ESPEN Guideline

ESPEN guideline on home enteral nutrition

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SUMMARY

This guideline will inform physicians, nurses, dieticians, pharmacists, caregivers and other home enteral nutrition (HEN) providers about the indications and contraindications for HEN, and its implementation and monitoring. Home parenteral nutrition is not included but will be addressed in a separate ESPEN guideline. This guideline will also inform interested patients requiring HEN. The guideline is based on current evidence and expert opinion and consists of 61 recommendations that address the indications for HEN, relevant access devices and their use, the products recommended, the monitoring and criteria for termination of HEN, and the structural requirements needed to perform HEN. We searched for meta-analyses, systematic reviews and single clinical trials based on clinical questions according to the PICO format. The evidence was evaluated and used to develop clinical recommendations implementing the SIGN method. The guideline was commissioned and financially supported by ESPEN and the members of the guideline group were selected by ESPEN.

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1. Introduction

Since its introduction in the 1970s, HEN has been established as a reliable and effective nutritional intervention, particularly relevant due to the increasing reliance on ambulatory care. Usually HEN is started during a hospital stay and continued as a long-term home therapy. Typically, there are only minor differences in the indication for HEN and for in-hospital enteral nutrition (EN). In HEN, additional criteria need to be considered carefully such as prognosis, health-related quality of life (QoL) and any ethical aspect of the treatments. In order to initiate HEN, the principle should be followed that without EN there is an expectation of significant deterioration of the patient’s nutritional state, affecting prognosis and QoL, which is a complex decision, if there is no effective treatment for the underlying medical condition.

Enteral nutrition support is a medical treatment but the decisions on route, content, and management of nutritional support are best made by multidisciplinary nutrition teams.

This guideline provides evidenced-based information on the use of HEN. There are numerous and often complex diseases that lead to the need for HEN, a description of which is not part of the present guideline, but they include:
• Swallowing disorders because of neurological diseases,
• Obstructions because of malignancies,
• Cachexia because of cancer,
• Chronic obstructive pulmonary disease,
• Heart disease,
• Chronic infections, and
• Malabsorption/maldigestion because of liver, pancreas, or intestinal diseases.

The specific nutritional requirements for these diseases are described in detail in other recently published ESPEN guidelines (see ESPEN website and Clinical Nutrition journal). The present guideline is focused on the methodology and clinical practice of HEN, the related monitoring, and strategies to avoid complications.

2. Methods

2.1. General methodology

The present guideline was developed according to the standard operating procedure for ESPEN guidelines [1], and based in part on the German guideline “Artificial Nutrition in the outpatient area” [2]. The guideline was developed by an expert group representing different professions including physicians (SCB, MC, CC, SMS, ZS), a pharmacist (PA), a nurse (KB) and dieticians (MC, IN, CJS), as well as a patient representative (ML).

Based on the standard operating procedures for ESPEN guidelines and consensus papers, the first development step of this guideline was the formulation of so-called PICO questions to address specific patient groups (or problems), Interventions, compare different therapies and be outcome-related [1]. In total, 19 PICO questions were created and split into five main chapters entitled “Indication and contraindication for HEN”, “Access devices for HEN”, “Products recommended for HEN”, “Monitoring and termination of HEN” and “Structural requirements to perform HEN”. To answer these PICO questions, a literature search was performed to identify suitable meta-analyses, systematic reviews and primary studies (for details see below, “search strategy”). Each PICO question was allocated to subgroups/experts for the different topics and 59 recommendations answering the PICO questions were formulated. The grading system of the Scottish Intercollegiate Guidelines Network (SIGN) [3] was used to grade the literature. The allocation of studies to the different levels of evidence is shown in Table 1. Supporting the recommendations, the working group added commentaries to explain their basis.

The grades of recommendation were decided according to the levels of evidence assigned (Table 2). In some cases, a downgrading from the generated grades of recommendation was necessary based on the levels of evidence according to Tables 1 and 2, e.g., due to a lack of quality of primary studies included in a meta-analysis. Such cases are described in the commentaries accompanying the respective recommendations. The wording of the recommendations reflects the grades of recommendations since level A is indicated by the use of the word “shall”, level B by the word “should” and level 0 by the word “can” or “may”. The good practice points (GPP) are based on experts’ opinions due to the lack of studies, for which the choice of wording was not restricted.

Between 27th June and 25th July 2018, an online voting on the recommendations was performed using the guideline-services.com platform. All ESPEN members were invited to agree or disagree with the recommendations and to provide comments. A first draft of the guideline was also made available to the participants on that occasion. Forty-three recommendations reached an agreement >90%, 14 recommendations reached an agreement between 75–90% and two recommendations an agreement ≤75%. Those recommendations with an agreement higher than 90% (indicating a strong consensus, Table 3) were directly passed, and all others were revised according to the comments and voted on again during a consensus conference which took place during the 2018 ESPEN Congress in Madrid on 2nd September 2018. Two recommendations (Recommendations 1 and 53) that originally had received more than 90% agreement were also voted on during the consensus conference due to major changes in wording. At that time, all recommendations except for eight of them received an agreement higher than 90%. During the consensus conference, two of the original recommendations were split into two separate recommendations. Therefore, the final guideline comprises of 61 recommendations. To support the recommendations and the assigned grades of recommendation, the ESPEN guideline office created evidence tables of relevant meta-analyses, systematic reviews and (randomized) controlled trials. These evidence tables are available online as supplemental material to this guideline (see clinicalnutritionjournal.com).

2.2. Search strategy

The literature search was performed separately for each PICO question in March 2018. The Pubmed, Embase and Cochrane databases were searched using the search filters “human”, “adult” and “English”. Some authors included their mother tongue as well. Depending on the PICO questions, different search terms presented in Table 4 were used in combination with “enteral nutrition”/“home enteral nutrition”/“tube feeding”/“home care services”/“intubation, gastrointestinal”/“feeding tube placement”/“PEG”/“gastrostomy”/“percutaneous endoscopic gastrostomy”/“RIG”/“jejunostomy”/“PEJ”/“PEGJ”/“gastric button”/“nasogastric intubation”/“nasogastric tube”/“nasogastric tube”/“enteral tube feeding”/“enteral feeding tube”. The results were pre-screened based on the abstracts. In addition to the named databases, websites from nutritional (nursing) societies in English speaking or bilingual countries including the English language were searched for practice guidelines.

3. Recommendations

3.1. Indication and contraindication for HEN

3.1.1. What are the indications for HEN?

Recommendation 1

HEN should be offered to patients at nutritional risk or malnourished who cannot meet their nutrient requirements by normal dietary intake, who have a functioning gastrointestinal tract, who are able to receive therapy outside of an acute care setting, and who agree and are able to comply with HEN therapy with the goal of improving body weight, functional status or QoL.

Grade of Recommendation GPP – Strong consensus (97% agreement)

Commentary

HEN is indicated in patients who are at high nutritional risk or malnourished, who are unable to meet nutritional requirements by the oral route, and who exhibit a functional gastrointestinal tract [5]. Thus, HEN can be defined as a life-sustaining therapy and should be considered if a patient’s nutritional intake is likely to be qualitatively or quantitatively insufficient for a week or more. According to ESPEN guidelines, an inadequate nutritional state is confirmed if patients cannot eat for a week or if the energy intake is less than 60% of estimated requirements for 1–2 weeks (corresponding approximately to a daily energy intake of less than 10 kcal/kg/d or a daily energy deficit of 600–800 kcal/d) [6–9]. Poor
According to the Scottish Intercollegiate Guidelines Network (SIGN) grading system,arduous treatment (e.g., chemotherapy) is concurrent[13].

The nutritional state may deteriorate more rapidly if foodabolic processes (e.g. infections, systemic inflammation) or if esophagectomy or total gastrectomy demonstrated that HEN by jejunostomy as a usual practice was feasible, safe and acceptable to patients and their caregivers. Furthermore, the authors showed a substantial increase in anthropometric (weight, mid-arm muscle circumference, triceps skinfold) and functional (handgrip strength) parameters as well as cost efficiency at a six-month follow-up[14]. The effectiveness of HEN on clinical outcomes was shown in two studies that included cancer and Crohn's patients[15,16]. Two non-randomized controlled studies (postoperative phase/during chemoradiation) in malnourished esophageal cancer patients found, HEN led to an improvement in QoL[17,18]. In another retrospective multicenter study with more 2842 patients, Klek et al. confirmed that — when indicated — HEN is a safe, well-tolerated and cost-effective procedure[19].

### Table 1

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>1 ++</td>
<td>Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>2 ++</td>
<td>High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
</tr>
<tr>
<td>2 ++</td>
<td>Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>2 ++</td>
<td>Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal</td>
</tr>
<tr>
<td>2 ++</td>
<td>Non-analytic studies, e.g. case reports, case series</td>
</tr>
<tr>
<td>2 ++</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>

According to the Scottish Intercollegiate Guidelines Network (SIGN) grading system[3].

nutritional intake is presumed when normal food ingestion covering individual requirements cannot be met despite the most skilled dietetic treatment and medical management of anorexia, gastrointestinal disorders, pain, and psychosocial stress. In this situation, initiation of EN should be within the week. Significant impairment of the nutritional state has to be assumed if the patient has lost >5% in one month (= >15% in three months) of body weight[10]. The nutritional state may deteriorate more rapidly if food absorption is less than 75% of the daily requirements based on general recommendations[11,12], or if there has been previous weight loss (e.g., loss of appetite, dysphagia) or concomitant catabolic processes (e.g. infections, systemic inflammation) or if arduous treatment (e.g., chemotherapy) is concurrent[13].

Before prescribing HEN, the absence of contraindications must be checked (recommendations 3–5). When HEN is prescribed, it is essential that the attending physician and a (nutrition) nurse specialist or dietician inform the patient in detail about potential benefits and risks of the treatment. The patient should give his/her consent and actively express their desire for the planned nutritional treatment. It is also important to discuss the choice of enteral access and appropriate care with the patient. Furthermore, the technical measures necessary for the preparation and administration of HEN have to be implemented to ensure that it can be performed safely, effectively and efficiently over the long term.

The primary aims of HEN are to correct significant nutritional deficiencies, to avoid further loss of body weight, and to stop the related deterioration of the patient's subjective QoL, all of which can result from poor oral nutritional intake. A multi-center randomized controlled trial (RCT) evaluating patients undergoing

### Table 2

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review, or RCT rated as 1 ++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1 ++, directly applicable to the target population, and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2 ++, directly applicable to the target population; or A body of evidence including studies rated as 2 ++, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1 ++ or 1 ++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 ++ or 2 ++</td>
</tr>
<tr>
<td>GPP</td>
<td>Good practice points/expert consensus: Recommended best practice based on the clinical experience of the guideline development group</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong consensus</td>
<td>Agreement of &gt;90% of the participants</td>
</tr>
<tr>
<td>Consensus</td>
<td>Agreement of &gt;75–90% of the participants</td>
</tr>
<tr>
<td>Majority agreement</td>
<td>Agreement of &gt;50–75% of the participants</td>
</tr>
<tr>
<td>No consensus</td>
<td>Agreement of &lt;50% of the participants</td>
</tr>
</tbody>
</table>

According to the AWMF methodology[4].

### 3.1.2. Who needs HEN?

**Recommendation 2**

Prior to discharge from hospital of patients at risk of malnutrition (e.g. patients with neurological disease, head injury, head and neck cancer, gastrointestinal and other malignancies, non-neoplastic gastrointestinal disease including malabsorptive syndromes), either oral nutritional supplements or HEN should be considered.

**Grade of Recommendation B – Strong consensus (96% agreement)**

**Commentary**

In epidemiological data collected from 3246 Italian patients over an 11-year period, a progressive annual increase in HEN therapy could be observed[20]. The mean incidence was 406 ± 58 patients/million inhabitants/year for patients living at home and 319 ± 44 for patients living in nursing homes (mean prevalence rate ± SD: 464 ± 129 cases/million inhabitants at home compared to 478 ± 164 in nursing homes)[20].

According to several epidemiological studies and European national registries, the most frequent indications for HEN in adults are neurological diseases (neurovascular and -degenerative), head and neck cancer, gastrointestinal cancer, and other cancers, cerebral palsy, non-neoplastic gastrointestinal disease (e.g., fistulae, esophageal stenosis, inflammatory bowel disease), head injury, malabsorptive syndromes (e.g., short bowel syndrome), severe intestinal motility disorders, inherited metabolic diseases, and cystic fibrosis (Table 5)[5,15,19–27].

A retrospective Italian study found a median duration of HEN is about 196 days[25]. Broken down by pathology, duration was 261 days for neurovascular disease, 251.5 days for neurodegenerative disease, 118 days for head and neck cancer, 82.5 days for abdominal cancer, 788 days for head injuries, and 387 days for congenital pathologies. Only 79% of the patients resumed oral nutrition, and the median survival rate was 9.1 months[25].

### 3.1.3. When is HEN not to be recommended? (Contraindication)

**Recommendation 3**

If life expectancy is estimated to be less than one month, HEN usually shall not be initiated.

**Grade of recommendation GPP – Consensus (78% agreement)**
Commentary
This recommendation is based on a previous recommendation of the German Society for clinical nutrition [2]. An effort should be made to estimate life expectancy to ensure optimal care [28]. For further recommendations regarding HEN, the ESPEN guideline on ethical aspects of artificial nutrition and hydration [29] and the ESPEN guideline on Clinical Nutrition in Neurology [30] should be considered.

Recommendation 4
HEN shall not be performed in patients with contraindications such as severe functional disturbances of the bowel, gastrointestinal obstruction, gastrointestinal tract bleeding, severe malabsorption or severe metabolic imbalances.

Grade of recommendation GPP – Consensus (84% agreement)

**Commentary**
This recommendation is based on good clinical practice and not specific to HEN. It applies similarly to EN in general.

Recommendation 5
If patient and/or their legal carers do not agree to a HEN program or are unlikely to comply with and/or if there are organizational/logistic problems which cannot be overcome, HEN should not be offered.

**Grade of recommendation GPP – Strong consensus (97% agreement)**

**Commentary**
This recommendation has been adopted from the German guideline “Artificial Nutrition in the outpatient area” [2] and fits to the “ESPEN ethical guideline” [29].

3.2. Access devices for HEN

**Recommendation 6**
HEN can be delivered through a nasal feeding tube in patients who need HEN only for a short period of time (up to 4–6 weeks).

**Grade of recommendation 0 – Consensus (90% agreement)**

**Commentary**
The most appropriate route for outpatient nutritional support depends on the functioning, accessibility and digestive and/or absorptive capacity of the gastrointestinal tract. There should be a careful consideration (incorporating contra-indications) when selecting the route for administration. If HEN is needed for a limited time (usually meaning up to six weeks), nasogastric tube feeding can be used. Even longer periods are possible, certainly with fine-bore nasogastric feeding tubes, when long term percutaneous endoscopic gastrostomy (PEG) or radiologically inserted gastrostomy (RIG) options are not suitable [25,31]. If there is already a device in situ that could be used for the provision of EN the use of that device should be considered.

**Recommendation 7**

**Table 4**

<table>
<thead>
<tr>
<th>PICO question</th>
<th>Search terms used in combination with “enteral nutrition”*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>“indication”</td>
</tr>
<tr>
<td>1.2</td>
<td>“diagnosis”, “outcome”</td>
</tr>
<tr>
<td>1.3</td>
<td>“contraindication”</td>
</tr>
<tr>
<td>2.3 + 2.4</td>
<td>“start”, “tube placement”, “PEG placement”, “bolus”, “continuous”, “pump”, “mobile device”, “jejuno jejunostomy feeding”, “home care”</td>
</tr>
<tr>
<td>2.5</td>
<td>“Home Care Services”, “Home Care Services, hospital-based”, “Home Residence Characteristics”, “Residential Treatment”, “Residential Facilities”, “Primary Health Care”, “primary care”, “primarycare” the above mentioned search terms were additionally combined with: “administration”, “parenteral drug administration”</td>
</tr>
<tr>
<td>3.1 + 3.2</td>
<td>“Home Care Services”, “Home Care Services, hospital-based”, “Home Residence Characteristics”, “Residential Treatment”, “Residential Facilities”, “Primary Health Care”, “primary care”, “primarycare” the above mentioned search terms were additionally combined with: “product or type or enteral feed or formula”</td>
</tr>
<tr>
<td>4.1</td>
<td>“case management”, “monitoring”, “follow-up”</td>
</tr>
<tr>
<td>4.2</td>
<td>“discontinuation”, “stop”, “weaning”, “oral autonomy”</td>
</tr>
<tr>
<td>4.3</td>
<td>“complications”</td>
</tr>
<tr>
<td>4.4</td>
<td>“quality of life”</td>
</tr>
</tbody>
</table>

*a The search terms displayed in this column were either combined by the operator “OR” or the different terms/spellings were used in different databases according to their specific headwords.

**Table 5**

| Indications for initiation of HEN including prevalence and outcomes improved by HEN. |
|-----------------------------------------------|-----------------------------------------------|
| HEN Indications                              | Overall HEN Prevalence | Overall HEN Outcomes |
| Cardiorespiratory diseases: 13.3% [5] | 2001, 95,2/106 [26] | Resumed full oral nutrition 18.7%. Switch to PN 0.32% [27] |
| Head and neck cancer: 7.5% [19, 17.3% [27, 11.5% [25] | 2003, 365/106 [26] | Resumed full oral nutrition: Neurological diseases 23.6%, digestive diseases 52.6%, head and neck cancer 31.3%, dementia 11.1%, anorexia 56.2%, AIDS 41.2% [26] |
| Cancer of other location: 15.3% [5, 8.2% [19] | 2009, 300/106 [26] | |
| Protein-calorie malnutrition: 2.7% [5, 3.0% [19] | 2010, 296/106 [26] | |
| Inherited metabolic disease: 5.8% [5, 2.3% [19, 2.6% [25] | 2013, 67,1106 [27, 47.6/106 [19] | |
| Malabsorption syndromes: 0.9% [27, 1.9% [24] | 2014, 80,8/106 [27] | |
| Intestinal motility disorders: 0.6% [27, 1.3% [24] | 2015, 90,5/106 [27] | |
...and QoL is possibly better [32], when long-term HEN is required. PEGJ is the preferred access device and should be placed similarly by both PEG and nasogastric feeding [35] whilst the risk of cancer patients, three systematic reviews on the same topic which PEG and nasogastric tubes were compared in head and neck tubes in dysphagic patients [36]. Body weight may be maintained [35], and earlier weaning after completion of radiotherapy [33,35]. The latter advantages limit the clear recommendation for the PEG group [37]. A systematic review including eleven RCT reported wound infection in a PEG group compared to the nasogastric tube ... during surgery with anastomotic leakage [39] and QoL is possibly better [32], although nasogastric tubes were associated with less dysphagia [35] and earlier weaning after completion of radiotherapy [33,35]. The latter advantages limit the clear recommendation for the PEG group suggested by the prior studies and lead to the “B” rather than “A” grade of recommendation. Another RCT conducted in oral cancer patients revealed a significant benefit regarding post-surgical wound infection in a PEG group compared to the nasogastic tube group [37]. A systematic review including eleven RCT reported fewer intervention failure (e.g., feeding interruption, blocking or leakage of the tube, better adherence to treatment) and better improvement in nutritional status (e.g. weight loss from baseline, mid-arm circumference) in the PEG group compared to the nasogastic tube group [36]. Also, QoL (e.g. inconvenience, discomfort, altered body image and social activities) was in favor of PEG. There was no significant difference in mortality rates and aspiration pneumonia between the two groups. Another systematic review could not draw firm conclusions as to whether or not PEG feeding was beneficial over nasogastric tube feeding in older non-stroke dysphagia patients [38], Fay et al. [39] came to the same conclusion in patients on long-term EN, although for an unknown reason early aspiration pneumonia was less frequent in the PEG group. On the other hand, in a multicenter prospective cohort study of long-term EN in elderly hospitalized people, PEG use was associated with improved survival, was better tolerated and was associated with a lower incidence of aspiration [40] compared to nasogastric feeding. Using a PEJ or PEJ/J (PEG with a jejunal extension) tube for HEN may be a suitable approach in case of gastrostodenal motility disorders, gastric outlet stenosis or high risk of aspiration [41,42].

**Recommendation 8**

A PEG should be preferred over a surgical gastrostomy for long-term HEN, mainly due a lower complication rate, cost-effectiveness and operating time.

**Grade of recommendation B — Strong consensus (93% agreement)**

**Commentary**

The recommendation to use a PEG or a PEJ for long-term HEN is based on a RCT [32] cited in the ESPEN Cancer guideline [6], in which PEG and nasogastric tubes were compared in head and neck cancer patients, three systematic reviews on the same topic [33–35], and a systematic review comparing PEG with nasogastric tubes in dysphagic patients [36]. Body weight may be maintained similarly by both PEG and nasogastric feeding [35] whilst the risk of tube dislodgement is lower [35,36] and QoL is possibly better [32], although nasogastric tubes were associated with less dysphagia [35] and earlier weaning after completion of radiotherapy [33,35]. Finally, a retrospective review revealed that the rates of tube dislodgement were significantly higher in the RIG group compared to the PEG group [50].

**Recommendation 10**

RIG or PRG can be used as alternative techniques for the placement of a feeding tube into the stomach, if an endoscopically guided tube placement cannot be performed.

**Grade of recommendation 0 — Strong consensus (97% agreement)**

**Commentary**

The risk of peritonitis and mortality is lowered if the gastrostomy is placed by an endoscopic rather than radiological technique [50–52]. Radiological techniques should be reserved for those patients in whom an endoscopic technique is not possible. However both PEG and PRG are effective for long-term EN support in selected individuals [48].

**Recommendation 11**

In case of inadvertent displacement or removal of the PEG more than four weeks after initial placement, direct replacement can be safely attempted before the track closes completely.

**Grade of recommendation GPP — Strong consensus (93% agreement)**
Commentary

A mature fibrous tract is a prerequisite for replacement of a PEG after inadvertent removal, dislodgement, occlusion or breakage. Patients who are at risk for inadvertent removal (e.g. dementia, delirium) require preventive measures to protect the tube. Adherence of the stomach to the abdominal wall normally takes place within 7–14 days but can be delayed in patients with impaired wound healing (e.g. malnutrition, ascites or corticosteroid treatment) [53]. Inadvertent removal of a recently placed percutaneous gastrostomy tube (<four weeks), is an emergency.

In the first two weeks, replacement is mostly done endoscopically or radiologically through the same site. Between two and for weeks after initial placement, besides endoscopic replacement, blind reposition can be attempted (upon medical decision) if the tube position is afterwards checked by a water-soluble contrast study [54]. Replacement should be executed expeditiously to maintain patency and prevent closure of the tract [41]. Balloon-type replacement tubes are mostly used for blind replacement. If a first tube change can be planned, it is recommended to perform it in a hospital, and afterwards replacement may be completed in a home care setting or nursing home by a nurse, if patients are not able to perform it [55]. If no commercially available gastrostomy tube with similar diameter is available for immediate replacement, a balloon-tipped Foley catheter of the same size can be used temporarily to keep the tract open and, if necessary, to administer EN, fluids or medications, although this is currently more difficult with universal safety connectors (e.g. “ENFit®” [55]. If there is any doubt of malposition after blind replacement then endoscopic or radiologic confirmation of correct position using a water-soluble contrast should be carried out prior to use of the tube. Alternative techniques to check proper position is pH confirmation of gastric content (pH 5 or less), irrigation of the tube with 3–50 ml sterile water without resistance or leakage from around the stoma, assessment of external length of the tube and manipulation of the tube via rotation and in–out movement [59,60].

3.2.2. How should the tubes, the tube insertions sites and consumables be handled during HEN?

Recommendation 12

Until the stoma tract is formed and the incision is healed, the PEG exit site should be daily monitored and kept clean and dry by using aseptic wound care (usually up to 5–7 days post procedure).

Grade of recommendation B — Strong consensus (100% agreement)

Recommendation 13

A glycerin hydrogel or glycogel dressing should be used as an alternative to classical aseptic wound care during the first week(s).

Grade of recommendation B — Strong consensus (97% agreement)

Recommendation 14

After stoma healing, dressings can be reduced to one or two times a week, and the entry site can be cleansed using soap and water of drinking quality.

Grade of recommendation 0 — Strong consensus (90% agreement)

Recommendation 15

Alternatively to recommendation 14, dressings can be omitted and the site can be left open.

Grade of recommendation GPP — Strong consensus (92% agreement)

Commentary to recommendations 12–15

During the first week after insertion of PEG one aim is to prevent stoma tract infection. It is not necessary to apply traction to the freshly inserted PEG tube system for the initial 24 h to achieve better adaptation of the gastric to the abdominal wall [56] The PEG exit site has to be monitored on a daily basis (for signs of bleeding, pain, erythema, induration, leakage, and inflammation) and cleansed (to remove any debris) with 0.9% w/v sodium chloride, sterile water or freshly boiled and cooled water. A sterile Y dressing to compress (that does not shed fibers), placed under the external disc plate, is commonly used, followed by a skin friendly and solvent-free breathable dressing. When the dressing is placed under the exterior bumper, tension has to be avoided [55,57]. Oclusive dressings should be avoided because they promote a moist wound environment and can lead to skin maceration [56,57].

According to previous guidelines [61,62] the grades of recommendations 12 and 13 have been upgraded to a “B”, even though the underlying primary literature evidence rather fits to a “O”. Within these guidelines, a direct comparison of “no care” versus “aseptic care” is missing, and instead only “cleansing” vs “disinfection” was examined for obvious (ethical) reasons.

Two RCTs in adults investigated alternative wound dressings compared with standard wound dressings. The more recent study demonstrated a statistically significant reduction of the mean infection scores at the end of the first and second week using a glycerin hydrogel wound dressing (applied the day after placement and changed every week during four weeks) [56,58]. However, the other study showed no advantage of a glycogel wound dressing regarding peristomal infection after one week of usage [59]. Both studies concluded that by omitting daily changes of regular wound dressings these adjunctive techniques or barriers can be a good cost-effective alternative. The findings were confirmed in a very recent RCT using a hydrogel in children [60].

After approximately one week (or if properly healed) the stoma site can be cleansed twice a week with a clean cloth using fresh tap water and soap and afterwards the skin can be gently and thoroughly dried. With a well healed exit site also, showering, bathing and swimming (it is advisable to cover the site with a waterproof dressing when swimming in public pools) is possible after a few weeks. For some patients it may be advisable to use an additional fixation or securement to minimize traction on the stoma site [57]. Once the patient is discharged it is important to guarantee further competent and high quality of care by means of clear and univocal verbal communication and written or visual materials for caregivers and/or patients. It should be also pointed out which department or service can be used as an (emergency) advice point [61].

Recommendation 16

Immediately after placement of the PEG, the external fixation plate should be subjected to very low traction, without tension.

Grade of recommendation GPP — Strong consensus (93% agreement)

Recommendation 17

Once the gastrostomy tract has been healed (after about one week), the tube should be rotated daily and should be moved inwards at least once a week (at least 2 cm, up to 10 cm).

Grade of recommendation GPP — Consensus (87% agreement)

Recommendation 18

After mobilization, the tube may be returned to its initial position with some free distance (0.5–1 cm) between the skin and the external bolster.

Grade of recommendation 0 — Strong consensus (93% agreement)

Recommendation 19

If the device is a gastrojejunostomy or gastrostomy with jejunal extension it should not be rotated (only weekly pushed in and out).
Grade of recommendation GPP — Strong consensus (92% agreement)

Commentary to recommendations 16—19

Buried bumper syndrome (BBS) is a severe complication in which the internal fixation device migrates alongside the tract of the stoma outside to the stomach. The device can end up anywhere between the stomach mucosa and the surface of the skin [62]. BBS is a usually long-term, uncommon, severe but preventable complication with adequate nursing aftercare. Alarming signals are any difficulty in mobilizing the tube, leakage around the insertion site when trying to flush the tube, frequent feeding pump alarms (that may indicate obstruction), abdominal pain, chronic site infections or resistance with administering EN or fluids [42]. The most important risk factor leading to BBS is excessive compression of tissue between the internal and external fixation device (most often with rigid or semi-rigid internal devices) [63]. The distance between the two bolsters should not be too loose or too restrictive. The tube should be advanced into the stomach for a minimum of about 2–3 cm, but with small movements there is a risk of just moving the abdominal wall, so ideally it should be even up to 5–10 cm [64]. This can start after approximately one week because earlier it can cause local pain and damage tract formation. A PEG can also be imbedded in the gastric mucosa even if it is still possible to rotate the PEG. This can happen when a gastric mucosa 'pocket' has grown over and round the bumper [64]. When stiches/sutures are present because the stomach is fixed to the abdominal wall (gastropexy), mobilization of the tube can be delayed until the sutures have been removed (usually after two weeks). Note that the device should not be rotated (but only moved in and out) if a jejunum extension is present within the tube or if the tube is a gastrojejunostomy [57,65].

Recommendation 20

In case of peristomal leakage of gastric contents at the stoma site, the surrounding skin can be properly protected using zinc oxide-based skin protectants.

Grade of recommendation 0 — Strong consensus (93% agreement)

Recommendation 21

Proton pump inhibitors can be used for decreasing leakage by minimizing gastric acid secretion and — if used — needs to be reviewed regularly.

Grade of recommendation 0 — Strong consensus (96% agreement)

Commentary to recommendations 20 and 21

A small peristomal liquid drainage in the week after placement can occur, but leakage of gastric content (very often in combination with signs of peristomal infection or gastrostomy tract enlargement) can lead to serious problems and even tube loss. Risk factors for peristomal leakage include skin infection, increased gastric acid secretion, gastroparesis, increased abdominal pressure, constipation, side torsion of the tube (which leads to ulceration and enlargement of the tract), increased tension between the internal and external bolster, BBS and the presence of granuloma tissue in the tract [55,66,67]. Also, patient-related factors can hinder wound healing such as diabetes (hyperglycemia), immunosuppression and malnutrition. In rare cases where leakage is obvious (or immediately after initial placement), EN should be delayed or stopped. Gastric decompression and starting proton pump inhibitors and/or prokinetics can be useful while simultaneously optimizing nutritional (e.g. with starting PN) and medical status [68]. In any case, to minimize skin breakdown due to leakage, a topical skin product as a powdered absorbing agent or a barrier film, paste or cream (containing zinc oxide) can be applied [69]. Also, foam dressings rather than gauze can be used to reduce local skin irritation (foam lifts the drainage away from the skin, whereas gauze can contribute to more skin maceration). Local fungal skin infections may also be associated with leakage and can be treated with topical antifungal agents. It is important to verify the proper tension between the two bolsters whilst avoiding unnecessary tube movement or excessive pressure (see also Recommendation 16). Side torsion resulting in a too large stoma tract, can be corrected by stabilizing the tube using a clamping device or switching to a low-profile device [53]. If a balloon retaining device is present, the volume content of the balloon has to correspond with the manufacturer’s recommendations and regularly checked (e.g. once a week). In case of a button gastrostomy, one needs to ensure that the correct balloon size and tube length are being used [57]. If local infection or excessive granulation tissue are present, this should be properly managed (see also Recommendations 22 and 24). Replacing the tube with a larger-diameter tube seems to be not very effective and can result in an enlarged stoma tract with more leakage [55]. In some refractory cases it can be tried to remove the tube for 24–48 hours, which permits slight spontaneously closure of the tract aiming that the replacement tube will fit more closely [70]. If all above mentioned measures fail, a new gastrostomy has to be placed at a new location.

Recommendation 22

Excessive granulation tissue is a common problem of PEG and should be avoided or treated using appropriate methods.

Grade of recommendation GPP — Strong consensus (93% agreement)

Commentary

The development of overgranulation tissue forming around the gastrostomy tube is a common complication in patients with a PEG tube. Granulation tissue is vascular, so it bleeds easily and is sometimes painful. Common causes of overgranulation include excess moisture, excess friction or movement from a poorly secured tube and critical colonization, leakage or infection (recommendations 22 and 24). A barrier film or cream may be administered to protect the surrounding skin and if the overgranulation tissue is exuding. The affected skin should be cleaned minimum once a day using an antimicrobial cleanser. Further, a wide variety of treatment options are possible such as the application of a topical antimicrobial agent under the fixation device, or a foam or silver dressing over the affected area which has to be changed only if there is evidence of significant exudate (but at least weekly). Another option is to apply cautery with silver nitrate directly onto the overgranulation tissue. Alternatively, a topical corticosteroid cream or ointment can be administered for 7–10 days in combination with a foam dressing to provide compression to the treatment site. Finally, surgical removal and argon plasma coagulation have been described in the literature. If the above steps prove ineffective, an alternative brand or type of gastrostomy tube can be tried [42,57,71].

Recommendation 23

Tube replacement should be accomplished in case of tube breakage, occlusion, dislodgement or degradation.

Grade of recommendation GPP — Strong consensus (93% agreement)

Commentary

Most transorally placed bumper-type tubes can be maintained for many years. The durability of a PEG tube system is primarily linked to its careful handling. There is no need to exchange a tube system at regular intervals [56]. Replacement will be required eventually because of breakage, occlusion, dislodgement or degradation [42]. A percutaneous enteral access device that shows signs of fungal colonization with material deterioration and compromised structural integrity should be replaced in a non-urgent but timely manner [41]. For a bumper-type tube, retrieval is performed by cutting the tube at the abdominal skin level and...
pushing the internal bumper into the intestinal lumen (‘cut and push’ technique) [72]. Migration is usually uneventful even with large-caliber tubes [73]. Nevertheless, endoscopic retrieval of the bumper is advocated in cases of previous bowel surgery and for patients at risk of strictures or an ileus, which could hinder spontaneous migration and elimination of the sectioned bumper [42]. The replacement can be performed in many ways: endoscopically, radiologically, surgically or at bedside (depending upon the type of gastrostomy tube being replaced) [57]. Balloon-type replacement tubes are mostly used for blind replacement through the same matured tract. The balloon is inflated with sterile (no saline) water (usually 5–10 mL) and water volume may be checked every week to prevent spontaneous balloon deflation because of water leakage. However, because of balloon degradation, this type of tube may require replacement every three to four months [42,74].

**Recommendation 24**

When a site infection is suspected or diagnosed, an antimicrobial agent can be topically applied to the entry site of the tube and the surrounding tissue, and if the site infection cannot be resolved by this treatment—combined with systemic broad-spectrum antibiotics.

**Grade of recommendation 0 — Strong consensus (93% agreement)**

**Recommendation 25**

If the infection cannot be resolved by the procedure described in Recommendation 24, the tube should be removed.

**Grade of recommendation GPP — Consensus (86% agreement)**

**Commentary to recommendations 24 and 25**

A site infection is a common complication after transoral gastrostomy tube placement [75]. Patients with diabetes, obesity, poor nutritional status and those on chronic corticosteroid therapy or other immunosuppressive therapy, are at increased risk for infection [76]. Also, hyper-hydrated or inflamed skin, due to leakage, can promote growth of microorganisms (see Recommendations 20 and 21). Prevention consists of first-line aseptic wound care after placement and early detection of signs and symptoms of infection such as loss of skin integrity, erythema, purulent and/or malodorous exudate, fever and pain [77]. One needs to ensure that the external bolster is not too tight, causing too much pressure between the internal and external bolster. The area can be swabbed for both bacterial and fungal infection. An antimicrobial ointment or a dressing with an antimicrobial agent which delivers a sustained release to the gastrostomy site can be used: these dressings typically get their antimicrobial activity from silver, iodine or polyhexamethylene biguanide and are available in different forms, e.g. foams, hydrocolloids or alginates. Be aware of allergies to any of the product components and silver dressings cannot be worn during magnetic resonance imaging procedures. Tailored systemic antibiotics or (if proven) antifungal agents can be used in combination with local therapy. Topical antibiotics should not be used. In case of stoma tract disruption, peristomal infection that persists despite appropriate antimicrobial treatment, skin excoriation or a fungal infection (particularly if a silicone tube is in situ) it is advisable to remove and/or replace the gastrostomy tube [57,77].

3.2.3. *When and how should HEN be started after tube placement?*

**Recommendation 26**

HEN may be started when patient is medically stable and (i) correct placement of the tube is verified; (ii) tolerance to enteral prescription (volume and formula) is demonstrated; and (iii) the patient and/or provider have appropriate knowledge and skills to manage HEN.

**Grade of Recommendation GPP — Strong consensus (100% agreement)**

**Commentary**

Hospitalized patients commencing HEN should be established on a stable feeding regimen before discharge from hospital. The patient’s ability to tolerate the volume and type of feed to be administered at home must be confirmed. If the patient has been admitted for a day procedure for the purpose of tube (re)placement, the gastrointestinal function needs to be ascertained before discharge to ensure safety. Commencement of HEN feeding depends on the type and position of the tube. For all tube types the correct position must be verified and if an interventional procedure has been performed e.g. gastrostomy or jejunostomy insertion, a period of observation to ensure no surgical complication is required. HEN patients and their carers, need training in managing their EN regimens by a multidisciplinary team [78]. Prior to discharge they need to be able to demonstrate competency in feed administration, equipment handling and some basic trouble shooting in case of tube or equipment failure [79].

**Recommendation 27**

The patient with a nasogastric tube can start HEN immediately according to the previously established nutritional care plan once appropriate tube placement has been confirmed.

**Grade of Recommendation GPP — Strong consensus (96% agreement)**

**Commentary**

Once naso-gastric tube position is confirmed HEN feeding can commence or continue according to previously established nutritional care plan. There is no evidence that feeds should be diluted at the start of HEN just for dilution purposes, unless additional liquid in form of water is needed [80]. Whatever tube access is used: caution should be exercised if refeeding syndrome is suspected. In such cases, appropriate guidelines should be followed to prevent metabolic complications.

**Recommendation 28**

Adults with uncomplicated gastrostomy tube placement can commence EN within 2–4 hours after the procedure.

**Grade of recommendation A — Strong consensus (100% agreement)**

**Commentary**

Traditionally, following gastrostomy insertion, EN commenced slowly with gradual increase in water or saline followed by enteral formula. Recent meta-analysis of RCTs showed no difference in complication when feeding was commenced <4 hours compared to delayed or next day feeding [42]. There is no evidence to support the practice of water trials prior to commencing EN via the gastrostomy tube or device [56,81,82].

**Recommendation 29**

A graduated program of commencement of jejunal HEN feeds should be followed.

**Grade of Recommendation B — Strong consensus (93% agreement)**

**Commentary**

This issue has been subject to clinical studies and these provide information to guide the clinician in the HEN setting. Jejunal feeding post abdominal surgery has increasingly become part of routine care [83]. The feed can be delivered into the jejunum via either naso-jejunal or jejunostomy tube. In either case, feed starting regimens have not been defined and there is a wide heterogeneity in practice. Studies recommend a starting infusion of 10 mL/h of 0.9% w/v sodium chloride in the first 24 hours after tube insertion, followed by commencing EN at 10 mL/h for 24 hours and then increasing the rate by 20 mL/h until nutrient target was reached usually by day 6 [84]. A prospective randomized trial conducted by Han-Geurts in 2007 used a starter regimen of 1.0 kcal/mL continuously delivered by pump commencing at 30 mL/h on the first post-operative day and increasing to 84 mL/h on the third day as.
A surgical procedure has been performed are poorly tolerated [85]. Ninety percent of patients tolerated this feeding well tolerated [86]. Though in some centers progression of feeding regimens meant that only half the patients reached target rate at day 8. Regimens for commencement of jejunal feeding where no surgical procedure has been performed are poorly defined in the literature, however provided that there is no resection of the gastrointestinal tract, and possibly less chance of ileus, starting regimens tend to be more liberal.

3.2.4. How should the HEN be administered (bolus or continuous), with pumps or mobile devices?

**Recommendation 30**
The method of HEN administration should be a decision of the multidisciplinary NST involved with the patient care, considering patient's disease, type of feeding tube in position, feed tolerance and patient preference.

*Grade of Recommendation GPP — Strong consensus (100% agreement)*

*Commentary*
Patient activity level, social environment and individual abilities should be considered when choosing delivery methods [87]. In some settings, the financial costs attributable to HEN treatment needs to be considered as it might influence the choice of administration methods.

**Recommendation 31**
Bolus or intermittent continuous or continuous infusion through a pump may be used depending on clinical need, safety and level of precision required.

*Grade of Recommendation GPP — Strong consensus (92% agreement)*

*Commentary*
Bolus infusion procedure requires the division of total feed volume into four to six feeds throughout the day. The infusion volume is typically between 200 and 400 mL of feed administered over a 15–60-minute period, depending on the patient's nutrient needs and tolerance. Bolus infusions are used either when a patient has a nasogastric tube in situ or gastrostomy tube. Feeds are administered with a 50 mL syringe with or without a plunger. Bolus feeding into the stomach is considered more physiological [88].

There is no evidence that bolus feeding predisposes to diarrhea, bloating, aspiration compared to continuous feeding [88]. Continuous infusion of enteral formula is usually through a pump. Enteral feeding pumps can accurately infuse solutions [89]. The use of an enteral feeding pump safely allows infusion of small volume of solutions for variable periods of time [90]. This is considered as an advantage in jejunal feeding as the jejunum relies on controlled delivery of isotonic substrates. High calorie feeds should be administered preferentially using a feeding pump.

Overnight pump-assisted feeding allows patients to be active during the day to carry out work/study and other social activities. Pump-assisted feeding allows patients to get uninterrupted sleep without the need to adjust flow rates during the night. Infusion of small volumes of solutions allows for safe jejunal infusion when feed tolerance is variable. Feeding pumps can be either static or mobile by placing the device in a specially designed rucksack. These can be placed on patient's back or attached e.g. to a wheelchair. Feeding pumps have evolved to be lighter and more intuitive in their operation allowing greater ease of HEN administration by patients and carers [89]. Combination of methods in practice (e.g. overnight continuous feeding and bolus feeding during the day) can provide autonomy to patients to meet their nutritional needs but at the same time allow for life style preferences.

**Recommendation 32**
Routine water flushing before and after feeding can prevent tube obstruction and should be part of patient/carer education.

*Grade of Recommendation GPP — Strong consensus (100% agreement)*

*Commentary*
Regardless of the administration route (gastral or jejunal), feeding tubes are prone to blockages, primarily due to the chemistry of the protein rich solutions, the viscosity of the fluid and the small diameter of the tube lumen. This problem is further exacerbated the longer the feeding tube is and if medications are administered through the tube. Tubes should be flushed with at least 30 mL of water of drinking quality before starting and after completion of feeds in case of bolus administration or 4-hourly if continuous feeding [91].

3.2.5. Can an enteral tube being used for HEN also be used for drug administration? If yes, how should an enteral tube be used for drug administration?

**Recommendation 33**
An enteral tube being used for EN can also be used for drug administration if the efficacy of drug administration can be confirmed.

*Grade of recommendation GPP — Strong consensus (92% agreement)*

**Recommendation 34**
If an enteral tube is used for drug administration, adequate information should be offered to patients and carers with the involvement of a pharmacist.

*Grade of recommendation GPP — Strong consensus (100% agreement)*

*Commentary to recommendations 33 and 34*
The administration of medicines through enteral feeding tubes is a widespread practice but a recent survey in the United Kingdom [92] found that over 30% of carers for patients requiring medicine administration through enteral feeding tubes received no information. Furthermore, that survey was undertaken through a national patient support group and so it could be that in a wider population even fewer carers may receive information. When using an enteral feeding tube for drug administration, it is important that the tube should not become blocked, and that those prescribing, supplying and administering the medicines are aware of their responsibility for any adverse events resulting from the use of unlicensed medicines or the off-label use of licensed medicines. The relevant Summary of Product Characteristics should be consulted to help understand the legal position regarding individual prescriptions and dosage forms. Using a product outside the terms of the Summary of Product Characteristics carries additional responsibility that should be accepted prior to medicine prescription, supply or administration. Crushing medicines should be avoided whenever possible because of the potential risks of exposure to the drug and inaccuracies of drug dosing. The choice of dosage form for administration through an enteral feeding tube also presents practical considerations. For example, whilst it is possible that there is a generally higher incidence of tube occlusions when using solid dosage forms through nasogastric and silicone PEG tubes care still needs to be taken with liquid medicines since they may contain sorbitol which is reported to contribute to diarrhea (48% of cases of osmotic diarrhea, n = 14) [93], or they be of an osmolality >500—600 mOsm/kg that is sufficiently high to cause gut disturbances [77].

A pharmacist is in an ideal position to advise on the administration of medicines though enteral feeding tubes and indeed the
involvement of pharmacists has been recommended in national guidelines [77]. The pharmacist may be able to suggest alternative medicines or alternative patient management options when asked to advise on the administration of a particular drug through an enteral feeding tube.

Recommendation 35
Appropriate ancillaries including syringes shall be used for drug administration through enteral tubes using connectors of a recognized standard in order to avoid misconnection errors.

Grade of recommendation A (ISO standard) — Strong consensus (100% agreement)

Recommendation 36
Measures shall be taken to ensure correct drug dosing when drugs are administered through enteral tubes, for example when using low-dose tip ENFit syringes. Shaking of a low-dose ENFit tip syringe to remove a drug moat shall not be done.

Grade of recommendation GPP — Strong consensus (100% agreement)

Commentary to recommendations 35 and 36
The recognized standard ISO 80369-3 for enteral tubes (“ENFit”) has been introduced following misconception errors, including fatal errors. This standard requires that tubing and ancillaries, including syringes, are of a specific design that cannot be connected with tubing and ancillaries intended for administration via a different route.

Due to concerns over the accuracy of drug administration using ENFit syringes, and particularly with low-dose ENFit syringes, the design of the 1 mL and 3 mL syringes was updated to incorporate a low-dose syringe tip design that cannot be connected with tubing and ancillaries intended for administration via a different route. Steps should be taken to avoid inaccurate dosing when using low-dose ENFit tip syringes when administering drugs through enteral tubes. Shaking a syringe to remove a moat of drug exposes the environment and people to the drug and could affect the dose delivered, and, therefore, in the absence of evidence, it is not a recommended practice.

Recommendation 37
The necessity and appropriateness for a drug to be administered through an enteral tube should be confirmed, taking into account factors including any effect of the site of drug delivery and potential drug interactions with enteral formula and enteral feeding tubes.

Grade of recommendation GPP — Strong consensus (100% agreement)

Commentary
The site of an enteral tube tip and therefore the site of drug delivery is an important factor when establishing likely drug efficacy. For example, a study of trovafloxacin administered into the stomach yielded similar efficacy with or without simultaneous enteral formula, but administration through a tube directly into the duodenum rather than through a tube into the stomach led to reduced drug availability [94]. Unfortunately, there was no note regarding the type or material of the nasogastric tube used in this publication.

When using an enteral feeding tube for the administration of medicines, no effect of bolus compared to continuous EN on tube blockage has been reported (p < 0.33) [93]. Nevertheless, the choice between bolus and continuous feeding could affect the practical administration of particular medicines, such as medicines which bind to enteral formula and therefore some medicines administered through an enteral feeding tube may need to be administered apart from enteral formula. Specific drug interactions with enteral formula that reduce drug efficacy have been reported, as have drug interactions directly between medicines and enteral feeding tubes. For example, phenytoin has been reported to bind directly with enteral formula, as well as separately to polyurethane enteral feeding tubes lubricated with polyvinylpyrrolidone (with pH an important factor) [95]. It has also been suggested that polyurethane PEGs are preferable to silicone PEGs when considering medicine administration through an enteral feeding tube because of higher retention of patency and subsequent ability to continue to use the tube [93].

Recommendation 38
Drugs may be administered individually through an enteral feeding tube, and the tube flushed before, between and after each drug, using 30 mL of water.

Grade of recommendation 0 — Strong consensus (100% agreement)

Commentary
It is almost universally accepted that medicines should not be mixed before administration through an enteral feeding tube due to risks including drug–drug interactions, and that adequate flushing of the tube between feed and/or medications is necessary. Using at least 30 mL of water for irrigation when giving medicines or when flushing small diameter nasogastric tubes may reduce the number of tube occlusions [93]. A survey of 105 Belgian community pharmacists found that they had limited knowledge regarding the administration of medicines through enteral feeding tubes. For example, fewer than half knew whether or not medicines should be mixed prior to administration [96]. However, the apparent lack of evidence behind the correct answers to those survey questions has been challenged, including because of a lack of evidence for not mixing medicines before administration through an enteral feeding tube [97]. Another similar survey [98] by the same group, but this time of Belgian residential care facilities for people with intellectual disability, found fewer than 40% of staff knew whether or not medicines may be mixed prior to administration, although the results are not generalizable because fewer than 20% of respondents had a nursing background and the remainder had no medical education. Furthermore, it was found in the same type of facility that recommendations for medicine administration through enteral feeding tubes were not followed [99]. The practice included over two thirds of the prepared medicines being mixed prior to administration, and in some cases up to eight medicines at once, despite almost half of the total medication records containing at least one drug–drug interaction [100]. Factors such as limited time and limited knowledge were blamed for the inappropriate medicine administrations [101].

3.3. Products recommended for HEN

3.3.1. Which nutritional products (standard formula) are recommended?

Recommendation 39
Standard commercial formula enteral tube feeds can be used, unless there is specific justification for a blended tube feed.

Grade of recommendation 0 — Strong consensus (92% agreement)

Commentary
There are no fundamental differences regarding the preferred nutritional products to be used to deliver HEN for patients that may have benign or malignant disease. Blended tube feeds rather than commercial tube feeds have been used frequently. For example, in a survey of adult Oley Foundation members, 69.5% of the 91 respondents indicated that they used blended tube feed [102]. In another survey of blended tube feed use in the community [103], 30 of 54 respondents reported improved tolerance and fewer adverse gut symptoms with blended tube feed whilst the remaining 24 respondents chose not to use blended tube feed for reasons that
included concerns over safety and a lack of knowledge regarding their preparation. Blended tube feeds have been considered to be time consuming and therefore costly to prepare, with one study finding that time and non-nutritional costs could account for >50% of the total feeding cost [104]. The same study also found there to be poor standardization of blended tube feeds, and risks of microbial contamination and product instability. It is of note that four of the five authors of this particular study were affiliated to commercial EN companies. Nevertheless, others have also expressed concern regarding higher microbial contamination of blended tube feed compared to commercial tube feed [105,106]. In addition, when 203 Polish patients were switched from blended tube feed administered as 50–100 mL boluses between five and six times each day to commercial tube feed administered as boluses or continuous infusion under the direction of a specialist, the outcomes included fewer hospital and intensive care admissions, and less frequent pneumonia, urinary tract infection and anemia requiring hospitalization [107]. In this study, a care package was provided to the patients in addition to the commercial tube feed which complicates the interpretation of the reported outcomes [107]. In another study, commercial tube feed was found to be relatively more beneficial over an 8-month period for patients with head and neck cancer compared to either blended tube feed or blended diet used as a tube feed [108]. All of the study groups had additional oral intake recommended, and therefore a consideration of their oral intake over the study period would have been beneficial. Blended food, although without clear benefit compared to commercial food, is still occasionally used in chronic patients at home, but not in hospitals. If used at all, it should be administered via a large tube (ch 14) or a PEG to prevent from clogging.

3.3.2. Which formula for special situations are needed?

Recommendation 40

Fiber-containing feeds shall normally be used for patients with diarrhea.

Grade of recommendation A – Strong consensus (92% agreement)

Recommendation 41

Fiber-containing feeds should be used for patients with constipation.

Grade of recommendation B – Strong consensus (96% agreement)

Commentary to recommendations 40 and 41

In a crossover study investigating the effect of fiber in EN of ten medically stable residents of a chronic care facility, fiber was found to nearly double both the frequency of opening bowels and the fecal wet weight (both p < 0.05), without diarrhea [109]. A reduction in measured glucose and an increase in albumin and hemoglobin was found when Israeli residents in long-term care facilities were given a tube feed containing fiber rather than not over an 8-week period, although the two tube feeds differed beyond only the fiber, for example in the density of amino acids and micronutrients [110]. Furthermore, the residents were not randomized to one or other of the tube feeds. More recently, in a systematic review and meta-analysis on the effects of fiber-containing enteral formula relevant to both acute and chronic settings, significant benefits of enteral formula containing fiber (especially fiber mixtures) were reported for patients with diarrhea as well as a trend of benefit of enteral formula containing fiber for patients with constipation [111].

Recommendation 42

A modified enteral formula with lower sugar content, containing slowly digestible carbohydrates and a fat content enriched in unsaturated fatty acids, especially mono-unsaturated fatty acids may be used for patients with diabetes.

Grade of recommendation 0 — Majority agreement (60% agreement)

Commentary

Specific tube feeds with a lower sugar content for patients with diabetes may be used, which are reported to be comparably tolerated to standard tube feeds [112]. For example, improved glycemic control was found for residents with type 2 diabetes in a long-term care facility who received an enteral tube feed with a third less energy from sugars (replaced with lipid, 16 patients in the lower sugar group and 14 patients in the control group) [113]. The lower sugar reached statistical significance for some results and tended to require less insulin although not statistically significant. One study participant in the higher sugar feed group did not complete the study because of uncontrolled blood glucose levels. A limitation of this study [113] that has previously been raised [112] is that the proportion of tube feed received by each study group was not reported. In another study of diabetes specific EN there was a reduction in both insulin requirement and in HbA1c after 84 days in patients with type 2 diabetes with neurological dysphagia [114]. One of the patients in the lower sugar tube feed group had diarrhea from the feed, and one of the patients in the standard sugar tube feed had severe hyperglycemia “possibly related to treatment”. A systematic review of diabetes-specific enteral formula (defined as oral supplements or tube feeds containing a high proportion (>60%) of fat, fructose and fiber) found improved glycemic control compared to standard enteral formula [115].

For a fixed sugar content, increasing the fat and protein content of diabetes specific enteral formula may affect glycemic control. For example, in a systematic review of the effects of different macronutrients on postprandial glycaemia, it was found that more insulin was required following high fat/protein meals [116].

Recommendation 43

For patients without diarrhea, constipation or diabetes, standard commercial tube feeds should be used according to the direction of a specialist.

Grade of recommendation GPP — Strong consensus (96% agreement)

Commentary

There are more limited reports for other special situations, which include a potential role for home-prepared low iodine tube feed for preparation for scanning and management of differentiated thyroid carcinoma [117]. In a study of EN with Crohn’s disease (which is complicated by all study participants being administered 200 mL of 10% w/v soybean lipid intravenously daily for an unknown duration), elemental formula gave benefit for disease remission as well as maintenance of remission compared to elemental formula plus drug treatment (prednisolone or sulphap-salazine), drug treatment alone (and a low residue diet), or no intervention [118]. A general note regarding ensuring clarity from the prescriber of nutritional goals if using modular protein supplements has been reported due to different products not being clinically equivalent to each other for the same quantity of amino acids [119]. Other reports appear to currently be less clinically relevant. Example include: standard enteral tube feed was found to be beneficial in 14 HIV positive patients with wasting, with no comparator group [120]; supplementation of enteral feed with digestive enzymes had non-significant effects on total protein and albumin levels in 16 elderly residents of a nursing care facility [121]; and the availability of only limited information regarding attempts to modify the gut microflora by the addition of fructo-oligosaccharides to tube feed [122].
3.4. Monitoring and termination of HEN

3.4.1. When and how should patients prescribed HEN be monitored?

Recommendation 44

HEN patients should be monitored for the efficacy and complications of HEN, which requires a good forward planning and communication between acting persons (physicians, nurses, caregivers etc.).

Grade of recommendation GPP – Strong consensus (96% agreement)

Recommendation 45

Monitoring of efficacy should be based primarily on body weight, body composition and hydration status, but may also include laboratory measurements, such as serum albumin or transthyretin (−prealbumin). Monitoring of complications should include tube- and EN-associated complications.

Grade of recommendation GPP – Consensus (83% agreement)

Commentary to recommendations 44 and 45

Monitoring should depend upon many factors, patient-related (underlying disease, nutritional status on discharge, active treatment or palliative care), and structure-related (presence or absence of a multidisciplinary team in charge of follow-up, homecare country legislation requiring prescription renewal at given intervals).

It may involve the prescribing multidisciplinary team (physician, dietician, nurse, pharmacist), the primary care physician and nurse, the home caregivers, as well as the patient him/herself, stressing the importance of training patients and/or caregivers on caring for the tube, hygiene and safety issues and basic problem solving.

Monitoring will be performed in the home setting or in the structure where the prescription originated. It may include:

- For efficacy: body weight, body composition (fat-free mass or muscle mass), hydration, muscle strength and performance, food intake, serum transthyretin (because of a much shorter half-life than albumin)
- For tolerance: tube-related complications (leakage, obstruction, displacement, local stoma complications) and respiratory and digestive tolerance

HEN aims at improving nutritional status or at least not letting it deteriorate. The prospective systematic follow-up of a Spanish cohort of 365 patients on HEN for various reasons showed after average 148 ± 104 (mean ± SD) days an improvement of all anthropometric (weight, arm circumference) and biochemical (albumin, transthyretin, transferrin, lymphocytes) parameters [22]. In a prospective study of 150 patients aged 70 ± 8 years (mean ± SD) who had a PEG tube placement for several diseases, among the 72 surviving at least 60 days there was no significant weight or serum albumin change after four months [123]. Among 80 patients who were randomized to receive supplemental HEN, HPN or nothing after major abdominal surgery and who were assessed up to one year after discharge, there was a global decrease in body weight (with however a maintained lean body mass) and an increase in serum albumin with time, with no differences between groups [124]. A small cohort study showing in 19 HEN patients biochemical evidence of micronutrient depletion [125] does not warrant a systematic screening for such a depletion, especially as these deficiencies usually correlate with malnutrition [126]. A retrospective study of 31 HEN patients showed that, despite a systematic monthly follow-up by a dedicated nurse, there were an average of 2.9 unscheduled healthcare contacts over 17.5 months, mostly for tube-related complications [127]. Another study, prospective, reported an average 5.4 unscheduled contacts over 10.5 months for complications [78]. A remote follow-up may prove useful: a prospective study of 188 HEN patients older than 65 years showed that the addition of a video consultation with the hospital team to a monthly home visit was able to reduce metabolic complications [128].

3.4.2. When should HEN be terminated?

Recommendation 46

HEN should be terminated when the desired weight has been reached and the patient’s oral intake matches his/her maintenance needs.

Grade of recommendation GPP – Strong consensus (92% agreement)

Commentary

Apart from end of life care, there are several situations in which HEN will be terminated:

- Restoration of oral feeding
- Severe complication (intractable diarrhea, aspiration pneumonia), leading to a prolonged contra-indication of HEN
- Transfer to a long-term care facility
- Termination of HEN indicated for trophic indications (short bowel syndrome)

The first situation is the most frequent. Patients may evolve from total EN to complementary EN to complete oral autonomy. A cohort of 417 patients on HEN was followed for 24–103 months. HEN had been stopped because of death in 75.2%, weaning in 32.6% and other reasons in 6.7%; only 5.5% were still dependent on HEN [26]. A Spanish cohort found in 365 HEN patients followed-up for 148 ± 104 days (mean ± SD) that as many patients had regained oral autonomy (47.2%) as those still needing EN support (47.8%) [22]. Two regional cohort studies (Alpes-Maritimes in France and Northern Alberta in Canada) report a much more frequent return to oral autonomy in patients with digestive diseases compared to patients with cancer or neurological diseases [5,26]. Follow-up of weight, with the usual weight as a target, as well as that of oral intake are therefore needed to determine when to discontinue HEN. No arguments are in favor of a progressive discontinuation rather than an abrupt one.

The end of life care situation has been covered by the recent ESPEN guideline on ethical aspects of artificial nutrition and hydration [29], in which it is said that “in case the feasibility or efficacy of artificial nutrition is uncertain it is advisable to administer the therapy on a trial basis. In the event of complications or if the desired success is not achieved, the attempt should be discontinued.”

3.4.3. What are the main complications of HEN and how should they be managed?

Recommendation 47

To reduce mechanical complications of HEN (blocking, dislodgement) percutaneous tubes should be used instead of nasal tubes for long-term needs (at least 4–6 weeks).

Grade of recommendation B – Strong consensus (98% agreement)

Commentary

General EN complications are applicable to patients on HEN, and can be classified as mechanic, aspiration, gastrointestinal, metabolic and stoma complications. The frequency of these complications has been studied in several retrospective and prospective studies, including different type of patients and enteral accesses [129–132].

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In a Cochrane systematic review, PEG feeding demonstrated a lower probability of intervention failure (defined as feeding interruption, blocking or leakage of the tube, no adherence to treatment), suggesting the endoscopic procedure is more effective and safer than nasogastric tube feeding [132]. This review included nine randomized controlled studies and intervention failure occurred in 19 of 156 patients in the PEG group and 63 of 158 patients in the nasogastric tube feeding group (RR 0.24, 95% CI 0.08 to 0.76, p = 0.01) in favor of PEG. There were no statistically significant differences in other complications, pneumonia and mortality between groups [132].

Mechanical complications are quite frequent in patients on HEN and include dislodgement and obstruction of the tubes. These complications are more frequent in nasal tubes, especially nasojejunal tubes, than in PEG tubes [129]. In a retrospective study, patients with neurological diseases had significantly more complications than cancer patients, with mechanical complications being the most frequent [130]. The authors attribute their results to the higher use of medications in neurological patients. Routine water flushing after feedings can prevent tube occlusion and is especially relevant in small-caliber tubes, like jejunostomies. If the tube does become clogged, simple water flushing can help regain patency in most cases of persistent obstruction, some experts, but not all, recommend infusion with cola-containing carbonated drinks or pancreatic enzymes may unclog the tube [133]. However, this maneuver is not recommended for several reasons, one being the sugar content of sodas enhancing the risk of tube contamination with bacteria. Others recommend the usage of 8.4% w/v sodium bicarbonate solution to unblock the tube; however, this is also not evidence-based medicine. If necessary, a guide wire or commercially available tube declogger can be used by an expert in case of PEG tubes [42]. Aspiration can occur in patients who are unable to protect their airways, especially patients with neurological problems. The incidence of aspiration has been reported to reach 20%. This can lead to pneumonia, respiratory failure, or death. Various strategies to reduce aspiration have been studied. These include elevation of the head of the bed, post-pyloric feeding (by nasojejunal, percutaneous gastrojejunosomy, or PEJ), and administration of motility agents to promote gastric emptying [42,133]. Gastrointestinal complications include constipation, diarrhea, vomits and abdominal pain. These complications may be caused by the underlying disease, the drug treatment, the enteral formula and the administration method [42,133]. Metabolic complications include hyperglycemia, electrolytic disturbances, micronutrient deficiency, and refeeding syndrome [42,133]. Stoma complications are frequent in patients with gastrostomy and include excessive granulation tissue, leakage, peristomal infection and the BBS [42,56]. See also Recommendations 7 and 8.

Recommendation 48
As home-made blenderized admixtures are less effective than EN formula or commercially produced ‘whole food’ solutions, they should not be utilized in patients on HEN.

Grade of recommendation GPP — Majority agreement (63% agreement)

Recommendation 49
As home-made blended admixtures are less safe than EN formula or commercially produced ‘whole food’ solutions, they should not be utilized in patients on HEN.

Grade of recommendation GPP — Consensus (76% agreement)

Commentary to recommendations 48 and 49
Blenderized or homebrewed diets are still popular in many countries due to its low cost in comparison to enteral formula. However, blended formulas are not standardized regarding macro and micronutrients composition and may entail a higher risk of contamination, as well as more cumbersome handling and administration [104]. In an observational study, the use of EN formula and a NST in comparison to blenderized admixtures improved weight and decreased infectious complications, hospital admissions and costs, but did not have any effect on other complications [134].

See also Recommendation 39.

Recommendation 50
A HEN team should adequately care of nasogastric and enteral tubes, as well as follow up the patients to decrease complications and rehospitalizations.

Grade of recommendation B — Strong consensus (100% agreement)

Commentary
Appropriate training of the patient/caregiver and continuity of care after discharge from the hospital are key factors for the success of HEN [135]. Most of the potential long-term complications are exclusively dependent on the quality of aftercare given to the tubing system and can be effectively avoided if the proper measures are taken. In a prospective study including 108 elderly patients in Italy, followed for twelve months, the authors found a low rate of complications, most of them mild. The mortality after first month and at one year was 7.4% and 23.1%, respectively, with a mean survival of 674 days that is almost three times longer than in the literature. The authors attribute their better results regarding other series of patients to the continuity of care by the same nutrition team [136]. In a quasi-experimental research in Taiwan with pretest/post-test evaluations in 233 patients with nasogastric tube feeding, systematic nursing intervention, including comprehensive educational pamphlets and video education in comparison to routine education, significantly improved the knowledge and skills of primary caregivers and decreased the incidence of 3-months complications [137]. In the absence of adequate gastrostomy aftercare, 6-months hospital readmission rates are as high as 23%. In a prospective study with 313 gastrostomy patients followed by a HEN team, 371 complications were encountered and most of them were resolved without hospitalization. Gastrostomy-related hospital readmissions were significantly reduced from 23 to 2% (p < 0.0001) [138]. In an observational multicenter study in Poland, the specialized HEN care program reduced morbidity and costs related to long-term EN at home [134]. In a randomized, prospective study in 100 patients older than 65 years treated with HEN in Italy, a video consultation between home visiting staff and hospital physicians specialized in clinical nutrition during monthly home visits was associated with a reduction of metabolic complications [128].

3.4.4. When and how should QoL be assessed in these patients?

Recommendation 51
During HEN treatment QoL should be measured periodically.

Grade of recommendation GPP — Strong consensus (92% agreement)

Commentary
QoL is one of the patient-related outcomes necessary to evaluate the effect of the treatments. HEN has a considerable physical, social and psychological effect on the lives of patients and their caregivers. Support at the time of tube placement, and regular ongoing support, can help to minimize the impact on both, enabling them to make the most of their daily lives, sleep better, and enjoy an overall higher QoL [139].

QoL should be measured at the beginning of HEN and periodically during the treatment to evaluate the impact of this intervention. In these patients QoL has been investigated using mainly generic questionnaires, such as SF-36, SF-12, WHO QoL-BREF and EQ-5D, showing a lower value than in the general population. Among the main factors than can influence HEN patient’s QoL are...
the underlying disease, age, gender and presence of caregiver. In a study with 38 long-term HEN patients in France, QoL was better in younger patients, without cancer and with more than one caregiver [140]. In this study, most of the participants improved their QoL following the initiation of HEN. In a multicenter study in Spain involving 267 patients, women and patients with neurological diseases rated a significantly lower value on their QoL compared to those of other groups [141]. In a study of 104 patients with PEG in Sweden, those with cancer diagnosis reported that PEG feeding interfered with their oral feeding more than patients with a neurological disease (p = 0.009) [142]. However, in a similar study of 122 participants in Australia there were no significant differences in QoL across different clinical areas [143]. The participants in this study suggested some improvements to the HEN service, including sooner follow-up after hospital discharge, more frequent reviews for long-term patients, and the availability of a multidisciplinary team to manage HEN patients. Also, the caregiver’s evaluation can be useful to have an approximation to the patient’s perception when he/she does not have the ability to communicate [144].

Recommendation 52
For evaluating QoL in HEN patients, validated specific questionnaires should be used.
Grade of recommendation GPP — Consensus (88% agreement)
Commentary
Patient’s Reported Outcomes Measures should be developed through a standardized process [145]. The process of validation of these tools entails the measure of the following psychometric properties (feasibility, reliability or reproducibility, responsiveness, determination of the minimal clinically significant difference, and validity). To measure QoL in HEN patients we can use generic or specific questionnaires. Generic tools lack sensitivity to reflect patients’ problems and differences in QoL between subgroups according to diseases or during the follow-up. Specific questionnaires are developed from patients’ symptoms, limitations, and problems in their daily life and are more sensitive to changes. To study QoL in HEN, some authors have used specific questionnaires for different pathologies (IBDQ, head and neck cancer QOL-EF, EORTC QLQ-C30) [146,147]. There are other specific questionnaires for PEG but with some methodological limitations. A specific questionnaire to evaluate QoL in patients on HEN regardless of the underlying disease and route of administrations has been validated in a Spanish population in a multicentric study including 355 subjects. This questionnaire, NutriQoL®r, consists of 17 items and evaluates QoL in two dimensions (physical performance, daily life activities, and social aspects). This questionnaire is reported to be valid, reliable and even if lowly sensitive to change it seems to be useful to measure QoL in this population [148,149].

3.5. Structural requirements to perform HEN

3.5.1. How and what to teach the patient and his family?
Recommendation 53
HEN should be standardized and coordinated by a multidisciplinary NST (physician, nurse, dietician, pharmacist) as this increases the quality of the measures, reduces the complication rates and thus makes a significant contribution to improve patients QoL and to the cost-effectiveness of the measures.
Grade of recommendation B — Strong consensus (96% agreement)
Recommendation 54
All information related to HEN should be provided not only verbally but also in writing or pictures.
Grade of recommendation B — Strong consensus (100% agreement)
Commentary to recommendations 53 and 54

3.5.2. What are the infrastructure requirements at home to safely perform HEN?

Recommendation 55
All healthcare professionals who are directly involved in patient care should receive education and training, relevant to their duties, on the different aspects related to the safe provision of HEN and the importance of providing adequate nutrition.
Grade of recommendation B — Strong consensus (100% agreement)
Recommendation 56
Healthcare professionals should ensure that all people who need nutrition support receive coordinated care from a multidisciplinary NST.
Grade of recommendation B — Strong consensus (100% agreement)
Recommendation 57
All hospitals who discharge patients with HEN should employ at least one specialized nutrition support nurse or dietician. Ideally, these hospitals should have a NST working within the clinical governance framework.
Grade of recommendation B — Strong consensus (96% agreement)
Recommendation 58
The environment for patients receiving HEN should be safe in order to administer the EN without the risk of complications.
Grade of recommendation B — Strong consensus (100% agreement)
Recommendation 59
Hygiene standards should be established to prevent contamination of the home enteral product and to prevent HEN-related infections.
Grade of recommendation GPP — Strong consensus (100% agreement)
Recommendation 60
All patients receiving HEN should have access to a professional for evaluation of the procedure and, especially in case of complications or emergencies, for adequate intervention.
Grade of recommendation GPP — Strong consensus (100% agreement)
Commentary to recommendations 55–60
The number of patients receiving HEN has increased considerably in recent years [79]. It is now estimated that more than twice as many patients receive EN in the community compared with those in hospital [150]. HEN is a complex therapy and should be closely monitored [150], otherwise serious complications can occur, like aspiration pneumonia, dislocated tubes, gastrointestinal complications, etc. Treatment is usually initiated in secondary care, but general practitioners can also refer patients for elective HEN with outpatient feeding tube placement. PEG tubes are the easiest feeding tubes to manage in the community. All hospitals who discharge patients with HEN should employ at least one specialist

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3.5.3. Which healthcare professionals should be involved in the management of HEN?

Recommendation 61

For optimal management of HEN, a NST approach may comprise – in addition to a physician, a dietician/nutritionist and a nurse – other allied healthcare professionals (for example, speech and language therapists, physiotherapists and occupational therapists, and pharmacists as necessary).

Grade of recommendation GPP – Strong consensus (97% agreement)

Commentary

The HEN team provides support to patients who are being fed via enteral feeding tube in the community. However, the organization of services to support the increasing number of people receiving HEN varies across regions. UK NICE guidelines outline that people receiving HEN in the community should “be supported by a coordinated multidisciplinary team” [150]. It seems that a standardized care coordination model involving a multidisciplinary team could be improve outcomes and reduce health care related costs. Nevertheless, inadequate data are available to determine the specific degree of effectiveness of any such intervention or team composition. The benefits of introducing community NSTs mainly come from observational work that has suggested benefit (e.g. audits following the introduction of expert review for HEN) in terms of reduced costs and improve outcome. In different countries, nurses and dieticians were the most listed team members of a multidisciplinary team, whereas primary care physicians and physician specialists were included in most of the different approaches for a multidisciplinary team too. In some cases, language or speech specialists, and other healthcare workers were also included [155].

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Conflicts of interest

The expert members of the working group were accredited by the ESPEN Guidelines Group, the ESPEN Education and Clinical Practice Committee, and the ESPEN executive. All expert members have declared their individual conflicts of interest according to the rules of the International Committee of Medical Journal Editors (ICMJE). If potential conflicts were indicated, they were reviewed by the ESPEN guideline officers and, in cases of doubts, by the ESPEN executive. None of the expert panel had to be excluded from the working group or from co-authorship because of serious conflicts. The conflict of interest forms are stored at the ESPEN guideline office and can be reviewed by ESPEN members with legitimate interest upon request to the ESPEN executive.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclnu.2019.04.022.

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