no significant difference in the risk of pneumonia and overall complications between PEG and NGT feeding. A meta-analysis was not possible for mortality and nutritional outcomes, but 3 studies suggested improved mortality outcomes with PEG feeding while 2 out of 3 studies reported PEG feeding to be better from a nutritional perspective (significance not reported in the abstract).

A Cochrane review<sup>140</sup> examined PEG versus percutaneous radiological gastrostomy for

swallowing disturbances. No relevant RCTs were identified. The authors noted that the large body of evidence in this field comes from retrospective and non-randomised controlled studies and case series.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

The 2017 surveillance found 2 reviews of PEG versus NGT. In the first, PEG was associated with less intervention failure than NGT but with no difference in mortality, adverse events or nutritional status. In the second review, the authors stated that firm conclusions could not be derived on whether PEG is beneficial over NGT as previously published literature were unclear or had a high risk of bias. They suggested that a well-designed and adequately powered RCT is needed. This evidence is currently unlikely to affect the recommendation in CG32 that 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.

A third review of PEG versus percutaneous radiological gastrostomy found no relevant RCTs. The authors stated that PEG and percutaneous radiological gastrostomy are effective for long-term enteral nutritional support in selected individuals, though current evidence is insufficient to recommend one technique over the other. CG32 does not currently make recommendations about percutaneous radiological gastrostomy and the lack of evidence in this technique means the guideline is currently unlikely to be affected.

New evidence is unlikely to change guideline recommendations.

### *Enteral nutrition versus usual care*

#### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Enteral tube feeding – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

A cluster RCT<sup>141</sup> (n=1059 mechanically ventilated, critically ill patients from 18 intensive care units) examined enhanced protein-energy provision via the enteral route plus a nursing educational intervention versus usual care (control). For the primary outcome, the proportion of prescribed protein and energy delivered by enteral nutrition was greater in the intervention sites compared to the control sites. Significant adjusted absolute mean differences between groups for protein and energy were seen in favour of intervention sites. The intervention sites had a similar improvement in protein and calories when appropriate parenteral nutrition was added to enteral

sources. Average time from intensive care unit admission to start of enteral nutrition did not differ significantly between groups. Complication rates were no different between the two groups.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

The 2017 surveillance found enteral feeding of critically ill patients led to increased protein and calorie intake with no difference in complication rates. The evidence appears to be aligned with CG32 to consider enteral tube feeding in people who are malnourished or at risk of malnutrition and have: inadequate or unsafe oral intake, and a functional, accessible gastrointestinal tract.

New evidence is unlikely to change guideline recommendations.

## *Nasoenteric tube versus jejunostomy*

### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Enteral tube feeding – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

An RCT<sup>142</sup> (n=59 patients who underwent oesophagectomy, total gastrectomy, or pancreaticoduodenectomy for upper gastrointestinal tract neoplasms) examined enteral nutrition via nasoenteric tube versus jejunostomy. The median length of enteral therapy use did not differ significantly between groups. The nasoenteric group required introduction of parenteral therapy significantly more frequently than the jejunostomy group. Complications related to the enteral route did not differ significantly between groups. In the nasoenteric group, there were 4 losses and 4 tube obstructions. In the jejunostomy group, there were 2 losses, 4 obstructions, and 2 cases of leakage around the tube. In the latter group, patients who underwent therapy for a longer time had significantly more tubal complications and longer intensive care unit and hospital stays.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

The 2017 surveillance found that in patients who underwent surgery for upper gastrointestinal tract neoplasms, nasoenteric tube and jejunostomy were associated with a similar number of complications, but jejunostomy more frequently avoided the need for parenteral nutrition. CG32 does not specifically discuss jejunostomy, and no evidence for jejunostomy versus nasoenteric tube was considered when the guideline was developed. The guideline recommends that people who meet the guideline criteria for enteral feeding, with upper gastrointestinal dysfunction (or an inaccessible upper gastrointestinal tract) should be considered for post-pyloric (duodenal or jejunal) feeding. It further recommends that gastrostomy feeding should be considered in people likely to need long-term (4 weeks or more) enteral tube feeding. The evidence for jejunostomy is from a single trial and further evidence may be needed to confirm results before an impact can be considered.

New evidence is unlikely to change guideline recommendations.

## *Management of tubes*

### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Enteral tube feeding – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

No relevant evidence was identified.

#### **Topic expert feedback**

##### *2017 surveillance*

Topic experts stated that the nasogastric placement section is weak given the National Patient Safety Agency alerts, and emphasis on patient safety, and believed this needs to be updated. They further noted the importance of good nursing care and education to reduce complications of enteral feeding (nasogastric tube insertion).

#### **Impact statement**

CG32 currently recommends that 'The position of all nasogastric tubes should be confirmed after placement and before each use by aspiration and pH graded paper (with X-ray if necessary) as per the advice from the National Patient Safety Agency (NPSA 2005)'

The 2005 advice currently cross-referred to by CG32 was [updated](#) in 2011 (though it states 'This Alert does not change the advice given in Patient Safety Alert 05 that pH testing remains the first line test, and x-ray checking remains the second line test.'). Further alerts have also been issued ([Rapid Response Report in 2011](#), and Patient Safety Alerts in [2013](#) and [2016](#)).

The guideline will be amended to refer to the latest Patient Safety Alerts, which should be referred to for detailed advice on reducing the harm caused by misplaced nasogastric feeding tubes.

Topic experts noted the importance of good nursing care and education. CG32 already recommends that 'People requiring enteral tube feeding should have their tube inserted by healthcare professionals with the relevant skills

and training.' No impact is therefore anticipated.

New evidence is unlikely to change guideline recommendations.

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

### Recommendations in this section of the guideline

#### Indications

- 1.8.1 Healthcare professionals should consider parenteral nutrition in people who are malnourished or at risk of malnutrition as defined in 1.3.1 and 1.3.2, respectively, and meet either of the following criteria:
- inadequate or unsafe oral and/or enteral nutritional intake
  - a non-functional, inaccessible or perforated (leaking) gastrointestinal tract.

#### Prescription

- 1.8.2 Parenteral nutrition should be introduced progressively and closely monitored, usually starting at no more than 50% of estimated needs for the first 24–48 hours. Parenteral nutrition can be withdrawn once adequate oral or enteral nutrition is tolerated and nutritional status is stable. Withdrawal should be planned and stepwise with a daily review of the patient's progress.
- 1.8.3 Patients who need parenteral nutrition should have their nutritional requirements determined by healthcare professionals with the relevant skills and training in the prescription of nutrition support. Before using most parenteral nutrition products, micronutrients and trace elements should be added and additional electrolytes and other nutrients may also be needed. Additions should be made under appropriate pharmaceutically controlled environmental conditions before administration.
- 1.8.4 Parenteral nutrition should be stopped when the patient is established on adequate oral and/or enteral support. There is no minimum length of time for the duration of parenteral nutrition.

#### Surgical patients

- 1.8.5 Healthcare professionals should consider supplementary peri-operative parenteral nutrition in malnourished surgical patients who meet the criteria in 1.8.1.
- 1.8.6 Peri-operative supplementary parenteral nutrition should not be given to surgical patients unless they meet the criteria set out in 1.8.1.
- 1.8.7 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.

#### Route of access

- 1.8.8 In hospital, parenteral nutrition can be given via a dedicated peripherally inserted central catheter as an alternative to a dedicated centrally placed central venous catheter. A free dedicated lumen in a multi-lumen centrally placed catheter may also be used.
- 1.8.9 Administration of parenteral nutrition via a peripheral venous catheter should be considered for patients who are likely to need short-term parenteral nutrition (less than 14 days) who have no need for central access for other reasons. Care should be taken in catheter choice, and in attention to pH, tonicity and long-term compatibility of the parenteral nutrition formulations in order to avoid administration or stability problems.
- 1.8.10 Tunnelling subclavian lines is recommended for long-term use (more than 30 days).
- 1.8.11 Catheters do not have to be tunnelled for short-term use (less than 30 days).

#### Mode of delivery

- 1.8.12 Continuous administration of parenteral nutrition should be offered as the preferred method of infusion in severely ill people who require parenteral nutrition.
- 1.8.13 Cyclical delivery of parenteral nutrition should be considered when using peripheral venous cannulae with planned routine catheter change.
- 1.8.14 A gradual change from continuous to cyclical delivery should be considered in patients requiring parenteral nutrition for more than 2 weeks.

#### Management of catheters

- 1.8.15 Only healthcare professionals competent in catheter placement should be responsible for the placement of catheters and they should be aware of the importance of monitoring and managing these safely.<sup>[12]</sup>

[12] Infection control: prevention of healthcare-associated infection in primary and community care. NICE Clinical Guideline 2 (2003).

#### Surveillance decision

This section of the guideline should not be updated.

#### *Parenteral nutrition – evidence identified prior to current 2017 surveillance review*

##### **2-year surveillance summary**

Update not required after review of evidence.

##### **5-year surveillance summary**

##### **Evidence Update 2013**

No relevant evidence was identified.

##### **8-year surveillance summary**

Two studies<sup>143,144</sup> on parenteral nutrition were identified. The first study<sup>143</sup> is the report of the EPaNIC trial that was identified at the 5-year review in 2011. The study compared early (within 24-48 hours, European guideline) versus late (after 7 days, American/Canadian guideline) initiation of parenteral nutrition when enteral nutrition fails to reach a caloric target and concluded that late initiation of parenteral nutrition was associated with faster recovery and fewer complications, as compared with early initiation.

The other study<sup>144</sup> aimed to assess outcomes of parenteral nutrition when the NICE guidance was adhered to. It concluded that implementing the guidelines may not be enough to reduce mortality and other outcomes. The authors also posited that in view of the fact that the guideline recommendations were mostly based on Grade D evidence due to absence of RCTs, new

interventions or changes in clinical practice should be considered to optimise the impact of parenteral nutrition on mortality.

It was also noted that there was a large ongoing multicentre UK RCT (the NIHR HTA-sponsored [CALORIE trial](#)) expected to report in December 2015, and it would be appropriate to wait for the publication of the results of the trial to look at this again.

##### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

##### **Impact statement**

At 8-year surveillance, no new evidence was identified which would change the direction of current guideline recommendations. It was noted that it would be appropriate to await the results of a large ongoing UK multi-centre study (the CALORIE trial) that is due for completion in December 2015.

[Note: The results of the CALORIE trial have now been published and are summarised in the above section in this document: 'Enteral tube feeding in hospital and the community: Enteral versus parenteral nutrition support']

New evidence is unlikely to change guideline recommendations.

### *Permissive parenteral underfeeding*

#### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Parenteral nutrition – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

A single-blinded RCT<sup>145</sup> (n=50 consecutive patients requiring short-term parenteral nutritional support) examined hypocaloric feeding (60% of estimated requirements) versus normocaloric feeding (100% of estimated requirements). Hypocaloric feeding was associated with significantly fewer septic complications (primary outcome), a significantly lower incidence of systemic inflammatory response syndrome, and significantly fewer feed related complications.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

The 2017 surveillance found that permissive underfeeding in patients requiring short term parenteral nutrition appears to be safe and may result in reduced septic and feed-related complications. This evidence appears to be consistent with CG32 that parenteral nutrition should be introduced progressively and closely monitored, usually starting at no more than 50% of estimated needs for the first 24–48 hours.

New evidence is unlikely to change guideline recommendations.

### *Insulin therapy in patients with traumatic brain injury on parenteral nutrition*

#### **2-year, 5-year and 8-year surveillance summaries, and 2013 Evidence Update**

See 'Parenteral nutrition – evidence identified prior to current 2017 surveillance review' above for details.

#### **2017 surveillance summary**

An open-label pilot RCT with blinded endpoint assessment<sup>146</sup> (n=26 traumatic brain injury patients on parenteral nutrition, without diabetes, pancreatitis, liver disease, or kidney complication) examined intensive insulin therapy (continuous insulin infusion to maintain glucose levels between 4.4 mmol/litre [80 mg/100 ml] and 6.6 mmol/litre [120 mg/100 ml]) versus conventional glucose control (no insulin unless glucose levels were greater than 10 mmol/litre [ $>180$  mg/100 ml]). Mean glucose concentration was significantly lower with intensive than conventional therapy. No primary outcome of a hypoglycemic episode occurred in either group. In the intensive group, triglyceride and C-reactive protein were

significantly decreased, and magnesium and phosphorus were significantly lower.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### **Impact statement**

The 2017 surveillance found some benefits of intensive insulin therapy over conventional glucose control in patients with traumatic brain injury on parenteral nutrition. CG32 does not directly discuss insulin therapy in parenteral nutrition (though in the monitoring section, it does note that glucose intolerance is common, and good glycaemic control is necessary). However, the new evidence is from a small pilot study whose authors stated that further data is needed to reach definitive conclusions, therefore the evidence is currently unlikely to affect the guideline.

New evidence is unlikely to change guideline recommendations.

## Supporting patients in the community

### Recommendations in this section of the guideline

- 1.9.1 Healthcare professionals should ensure that patients having enteral or parenteral nutrition in the community and their carers:
- are kept fully informed and have access to appropriate sources of information in formats, languages and ways that are suited to an individual's requirements. Consideration should be given to cognition, gender, physical needs, culture and stage of life of the individual
  - have the opportunity to discuss diagnosis, treatment options and relevant physical, psychological and social issues
  - are given contact details for relevant support groups, charities and voluntary organisations.

#### **Enteral tube feeding**

- 1.9.2 All people in the community having enteral tube feeding should be supported by a coordinated multidisciplinary team, which includes dietitians, district, care home or homecare company nurses, GPs, community pharmacists and other allied healthcare professionals (for example, speech and language therapists) as appropriate. Close liaison between the multidisciplinary team and patients and carers regarding diagnoses, prescription, arrangements and potential problems is essential.
- 1.9.3 Patients in the community having enteral tube feeding and their carers should receive an individualised care plan which includes overall aims and a monitoring plan.
- 1.9.4 Patients in the community having enteral tube feeding and their carers, should receive training and information from members of the multidisciplinary team on:
- the management of the tubes, delivery systems and the regimen, outlining all procedures related to setting up feeds, using feed pumps, the likely risks and methods for troubleshooting common problems and be provided with an instruction manual (and visual aids if appropriate)
  - both routine and emergency telephone numbers to contact a healthcare professional who understands the needs and potential problems of people on home enteral tube feeding
  - the delivery of equipment, ancillaries and feed with appropriate contact details for any homecare company involved.

#### **Parenteral nutrition**

- 1.9.5 All people in the community having parenteral nutrition should be supported by a co-ordinated multidisciplinary team, which includes input from specialist nutrition nurses, dietitians, GPs, pharmacists and district and/or homecare company nurses. Close liaison between the multidisciplinary team and patients and carers regarding diagnoses, prescription, arrangements and potential problems is essential.
- 1.9.6 People in the community having parenteral nutrition and their carers should receive an individualised care plan which includes overall aims and a monitoring plan.
- 1.9.7 People in the community having parenteral nutrition and their carers should receive training and information from members of the multidisciplinary team on:
- the management of the delivery systems and the regimen, outlining all procedures related to setting up feeds, using feed pumps, the likely risks and methods for troubleshooting common problems and be provided with an instruction manual (and visual aids if appropriate)
  - routine and emergency telephone numbers to contact a healthcare professional with the relevant competencies (specialist nutrition nurse, pharmacist)
  - the arrangements for the delivery of equipment, ancillaries and feed with appropriate contact details for any homecare company involved.

## Surveillance decision

This section of the guideline should not be updated.

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### *Nutritional interventions (other than enteral / parenteral nutrition) for older people living in the community*

#### **2-year surveillance summary**

Update not required after review of evidence.

#### **5-year surveillance summary**

No relevant evidence was identified.

#### **Evidence Update 2013**

No relevant evidence was identified.

#### **8-year surveillance summary**

No relevant evidence was identified.

#### **2017 surveillance summary**

##### *Home-based physical training and nutritional intervention programme*

An RCT<sup>147</sup> (n=80 prefrail and frail community-dwelling older people; mean age 83 years) examined a home-based and volunteer-administered physical training and nutritional intervention programme versus a social support intervention (control). The community-dwelling older persons in both groups were visited twice a week by trained nonprofessional volunteers. In the physical training/nutrition group, both the buddies and older persons performed 6 strength exercises within a circuit training session and discussed nutrition-related aspects. The active control group had the opportunity to perform cognitive training in addition to the social contact. Significant improvements in the Mini Nutritional Assessment-long form score and the Health, Ageing and Retirement in Europe-Frailty Instrument for Primary Care score were observed in the physical training/nutrition group after 12 weeks. In both groups, the prevalence of impaired nutritional status, and prevalence of frailty, decreased significantly by a similar amount in both groups. The presence of impaired nutritional status at baseline was independently significantly associated with greater changes in the nutritional and frailty status after 12 weeks.

##### *Tailored nutritional guidance with home visits*

An RCT<sup>148</sup> (n=78 people [40% at risk for malnutrition] with Alzheimer's disease living with a spouse; mean age 77 years) examined tailored nutritional guidance with home visits

during one year versus a written guide about nutrition in older adults (control). No difference in the primary outcome of weight change was found between the groups. At 12 months, protein intake and health-related quality of life went up in the intervention group and down in the control group, and differed significantly between the groups (adjusted for baseline value, age, sex, Mini-Mental State Examination and BMI). Dimensions of health-related quality of life that differed included mental functioning, breathing, usual activities and depression. The fall rate was lower in the intervention than control group (adjusted for age, sex and Mini-Mental State Examination).

##### *Referral to a dietitian*

An RCT<sup>149</sup> (n=146 community-dwelling undernourished individuals aged >65 years in primary care) examined effects of a dietetic treatment (referral to and treatment by a trained dietitian) versus control (no referral). After 6 months, no treatment effect was found on the primary outcomes of body weight, physical performance, and handgrip strength. Furthermore, no treatment effect was found for the secondary outcomes (energy intake, protein intake and fat-free mass). Predefined subgroup analyses showed a treatment effect on body weight in physically active participants and not in inactive participants.

A cost effectiveness analysis<sup>150</sup> of the above RCT<sup>149</sup> was also performed. After 6 months, no statistically significant differences were found between the dietetic treatment and control in total costs. The incremental cost-utility ratio for quality-adjusted life years (QALYs) was not interpretable. The incremental cost-effectiveness ratio for body weight gain was 2111. The probability that dietetic treatment is cost-effective compared with usual care was 0.78 for a ceiling ratio of €5000 for body weight and 0.06 for a ceiling ratio of €20,000 for QALY. The authors concluded that dietetic treatment in older, undernourished, community-dwelling individuals was not cost-effective compared with usual care.

## Topic expert feedback

### 2017 surveillance

Topic experts noted a lack of emphasis in the guideline on frailty sarcopenia and nutrition especially in the older adult population.

Topic experts also noted that like in America, our nutrition teams are focused in acute settings and asked if the guidance can provide more direction for community settings. The structure of the NHS is changing, more care is transferring from acute to community. They queried if the nutrition guidelines were initiated in the community and followed the patient into the acute (where necessary) what benefits would it have for the patient and their overall outcome? No evidence was provided for this, but an opportunity to explore this possibility with community based teams would be valuable.

It was further noted that the guidance does not make reference to the need to engage the whole system e.g. commissioners, public health, social care, and third sector.

## Impact statement

The 2017 surveillance found evidence that nutritional interventions involving home visits for older people living in the community can improve nutritional status, frailty, protein intake, and health-related quality of life, and reduce the number of falls. Given the interest from topic experts in exploring community interventions, and that CG32 does not specifically discuss home-based nutrition programmes for older people living in the community, guidance in this area may therefore be needed. However, this evidence relates more to health promotion in older and frail people, and will be logged for consideration in surveillance of other NICE guidelines in public health and social care.

Treatment by trained dietitians did not appear to be beneficial and was not cost-effective, and is unlikely to affect CG32 which does not specifically recommend referral to and treatment by a trained dietitian in primary care.

New evidence is unlikely to change guideline recommendations.

## Home parenteral nutrition education

### 2-year surveillance summary

Update not required after review of evidence.

### 5-year surveillance summary

No relevant evidence was identified.

### Evidence Update 2013

No relevant evidence was identified.

### 8-year surveillance summary

No relevant evidence was identified.

### 2017 surveillance summary

An RCT<sup>151</sup> (n=51 patients in a quaternary care medical centre, mean age 46 years, with a tunnelled catheter/peripherally inserted central catheter) examined usual care plus voiceover interactive PowerPoint catheter care education prehospital discharge versus usual care education (control). Across the groups, mean home parenteral nutrition duration was 2.2 months. Between-group knowledge and changes in knowledge were similar in both groups at preeducation, immediate posteducation, and 7–10 days postdischarge. At 90 days, there were no differences between groups in catheter-related bloodstream

infection (CRBSI) incidence, rehospitalisation, CRBSI-related rehospitalisation rates, and non-CRBSI complications between groups. The interactive education group had more patient calls to the home parenteral nutrition clinicians than control.

### Topic expert feedback

No topic expert feedback was relevant to this evidence.

### Impact statement

The 2017 surveillance found that interactive catheter care education pre-discharge led to more patient calls to the home parenteral nutrition clinicians but made no difference to infection, rehospitalisation, and complications. The evidence is from a single small trial and is unlikely to affect CG32, which already recommends that all people in the community having enteral tube feeding should be supported by a coordinated multidisciplinary team, and should receive training and information from members of the multidisciplinary team.

New evidence is unlikely to change guideline recommendations.

*Working in partnership with patients, families, and carers*

**2-year surveillance summary**

Update not required after review of evidence.

**5-year surveillance summary**

No relevant evidence was identified.

**Evidence Update 2013**

No relevant evidence was identified.

**8-year surveillance summary**

No relevant evidence was identified.

**2017 surveillance summary**

A report<sup>152</sup> was identified by topic experts. The report was based on a questionnaire devised to obtain views and insights of patients/carers on 3 areas of health and social care, with a specific focus on nutrition and hydration:

1) Nutrition and hydration services: priorities and trends over time; 2) Patient experience; 3) Inequalities. Thirty organisations were contacted to scope the issues concerned, with the view to organise an in-depth facilitated discussion using a qualitative approach.

Relevant key messages from the report included:

- Patient and population groups are willing to be involved in their care – ‘we will contribute to our care’.
- Real engagement with patients.
- See us as a person, not only as a problem.
- Ask us what is important to us.
- Let’s discuss and agree on the goals of our treatment – we may not have the same priorities as you.
- We will contribute to our care if we are allowed to.
- Check our understanding of what you have told us – we may be embarrassed to ask again or not want to seem a nuisance.
- Communicate with us clearly at the right time – this is essential.

Another report<sup>153</sup> was identified by topic experts. The report was based on: patient sources (the national Patients Association

Helpline, patient surveys, feedback in interviews with patients and carer); a review of recent work into malnutrition by government and concerned charitable organisations including the Patients Association 2011 report ‘Malnutrition in the Community and Hospital’; 2 specific dedicated surveys; and Freedom of Information requests to NHS Trusts.

Relevant recommendations from the report included:

- [...] ensure that nutritional advice is part of the discharge process, when required.
- Information about diet and nutrition should be provided during in-patient stay and/or on discharge
- [...] people discharged from hospital with nutritional needs are well supported in the community

The report also noted that ‘More effort needs to be put in ensuring that care providers follow best practice guidelines such as those from NICE including CG32’

**Topic expert feedback**

Topic experts highlighted two reports by BAPEN<sup>152</sup> and the Patients Association<sup>153</sup> which are discussed above.

**Impact statement**

The 2017 surveillance identified evidence from 2 reports which is broadly aligned with recommendations in CG32 to ensure that patients having enteral or parenteral nutrition in the community and their carers: are kept fully informed and have access to appropriate sources of information in formats, languages and ways that are suited to an individual’s requirements; have the opportunity to discuss diagnosis, treatment options and relevant physical, psychological and social issues; and are given contact details for relevant support groups, charities and voluntary organisations. No impact on the guideline is therefore anticipated.

New evidence is unlikely to change guideline recommendations.

## Areas not currently covered in the guideline

### Nutrition support in specific conditions

This area was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new area.

### Surveillance decision

This area should not be added.

#### *Nutrition support in specific conditions*

##### **2-year surveillance summary**

No relevant evidence was identified.

##### **5-year surveillance summary**

Nutrition in people requiring specific long-term therapeutic regimens for the treatment of diseases was excluded from the original scope. Thus no study was identified from the high level searches on this area. However, during consultation, 1 stakeholder suggested that this was an important area that warranted inclusion in the guideline and provided information on publications relating to nutrition in chronic liver disease.

##### **Evidence Update 2013**

###### *Stroke*

A Cochrane review<sup>154</sup> investigated interventions for dysphagia and nutrition support in patients with stroke. 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. Alongside general recommendations for nutrition support in CG32, guidance specific to nutrition support in stroke is covered by the NICE 'Stroke' guideline CG68; the identified new evidence is unlikely to have an impact on the stroke guideline recommendations and is broadly consistent with recommendations for general nutrition support in CG32.

###### *Liver disease*

A Cochrane review on nutritional support for liver disease<sup>155</sup> revealed no significant differences for most analyses. The evidence suggests that the benefits of nutrition support in

patients with liver disease appear to be restricted, but limitations of current data prevent firm conclusions and more robust evidence is needed to confirm findings.

##### **8-year surveillance summary**

###### *Cirrhosis*

A systematic review and meta-analysis<sup>156</sup> of RCTs of oral or enteral nutritional supplementation in adult patients with cirrhosis was found. Results showed that there was no reduction in mortality when all studies were combined. The authors concluded that there is insufficient evidence to definitively state that the intervention impacts clinical outcomes in liver cirrhosis.

##### **2017 surveillance summary**

###### *Tuberculosis*

A Cochrane review<sup>157</sup> of 35 RCTs (n=8283) examined oral nutritional supplements for people being treated with antituberculous drug therapy for active tuberculosis. A second systematic review and meta-analysis<sup>158</sup> of 19 RCTs (n=3681) examined adjuvant efficacy of nutrition support during pulmonary tuberculosis treatment with antituberculous drug therapy. Across the 2 reviews, only 1 study was from the UK, with the rest mainly from Asia and Africa. The UK study found that adjunctive vitamin D during intensive-phase antimicrobial treatment of pulmonary tuberculosis did not significantly affect the primary outcome of time to sputum culture conversion in the whole study population (though it did benefit a subgroup of participants with the tt genotype of the TaqI vitamin D receptor polymorphism).

### *Hepatitis C*

An RCT<sup>159</sup> (n=53 patients with chronic hepatitis C receiving PEG-interferon containing therapy) examined preventive nutrition support (regular dietary advice plus energy- and protein-rich evening snack) versus on-demand nutritional support (nutritional intervention if weight loss >5%). At baseline, 46% of patients performed paid labour and 62% performed some kind of physical exercise. Furthermore, most patients were able to carry out normal activity with only minor symptoms of disease (mean Karnofsky performance score: 94). Decreases of paid labour productivity, physical exercise activity and Karnofsky performance scores were significantly less in the preventive than on-demand group after 24 weeks of treatment. Effects of preventive nutritional support were even more pronounced after 48 weeks.

### *Cystic fibrosis*

A Cochrane review<sup>160</sup> of 3 RCTs (n=131) examined oral calorie supplements for cystic fibrosis. Included trials lasted between 3 and 12 months. Two trials compared supplements to additional nutritional advice and 1 to no intervention. Two of the included trials recruited only children. There were no significant differences between people receiving supplements or dietary advice alone for change in weight, height, body mass index, z score or other indices of nutrition or growth. Total calorie intake was significantly greater in people taking supplements at 12 months. There were no significant differences between the groups for anthropometric measures of body composition, lung function, gastrointestinal adverse effects or activity levels.

### *Amyotrophic lateral sclerosis*

A double-blind, phase 2 RCT<sup>161</sup> (n=24 patients with amyotrophic lateral sclerosis and no history of diabetes, liver or cardiovascular disease, already receiving percutaneous enteral nutrition) examined hypercaloric enteral nutrition. Patients were randomly assigned to 1 of 3 interventions: 1) a high-carbohydrate hypercaloric tube-fed diet (HC/HC); 2) a high-fat hypercaloric tube-fed diet (HF/HC); 3) control (replacement calories using an isocaloric tube-fed diet). Patients received the intervention diets for 4 months and were followed up for 5 months. The primary outcomes were safety and tolerability. Patients who received the HC/HC diet had significantly

fewer serious adverse events than did those on the control diet, but the total number of adverse events did not differ significantly between groups. Fewer patients in the HC/HC than in the control group discontinued their study diet due to adverse events (significance not reported in the abstract). During the 5 month follow-up, significantly fewer deaths occurred in the HC/HC than the control group. Adverse events, tolerability, deaths, and disease progression did not differ significantly between the HF/HC group and the control group.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### **Impact statement**

At 8-year surveillance, it was concluded that findings of studies up to this timepoint did not warrant any changes to CG32.

The 2017 surveillance found the following evidence for several specific conditions:

- Tuberculosis: Vitamin D hastened sputum culture conversion in participants with a particular vitamin D receptor polymorphism.
- Hepatitis C: Preventive nutritional support can ameliorate decreases in paid labour productivity, physical exercise and performance status.
- Cystic fibrosis: Total calorie intake was significantly greater in people taking supplements, but there appeared to be no physical or clinical benefits. Two of the 3 included trials in the review were in children therefore the evidence is of limited value to CG32.
- Amyotrophic lateral sclerosis: Hypercaloric enteral nutrition appears to be safe and tolerable, however the trial included only 24 patients.

The above evidence appears to broadly align with the general recommendations in CG32 that nutrition support should be considered in people with, or at risk of, malnutrition, and if there is concern about the adequacy of micronutrient intake, a complete oral multivitamin and mineral supplement should be considered.

New evidence is unlikely to impact on the guideline.

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## Immunonutrition (including the use of novel substrates such as glutamine or arginine)

This area was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new area.

### Surveillance decision

This area should not be added.

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#### *Immunonutrition*

##### **2-year surveillance summary**

No relevant evidence was identified.

##### **5-year surveillance summary**

Although the use of novel substrates such as glutamine or arginine was excluded from the scope of the guideline, at the 5-year review, immunonutrition was considered an emerging topic that might warrant inclusion in the scope of a future update of the guideline. A focused search on immunonutrition was therefore undertaken and 35 studies<sup>162-196</sup> were identified for inclusion in the review.

Six studies were related to the area of parenteral immunonutrition in a varied patient population (gastrointestinal cancer, severe acute pancreatitis and critically ill patients). Three studies analysed the effect of varying quantities of omega 3 and fish oils in total parenteral nutrition<sup>172,194,195</sup>, 2 studies addressed the effect of varying lipid composition of total parenteral nutrition<sup>181,183</sup>, and 1 study looked at the effects of varying the amino acid content of total parenteral nutrition<sup>189</sup>. The largest study (166 patients in an intensive care setting) found no difference between groups with respect to inflammatory markers<sup>172</sup>. Other, smaller studies found that the intervention reduced the concentration of inflammatory markers<sup>195</sup>, and had beneficial effects on serum lipid profiles<sup>183</sup> and reduced postoperative morbidity<sup>189</sup>. Two studies could potentially inform health economic considerations of this new topic once conclusive clinical evidence is available<sup>175,197</sup>.

Ten studies were found that specifically looked at parenteral nutrition with glutamine versus standard parenteral nutrition<sup>162,168-171,176,179,180,190,196</sup>. 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<sup>162</sup> and increased survival<sup>169</sup> 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 TNF-alpha<sup>180</sup>. 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, C-reactive protein, lymphocyte count, T cell and CD8 count after surgery<sup>196</sup>. Studies also showed improved survival<sup>169</sup>, incidence of specific infections<sup>170</sup>, and decreased intolerance to feeding<sup>198</sup>.

Eleven studies pertaining to the area of enteral immunonutrition were identified. Studies involved looking at immunonutrition versus standard enteral nutrition<sup>163,164,166,177,182,184,185,187,191-193</sup>. One study looked at immunoenhanced enteral nutrition versus standard parenteral nutrition. In the majority of studies patients receiving immunonutrition tend to have better outcomes with regards to inflammatory markers, mortality, ventilator and intensive care unit-free days<sup>106,163-165,177,182,184,185,187,191-193</sup>.

There were 7 studies pertaining to the area of oral immunonutrition<sup>166,167,173,174,178,186,188</sup>. 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<sup>166,178,186</sup>, 1 study looked at stroke patients<sup>173</sup>, and 1 looked at patients with gastrointestinal tumours<sup>174</sup>. Some studies showed a trend towards decrease in hospital admissions, decreased length of stay, and decreased mortality<sup>166,167,173</sup>. 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<sup>178</sup>. Two studies looked at biochemical indices, one study found a beneficial reduction in TNF-alpha mRNA and IL-6 mRNA in the intervention group<sup>186</sup>, and another study found that biochemical markers indicated a decrease in immune suppression in patients receiving immunonutrition intervention<sup>188</sup>. 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.

### **Evidence Update 2013**

A Cochrane review<sup>66</sup> found that immune enhancing nutrition may reduce postoperative complications in patients undergoing non-emergency gastrointestinal surgery.

### **8-year surveillance summary**

Nine studies<sup>199-207</sup> were identified through a high level search.

One systematic review and meta-analysis<sup>200</sup> of RCTs published between 1985 and 2009 that assessed the clinical impact of perioperative enteral immunonutrition in major gastrointestinal elective surgery was found. The authors concluded that perioperative enteral immunonutrition decreases morbidity and hospital stay but not mortality after major gastrointestinal surgery.

One large RCT<sup>199</sup> conducted in Scotland showed no effect on new infections or on mortality when parenteral nutrition was supplemented with glutamine or selenium.

One large multi-centre RCT<sup>201</sup> conducted in Europe and North America concluded that early provision of glutamine or antioxidants did not improve clinical outcomes, and that glutamine

was associated with an increase in mortality among critically ill patients with multiorgan failure.

Preliminary data from 1 small French RCT<sup>205</sup> showed that immunonutrition improves functional capacities in head, neck and oesophageal cancer patients undergoing radiochemotherapy.

One small RCT<sup>207</sup> conducted in China concluded that arginine-supplemented enteral nutrition significantly improves long-term survival and restores immunity in malnourished gastric cancer patients.

A systematic review and meta-analysis<sup>202</sup> of RCTs found that fish oil-containing lipid emulsions may be able to decrease mortality and ventilation days in the critically ill. However, the authors concluded that because of the paucity of clinical data, there is inadequate evidence to recommend the routine use of parenteral fish oil and that large, rigorously designed RCTs are required to elucidate the efficacy of parenteral fish oil in the critically ill.

Another systematic review and meta-analysis<sup>204</sup> concluded that omega-3 fatty acid supplementation of parenteral nutrition does not improve mortality, infectious complications, and intensive therapy unit length of stay in comparison with standard parenteral nutrition in critically ill adult patients.

One small RCT<sup>203</sup> conducted in Brazil found that fish oil decreases C-reactive protein/albumin ratio and plasma fatty acid profile and potentially prevents weight loss in people with colorectal cancer.

One small RCT<sup>206</sup> conducted in Taiwan found that Omega-3 fatty acid-, micronutrient-, and probiotic-enriched nutrition helps body weight stabilisation in head and neck cancer cachexia.

### **2017 surveillance summary**

#### *Preoperative – gastrointestinal surgery*

An RCT<sup>208</sup> (n=95 well-nourished and malnourished patients undergoing elective upper and lower gastrointestinal surgery) examined a commercial immuno-enhancing supplement 5 days preoperatively versus no supplement (control). The primary outcome of length of stay did not differ significantly between groups, nor in a subgroup of malnourished patients only. Complications and unplanned intensive care admission rates were very low in both groups. The average admission cost did not differ significantly between groups.

### *Severe burns*

A Cochrane review<sup>209</sup> of 16 RCTs (n=678) examined immunonutrients (glutamine, arginine, branched-chain amino acids, n-3 fatty acids, combined immunonutrients or precursors to known immunonutrients) versus an isonitrogenous diet (overall protein content held constant, but individual constituents may be changed) in patients with severe burn injury. Glutamine was the most common immunonutrient and was given in 7 of the 16 included studies. Use of glutamine compared with an isonitrogenous control led to a significant reduction in length of hospital stay and significantly reduced mortality. However, the authors noted that because of the small sample size, it is likely that these results reflect a false-positive effect. No study findings suggest that glutamine has an effect on burn wound infection or on non-wound infection. All other agents investigated showed no evidence of an effect on mortality, length of stay or burn wound infection or non-wound infection rates.

### *Chemoradiotherapy in head and neck cancer*

An RCT<sup>210</sup> (n=40 patients with head and neck cancer treated with curative concurrent chemoradiotherapy) examined immune-enhanced nutrition supplements versus control (no supplements). All patients received a regular diet and dietary counselling by a protocol dietician. Seven patients from the immunonutrition group withdrew from the study; 1 patient could not tolerate the side effect of chemotherapy and 6 patients could not tolerate the taste of oral immune-enhanced nutrition. One patient from the control group withdrew consent. There was no significant weight loss with immunonutrition but significant weight loss was seen with control. Median percentage change from baseline of energy intake, and circulating levels of nutritional markers, pre-albumin and albumin declined in both groups (significance not reported in the abstract). There was a significantly decreased level of albumin in the control compared to the immunonutrition group at the end of treatment. During chemoradiotherapy 4 patients in the control group and 1 patient in the immunonutrition group developed grade 3 mucositis. One patient in the control group had grade 3 radiation dermatitis. Grade 3-4 hematologic toxicities, mainly in absolute neutrophil count, were significantly higher in the control than the immunonutrition group.

A double-blind RCT<sup>211</sup> (n=91 patients with head and neck cancer undergoing curative radio[chemo]therapy) examined echium oil (a plant source of n-3 polyunsaturated fatty acids [PUFA]; 7.5 ml twice per day, 235 mg/ml alpha-linolenic acid [ALA] + 95 mg/ml stearidonic acid [SDA] + 79 mg/ml gamma-linolenic acid [GLA]) versus control (n-3 PUFA deficient sunflower oil high oleic; 7.5 ml twice a day). Standard nutritional support was also supplied during treatment. Dietary supplement adherence was comparable in both groups. At week 4, intention-to-treat analysis did not reveal any protective effect of echium oil against weight loss, and no significant improvement was observed in any other evaluated anthropometric parameters.

### *Unresectable pancreatic cancer*

A systematic review and meta-analysis<sup>212</sup> of 11 RCTs examined n-3 PUFA in unresectable pancreatic cancer. Compared with conventional nutrition, an oral nutrition supplement enriched with n-3 PUFAs led to a significant increase in body weight and lean body mass, a significant decrease in resting energy expenditure, and an increase in overall survival (significance not reported in the abstract).

### *Gastrointestinal cancer surgery*

A systematic review and meta-analysis<sup>213</sup> of 15 RCTs examined perioperative n-3 PUFAs in gastrointestinal cancer surgical patients. Compared with conventional nutrition, a significant association was seen between n-3 PUFA intake and reduced length of stay, duration of systemic inflammatory response syndrome, reduced serum C-reactive protein levels, and reduced incidence of postoperative infectious complications.

### *Enteral nutrition – critically ill patients*

A systematic review and meta-analysis<sup>214</sup> of 10 RCTs examined glutamine-enriched enteral nutrition in critically ill patients. There was no significant difference in mortality, and a funnel plot found no evidence of publication bias. A fixed effect model showed a significant reduction in gut permeability with enteral feeding enriched with glutamine, and the funnel plot did not show publication bias.

### *Enteral and parenteral nutrition – cancer surgery*

An RCT<sup>215</sup> (n=776 well-nourished and malnourished patients undergoing gastric or pancreatic resection for cancer; mean age 61 years) compared the following

4 perioperative nutrition support strategies: standard enteral nutrition (SEN), immunomodulating enteral nutrition (IMEN), standard parenteral nutrition (SPN), or immunomodulating parenteral nutrition (IMPN). All malnourished patients received preoperative parenteral nutrition. No statistically significant differences were observed in well-nourished patients, during either enteral or parenteral intervention, independent of the type of intervention (standard or immunomodulating). However, the malnourished group saw a significant positive impact of enteral immunonutrition on reduction of postoperative complications and length of stay compared with a standard enteral diet. The cross-analysis of SEN, IMEN, SPN, and IMPN was insignificant.

A systematic review and meta-analysis<sup>216</sup> of 9 RCTs (n=785) examined enteral immunonutrition versus standard enteral nutrition in patients undergoing surgery for gastric cancer. Meta-analysis showed that enteral immunonutrition did not significantly improve postoperative complications or length of hospitalisation.

An RCT<sup>217</sup> (n=41 patients undergoing upper gastrointestinal surgery for cancer) examined enteral immunonutrition versus control (standard enteral nutrition). These regimens were followed for 7 days perioperatively by all patients. Patients in the immunonutrition group showed a more marked significant decrease in the rate of postoperative infections and anastomotic leakage, and had a significantly shorter length of hospital stay, than controls. Rates of overall morbidity and mortality were similar in the two groups.

#### *Parenteral nutrition – pancreatitis*

A systematic review and meta-analysis<sup>218</sup> of 7 RCTs examined parenteral immunonutrition in patients with acute pancreatitis. Parenteral immunonutrition significantly reduced the risk of infectious complications and mortality. Length of stay was also significantly shorter in patients who received immunonutrition.

#### **Topic expert feedback**

##### *8-year surveillance*

One GDG member commented that the field of immunonutrition was not included in the original guidance but since then a lot of research has been published which has led to massive variation in practice related to the prescription or otherwise of these more expensive nutritional support interventions.

#### **Impact statement**

The 5-year surveillance concluded that no sufficient evidence was identified that would merit adding immunonutrition to the guideline.

The 2013 Evidence Update concluded that limitations of the evidence, combined with potential issues of adverse reactions to immune enhancing supplements, meant that findings were unlikely to affect CG32

The 8-year surveillance concluded that evidence relating to immunonutrition was promising – benefits were found in subgroups of high-risk and malnourished patients. However, conflicting results on the benefit of immunonutrition from several studies (and even evidence of harm in at least 1 study) did not allow for any firm conclusions. The evidence was deemed insufficient to include immunonutrition in the guideline.

The 2017 surveillance found the following effects of immunonutrition (listed according to populations and intervention):

- Preoperative therapy in gastrointestinal surgery (unspecified immunonutrition): Did not reduce length of stay or cost.
- Severe burns (unspecified immunonutrition): Reduced length of stay and mortality (Cochrane authors noted this finding should be taken with care due to study limitations, and larger studies are needed).
- Chemoradiotherapy in head and neck cancer (unspecified immunonutrition in 1 trial, and n-3 PUFA in 1 trial): Mixed outcomes for weight loss, but reduced toxicity of chemoradiotherapy.
- Unresectable pancreatic cancer (n-3 PUFA): Increased body weight and lean body mass.
- Gastrointestinal cancer surgery (n-3 PUFA): Reduced length of stay, duration of systemic inflammatory response syndrome, C-reactive protein, and postoperative infectious complications.
- Enteral nutrition – critically ill patients (glutamine): No effect on mortality, but decreased gut permeability.
- Enteral nutrition – gastrointestinal cancer surgery (unspecified immunonutrition): Mixed outcomes for postoperative complications and length of stay, but decreased anastomotic leakage. Authors

noted that more studies are warranted to further establish effects.

- Parenteral nutrition – pancreatitis (unspecified immunonutrition): Reduced infectious complications, mortality and length of stay.

Overall, evidence for immunonutrition remains mixed with benefits seen with some types of immunonutrition in some populations

undergoing some interventions, but with no effects seen in other populations. Evidence is inconsistent and unlikely to affect CG32, the scope of which currently excludes the use of novel substrates such as glutamine or arginine.

New evidence is unlikely to impact on the guideline.

## Satiety hormone suppression

This area was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new area.

### Surveillance decision

This area should not be added.

#### *Satiety gut hormone suppression with octreotide acetate after oesophagectomy*

##### **2-year surveillance summary**

No relevant evidence was identified.

##### **5-year surveillance summary**

No relevant evidence was identified.

##### **Evidence Update 2013**

No relevant evidence was identified.

##### **8-year surveillance summary**

No relevant evidence was identified.

##### **2017 surveillance summary**

A double-blind, crossover RCT<sup>219</sup> (n=10 disease-free patients at least 1 year post oesophagectomy with gastric conduit reconstruction; and n=8 unoperated controls) examined satiety gut hormone suppression with subcutaneous octreotide acetate (1ml; 100 micrograms) versus control (1ml saline). Interventions were followed by a standardised ad libitum meal. Patients with oesophagectomy demonstrated significant weight loss at 3, 6, 12, and 24 months postoperatively. Ghrelin levels were similar for both groups, but postprandial glucagon-like peptide 1 and peptide YY

responses were significantly greater among patients with oesophagectomy compared with controls. After octreotide, ad libitum calorie intake significantly increased among patients with oesophagectomy but not controls.

##### **Topic expert feedback**

It was noted that octreotide acetate is not licensed for the indication examined in the study.

##### **Impact statement**

The 2017 surveillance found that patients with oesophagectomy demonstrated an exaggerated postprandial satiety gut hormone response that could be attenuated by octreotide leading to increased calorie intake. Although CG32 does not discuss drug treatment of satiety, the evidence was from a single small trial in an unlicensed indication and further evidence to confirm results is needed before any impact on the guideline can be considered.

New evidence is unlikely to impact on the guideline.

## Editorial and factual corrections identified during surveillance

During surveillance editorial or factual corrections were identified.

- Recommendations 1.4.6, 1.6.1 and 1.6.3 make reference to a box but do not specify the box number.
- Footnote 5 to recommendation 1.3.4 references the document 'Withholding and withdrawing life prolonging treatments: good practice in decision making' by the General Medical Council. This was [withdrawn](#) in July 2010 and has now been replaced with '[Treatment and care towards the end of life: decision making](#)'. The reference will need to be updated.
- Footnote 6 to recommendation 1.3.4 references the document 'Reference guide to consent for examination or treatment' (2001) Department of Health. This has now been updated to a [second edition](#) published in 2009, therefore the year of publication will need to be amended.
- Recommendation 1.7.17 states 'The position of all nasogastric tubes should be confirmed after placement and before each use by aspiration and pH graded paper (with X-ray if necessary) as per the advice from the National Patient Safety Agency (NPSA 2005).' The 2005 advice was [updated](#) in 2011 (though it states 'This Alert does not change the advice given in Patient Safety Alert 05 that pH testing remains the first line test, and x-ray checking remains the second line test.'). Further alerts have also been issued ([Rapid Response Report in 2011](#), and Patient Safety Alerts in [2013](#) and [2016](#)). The guideline will need to be updated to refer to the latest advice.
- Footnote 12 to recommendation 1.8.15 cross-refers to NICE clinical guideline 2. This has been updated and replaced by NICE guideline 139 and the cross-referral will need updating.

## Research recommendations

**RR – 01 Further research is needed to ascertain whether an educational intervention (for example, three 1- week modular courses, over 6 months) for all healthcare professionals, in particular medical and nursing staff including those who work with people with dementia would have an effect on patient care (that is, effect on nutritional status, length of hospital stay, frequency of GP visits, complications and quality of life) compared to no formal education.**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 02 What are the benefits to patients of a nutritional screening programme (using a simple tool such as the ‘Malnutrition Universal Screening Tool’ [MUST]) compared with not screening people in: a) primary care (attending GP clinics); b) care homes; c) hospital inpatients; d) hospital outpatients; e) patients with dementia in terms of determining the number of people at risk of malnutrition, complications, survival, hospital admission rates, length of stay, quality of life and cost effectiveness?**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 03 Further research is needed to identify which components of nutrition monitoring are clinically and cost effective**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 04 What are the benefits of patients (in hospital or the community, including older people) identified as at high risk of malnutrition by a screening tool such as MUST being offered either oral nutritional supplements compared with a) dietary modification and/or food fortification, or b) dietary modification and/or food fortification together with dietary counselling, in terms of determining complications, survival, length of hospital stay, quality of life and cost effectiveness?**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 05 What are the benefits of enteral tube feeding to patients compared with no enteral tube feeding in people with dysphagia and early to mid-stage dementia in terms of reduced complications associated with swallowing, improved nutritional status, delayed onset of advanced stage dementia, hospital admissions, cost effectiveness and survival?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 06 Further research investigating the optimal levels of energy and nitrogen provision for severely ill or injured patients during the early part of their illness is needed using clinical endpoints such as infection and mortality rates rather than changes in anthropometry and estimated nutrient balance.**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 07 What are the benefits to patients in hospital identified as at high risk of malnutrition by a screening tool such as the ‘Malnutrition Universal Screening Tool’ (‘MUST’) being offered either a) complete oral nutritional supplements b) combined micro and macronutrient supplements or c) micronutrient supplementation in terms of survival, hospital admissions, quality of life and cost effectiveness?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 08 What are the benefits to patients in primary care identified as high risk of malnutrition by a screening tool such as the ‘Malnutrition Universal Screening Tool’ (‘MUST’) being offered either oral nutritional supplements compared to being offered; a) combined micro and macronutrient supplement or b) micronutrient supplementation alone or c) standard care**

**(no specific dietary intervention) in terms of survival, hospital admissions, quality of life and cost effectiveness**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

#### **Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 09 Do patients with oro-pharyngeal dysphagia (as assessed by a trained practitioner) who are given thickened liquids compared to standard/ unthickened liquids benefit in terms of improved mood, increased nutritional intake, reduce dehydration, less aspiration incidents, mortality and avoidance of the need for enteral feeding?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

#### **Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 10 Do patients with oro-pharyngeal dysphagia (as assessed by a trained practitioner) who are given pureed food compared to standard/ soft food benefit in terms of improved nutritional intake, the safety and efficiency of swallow, the number of aspiration incidents and avoidance of the need for enteral feeding?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

#### **Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 11 What are the benefits to Intensive care patients likely to stay for >5 days, who are offered ETF only compared to ETF and PN if they fail to tolerate >60% of their target nutritional needs 2 days after starting ETF in terms of survival, complications and hospital costs?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

#### **Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 12 What are the benefits to malnourished surgical patients who have indications for ETF being offered ETF only compared to ETF and PN if they fail to tolerate >60% of their target nutritional needs two days after starting ETF in terms of survival, complications and hospital costs?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 13 What are the benefits to patients who need short term PN support being offered standard PN compared to either PN and minimal ETF (<25ml/hr) or PN with Glutamine and minimal ETF (<25ml/hr) in terms of survival, complications and hospital costs?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 14 What are the benefits to patients who present with the indications for PN being fed only 50% of estimated protein and energy needs but with full micronutrient and electrolyte provision for first 5 days, followed by feeding at full needs compared to being fed 100% of estimated needs from the first day of feeding in terms of; metabolic complications, infection rates, length of PN feeding, mortality, length of hospital stay, and time to ‘medically fit for discharge.**

[New evidence](#) relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 15 What are the benefits to patients who have indications for PN due to acute but reversible intestinal failure (e.g. prolonged ileus) being commenced on PN within 6 days of developing that failure compared to not commencing until 12 days after the development of that failure if the feeding problem has not resolved in terms of; metabolic complications, infection rates, duration of PN feeding, mortality, duration of hospital stay, time to ‘medically fit for discharge.**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

### Surveillance decision

This research recommendation will be considered again at the next surveillance point.

**RR – 16 What are the benefits to Intensive care patients likely to stay for >5 days who have contraindications to ETF being offered standard PN compared to either PN with additional glutamine, PN with additional selenium, or PN with**

**additional glutamine and selenium in terms of survival, complications including catheter related infections and hospital costs?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

**Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 17 Do patients managed by specialised centres have a better outcome (mortality, morbidity, complications, QOL) than those managed by a local hospital?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

**Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 18 What factors contribute to the different numbers and indications for long term HETF and long term HPN in different regions in the UK (and in different countries)?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

**Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 19 What are the health economic implications (cost effectiveness) of long term HETF and long term HPN?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

**Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

**RR – 20 How are specific complications best treated (and avoided) in the community (e.g. tube / catheter blockage)?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

**Surveillance decision**

This research recommendation will be considered again at the next surveillance point.

## References

1. NIHR and BAPEN. (2015) The cost of malnutrition in England and potential cost savings from nutritional interventions.
2. Ha L, Hauge T, Spenning AB et al. (2010) 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* 29:567-573.
3. Rabinovitch R. (2006) 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* 28:287-296.
4. Beck AM, Holst M, and 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.
5. 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.
6. 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.
7. Neelemaat F, Bosmans JE, Thijs A et al. (2012) Oral nutritional support in malnourished elderly decreases functional limitations with no extra costs. *Clinical Nutrition* 31:183-190.
8. 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* 65:735-742.
9. Kim H, Suh EE, Lee HJ et al. (2013) The Effects of Patient Participation-Based Dietary Intervention on Nutritional and Functional Status for Patients With Gastrectomy: A Randomized Controlled Trial. *Cancer Nurs* .
10. Perry L, Hamilton S, Williams J et al. (2013) Nursing interventions for improving nutritional status and outcomes of stroke patients: descriptive reviews of processes and outcomes. *Worldviews on evidence-based nursing / Sigma Theta Tau International, Honor Society of Nursing* 10:17-40.
11. Young AM, Mudge AM, Banks MD et al. (2013) Encouraging, assisting and time to EAT: Improved nutritional intake for older medical patients receiving Protected Mealtimes and/or additional nursing feeding assistance. *Clinical Nutrition* 32:543-549.
12. Badia T, Formiga F, Ferrer A et al. (2015) Multifactorial assessment and targeted intervention in nutritional status among the older adults: a randomized controlled trial: the Octabaix study. *BMC geriatrics* 15:45.
13. Beck AM, Christensen AG, Hansen BS et al. (2016) Multidisciplinary nutritional support for undernutrition in nursing home and home-care: A cluster randomized controlled trial. *Nutrition (Burbank, Los Angeles County, Calif.)* 32:199-205.
14. Cong MH, Li SL, Cheng GW et al. (2015) An interdisciplinary nutrition support team improves clinical and hospitalized outcomes of esophageal cancer patients with concurrent chemoradiotherapy. *Chinese medical journal* 128:3003-3007.

15. Schultz TJ, Kitson AL, Soenen S et al. (2014) Does a multidisciplinary nutritional intervention prevent nutritional decline in hospital patients? A stepped wedge randomised cluster trial. *e-SPEN Journal* 9:e84-e90.
16. Duncan DG, Beck SJ, Hood K et al. (2006) 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* 35:148-153.
17. fenacht U, hlin M, Wegmann M et al. (2010) Nutritional counseling improves quality of life and nutrient intake in hospitalized undernourished patients. *Nutrition* 26:53-60.
18. Isenring EA BJC. (2007) 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* 107:404-412.
19. Bourdel-Marchasson I, Blanc-Bisson C, Doussau A et al. (2014) Nutritional advice in older patients at risk of malnutrition during treatment for chemotherapy: A two-year randomized controlled trial. *PLoS ONE* 9:no.
20. Poulsen GM, Pedersen LL, Osterlind K et al. (2014) Randomized trial of the effects of individual nutritional counseling in cancer patients. *Clinical nutrition (Edinburgh, Scotland)* 33:749-753.
21. Uster A, Rufenacht U, Ruehlin M et al. (2013) Influence of a nutritional intervention on dietary intake and quality of life in cancer patients: a randomized controlled trial. *Nutrition (Burbank, Los Angeles County, Calif.)* 29:1342-1349.
22. Caccialanza R, Palladini G, Cereda E et al. (2015) Nutritional counseling improves quality of life and preserves body weight in systemic immunoglobulin light-chain (AL) amyloidosis. *Nutrition* 31:1228-1234.
23. Baldwin C, Kimber KL, Gibbs M et al. (20-12-2016) Supportive interventions for enhancing dietary intake in malnourished or nutritionally at-risk adults. *Cochrane database of systematic reviews (Online)* 12:CD009840.
24. Abbott RA, Whear R, Thompson-Coon J et al. (2013) Effectiveness of mealtime interventions on nutritional outcomes for the elderly living in residential care: a systematic review and meta-analysis. *Ageing Res Rev* 12:967-981.
25. Wijnhoven HAH, van dM, B S et al. (2015) Variety within a cooked meal increases meal energy intake in older women with a poor appetite. *Appetite* 95:571-576.
26. 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* 16:562-568.
27. Carey S, Ferrie S, Ryan R et al. (2013) Long-term nutrition intervention following major upper gastrointestinal surgery: A prospective randomized controlled trial. *European journal of clinical nutrition* 67:324-329.
28. Green SM and James EP. (2013) Barriers and facilitators to undertaking nutritional screening of patients: a systematic review. *J Hum.Nutr Diet* 26:211-221.
29. Li HJ, Cheng HS, Liang J et al. (2013) Functional recovery of older people with hip fracture: does malnutrition make a difference? *J Adv.Nurs* 69:1691-1703.
30. Nykanen I, Lonnroos E, Kautiainen H et al. (2013) Nutritional screening in a population-based cohort of community-dwelling older people. *Eur.J Public Health* 23:405-409.
31. Omidvari AH, Vali Y, Murray SM et al. (2013) Nutritional screening for improving professional practice for patient outcomes in hospital and primary care settings. *Cochrane database of systematic reviews (Online)* 6:CD005539.

32. Roque M, Salva A, and Vellas B. (2013) Malnutrition in community-dwelling adults with dementia (Nutrialz Trial). *Journal of Nutrition, Health and Aging* 17:295-299.
33. Tamura BK, Bell CL, Masaki KH et al. (2013) Factors Associated With Weight Loss, Low BMI, and Malnutrition Among Nursing Home Patients: A Systematic Review of the Literature. *J AM MED DIR ASSOC* 14:649-655.
34. Vashi PG, Gupta D, Lammersfeld CA et al. (2013) The relationship between baseline nutritional status with subsequent parenteral nutrition and clinical outcomes in cancer patients undergoing hyperthermic intraperitoneal chemotherapy. *Nutrition Journal* 12.
35. Vivanti A, Isenring E, Baumann S et al. (2015) Emergency department malnutrition screening and support model improves outcomes in a pilot randomised controlled trial. *Emergency medicine journal : EMJ* 32:180-183.
36. Cox S, Powell C, Carter B et al. (2016) Role of nutritional status and intervention in oesophageal cancer treated with definitive chemoradiotherapy: outcomes from SCOPE1. *British journal of cancer* 115:172-177.
37. Roller RE, Eglseer D, Eisenberger A et al. (2016) The Graz Malnutrition Screening (GMS): a new hospital screening tool for malnutrition. *The British journal of nutrition* 115:650-657.
38. Bally MR, Blaser Y, Prisca Z et al. (2016) Nutritional Support and Outcomes in Malnourished Medical Inpatients: A Systematic Review and Meta-analysis. *JAMA internal medicine* 176:43-53.
39. 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.
40. Zeki S, Culkun A, Gabe SM et al. (2011) Refeeding hypophosphataemia is more common in enteral than parenteral feeding in adult in patients. *Clinical nutrition (Edinburgh, Scotland)* 30:365-368.
41. Doig GS, Simpson F, Heighes PT et al. (2015) Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial. *Lancet Respir.Med* 3:943-952.
42. Arabi YM, Aldawood AS, Haddad SH et al. (2015) Permissive underfeeding or standard enteral feeding in critically ill adults. *New England Journal of Medicine* 372:2398-2408.
43. Arabi YM, Aldawood AS, Al-Dorzi HM et al. (2-9-2016) Permissive Underfeeding or Standard Enteral Feeding in High and Low Nutritional Risk Critically Ill Adults: Post-hoc Analysis of the PermiT trial. *Am J Respir.Crit.Care Med* .
44. Choi EY, Park D, and Park J. (2015) Calorie intake of enteral nutrition and clinical outcomes in acutely critically ill patients: a meta-analysis of randomized controlled trials. *JPEN.Journal of parenteral and enteral nutrition* 39:291-300.
45. Marik PE and Hooper MH. (2016) Normocaloric versus hypocaloric feeding on the outcomes of ICU patients: a systematic review and meta-analysis. *Intensive Care Medicine* 42:316-323.
46. Petros S, Horbach M, Seidel F et al. (2016) Hypocaloric vs Normocaloric Nutrition in Critically Ill Patients. *Journal of Parenteral and Enteral Nutrition* 40:242-249.
47. Charles EJ, Petroze RT, Metzger R et al. (2014) Hypocaloric compared with eucaloric nutritional support and its effect on infection rates in a surgical intensive care unit: a randomized controlled trial. *Am J Clin Nutr* 100:1337-1343.
48. Rugeles SJ, Rueda JD, Diaz CE et al. (2013) Hyperproteic hypocaloric enteral nutrition in the critically ill patient: A randomized controlled clinical trial. *Indian Journal of Critical Care Medicine* 17:343-349.

49. Tian F, Wang X, Gao X et al. (2015) Effect of initial calorie intake via enteral nutrition in critical illness: a meta-analysis of randomised controlled trials. *Critical care (London, England)* 19:180.
50. Anbar R, Beloosesky Y, Cohen J et al. (2014) Tight calorie control in geriatric patients following hip fracture decreases complications: a randomized, controlled study. *Clinical nutrition (Edinburgh, Scotland)* 33:23-28.
51. Beck AM DK. (2008) Multifaceted nutritional intervention among nursing-home residents has a positive influence on nutrition and function. *Nutrition (Burbank, Los Angeles County, Calif)* 24:1073-1080.
52. Beck AM, Damkjaer K, and rbye LW. (2010) 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* 50:351-355.
53. Botella-Carretero JI, Iglesias B, Balsa JA et al. (2008) 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* 32:120-128.
54. Botella-Carretero JI, Iglesias B, Balsa JA et al. (2010) Perioperative oral nutritional supplements in normally or mildly undernourished geriatric patients submitted to surgery for hip fracture: a randomized clinical trial. *Clinical Nutrition* 29:574-579.
55. Castellanos VH, Marra MV, and Johnson P. (2009) 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* 109:445-451.
56. McMurdo ME, Price RJ, Shields M et al. (2009) Should oral nutritional supplementation be given to undernourished older people upon hospital discharge? A controlled trial. *Journal of the American Geriatrics Society* 57:2239-2245.
57. Minig L, Biffi R, Zanagnolo V et al. (2009) Early oral versus "traditional" postoperative feeding in gynecologic oncology patients undergoing intestinal resection: a randomized controlled trial. *Annals of Surgical Oncology* 16:1660-1668.
58. Navratilova M, Jarkovsky J, Ceskova E et al. (2007) Alzheimer disease: Malnutrition and nutritional support. *Clinical and Experimental Pharmacology and Physiology* 34:S11-S13.
59. Norman K, Kirchner H, Freudenreich M et al. (2008) 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* 27:48-56.
60. Ravasco P. (2005) Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. *Head & Neck* 27:659-668.
61. Simmons SF ZX. (2010) Cost-effectiveness of nutrition interventions in nursing home residents: a pilot intervention. *The journal of nutrition, health & aging* 14:367-372.
62. van Anholt RD, Sobotka L, Meijer EP et al. (2010) Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in non-malnourished patients. *Nutrition* 26:867-872.
63. Wouters-Wesseling W. (2006) Early nutritional supplementation immediately after diagnosis of infectious disease improves body weight in psychogeriatric nursing home residents. *Aging clinical and experimental research* 18:70-74.
64. Baldwin C and Weekes CE. (2011) Dietary advice with or without oral nutritional supplements for disease-related malnutrition in adults. *Cochrane Database of Systematic Reviews* CD002008.

65. Baldwin C, Spiro A, Ahern R et al. (7-3-2012) Oral nutritional interventions in malnourished patients with cancer: a systematic review and meta-analysis. *Journal of the National Cancer Institute* 104:371-385.
66. Burden S, Todd C, Hill J et al. (2012) Pre-operative Nutrition Support in Patients Undergoing Gastrointestinal Surgery. *Cochrane Database of Systematic Reviews* CD008879.
67. Collins PF, Stratton RJ, and Elia M. (2012) Nutritional support in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *American Journal of Clinical Nutrition* 95:1385-1395.
68. Collins PF, Elia M, and Stratton RJ. (1-5-2013) Nutritional support and functional capacity in chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Respirology* 18:616-629.
69. Ferreira IM, Brooks D, White J et al. (2012) Nutritional supplementation for stable chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* CD000998.
70. 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 & Ageing* 42:39-45.
71. 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.
72. Bouillanne O, Curis E, Hamon-Vilcot B et al. (2013) Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: a randomized controlled trial. *Clin Nutr* 32:186-192.
73. Gurgun A, Deniz S, Argin M et al. (2013) Effects of nutritional supplementation combined with conventional pulmonary rehabilitation in muscle-wasted chronic obstructive pulmonary disease: A prospective, randomized and controlled study. *Respirology* 18:495-500.
74. Karandish M, Tamimi M, Shayesteh AA et al. (2013) The effect of magnesium supplementation and weight loss on liver enzymes in patients with nonalcoholic fatty liver disease. *Journal of Research in Medical Sciences* 18:572-578.
75. Khoshbaten M, Ghaffarifar S, Jabbar Imani A et al. (2013) Effects of early oral feeding on relapse and symptoms of upper gastrointestinal bleeding in peptic ulcer disease. *Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society* 25:125-129.
76. Lee J and Finucane T. (2013) Thought for food: Is nutritional supplementation an effective treatment for malnutrition? *Journal of the American Geriatrics Society* 61:S161.
77. Lee LC, Tsai AC, Wang JY et al. (3-5-2013) Need-based intervention is an effective strategy for improving the nutritional status of older people living in a nursing home: A randomized controlled trial. *Int J Nurs Stud* .
78. Leslie WS, Woodward M, Lean ME et al. (2013) Improving the dietary intake of under nourished older people in residential care homes using an energy-enriching food approach: a cluster randomised controlled study. *J Hum.Nutr Diet* 26:387-394.
79. Locher JL, Vickers KS, Buys DR et al. (7-9-2013) A Randomized Controlled Trial of a Theoretically-Based Behavioral Nutrition Intervention for Community Elders: Lessons Learned from the Behavioral Nutrition Intervention for Community Elders Study. *Journal of the Academy of Nutrition and Dietetics* .
80. Marinari S, Manigrasso MR, and De BF. (2013) Effects of nutraceutical diet integration, with coenzyme Q10 (Q-Ter multicomposite) and creatine, on dyspnea, exercise tolerance, and quality of life in COPD patients with chronic respiratory failure. *Multidisciplinary Respiratory Medicine* 8.

81. Stange I, Bartram M, Liao Y et al. (2013) Effects of a low-volume, nutrient- and energy-dense oral nutritional supplement on nutritional and functional status: A randomized, controlled trial in nursing home residents. *Journal of the American Medical Directors Association* 14:628.
82. Stratton RJ, Hebuterne X, and Elia M. (2013) A systematic review and meta-analysis of the impact of oral nutritional supplements on hospital readmissions. *Ageing Research Reviews* 12:884-897.
83. Wang Y, Liu XJ, Robitaille L et al. (2013) Effects of vitamin C and vitamin D administration on mood and distress in acutely hospitalized patients. *American Journal of Clinical Nutrition* 98:705-711.
84. Rondanelli M, Klersy C, Terracol G et al. (2016) Whey protein, amino acids, and Vitamin D supplementation with physical activity increases fat-free mass and strength, functionality, and quality of life and decreases inflammation in sarcopenic elderly. *American Journal of Clinical Nutrition* 103:830-840.
85. Yoshimura Y, Uchida K, Jeong S et al. (2016) Effects of nutritional supplements on muscle mass and activities of daily living in elderly rehabilitation patients with decreased muscle mass: A randomized controlled trial. *Journal of Nutrition, Health and Aging* 20:185-191.
86. Collins J and Porter J. (2015) The effect of interventions to prevent and treat malnutrition in patients admitted for rehabilitation: a systematic review with meta-analysis. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association* 28:1-15.
87. Deutz NE, Matheson EM, Matarese LE et al. (2016) Readmission and mortality in malnourished, older, hospitalized adults treated with a specialized oral nutritional supplement: A randomized clinical trial. *Clinical nutrition (Edinburgh, Scotland)* 35:18-26.
88. Elia M, Normand C, Laviano A et al. (2016) A systematic review of the cost and cost effectiveness of using standard oral nutritional supplements in community and care home settings. *Clinical Nutrition* 35:125-137.
89. Elia M, Normand C, Norman K et al. (2016) A systematic review of the cost and cost effectiveness of using standard oral nutritional supplements in the hospital setting. *Clinical Nutrition* 35:370-380.
90. Huynh DTT, Devitt AA, Paule CL et al. (2015) Effects of oral nutritional supplementation in the management of malnutrition in hospital and post-hospital discharged patients in India: a randomised, open-label, controlled trial. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association* 28:331-343.
91. Jobse I, Liao Y, Bartram M et al. (2015) Compliance of nursing home residents with a nutrient- and energy-dense oral nutritional supplement determines effects on nutritional status. *The journal of nutrition, health & aging* 19:356-364.
92. Kiss N, Seymour JF, Prince HM et al. (2014) Challenges and outcomes of a randomized study of early nutrition support during autologous stem-cell transplantation. *Current oncology (Toronto, Ont.)* 21:e334-e339.
93. Parsons EL, Stratton RJ, Cawood AL et al. (2016) Oral nutritional supplements in a randomised trial are more effective than dietary advice at improving quality of life in malnourished care home residents. *Clinical nutrition (Edinburgh, Scotland)* .
94. Tylner S, Cederholm T, and Faxen-Irving G. (2016) Effects on Weight, Blood Lipids, Serum Fatty Acid Profile and Coagulation by an Energy-Dense Formula to Older Care Residents: A Randomized Controlled Crossover Trial. *Journal of the American Medical Directors Association* 17:275.
95. van dB, Gerda H, Lindeboom R et al. (2015) The effects of the administration of oral nutritional supplementation with medication rounds on the achievement of nutritional goals: a randomized controlled trial. *Clinical nutrition (Edinburgh, Scotland)* 34:15-19.

96. Klappenbach RF, Yazzi FJ, Alonso Q et al. (2013) Early oral feeding versus traditional postoperative care after abdominal emergency surgery: a randomized controlled trial. *World journal of surgery* 37:2293-2299.
97. Sharma M, Wahed S, O'Dair G et al. (2013) A randomized controlled trial comparing a standard postoperative diet with low-volume high-calorie oral supplements following colorectal surgery. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland* 15:885-891.
98. Imamura H, Nishikawa K, Kishi K et al. (2016) Effects of an Oral Elemental Nutritional Supplement on Post-gastrectomy Body Weight Loss in Gastric Cancer Patients: A Randomized Controlled Clinical Trial. *Annals of Surgical Oncology* 23:2928-2935.
99. Ostadrahimi A, Nagili B, Asghari-Jafarabadi M et al. (2016) A Proper Enteral Nutrition Support Improves Sequential Organ Failure Score and Decreases Length of Stay in Hospital in Burned Patients. *Iranian Red Crescent medical journal* 18:e21775.
100. Munk T, Beck AM, Holst M et al. (2014) Positive effect of protein-supplemented hospital food on protein intake in patients at nutritional risk: a randomised controlled trial. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association* 27:122-132.
101. Pouyssegur V, Brocker P, Schneider SM et al. (2015) An innovative solid oral nutritional supplement to fight weight loss and anorexia: open, randomised controlled trial of efficacy in institutionalised, malnourished older adults. *Age and ageing* 44:245-251.
102. Stelten S, Dekker IM, Ronday EM et al. (2015) Protein-enriched 'regular products' and their effect on protein intake in acute hospitalized older adults; a randomized controlled trial. *Clinical Nutrition* 34:409-414.
103. Van W, V, Brondel L et al. (2016) An innovative brioche enriched in protein and energy improves the nutritional status of malnourished nursing home residents compared to oral nutritional supplement and usual breakfast: FARINE+ project. *Clinical Nutrition ESPEN* 15:93-100.
104. Arefian NM, Teymourian H, and Radpay B. (2007) Effect of partial parenteral versus enteral nutritional therapy on serum indices in multiple trauma patients. *Tanaffos* 6:37-41.
105. Desachy A. (2008) Initial efficacy and tolerability of early enteral nutrition with immediate or gradual introduction in intubated patients. *Intensive Care Medicine* 34:1054-1059.
106. Doley RP YTWJK. (2009) Enteral nutrition in severe acute pancreatitis. *JOP : Journal of the pancreas* 10:157-162.
107. Elia M and Stratton RJ. (1-6-2008) A cost-utility analysis in patients receiving enteral tube feeding at home and in nursing homes. *Clinical nutrition (Edinburgh, Scotland)* 27:416-423.
108. Grizas S G. (2008) A comparison of the effectiveness of the early enteral and natural nutrition after pancreatoduodenectomy. *Medicina (Kaunas, Lithuania)* 44:678-686.
109. Hyltander A. (2005) 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* 3:466-474.
110. Joos AK PP. (2008) 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* 10:605-609.
111. Kang WM YJZ. (2008) Effects of enteral and parenteral nutrition on gastrointestinal 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* 23:113-116.

112. Lam NN TNKC. (2008) 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* 34:192-196.
113. Nagata S F. (2009) Comparison of enteral nutrition with combined enteral and parenteral nutrition in post-pancreaticoduodenectomy patients: a pilot study. *Nutrition Journal* Vol.8, pp.24, 2009..
114. Nguyen NQ. (2008) The impact of delaying enteral feeding on gastric emptying, plasma cholecystokinin, and peptide YY concentrations in critically ill patients. *Critical care medicine* 36:1469-1474.
115. Ryu J. (2009) Clinical outcomes comparing parenteral and nasogastric tube nutrition after laryngeal and pharyngeal cancer surgery. *Dysphagia* 24:378-386.
116. Vaithiswaran V. (2008) Effect of early enteral feeding after upper gastrointestinal surgery. *Tropical gastroenterology : official journal of the Digestive Diseases Foundation* 29:91-94.
117. White H. (2009) 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)* 13:R187, 2009.
118. Wang Q, Liu ZS, Qian Q et al. (28-8-2008) Treatment of upper gastrointestinal fistula and leakage with personal stage nutrition support. *World Journal of Gastroenterology* 14:5073-5077.
119. Wu XM. (2010) Total enteral nutrition in prevention of pancreatic necrotic infection in severe acute pancreatitis. *Pancreas* 39:248-251.
120. Alagiakrishnan K, Bhanji RA, and Kurian M. (2013) Evaluation and management of oropharyngeal dysphagia in different types of dementia: a systematic review. *Archives of Gerontology & Geriatrics* 56:1-9.
121. Gomes Jr CAR, Lustosa SAS, Matos D et al. (2012) Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances. *Cochrane Database of Systematic Reviews* CD008096.
122. 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* 59:2009-2016.
123. 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* 112:150-155.
124. 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.
125. Cobell WJ, Hinds AM, Lim RG et al. (2013) Feeding after percutaneous endoscopic gastrostomy: Experience of early versus delayed feeding. *Gastrointestinal Endoscopy* 77:AB150-AB151.
126. Doig GS, Chevrou-Severac H, and Simpson F. (2013) Early enteral nutrition in critical illness: a full economic analysis using US costs. *Clinicoecon.Outcomes Res* 5:429-436.
127. Nugent B, Lewis S, and O'Sullivan JM. (2013) Enteral feeding methods for nutritional management in patients with head and neck cancers being treated with radiotherapy and/or chemotherapy. *Cochrane database of systematic reviews (Online)* 1:CD007904.
128. Alkhwaja S, Martin C, Butler RJ et al. (2015) Post-pyloric versus gastric tube feeding for preventing pneumonia and improving nutritional outcomes in critically ill adults. *The Cochrane database of systematic reviews* 8:CD008875.

129. Silva Cristiane Costa Reis da, Bennett C, Saconato H et al. (2015) Metoclopramide for post-pyloric placement of naso-enteral feeding tubes. The Cochrane database of systematic reviews 1:CD003353.
130. Harvey SE, Parrott F, Harrison DA et al. (2016) A multicentre, randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of early nutritional support via the parenteral versus the enteral route in critically ill patients (CALORIES). Health technology assessment (Winchester, England) 20:1-144.
131. Chow R, Bruera E, Chiu L et al. (2016) Enteral and parenteral nutrition in cancer patients: a systematic review and meta-analysis. Annals of palliative medicine 5:30-41.
132. Zhang Y, Gu F, Wang F et al. (2016) Effects of early enteral nutrition on the gastrointestinal motility and intestinal mucosal barrier of patients with burn-induced invasive fungal infection. Pakistan Journal of Medical Sciences 32:599-603.
133. Takesue T, Takeuchi H, Ogura M et al. (2015) A Prospective Randomized Trial of Enteral Nutrition After Thoracoscopic Esophagectomy for Esophageal Cancer. Annals of Surgical Oncology 22:802-809.
134. Andersen S, Kennedy G, and Banks M. (2015) A randomised controlled comparison of enteral versus parenteral nutritional support post allogeneic haematopoietic cell transplantation. Clinical Nutrition 10:e102â€“e106.
135. Zhong J, Kang K, and Shu X. (2015) Effect of nutritional support on clinical outcomes in perioperative malnourished patients: a meta-analysis. Asia Pacific journal of clinical nutrition 24:367-378.
136. Baker J, Janda M, Graves N et al. (2015) Quality of life after early enteral feeding versus standard care for proven or suspected advanced epithelial ovarian cancer: Results from a randomised trial. Gynecologic oncology 137:516-522.
137. Ekinci O, Yanik S, Terzioglu B et al. (2016) Effect of Calcium beta-Hydroxy-beta-Methylbutyrate (CaHMB), Vitamin D, and Protein Supplementation on Postoperative Immobilization in Malnourished Older Adult Patients With Hip Fracture: A Randomized Controlled Study. Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition .
138. Gomes Claudio AR, Jr, Andriolo RB et al. (2015) Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances. The Cochrane database of systematic reviews 5:CD008096.
139. Jaafar MH, Mahadeva S, Morgan K et al. (2015) Percutaneous endoscopic gastrostomy versus nasogastric feeding in older individuals with non-stroke dysphagia: a systematic review. The journal of nutrition, health & aging 19:190-197.
140. Yuan Y, Zhao Y, Xie T et al. (2016) Percutaneous endoscopic gastrostomy versus percutaneous radiological gastrostomy for swallowing disturbances. The Cochrane database of systematic reviews 2:CD009198.
141. Heyland DK, Murch L, Cahill N et al. (2013) Enhanced protein-energy provision via the enteral route feeding protocol in critically ill patients: results of a cluster randomized trial. Critical care medicine 41:2743-2753.
142. Torres J, Luiz G, de VS et al. (2014) Randomized clinical trial: nasoenteric tube or jejunostomy as a route for nutrition after major upper gastrointestinal operations. World journal of surgery 38:2241-2246.
143. Casaer MP, Mesotten D, Hermans G et al. (2011) Early versus Late Parenteral Nutrition in Critically Ill Adults. New England Journal of Medicine 365:506-517.

144. Vincent RP, Omar S, Elnenaei MO et al. (2013) Adherence to the National Institute of Clinical Excellence guidance on parenteral nutrition screening is not enough to improve outcomes. *Clinical nutrition (Edinburgh, Scotland)* 32:73-76.
145. Owais AE, Kabir S, I, McNaught C et al. (2014) A single-blinded randomised clinical trial of permissive underfeeding in patients requiring parenteral nutrition. *Clinical Nutrition* 33:997-1001.
146. Mousavi SN, Nematy M, Norouzy A et al. (2014) Comparison of intensive insulin therapy versus conventional glucose control in traumatic brain injury patients on parenteral nutrition: A pilot randomized clinical trial. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences* 19:420-425.
147. Luger E, Dorner TE, Haider S et al. (2016) Effects of a Home-Based and Volunteer-Administered Physical Training, Nutritional, and Social Support Program on Malnutrition and Frailty in Older Persons: A Randomized Controlled Trial. *Journal of the American Medical Directors Association* 17:671.
148. Suominen MH, Puranen TM, Jyvakorpi SK et al. (2015) Nutritional Guidance Improves Nutrient Intake and Quality of Life, and May Prevent Falls in Aged Persons with Alzheimer Disease Living with a Spouse (NuAD Trial). *The journal of nutrition, health & aging* 19:901-907.
149. Schilp J, Kruiuzenga HM, Wijnhoven Hanneke AH et al. (2013) Effects of a dietetic treatment in older, undernourished, community-dwelling individuals in primary care: a randomized controlled trial. *European journal of nutrition* 52:1939-1948.
150. Schilp J, Bosmans JE, Kruiuzenga HM et al. (2014) Is dietetic treatment for undernutrition in older individuals in primary care cost-effective? *Journal of the American Medical Directors Association* 15:226.
151. Emery D, Pearson A, Lopez R et al. (2015) Voiceover Interactive PowerPoint Catheter Care Education for Home Parenteral Nutrition. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition* 30:714-719.
152. BAPEN. (2014) Nutritional Care and the Patient Voice – are we being listened to?
153. Patients Association. (2015) MANAGING ADULT MALNUTRITION IN THE COMMUNITY: A Spotlight on Information, Help and Support available for Patients and Carers in England.
154. 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* CD000323.
155. Koretz RL, Avenell A, and Lipman TO. (2012) Nutritional support for liver disease. *Cochrane Database of Systematic Reviews* 5:CD008344.
156. Ney M, Vandermeer B, van Zanten SJV et al. (2013) Meta-analysis: oral or enteral nutritional supplementation in cirrhosis. *Alimentary pharmacology & therapeutics* 37:672-679.
157. Grobler L, Nagpal S, Sudarsanam TD et al. (2016) Nutritional supplements for people being treated for active tuberculosis. *The Cochrane database of systematic reviews* CD006086.
158. Si Z, Kang L, Shen X et al. (2015) Adjuvant Efficacy of Nutrition Support During Pulmonary Tuberculosis Treating Course: Systematic Review and Meta-analysis. *Chinese medical journal* 128:3219-3230.
159. Huisman EJ, van M, S et al. (2016) Effects of preventive versus "on-demand" nutritional support on paid labour productivity, physical exercise and performance status during PEG-interferon-containing treatment for hepatitis C. *Clinics and Research in Hepatology and Gastroenterology* 40:221-229.
160. Smyth RL and Rayner O. (2014) Oral calorie supplements for cystic fibrosis. *The Cochrane database of systematic reviews* 11:CD000406.

161. Wills AM, Hubbard J, Macklin EA et al. (2014) Hypercaloric enteral nutrition in patients with amyotrophic lateral sclerosis: A randomised, double-blind, placebo-controlled phase 2 trial. *The Lancet* 383:2065-2072.
162. Blijlevens NM. (2005) 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* 13:790-796.
163. Buijs N, van Bokhorst-de van der Schueren MA, Langius JA et al. (2010) Perioperative arginine-supplemented nutrition in malnourished patients with head and neck cancer improves long-term survival. *American Journal of Clinical Nutrition* 92:1151-1156.
164. Casas-Rodera P, mez-Candela C, tez S et al. (2008) Immunoenhanced enteral nutrition formulas in head and neck cancer surgery: a prospective, randomized clinical trial. *Nutricion Hospitalaria* 23:105-110.
165. Celik JB GK. (2009) The role of immunonutrition in gynecologic oncologic surgery. *European journal of gynaecological oncology* 30:418-421.
166. Cereda E G. (2009) 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* 57:1395-1402.
167. Chapman IM, Visvanathan R, Hammond AJ et al. (2009) 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* 89:880-889.
168. Culkin A. (2008) A double-blind, randomized, controlled crossover trial of glutamine supplementation in home parenteral nutrition. *European journal of clinical nutrition* 62:575-583.
169. da Gama Torres HO. (2008) Efficacy of glutamine-supplemented parenteral nutrition on short-term survival following allo-SCT: a randomized study. *Bone marrow transplantation* 41:1021-1027.
170. Estivariz CF GDL. (2008) Efficacy of parenteral nutrition supplemented with glutamine dipeptide to decrease hospital infections in critically ill surgical patients. *JPEN Journal of parenteral and enteral nutrition*. 32:389-402.
171. Fan YP. (2009) 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* 24:55-59.
172. Friesecke S L. (2008) Fish oil supplementation in the parenteral nutrition of critically ill medical patients: a randomised controlled trial. *Intensive Care Medicine* 34:1411-1420.
173. Garbagnati F, Cairella G, De MA et al. (2009) Is antioxidant and n-3 supplementation able to improve functional status in poststroke patients? Results from the Nutristroke Trial. *Cerebrovascular Diseases* 27:375-383.
174. Gunerhan Y. (2009) Effect of preoperative immunonutrition and other nutrition models on cellular immune parameters. *World journal of gastroenterology : WJG* 15:467-472.
175. Jiang ZM. (2010) Randomized clinical trial of intravenous soybean oil alone versus soybean oil plus fish oil emulsion after gastrointestinal cancer surgery. *The British journal of surgery* 97:804-809.
176. Jo S. (2006) 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* 30:1974-1982.

177. Klek S K. (2008) Standard and immunomodulating enteral nutrition in patients after extended gastrointestinal surgery--a prospective, randomized, controlled clinical trial. *Clinical nutrition (Edinburgh, Scotland)* 27:504-512.
178. Langkamp-Henken B. (2006) Nutritional formula improved immune profiles of seniors living in nursing homes. *Journal of the American Geriatrics Society* 54:1861-1870.
179. Luo M. (2008) 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)* 24:37-44.
180. Luo Y, Xu W-G, Dong H-J et al. (2005) Glutamine for immunomodification and metabolic support in patients with chronic obstructive pulmonary disease. *Chinese Journal of Clinical Rehabilitation* 9:234-236.
181. Piper SN. (2008) 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* 25:557-565.
182. Pontes-Arruda A. (2006) 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* 34:2325-2333.
183. Puiggros C. (2009) 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 Journal of parenteral and enteral nutrition.* 33:501-512.
184. Qin HL. (2008) Effect of *Lactobacillus plantarum* enteral feeding on the gut permeability and septic complications in the patients with acute pancreatitis. *European journal of clinical nutrition* 62:923-930.
185. Ryan AM. (2009) 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* 249:355-363.
186. Schiffrin EJ, Thomas DR, Kumar VB et al. (2007) Systemic inflammatory markers in older persons: the effect of oral nutritional supplementation with prebiotics. *Journal of Nutrition, Health & Aging* 11:475-479.
187. Slotwinski R, Olszewski WL, Lech G et al. (2008) Immunonutrition after major pancreatic surgery. *Central-European Journal of Immunology* 33:67-73.
188. Sorensen D. (2009) Perioperative immunonutrition in head and neck cancer. *The Laryngoscope* 119:1358-1364.
189. Sun LC, Shih YL, Lu CY et al. (2008) Randomized, controlled study of branched chain amino acid-enriched total parenteral nutrition in malnourished patients with gastrointestinal cancer undergoing surgery. *American Surgeon* 74:237-242.
190. Tang ZF LYL. (2007) Glutamine and recombinant human growth hormone protect intestinal barrier function following portal hypertension surgery. *World journal of gastroenterology : WJG* 13:2223-2228.
191. Theilla M, Singer P, Cohen J et al. (2007) A diet enriched in eicosapentaenoic 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* 26:752-757.
192. van Stijn MF. (2010) Antioxidant-enriched enteral nutrition and immuno-inflammatory response after major gastrointestinal tract surgery. *The British journal of nutrition* 103:314-318.

193. van Stijn MF. (2008) Antioxidant enriched enteral nutrition and oxidative stress after major gastrointestinal tract surgery. *World journal of gastroenterology* : WJG 14:6960-6969.
194. Wang X. (2008) 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 Journal of parenteral and enteral nutrition*. 32:236-241.
195. Wang X. (2009) Fish oil-supplemented parenteral nutrition in severe acute pancreatitis patients and effects on immune function and infectious risk: a randomized controlled trial. *Inflammation* 32:304-309.
196. Yeh CN. (2008) 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* 393:849-855.
197. Klek S K. (2008) The impact of immunostimulating nutrition on infectious complications after upper gastrointestinal surgery: a prospective, randomized, clinical trial. *Annals of Surgery* 248:212-220.
198. McQuiggan M. (2008) Enteral glutamine during active shock resuscitation is safe and enhances tolerance of enteral feeding. *JPEN Journal of parenteral and enteral nutrition*. 32:28-35.
199. Andrews PJ, Avenell A, Noble DW et al. (17-3-2011) Randomised trial of glutamine, selenium, or both, to supplement parenteral nutrition for critically ill patients. *BMJ* 342.
200. Cerantola Y, Hubner M, Grass F et al. (1-1-2011) Immunonutrition in gastrointestinal surgery. *British Journal of Surgery* 98:37-48.
201. Heyland D, Muscedere J, Wischmeyer PE et al. (17-4-2013) A Randomized Trial of Glutamine and Antioxidants in Critically Ill Patients. *New England Journal of Medicine* 368:1489-1497.
202. Manzanares W, Dhaliwal R, Jurewitsch B et al. (1-1-2014) Parenteral Fish Oil Lipid Emulsions in the Critically Ill: A Systematic Review and Meta-Analysis. *Journal of Parenteral and Enteral Nutrition* 38:20-28.
203. Mocellin MC, Pastore E Silva, Camargo CDQ et al. (2013) Fish oil decreases C-reactive protein/albumin ratio improving nutritional prognosis and plasma fatty acid profile in colorectal cancer patients. *Lipids* 48:879-888.
204. Palmer AJ, Ho CK, Ajibola O et al. (2013) The role of omega-3 fatty acid supplemented parenteral nutrition in critical illness in adults: a systematic review and meta-analysis. *Critical care medicine* 41:307-316.
205. Vasson MP, Talvas J, Perche O et al. (20-6-2013) Immunonutrition improves functional capacities in head and neck and esophageal cancer patients undergoing radiochemotherapy: A randomized clinical trial. *Clin Nutr* .
206. Yeh KY, Wang HM, Chang JW et al. (2013) Omega-3 fatty acid-, micronutrient-, and probiotic-enriched nutrition helps body weight stabilization in head and neck cancer cachexia. *Oral Surg Oral Med Oral Pathol.Oral Radiol* 116:41-48.
207. Zhao H, Wang Y, Jing H et al. (2013) Randomized clinical trial of arginine-supplemented enteral nutrition versus standard enteral nutrition in patients undergoing gastric cancer surgery. *Journal of Cancer Research and Clinical Oncology* 139:1465-1470.
208. Barker LA, Gray C, Wilson L et al. (2013) Preoperative immunonutrition and its effect on postoperative outcomes in well-nourished and malnourished gastrointestinal surgery patients: a randomised controlled trial. *European journal of clinical nutrition* 67:802-807.
209. Tan HB, Danilla S, Murray A et al. (2014) Immunonutrition as an adjuvant therapy for burns. *The Cochrane database of systematic reviews* 12:CD007174.

210. Chitapanarux I, Pisprasert V, Tharavichitkul E et al. (2016) Randomized study of nutritional status and treatment toxicities of oral arginine, glutamine, and omega-3 fatty acids during concurrent chemoradiotherapy for head and neck cancer patients. *Functional foods in health and disease* 6:121-132.
211. Pottel L, Lycke M, Boterberg T et al. (2014) Echium oil is not protective against weight loss in head and neck cancer patients undergoing curative radio(chemo)therapy: a randomised-controlled trial. *BMC complementary and alternative medicine* 14:382.
212. Ma Y, Yu J, Xiao J et al. (2015) The consumption of omega-3 polyunsaturated fatty acids improves clinical outcomes and prognosis in pancreatic cancer patients: a systematic evaluation. *Nutrition and cancer* 67:112-118.
213. Ma Y, Liu L, Xiao J et al. (2016) Perioperative omega-3 Polyunsaturated Fatty Acid Nutritional Support in Gastrointestinal Cancer Surgical Patients: A Systematic Evaluation. *Nutrition and cancer* 68:568-576.
214. Mottaghi A, Yeganeh MZ, Golzarand M et al. (2016) Efficacy of glutamine-enriched enteral feeding formulae in critically ill patients: a systematic review and meta-analysis of randomized controlled trials. *Asia Pacific journal of clinical nutrition* 25:504-512.
215. Klek S, Szybinski P, and Szczepanek K. (2014) Perioperative immunonutrition in surgical cancer patients: a summary of a decade of research. *World journal of surgery* 38:803-812.
216. Song GM, Tian X, Liang H et al. (2015) Role of enteral immunonutrition in patients undergoing surgery for gastric cancer: A systematic review and meta-analysis of randomized controlled trials. *Medicine (United States)* 94:no.
217. Yildiz SY, Yazicioglu MB, Tiryaki C et al. (2016) The effect of enteral immunonutrition in upper gastrointestinal surgery for cancer: A prospective study. *Turkish Journal of Medical Sciences* 46:393.
218. Jafari T, Feizi A, Askari G et al. (2015) Parenteral immunonutrition in patients with acute pancreatitis: A systematic review and meta-analysis. *Clinical Nutrition* 34:35-43.
219. Elliott JA, Jackson S, King S et al. (2015) Gut hormone suppression increases food intake after esophagectomy with gastric conduit reconstruction. *Annals of Surgery* 262:824-830.