

Editorial

Standard operating procedures for ESPEN guidelines and consensus papers



S U M M A R Y

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Guideline
Position paper
Standard operating procedure
Evidence level
Recommendation grading
Clinical nutrition

The ESPEN Guideline standard operating procedures (SOP) is based on the methodology provided by the Association of Scientific Medical Societies of Germany (AWMF), the Scottish Intercollegiate Guidelines Network (SIGN), and the Centre for Evidence-based Medicine at the University of Oxford. The SOP is valid and obligatory for all future ESPEN-sponsored guideline projects aiming to generate high-quality guidelines on a regular basis. The SOP aims to facilitate the preparation of guideline projects, to streamline the consensus process, to ensure quality and transparency, and to facilitate the dissemination and publication of ESPEN guidelines. To achieve this goal, the ESPEN Guidelines Editorial board (GEB) has been established headed by two chairmen. The GEB will support and supervise the guideline processes and is responsible for the strategic planning of ESPEN guideline activities. Key elements of the SOP are the generation of well-built clinical questions according to the PICO system, a systemic literature search, a classification of the selected literature according to the SIGN evidence levels providing an evidence table, and a clear and straight-forward consensus procedure consisting of online voting's and a consensus conference. Only experts who meet the obligation to disclosure any potential conflict of interests and who are not employed by the Industry can participate in the guideline process. All recommendations will be graded according to the SIGN grading and novel outcome models besides biomedical endpoints. This approach will further extent the leadership of ESPEN in creating up-to-date and suitable for implementation guidelines and in sharing knowledge on malnutrition and clinical nutrition.

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1. Introduction

The European Society for Clinical Nutrition and Metabolism (ESPEN) is an international Society that fosters the development of guidelines in the field of clinical nutrition. Since 1997, ESPEN publishes guidelines and position papers on a regulatory basis in *Clinical Nutrition*, e.g. on liver and renal insufficiency or acute pancreatitis [1–4] or on screening, anthropometry and feeding tubes [5–8]. In 2005, ESPEN/ESPGHAN guidelines on pediatric parenteral nutrition were published in the *Journal of Pediatric Gastroenterology and Nutrition* [9]. In 2006, a first comprehensive bunch of ESPEN guidelines on enteral nutrition was published in *Clinical Nutrition* [10]. These guidelines were based to a large extent on German guidelines published before in German language. In 2009, the ESPEN guidelines for adult parenteral nutrition were published in *Clinical Nutrition* [11]. In 2012, the guidelines for perioperative care were published together with the Enhanced Recovery After Surgery (ERAS) Society in *Clinical Nutrition* [12–14]. In 2013, the French recommendations on Nutritional therapy in major burns were endorsed by ESPEN and published in *Clinical Nutrition* [15].

The methodology and quality of these guidelines varied fairly. Because of this reason, but also because the two major bundles of ESPEN guidelines, that on enteral nutrition in adults from 2006, and that of parenteral nutrition in adults from 2009 expired, ESPEN

launched a new guideline concept in 2010 proposed for four years. The concept was focused on 'Medical nutrition' that aims to prevent and treat malnutrition in the context of diseases. This 'disease-specific guideline framework' does no more separate enteral and parenteral nutrition. Instead, a comprehensive approach comprising screening, assessment, nutritional counseling, oral nutritional supplements, as well as enteral and parenteral nutrition is envisioned [16].

This concept was launched by the authors of the invited editorial on ESPEN disease-specific guideline framework [16], S. Schneider and J. C. Preiser, who initiated four working groups on different topics (cystic fibrosis, cancer, dementia, and chronic intestinal failure) that largely completed their work expected to be published 2015 in *Clinical Nutrition*. The guideline process was shortly described in the editorial; however, it could not been fully brought into practice. Thus, the process of these five guidelines was not fully standardized yet. Therefore, ESPEN decided to re-launch the guideline process with a modified methodology adapted from a German Guidance Manual [17]. This manual derived from the AWMF (Association of the Scientific Medical Societies of Germany) served successfully for the German guidelines on clinical nutrition published since 2013 (<http://dgem.de/leit.htm>). ESPEN will make use not only from this methodology but also from the existing German and other national guidelines whenever appropriate.

However, such guidelines will not be endorsed by ESPEN, but updated and modified to the European needs following a shortened methodology under the authorship of national and international experts.

The details of the new methodology that aims to create so-called “S3 guidelines” according to the AWMF nomenclature [17] with a high scientific and methodological standard will be presented in the following standard operation procedure (SOP). The *ESPEN Guideline SOP* will underlie all future ESPEN guidelines and position papers to ensure maximal quality and coherence. This approach will further extend the leadership of ESPEN in creating up-to-date and suitable for implementation guidelines and in sharing knowledge on malnutrition and clinical nutrition.

2. Methodology

Apart from the German methodology provided by the AWMF [17], the *ESPEN Guideline SOP* is based on the well-established Scottish methodology presented on the websites of the Scottish Intercollegiate Guidelines Network (SIGN) [18], as well as on the similar British methodology presented on the websites of the National Institute for Health and Care Excellence (NICE) [19]. Moreover, we adapted our methodology at some points to the SOP for guidelines authorized by the European Crohn's and Colitis Organization (ECCO) [20], to the GRADE practice on rating quality of evidence and strength of recommendations [21], and to the Oxford methodology presented at the University of Oxford website of the Centre for Evidence-based Medicine (<http://www.cebm.net>).

During project planning, a decision should be made as early as possible about the planned “S class” as defined in the AWMF Guideline Manual and Rules [17]. The AWMF classification grid is used to differentiate between the S1 expert recommendations and S2e, S2k and S3 guidelines. Every class stands for a specific methodological concept that should be described in a plausible way for the user. S-Classes are meant to indicate the degree to which a guideline development process was systematic. The class is selected depending on how much effort is suitable and required to legitimate the implementation of the guideline and to convince the target group. Usually, ESPEN guidelines will fulfill the criteria of a “S3 guideline” that refer to the DELBI instrument [17] and AGREE II (see <http://www.agreetrust.org/>):

- The guideline working group should be representative of the target users and the participating medical society(ies) and/or organization(s)
- A systematic literature search and selection, including systematic search for guidelines on the same topic to assess whether individual recommendations can be used and/or adapted, as well as a critical appraisal of the scientific evidence with regard to the relevant clinical questions is necessary.
- Systematic methods are used to search for the evidence, i.e. the search strategy should be described in detail with a list of search terms and sources used (electronic databases, databases of systematic reviews, manually-searched journals, conference proceedings and other guidelines)
- The selection criteria for the evidence are presented explicitly, especially the exclusion criteria
- The evidence researched and selected according to criteria established a priori is assessed with respect to its methodological quality and the results are summarized in an evidence table.
- The result of the appraisal allows the strength of the evidence (“recommendation grades or grades of evidence”) to be established.

- The methods for generating (nominal group process or Delphi method) and establishing consensus-based recommendations (consensus conference) are clearly described.
- Every recommendation is discussed and voted on as part of a structured consensus development with a neutral moderator. Objectives are to find a solution to pending decision-making issues, a conclusive appraisal of the recommendations and measure the strength of consensus.
- Based on the evidence of the existing literature and on the results of the structured consensus process the grade of recommendation A (strong recommendation), B (recommendation) or O (open recommendation) will be determined.
- The finalized guideline will indicate for each recommendation level of evidence (based on study methodology), grade of recommendation (based on study methodology plus consistency of results and various aspects of clinical implementation) for each recommendation and strength of consensus (>90%, >75%, >50%, <50%)
- A description of the methodological strategy (guideline report) is attached to the guideline

3. Scope of application and aim

The *ESPEN Guideline SOP* is valid and obligatory for all ESPEN-sponsored guideline projects. ESPEN guidelines comprise all consensus guidelines and position papers on the diagnosis, classification, or management of malnutrition, disease-related malnutrition, and nutrition-related diseases authorized by ESPEN. All ESPEN guidelines and position papers will be reviewed by the *ESPEN Guidelines Editorial board* (GEB) and finally approved by the *ESPEN Executive Committee* (ExeCom). Exceptions not adhering to this SOP should be limited to rare cases and need written approval by the ExeCom.

The *ESPEN Guideline SOP* aims to facilitate the selection and preparation of guideline projects by ESPEN, to streamline the consensus process for guidelines, to ensure maximal scientific evidence for the recommendations, to increase transparency of the entire process leading to novel guidelines, updates of established guidelines or position papers, to prevent delays in the process by implementing predefined timelines and by facilitating review and approval, and to facilitate and standardize the dissemination and publication of ESPEN guidelines and position papers.

4. ESPEN guidelines Editorial board (GEB)

The GEB is nominated by the ESPEN ExeCom usually for four years (Fig. 1). The GEB advisory board consists of up to five persons, 2 chairmen, the ESPEN chairman, and two other experts (e.g. another ESPEN ExeCom member, the GEB secretary, a guideline methodologist). The GEB members can be renominated for a second turn by the ESPEN ExeCom. The GEB runs an office consisting of the GEB secretary and headed by the GEB chairman, or by one of the GEB chairmen, if there are two in action. The GEB supports and supervises the guideline processes and is responsible for the strategic planning of guideline activities. Principle decisions such as approval of a new guideline proposal and other decisions with substantial financial consequences needs approval not only by the GEB but also by the ESPEN ExeCom. In detail, each guideline is supervised by a GEB chairman, who is co-author of the guideline. The GEB office secretary will coordinate all guideline processes, communication between group members and the GEB and other participating institutions. Moreover, the GEB office secretary will organize the meetings and voting's for the consensus process,

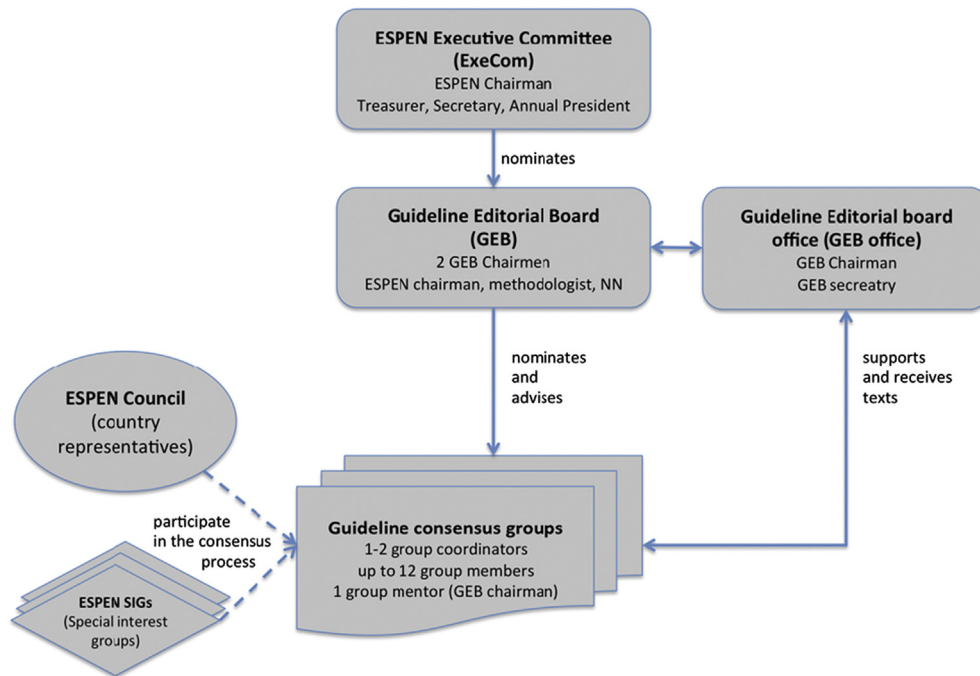


Fig. 1. Responsibilities within the ESPEN guideline generation process. At present, the GEB members are Stephan C. Bischoff and Pierre Singer (GEB chairmen), André van Gossum (ESPEN chairman), Michael Koller (methodologist), and Tommy Cederholm. For further explanation see text.

advise the working group, create the evidence tables and edit the manuscripts in collaboration with the GEB supervisor prior to publication. A map of all guideline projects will be maintained and updated by the GEB and the ESPEN office.

5. Submitting a proposal to develop ESPEN guidelines

Unsolicited proposals may be submitted to the ESPEN office or directly to the GEB office by any individual ESPEN member or by a group of individuals of whom at least one is an ESPEN member, or by an ESPEN Special interest group (SIG) using a standard form (see <http://www.espen.org/education/espen-guidelines>).

In particular, young ESPEN fellows are encouraged to submit applications for new guidelines. All proposers are asked to enclose a CV and a motivation statement along with their application. Further details about the application process are found at the ESPEN website.

The proposal should describe a short rationale, all topics that will be covered, the members of the initial task force and one responsible coordinator, the proposed timelines for the consensus work and for the final publication and the estimated budget. Advice can be sought through the GEB or the ESPEN ExeCom.

Every proposal will be reviewed by the GEB and a recommendation made to the ESPEN ExeCom will be provided within one month after receipt of the submission. The ESPEN ExeCom will respond within three months in terms of approval, tentative acceptance with revisions, or disapproval of the proposal. Once approved, the GEB will nominate the responsible coordinator of the group, the group members and the GEB supervisor of the group. Furthermore, the GEB will prepare the contract between the group and ESPEN in which all details will be regulated.

Solicited proposals can be announced by the GEB after approval by the ESPEN ExeCom. Either, open calls can be sent to all ESPEN members or announced at the ESPEN website, or selected experts can be contacted and asked for contribution. In a first step, the responsible coordinator will be recruited, followed

by a second call or recruitment for participants of the group. The second step will be coordinated by the GEB in collaboration with the group coordinator. All new guideline projects will be announced at the ESPEN website. Every ESPEN member has the possibility to ask for joining a guideline group within a given time frame (usually one month) by writing to the responsible GEB supervisor with a rationale explaining their expertise (maximum 10 lines, supported by a maximum of 5 key references). All correspondence can be addressed to the ESPEN office (which will be forwarded to the GEB chairs within two weeks) or directly to the GEB office or chairs.

6. Selection of the working group

The composition of the working groups should be based on the topics suggested in the initial proposal, although additional working parties can be added or topics can be merged or readjusted as deemed appropriate by the GEB. Criteria for selection of working party members will primarily depend on academic expertise, but appropriate consideration of gender balance, geographical location, participation in current or previous guideline projects is expected, to avoid the perception of bias. Inclusion of ESPEN members active in SIG's and young ESPEN members is encouraged.

The GEB will decide about the final composition of the group. The group members will be selected in accordance with the responsible coordinator and the responsible GEB supervisor. A GEB chairman acts as GEB supervisor in order to ensure that the guideline project is carried out according to the *ESPEN Guideline SOP*.

Before the selection process is finalized, an *ESPEN declaration of conflict of interest (COI)* form will be sent to all contributors via the ESPEN office and only those individuals who have declared their COI are entitled to participate in the consensus. Employees of the Pharmaceutical Industry are explicitly excluded from the systematic literature review or meetings of the consensus, even as observers.

7. Guideline budget

The costs of the guidelines will be covered by ESPEN. The use of an appropriate guideline platform for up to two voting rounds on the prepared recommendations, and a voting system during the final consensus meeting will be provided. Moreover, the office will support the groups by methodological advice, by creating evidence tables and by participating in preparing the manuscript for publication.

Industry support for consensus projects can only be made through unrestricted grants to ESPEN and should be agreed with the ESPEN ExeCom prior to any commitment. A direct sponsoring of a specific guideline project through industry is not allowed.

If the guideline project is an orchestrated effort involving ESPEN and other Scientific Societies/Organizations, the selection process only applies to the contribution of ESPEN to the project. Other societies and organizations should follow their own procedures. However, employees of the Pharmaceutical Industry remain excluded from any guideline project accredited by ESPEN.

Approval of the guideline topic, the coordinator and the group members as well as the timeline and the budget plan is milestone 1. An overview of all milestones is shown within the flow chart for the structured generation of ESPEN guidelines (Figs. 2 and 3).

8. 'PICO questions' to be answered by the guideline

The first stage of EBM is to ask clearly focused questions, because it makes it much easier to find a reliable answer. Therefore, the guideline process starts by defining the major topics/questions that will be addressed by the guideline. This process is done within the guideline group under the leadership of the responsible guideline coordinator.

To benefit patients and clinicians, well-built clinical questions need to be both directly relevant to patients' problems and phrased in ways that direct the search to relevant and precise answers. In practice, such questions usually contain four elements, (i) **p**atient or problem-based question, such as what is the target group, what is the problem; (ii) **i**ntervention-related question, e.g. what is the action such as advice, counseling, treatment, (iii) a **c**omparison of intervention, if necessary, e.g. in comparison to standard therapy alone, and (iv) **o**utcome-related question or topic, e.g. normal body weight, morbidity, length of stay, or quality of life (Table 1). The four elements have been abbreviated by the letters PICO, and the questions generated by this way are named *PICO questions*. At the University of Oxford website, an example is provided how to formulate a search question using the PICO system (see <http://www.cebm.net>).

Once the list of topics and the PICO questions have been approved within the group, they will be sent to the GEB group supervisor together with the search key words for final approval (milestone 2).

9. Literature search

Before starting with the classical literature search, one should look for secondary sources such as published valid guidelines (e.g. NICE, SIGN; US National Guidelines Clearinghouse, guidelines of European or international societies in the field) and systematic reviews (e.g. Cochrane Library, see also www.tripdatabase.com).

Next, a search for primary sources is required (e.g. PubMed) using methodological filters to target the right type of study (e.g. therapy, diagnosis, prognosis, etiology). The development of guideline recommendations and the supporting text should always include a systematic literature search with the appropriate key words using Medline/Pubmed and other databases. The *search key words* and

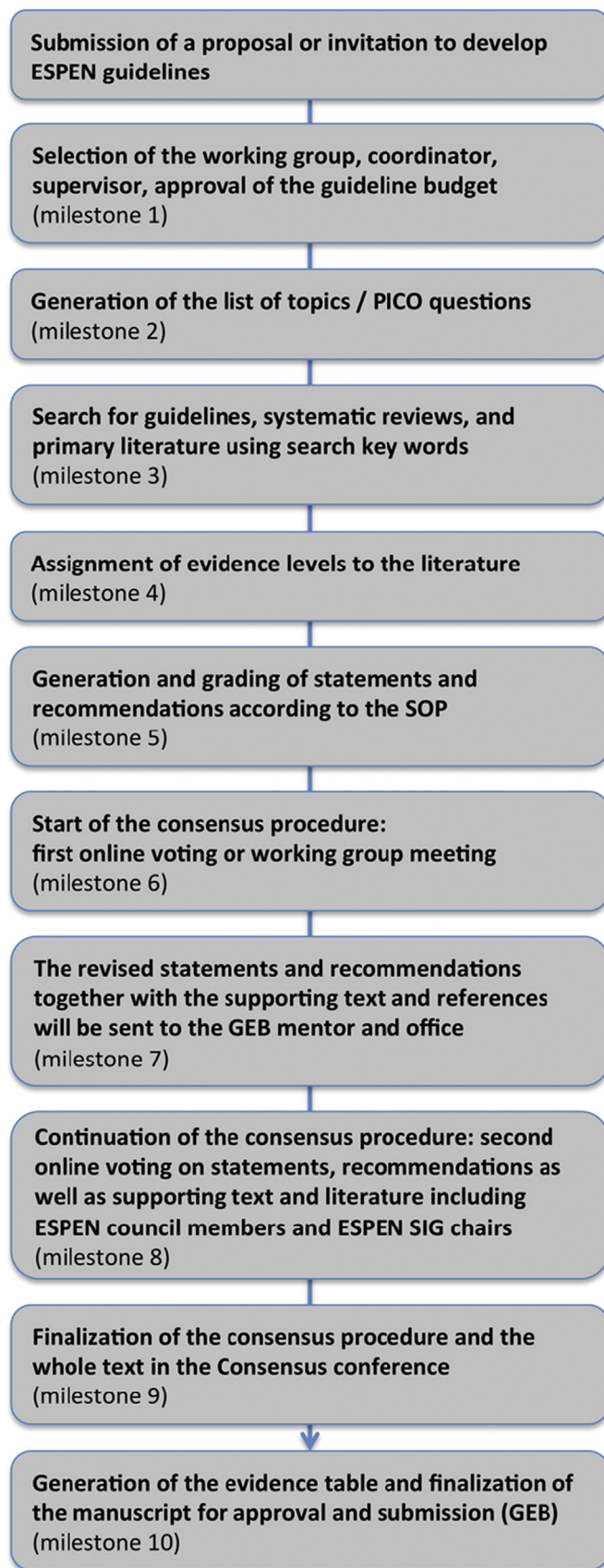


Fig. 2. Flow chart for the structured generation of an ESPEN guideline. The procedure consists of 10 milestones. Further explanation in the text.

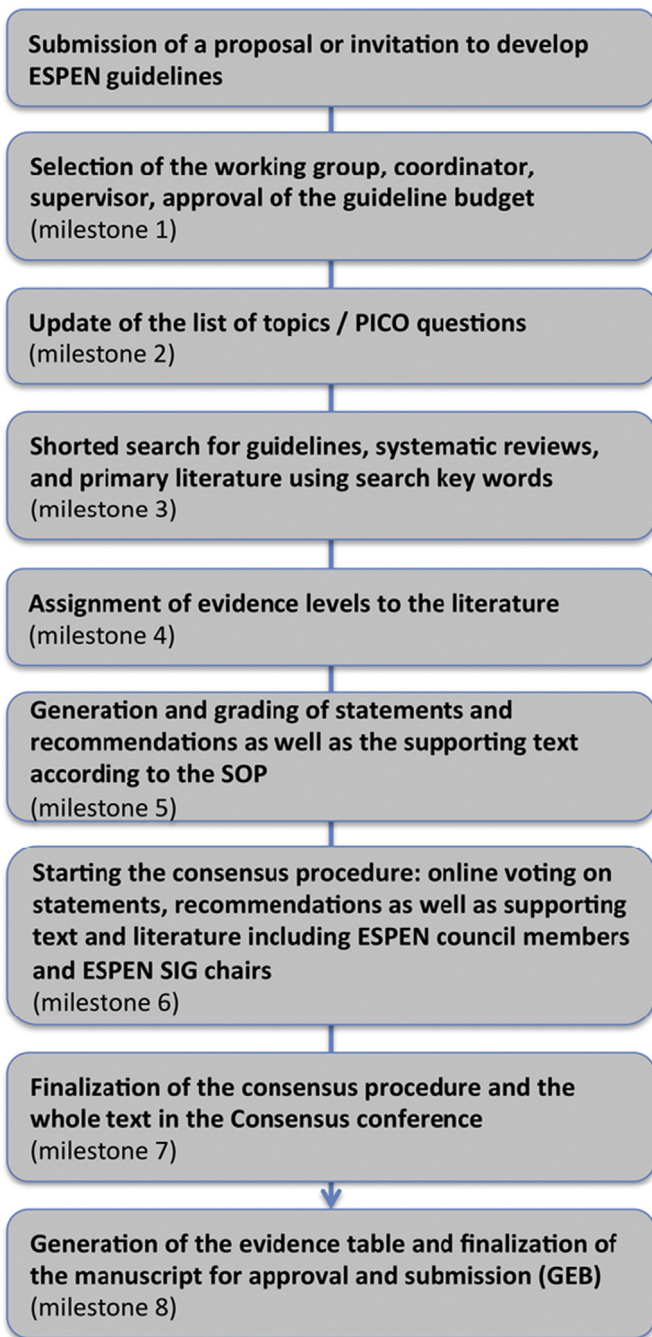


Fig. 3. Flow chart for the structured generation of an ESPEN guideline based on an existing valid guideline (shorted procedure). The shorted procedure consists of 8 milestones. Further explanation in the text.

the results retrieved thereby must be documented. If required by the group coordinator, the GEB office can assist in performing the search, or even perform it according to the *PICO questions* and the *search key words* provided by the working group (milestone 3).

10. Classification of the literature according to evidence levels

The result of the literature search is sent back to the working group for selection and analysis of the literature of relevance for the recommendations. Usually, the appropriate literature will be selected by the group coordinator from the search result and

categorized into clinical trials relevant for the recommendations, and other publications required for the supporting text of the guideline. The selection process requires appropriate documentation. Only the publications that are thought to be of relevance for the recommendations need to be classified according to an *evidence level* (EL) standard. The EL is the major basis for the *recommendation grade* (RG) each recommendation has to be attributed with.

A variety of classification systems are available for assigning EL of existing studies among which the most popular ones are the Oxford classification dated 2009 (www.cebm.net/index.aspx?o=1025), the SIGN classification 1999–2012 (www.sign.ac.uk/guidelines/fulltext/59/evidence.html), and the GRADE system (www.gradeworkinggroup.org/intro.htm). The Oxford and SIGN classification systems focus on the quality of the individual studies. The GRADE approach views the available evidence from the outcome perspective (critical appraisal of the “body of evidence” from the studies for each relevant endpoint) [17].

For the ESPEN guidelines we use the SIGN classification for EL (Table 2) and RG (Table 3). The only substantial difference between the SIGN and the Oxford classification for EL is that the Oxford classification distinguishes between cohort studies (level 2) and case–control studies (level 3), whereas SIGN merges the two levels to one. Therefore, the Oxford classification consists of 5 levels, the SIGN classification of 4. In order to make the process as simple as possible, we selected the SIGN classification for EL. Also regarding RG, the SIGN and the Oxford classification are almost identical, except that the SIGN classification system offers apart from the classical three class grading (A/B/O) the category ‘Good practice points’ (GPP), also named “expert consensus”, which recommends best practice based on the clinical experience of the guideline development. This category is of particular importance in fields like nutrition, in which relevant questions are not always covered by appropriate trials, e.g. because of ethical reasons or methodological limitations such as impossibility of blinding the intervention products. Finally, SIGN offers apart from the grades of recommendations also ‘forms of recommendation’ that classify recommendations into strong (A) and conditional recommendation (B) against or for something, respectively, which might be even more relevant for the user than the classical grading system.

At the University of Oxford website, ‘Critical Appraisal Worksheets’ are available supporting the analysis of systematic reviews, diagnosis and therapy papers as well as clinical trial publications (<http://www.cebm.net/critical-appraisal/>). Alternatively, the SIGN checklists can be used, which are available for systematic reviews and meta-analyses, randomized controlled trials, cohort studies, case–control studies, diagnostic studies, and economic studies (<http://www.sign.ac.uk/methodology/checklists.html>).

In this context, it is strongly recommended to calculate the *Number Needed to Treat* (NNT) to better estimate the relevance of the result. The NNT is the number of patients one need to treat to prevent one additional bad outcome (death, infection, etc.). To calculate the NNT, one needs to know the *Absolute Risk Reduction* (ARR), which is defined as $ARR = CER \text{ (Control Event Rate)} - EER \text{ (Experimental Event Rate)}$. The NNT is the inverse of the ARR ($NNT = 1/ARR$) and is always rounded up to the nearest whole number [22]. Sometimes, odds ratios (ORs) are indication in publications instead of event rates or NNT. In this case, a formula for converting ORs to NNTs can be used: $NNT = (1 - (PEER * (1 - OR))) / ((1 - PEER) * (PEER * (1 - OR)))$, whereas PEER stands for patient's expected event rate if they receive the control treatment.

The literature selection is done by the working group coordinator, the attribution of EL for those publications marked as relevant for the recommendations is done by the GEB office according to the SIGN classification (milestone 4).

Table 1
The PICO question system.

	1	2	3	4
	Patient or problem	Intervention (a cause, prognostic factor, treatment, etc.)	Comparison intervention (if necessary)	Outcomes
	P	I	C	O
Tips for Building	Define the patient target group (e.g. patients with liver cirrhosis) or the problem (e.g. mal-nutrition in the ICU) Balance precision with brevity.	Define the type of intervention (e.g. nutrition counseling, oral nutrition supplement, enteral/parenteral nutrition). Be specific.	Ask “What is the main alternative to compare with the intervention?” The alternative can be usual care or an alternative intervention.	Ask “What can I hope to accomplish?” or “What could this exposure really affect?”, for example weight gain, improvement of quality of life, reduction of morbidity/mortality.
Example	“In patients with stable liver cirrhosis ...”	“... would adding an oral nutrition supplement to standard nutrition counseling ...”	“... when compared with standard care alone ...”	“... lead to lower mortality or morbidity from malnutrition.”

Modified from Asking Focused Questions. Centre for Evidence-based medicine. University of Oxford (<http://www.cebm.net/asking-focused-questions/>).

Table 2
Levels of evidence.

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or 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
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2–	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

According to the Scottish Intercollegiate Guidelines Network (SIGN) grading system. Source: SIGN 50: A guideline developer's handbook. Quick reference guide October 2014 [19].

Table 3
Grades and forms of recommendations.

a. Grades of recommendation ^a	
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or
B	A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
	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
0	Extrapolated evidence from studies rated as 1++ or 1+
	Evidence level 3 or 4; or
	Extrapolated evidence from studies rated as 2++ or 2+
GPP	Good practice points/expert consensus: Recommended best practice based on the clinical experience of the guideline development group
b. Forms of recommendation ^b	
Judgment	Recommendation
Undesirable consequences clearly outweigh desirable consequences	Strong recommendation against
Undesirable consequences probably outweigh desirable consequences	Conditional recommendation against
Balance between desirable and undesirable consequences is closely balanced or uncertain	Recommendation for research and possibly conditional recommendation for use restricted to trials
Desirable consequences probably outweigh undesirable consequences	Conditional recommendation for
Desirable consequences clearly outweigh undesirable consequences	Strong recommendation for

^a There is not necessarily a 1:1 relation between grade of recommendation (A,B,0) and the quality of the evidence. Grade of recommendation should also take into account criteria such as consistency of study results, clinical relevance of endpoints (outcomes) and effect sizes, risk-benefit ratio, patient preferences, application to the relevant patient group, application to health care setting, legal and economic considerations. Based on these criteria, upgrading or downgrading of grades of recommendation is permissible.

^b Modified from the Scottish Intercollegiate Guidelines Network (SIGN) grading system. Source: SIGN 50: A guideline developer's handbook. Quick reference guide October 2014 [19].

11. Consensus procedure

Based on the PICO questions and the selected literature, the working groups will generate a first draft of recommendations. Optionally, this procedure can be divided into working subgroups formed by the group coordinator(s). Finally, the recommendations have to be approved by the whole working group.

A recommendation is defined as a statement that contains a course of action such as a diagnostic procedure or a preventive or

treatment activity. Recommendations should contain the verbs can/may (RG 0), should (RG B), or shall (RG A) depending on the recommendation grade. The recommendations will be presented with standardized naming and consecutive numbering, e.g. ‘ESPEN-XXX Recommendation 1’.

The recommendations need to be graded according to the SIGN RGs and recommendation forms (Table 3). Moreover, the recommendations should be attributed to one out of five outcome models (Table 4) according to Koller et al. [23]. These models have

substantial implications for evaluating trials in clinical nutrition and comprise biomedical, patient-centered/-reported, health economic, decision-making, and integration of classical and patient-reported endpoints. Most published studies in the field of clinical nutrition make use of biomedical endpoints, but the growing importance of patient-centered/-reported and health economic outcomes is recognized. Therefore, ESPEN guidelines will not only focus on biomedical endpoints in clinical nutrition studies, whenever applicable.

In detail, the working group has to deliver (i) the recommendation, (ii) the literature on which the recommendation is based on, (iii) the grade and form of recommendation, (iv) the attributed outcome model. These materials have to be sent to the GEB office (milestone 5).

To facilitate the discussion among the working group and to quantify opinions among all working group members and other experts an online guideline platform that will be maintained by the GEB office will be used for all guideline projects. Usually, one or two rounds of online voting will be performed. The first round will take place after finalization of the recommendations and will involve all participants of the working group including the GEB supervisor. Participants that do not participate in the online voting process within the given time frame may be excluded from the guideline project. The feedback from the first online voting will be used to modify and improve the initial recommendations in order to reach the highest degree of acceptance at the second online voting and the final consensus meeting. Alternatively, the first online voting can be replaced by a physical meeting of the group for discussion and voting. The results have to be sent to the GEB office (milestone 6). If the guideline is prepared based on an existing valid national guideline, milestone 6 (1st voting) can be omitted.

12. Supporting text

A supporting text (also called background text) by the detailed evidence from the literature is composed by the working group, or optionally by working subgroup if applicable. The supporting text should be submitted as a MS Word document with references, the references should be also be provided as a file in a reference program (Endnote or Reference Manager) to allow rapid merging of manuscripts from different working subgroups, and inclusion of updates and modifications of the manuscript by the guideline coordinator (not by the GEB office).

Best practice has a timeline that requires a complete draft of supporting text submitted to the GEB monitor of the guideline project prior to the second online voting, latest prior to the consensus panel. This is often most readily achieved by ensuring that the group coordinator is tasked to write this – possibly based on the input from the working subgroups. In any case, the final editing of the text is done by the responsible coordinator of the guideline project.

The supporting text should be concise and should focus on relevant publications to support the evidence of the

recommendations. If necessary, a few additional publications can be cited to support and explain the supporting text. It should not provide an extensive review of the literature. Generally, a guideline manuscript should not exceed more than 15,000 words without references, and not more than 100 recommendations. Exceptions need approval by the GEB and the Editor-in-Chief of *Clinical Nutrition*. A supporting text should be usually not longer than 250 words and should not contain more than 10 references (usually 3–6 references). The complete supporting text with the recommendations has to be sent to the GEB supervisor and the GEB office (milestone 7). If the guideline is prepared based on an existing valid national guideline, milestone 7 can be omitted provided that the recommendations will be provided together with the supporting text within milestone 5.

A second online voting round (first voting round in case of guideline prepared based on an existing guideline) will then take place once the background/supporting text with references come available. In addition to all the working group members, the ESPEN council members and those ESPEN members that applied for the guideline but were rejected due to space limitations will be involved in this online voting. The results will be classified into four classes (Table 5). The feedback of the second online voting round will again be used to modify and improve the recommendations in order to reach the highest degree of acceptance at the final consensus meeting or to make voting dispensable at the final consensus meeting. If the guideline group feels that suggestions are inappropriate and no further amendments are needed, recommendations may stay unchanged. In contrast to the first online voting, the second online voting is obligatory. The revised text after the second online voting has to be sent to the GEB office (milestone 8).

13. Consensus conference

A final consensus meeting will take place after the second online voting round and after the supporting test has been completed. All ESPEN members that were involved in the guideline should aim to attend this meeting. There will be only one consensus meeting per ESPEN guideline project. All recommendations will be presented there. All recommendations with more than 75% agreement in the second online voting round do not need any additional voting in the consensus panel meeting. All recommendations with less than 75% agreement will be voted upon and may be modified according to the feedback of the consensus panel members in order to achieve a higher degree of agreement.

Recommendations with more than 75% of agreement in the final consensus meeting or the second online voting round are accepted as final consensus recommendations. Those with less than 50% agreement in the final consensus meeting are rejected, as there has been no majority among the experts. Those recommendations with 50–75% agreement represent a majority vote which should result in a downgrading of the recommendation grade. The final publication should explain the full process by which Consensus

Table 4
Outcome models in clinical studies.

Endpoints with implications for evaluating trials in clinical nutrition	Examples
Biomedical endpoint (BM)	e.g. improvement of body weight, body composition, morbidity, mortality
Patient-centered/-reported endpoint (PC)	e.g. validated quality-of-life score
Health economic endpoint (HE)	e.g. QALYs or budget savings
Decision-making endpoint (DM)	e.g. clinical parameters or biomarkers that allow to make a clinically relevant decision such as transfer from ICU to a normal ward or nutritional support yes/no
Integration of classical and patient-reported endpoint (IE)	The combination of BM and PC, e.g. complex scores such as the Frailty Index

Adapted from Koller et al. [23].

Table 5
Classification of the strength of consensus.

Strong consensus	Agreement of >90% of the participants
Consensus	Agreement of >75–90% of the participants
Majority agreement	Agreement of >50–75% of the participants
No consensus	Agreement of <50% of the participants

According to the AWMF methodology [17].

was obtained, the methods used to search the literature and how consensus was reached and how this was defined.

The set of guideline recommendations once accepted at the consensus meeting is final and is not open to further change by any process other than reconvening the SOPs for ESPEN-authorized guidelines (as of Jan. 6th, 2015). A copy of the final set of recommendations, together with the final supporting text and the references marked as relevant for the recommendation or not, needs to be submitted to the GEB chairs and the GEB office (milestone 9).

The guideline group members as well as any other involved person are not allowed to make recommendations available or visible outside the consensus panel. Exceptions need written approval by the GEB.

The GEB office will create the evidence table based on the materials obtained from the guideline group coordinator. Provided that the materials are complete, the GEB office will complete the evidence table usually within one month, at maximum within two months.

14. Finalization of the manuscript and publication

All ESPEN guidelines will be published in the ESPEN journal, which is currently *Clinical Nutrition*. Dual publications should be generally avoided. A careful discussion with the Editor-in-Chief of *Clinical Nutrition* is necessary at the earliest opportunity and expressly before any agreement is reached or any memorandum of understanding is signed, before joint guidelines are further preceded. If publication is not resolved before the start of the Guideline process, then misunderstandings are common that may be very difficult to resolve at a later date. All variation of this policy needs approval by the GEB.

Generally, one paper per guideline should be prepared, exceptions need approval by the GEB and the Editor-in-Chief of *Clinical Nutrition*. The readability of a large guideline is usually improved by structuring the guideline into different chapters with consecutive numbering. Each manuscript starts with a title page and a content. An introduction with a brief outline of the methods and criteria that have been used, and how authors were selected should be present in all ESPEN consensus papers. It can refer to published methodology that will be published separately by the GEB chairs with the support of the GEB office.

All the contributing consensus participants will be acknowledged in a list of contributors. A maximum of 15 participants can be included as authors on a guideline paper. Exceptions need approval by the GEB and the Editor-in-Chief of *Clinical Nutrition*. Generally, the group coordinator will be the first and corresponding author, and the group supervisor who is one of the GEB chairmen will be the last author. The group coordinator will propose the co-authors from the working group. Each paper should be signed by the coordinator and corresponding authors (usually the same). All work subgroup leaders will appear first (if applicable) and other group members will appear in alphabetical order. Authorship of guidelines is best agreed in advance within the working group. If the working group was led by two coordinators who have contributed equally, this can be denoted by an

asterisk. In case of conflict, the GEB will decide about the authorship issue.

All texts should be sent back to all authors for final approval (allowing at least two weeks for review). The GEB office and the GEB chairs will cross-read all manuscripts before they are sent to the journal Editor. At this step, the format will be counter-checked to ensure a consistent layout of all ESPEN guidelines. In case of major changes, the working group coordinator will be asked to approve the final version within one week. Then, the GEB office will send the guideline for final approval to the ESPEN ExeCom and to the presidents of other societies, if other societies are involved. If no formal objection is obtained within two weeks, the GEB office will send the paper to the journal Editor (milestone 10).

All ESPEN-sponsored and approved guideline and position papers have to be published in *Clinical Nutrition* and Open Access to all guideline papers will be guaranteed by ESPEN and the publisher of *Clinical Nutrition* without charge. Exemptions will require approval by the ESPEN ExeCom, the GEB and the coordinator of the guideline. Also for joint guidelines with other societies a single guideline paper should be aimed for and it should be published in *Clinical Nutrition*. Dual publications should be generally avoided, but can be considered as rare exceptions.

The guideline recommendations are not eligible for external review, neither by peer reviewers, nor by ESPEN corporate sponsors. They remain the property of ESPEN, or (in the case of jointly sponsored guidelines) the joint property of ESPEN and the collaborating organization.

A final Word document file and a final Endnote file with the most recent and submitted version of the manuscript and the references needs to be submitted to the GEB and the ESPEN office for storage. These files can be used for future updates of guidelines and may substantially facilitate the work on guideline updates.

15. Implementation and update

In order to ensure the implementation of ESPEN guidelines a number of activities are previewed.

1. Careful examination of the guideline for clarity of language and format
2. Proofreading by a representative from a patient's organization
3. Presentation of the guideline in different formats (full format for experts, short format for practitioners, easy-to-read format for patients) and media (print and website)
4. Supplementation of the guideline with algorithms, care pathways, and electronic decision support tools
5. Linking the guideline with related organizations and stakeholders
6. Dissemination of the guidelines via slide sets, oral presentations, and teaching lessons (e.g. national conferences, LLL education, etc.)

In order to ensure timeliness of ESPEN guidelines, they will be updated at regular intervals (usually every 3–4 years, latest after 5 years).

The need for continuous supplementation and updating of a guideline is not only a function of the availability of new and emerging scientific knowledge, but also depends on the results obtained from an analysis of the guideline's previous usage. The latter helps to identify potentials for improvement. The methodological requirements are specified in the DELBI instrument and the guideline requirements described in the AWMF Guidance Manual [17].

Conflict of interest

None declared.

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