



## Applied nutritional investigation

## Detection and treatment of medical inpatients with or at-risk of malnutrition: Suggested procedures based on validated guidelines



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## ABSTRACT

**Objective:** Despite the high prevalence of malnutrition in the general inpatient population, there is a lack of knowledge in regard to detecting disease-related malnutrition and implementing nutritional support. Our aim was to suggest practical procedures for screening and treating malnourished or at-risk patients hospitalized in medical wards, thereby fostering a straightforward implementation of nutritional therapy independent of the underlying disease and comorbidities.

**Methods:** A working group of experts in clinical nutrition selected and analyzed published disease-specific European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines relevant for our aim. Eight questions in population, intervention, control, outcome format were defined to cover topics such as screening, nutritional targets, and routes of feeding. Individual studies were extracted from the guidelines by applying inclusion and exclusion criteria targeting the heterogeneous population of medical inpatients with or at-risk of disease-related malnutrition. We used those studies as evidence, as well as recommendations from the selected ESPEN guidelines, to formulate answers to the questions. Final agreement with the statement was obtained by consensus of the whole working group.

L.B. and F.G. contributed equally to this study. We thank warmly all member of the expert working group for their contribution to the development of these suggested procedures. The working group (see Acknowledgment section) selected relevant ESPEN disease specific guidelines, defined topics of interest, and developed the clinical questions. L.B. and F.G. extracted the studies from each selected guidelines after defining the inclusion and exclusion criteria applying to participants, outcomes, and study design; compiled the recommendations of the selected ESPEN guidelines; analyzed the extracted evidence, formulated the statements for each question, and drafted the manuscript. All

members of the working group expressed their level of agreement with each statement. All authors reviewed and approved the manuscript. P.S. has primary responsibility for final content. P.S. is supported by the Swiss National Science Foundation (SNSF Professorship, PP00 P3\_150531/1) and the Research Council of the Kantonsspital Aarau, Switzerland (1410.000.044). Nestlé Suisse SA supported the research project with an unrestricted research grant. Abbott AG provided a fellowship grant for the development of nutritional guidelines.

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**Results:** Procedures on how to provide integrated nutritional therapy (oral, enteral, and parenteral) to a heterogeneous patient population were suggested, including how to identify malnourished or at-risk patients, nutrient targets, choice of feeding route, monitoring, and assessment of patients. We also developed a simple algorithm to facilitate the implementation of a nutritional care plan for the general medical inpatient population.

**Conclusion:** By compiling evidence and recommendations from disease-specific guidelines, we were able to suggest a nutritional strategy applicable to large and heterogeneous group of malnourished or at-risk patients admitted to hospitals. A large randomized controlled trial is currently investigating whether this strategy improves clinical outcomes of patients.

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## Introduction

Patients admitted to medical wards of hospitals, for instance after an acute exacerbation of a chronic condition, are at high risk to have or develop disease-related malnutrition (DRM) resulting from loss of appetite, poor nutritional intake, and disease-related catabolism [1,2]. If untreated, DRM ultimately leads to significant loss of lean and adipose tissues and affects the function and recovery of multiple organ systems [3]. Among hospitalized patients, the prevalence of DRM is estimated between 20% and 55%, with about 20% of patients affected in Switzerland [4–7]. Hospitalized elderly patients are particularly vulnerable to develop DRM as a consequence of preexisting decreased lean body mass and impaired intake of protein, energy, and fluids [8]. DRM in turn has profound effects on disease course and recovery [9,10]. Several clinical studies have linked DRM to a higher morbidity, mortality, risk of infection, longer stay in the hospital, and higher costs [11]. In addition, several randomized controlled trials (RCTs) found beneficial effects associated with nutritional therapy in the malnourished inpatient population. In fact, a recent meta-analysis focusing on nutritional support in the medical inpatient population found nutritional interventions to be associated with high intake of energy and protein and an increase in body weight [12]. Risk for unplanned readmission after hospital discharge was significantly decreased as was length of stay in the malnourished population.

Current guidelines published by the European Society for Clinical Nutrition and Metabolism (ESPEN) provide primarily recommendations for nutritional therapy specific to particular organ dysfunctions and medical specialty (e.g. liver, oncology, and geriatrics). Yet, those recommendations are often neglected and or not implemented in the large and highly heterogeneous medical inpatient population of medical wards. This may be one of the reasons why, in many medical wards of hospitals, no systematic screening and nutritional therapy programs are currently in place, which contributes to the alleged undertreatment of patients with this condition. A study from 2010, including patients admitted to the departments of internal medicine of seven Swiss hospitals during a 3 years period, showed that among those with a strong indication for nutrition therapy, only 70% obtained nutritional interventions.

We created a multiprofessional working group composed of experts in clinical nutrition, used current ESPEN guidelines, and the research findings they were built on, to establish a consensus on how to provide nutritional therapy to the heterogeneous malnourished or at-risk medical inpatient population. We detail our rationale and supporting evidence for our suggestions and present them as an algorithm to enable easy and quick decision making for nutritional therapy for general medical inpatients with or at-risk of DRM. The present study was carried out in

preparation for a large-scale, Swiss-wide, multicenter RCT (<https://clinicaltrials.gov/ct2/show/NCT02517476>) in a mixed internal medicine population, where the proposed algorithm is currently being validated.

## Methods and materials

A working group of experts in clinical nutrition was formed (see Acknowledgment section). During a workshop that took place in Basel, Switzerland, on February 21, 2014, a subworking group selected ESPEN guidelines specific to diseases and medical specialties (e.g. liver disease and oncology) to be used as a source of supporting evidence relevant to the patient population of general medical inpatients (Appendix A available online at [www.nutritionjrn.com](http://www.nutritionjrn.com)). Guidelines for the geriatric population were also considered since a large part of malnourished or at-risk patients in medical wards of hospitals are elderly (i.e. over 75 y old). All guidelines we selected were updated for the last time in 2006 and 2009 (guidelines for enteral and parenteral nutrition, respectively). The subworking group also defined topics of interest to be covered in the suggested procedures (such as screening method, energy, protein, micronutrient and other nutritional targets, route of feeding). Eight clinical questions in population, intervention, control, outcome format were developed to address those topics.

In a second step, we defined inclusion and exclusion criteria applying to participants, outcomes and study design to explore the evidence behind the selected ESPEN guidelines (Appendix B available online at [www.nutritionjrn.com](http://www.nutritionjrn.com)). Thereafter, we screened the abstracts of the studies found in the ESPEN guidelines and selected those that met our inclusion criteria and provided answers to our questions. The years of publication (1982–2007), design, number, and main diagnostic of patients of each included study are reported in Table 1. Recommendations applying to at-risk or malnourished patients found in the selected ESPEN guidelines and providing answers to each of our clinical questions were also extracted and are presented in Appendix A available online at [www.nutritionjrn.com](http://www.nutritionjrn.com). For each clinical question, we formulated statements based on 1) the analysis of the studies we selected from the ESPEN guidelines (Table 1), and 2) the recommendations found in those guidelines (Appendix A available online at [www.nutritionjrn.com](http://www.nutritionjrn.com)).

Statements were presented in a table (Table 2) that was sent by email to all members of the working group. The members were asked to express their level of agreement with each statement by choosing between a “strong” (i.e. we recommend or “should”) or “weak” (we suggest or “may”) agreement and by providing a rationale supporting their opinion. After collecting all agreements, statements were adapted according to their associated predominant level and a final consensus procedure on the detection and treatment of malnutrition in medical inpatients was suggested. We developed ultimately a nutrition algorithm to display our conclusions in a graphical format (Fig. 1).

## Results

### Indication

*Question 1. Is the Nutritional Risk Screening 2002 (NRS) an appropriate tool to identify inpatients who are malnourished or at risk for malnutrition, and predict positive outcome if followed by nutritional support, when compared to other validated methods?*

Although there is no universally accepted definition of malnutrition, several nutritional screening and assessment tools have been developed to detect the risk of DRM and/or existing DRM in hospitalized patients.

**Table 1**  
Studies extracted from selected ESPEN guidelines and used to answer each clinical question

Search question	Source, year	Studies included (author, year)	Study design	Participants (main diagnostic, N)
Question 1	ESPEN Guidelines for Nutrition Screening 2002, 2003	Kondrup et al., 2003	Retrospective analysis	Various acute illnesses, 8944
		Johansen et al., 2003	RCT	Various diagnostics, 212
Question 2	ESPEN Guidelines for Nutrition Screening 2002, 2003 ESPEN Guidelines on Enteral Nutrition: Liver disease, 2006 ESPEN Guidelines on Enteral Nutrition: Cardiology and Pulmonology, 2006 ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology, 2006	Johansen et al., 2003	RCT	Various diagnostics, 212
		Mendenhall 1993	Non-randomized trial	Severe alcoholic hepatitis, 273
		Kerns 1992	RCT	Alcoholic liver disease, 31
		Heymsfield 1989	Non-randomized trial	Congestive heart failure, 8
		Ferreira 2012	Systematic review	Obstructive pulmonary disease, 325
Question 3	ESPEN Guidelines on Enteral Nutrition: Adult Renal Failure, 2006 ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology, 2006 ESPEN Guidelines on Enteral Nutrition: Gastroenterology, 2006 ESPEN Guidelines on Enteral Nutrition: Pancreas, 2006 ESPEN Guidelines on Parenteral Nutrition: Hepatology, 2009 ESPEN Guidelines on Enteral Nutrition: Cardiology and Pulmonology, 2006	Ollenschläger 1992	RCT	Acute leukemia, 29
		Schneeweiss 1990	Non-randomized trial	Acute renal failure, 86
		Knox 1983	Observational study	Cancer, 200
		Dempsey 1984	Observational study	Gastrointestinal cancer, 173
		Klein 1988	Observational study	Ulcerative colitis, 8
		Dickerson 1991	Observational study	Acute pancreatitis, 48
		John, W.J., 1989	Non-randomized trial	Alcoholic hepatitis, 20
		Madden 1999	Non-randomized trial	Alcoholic hepatitis, 141
		Poehlman 1994	Non-randomized trial	Congestive heart failure, 60
		Question 4	ESPEN Guidelines on Enteral Nutrition: Gastroenterology, 2006 ESPEN Guidelines on Enteral Nutrition: Wasting in HIV and other chronic infectious diseases, 2006 ESPEN Guidelines on Enteral Nutrition: Liver disease, 2006 ESPEN Guidelines on Parenteral Nutrition: Hepatology, 2009	Klein 1988
Selberg 1995	Non-randomized trial			HIV, 6
Bunout 1989	RCT			Alcoholic liver disease, 36
Calvey 1985	RCT			Alcoholic hepatitis, 64
Swart 1989	Non-randomized trial			Liver cirrhosis, 8
Question 5	ESPEN Guidelines on Enteral Nutrition: Pancreas, 2006 ESPEN Guidelines on Parenteral Nutrition: Pancreas, 2009 ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology, 2006	Nielsen 1993	Observational study	Alcoholic liver cirrhosis, 37
		Du 2003	RCT	Acute pancreatitis, 84
		Siriwardena 2007	RCT	Acute pancreatitis, 43
Question 6	ESPEN Guidelines on Enteral Nutrition: Geriatrics, 2006	Fearon 2003	RCT	Cancer, 200
		Bruera 2003	RCT	Cancer, 60
		Gogos 1998	RCT	Cancer, 30
		Milne 2002	Systematic review	Geriatrics, 2464 (of whom 1623 unwell, 854 undernourished)
		Milne 2006	Meta-analysis	Geriatrics, 9187
		Potter 2001	RCT	Various diagnostics, geriatrics, 381
		McEvoy 1982	RCT	Various diagnostics, geriatrics, 51
		Volkert 1996	RCT	Various diagnostics, geriatrics, 46
Question 7	ESPEN Guidelines on Enteral Nutrition: Pancreas, 2006	Saudny-Unterberger 1997	RCT	Acute Exacerbation of Chronic Obstructive Pulmonary Disease, 33
		Pandey 2004	RCT	Acute pancreatitis, 28
Question 8	ESPEN Guidelines on Parenteral Nutrition: Pancreas, 2009	Marick 2004	Meta-analysis	Acute pancreatitis, 263

RCT, randomized controlled trial

The NRS is a nutrition screening tool that includes the evaluation of nutritional risk, disease severity and age of the patient. It was developed based on a retrospective analysis of 128 RCTs of nutritional therapy versus no therapy on clinical outcome in hospitalized patients [13]. This analysis suggested that the NRS was able to identify patients at risk of malnutrition and to determine who would or would not benefit from nutritional support, being a score of at least 3 indicative of an increased risk of DRM and potential benefits from nutritional interventions. The trials included in the study were performed in clinically heterogeneous groups of patients including surgical, critically ill, and long-term care patients. Following this retrospective analysis, a prospective RCT focusing on 212 patients, predominantly hospitalized on medical wards (68% of the included patients)

was conducted. The NRS enabled to identify individuals at risk of DRM, yet the intervention did not result in significant effects on complications rate, length of hospital stay or quality of life (QoL), questioning therefore the capacity of the NRS to predict positive outcomes following nutritional therapy in the medical inpatient population [14].

For the hospital setting, ESPEN recommends using the NRS to determine the risk of malnutrition within 48 h post-admission [15]. Most disease and organ-specific selected guidelines, however, do not provide recommendation on the choice of malnutrition screening and assessment tools, rather relying on weight loss or BMI to identify patients at risk of malnutrition. Those parameters are also commonly used to diagnose DRM.

**Table 2**  
Consensus opinion on nutritional therapy for general patients in medical wards of hospitals

Topics	Recommendations	Agreement
Indication	The NRS should be used in medical wards to identify patients at risk of malnutrition (i.e. with a score of at least 3 points), within 48 h post-hospital admission. A full nutritional assessment (including an in-depth evaluation of anthropometric, biochemical, clinical, and dietary information) should be performed in patients with an NRS $\geq 3$ to determine if the patient is truly malnourished, to understand the causes of malnutrition and thus to support the development of a tailored nutrition care plan.	Strong
	Nutritional therapy should be considered in malnourished or at-risk medical inpatients for at least 5 to 7 d in order to improve nutrition-related outcomes.	Strong
Energy and protein requirements	REE should be individually measured by indirect calorimetry.	Strong
	When indirect calorimetry cannot be used, we suggest calculating REE with the body weight-adjusted Harris-Benedict formula as long as clinical judgment and experience is also used to determine the final caloric targets.	Weak
	Intakes of protein increased to at least 1.2 g/kg BW/d should be provided to correct or prevent protein malnutrition in malnourished or at-risk medical inpatients.	Strong
	We suggest lowering the protein intake to 0.8 to 1 g/kg BW/d for patients with acute and chronic renal failure without renal replacement therapy.	Weak
Micronutrients and other nutrients requirements	We suggest supplementing malnourished or at-risk medical inpatients on oral nutrition with multivitamins and multiminerals to reach the recommended dietary allowance for micronutrients, thereby correcting or preventing deficiencies. However, an individual assessment of patients remains crucial to specifically correct deranged values of micronutrients.	Weak
Additional oral supplementation	ONS should be used in addition to hospital meals ideally adapted to individual preferences, to meet nutritional requirements and improve outcomes of malnourished or at-risk medical inpatients. Fortification of meals and providing patients with between-meal snacks should be at least equally part of the strategy to supplement intakes.	Strong
Route, monitoring and reassessment	Enteral tube feeding, ideally maintaining some oral food intake, should be implemented in medical inpatients with or at-risk of DRM who could not reach 75% of their energy and protein targets (or consume more than 75% of the food served daily) within 5 d of oral feeding and for whom clinical judgment predicted that oral nutrition would not be sufficient to improve nutritional intakes. Intakes should be reassessed every 24 to 48 h.	Strong
	We recommend starting parenteral nutrition with a minimal oral or enteral feeding when possible, if oral and/or enteral nutrition is not possible or if at least 75% of energy and protein targets have not been reached during the 5 d following the beginning of enteral nutrition. Intakes should be reassessed every 24 to 48 h	Strong

BW, body weight; d, days; DRM, disease-related malnutrition; ONS, oral nutritional supplements; NRS, Nutritional Risk Screening; REE, resting energy expenditure

Based on the available evidence, the NRS should be used in medical wards to identify patients at risk of malnutrition and start nutritional therapy in patients with a score of at least 3 points within 48 h post hospital admission. Yet, the NRS is not intended to establish the diagnosis of existing malnutrition. When possible, a full nutrition assessment (including an in-depth evaluation of anthropometric, biochemical, clinical, and dietary information) should be performed in patients with an NRS  $\geq 3$  to determine if the patient is truly malnourished, to understand the causes of malnutrition, and thus to support the development of a tailored nutrition care plan. The recently diagnostic criteria proposed by ESPEN may be considered [16]. On the other hand, uncertainty remains about whether or not at-risk medical inpatients receiving nutritional therapy will indeed benefit from this intervention. This topic is covered by the next question.

*Question 2. In malnourished or at-risk medical inpatients, does nutritional therapy result in improved outcomes when compared with usual care?*

Studies describing any type of nutritional therapy interventions (oral, enteral, or parenteral) in medical inpatients with or at-risk of DRM were considered.

From six studies extracted, 1 systematic review of 325 patients showed weight gain and improved health-related QoL (measured by St George's Respiratory Questionnaire) in patients with chronic obstructive pulmonary disease (COPD) receiving oral, enteral, or parenteral feeding versus control [17]. We found three RCTs, two of which confirmed positive effects of nutritional therapy on weight stabilization (31 randomized patients with alcoholic hepatitis fed by the enteral route) [18] and weight gain (29 patients with acute leukemia receiving dietary counselling) [19]. The third found no effect in 212 patients with various diseases receiving dietary counselling and tailored nutritional support [14]. In the same study, the intervention resulted in

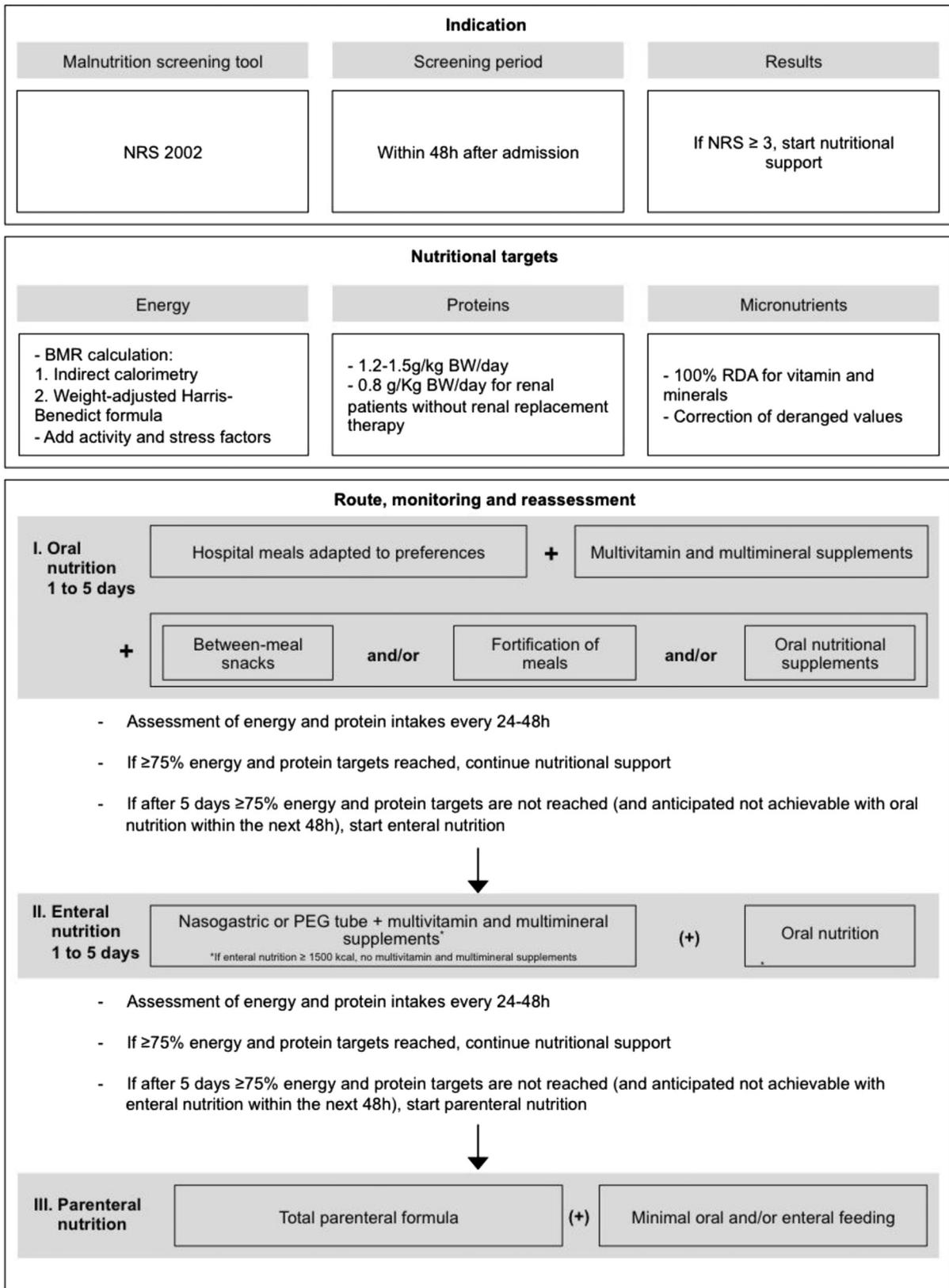
increased protein and energy intake. One very small non-randomized trial from 1989 performed on eight patients with congestive heart failure treated with enteral feeding resulted in gain of lean body mass but loss of weight [20]. In the sixth study, a non-randomized trial of 273 patients with alcoholic hepatitis receiving high-calorie, high-protein supplements with oxandrolone versus low-calorie, low-protein supplements without the drug, reduction of mortality, severity of disease and malnutrition was observed [21]. None of the studies included demonstrated effects of nutritional therapy interventions on length of stay (LOS) [14] or prevention of infection [19].

Due to inconsistent results and/or the lack of well-designed high-quality evidence, some of the disease-specific guidelines we selected are not providing recommendations about nutritional therapy in malnourished or at-risk patients. Available recommendations, however, consistently support this practice to improve nutritional status. Nutritional therapy is also recommended to improve other outcomes in particular groups of patients (e.g., improve survival in liver failure or geriatric patients).

Based on the limited available evidence and recommendations found in selected guidelines, there is a good rationale that nutritional therapy should be considered in malnourished or at-risk medical inpatients for at least 5 to 7 d in order to improve nutrition-related outcomes. More studies are needed in this group of patients to better understand if other outcomes can be improved in general medical inpatients (e.g. clinical, health resources and patient-centered outcomes).

#### *Energy and protein requirements*

*Question 3. In malnourished or at-risk medical inpatients, should the gold-standard method indirect calorimetry be used to determine individual energy requirements, when compared with predictive equations?*



NRS = Nutritional Risk Screening; BW = body weight; RDA = recommended dietary allowance

Fig. 1. Nutritional algorithm: graphical representation of the suggested procedures.

Energy requirements of hospitalized patients differ depending on total energy expenditure, which is largely affected by the body size, composition, as well as type and severity of disease. Indirect calorimetry is the gold standard method to determine total energy expenditure by measuring resting energy expenditure (REE) and including energy expenditure linked with physical activity and consumption of food [22,23]. However, the costs, availability, and practical considerations (e.g., requirement of trained personal to perform measurements or fasting periods before measurement) impose major barriers in using this method and might explain its underuse often observed in medical wards of hospitals [24]. The Harris-Benedict equation is more frequently used in hospitals to calculate REE and estimate caloric requirements, taking in consideration activity and stress factors. In under- and overweight patients, this equation does not enable precise calculation of REE. Using the Harris-Benedict equation with adjusted body weight (BW) calculated with the formula  $\text{adjusted BW} = (\text{actual BW} - \text{ideal BW}) \times 25\% + \text{ideal BW}$  might improve its accuracy, although it is still unclear how to ideally adjust BW in patients with a body weight outside of the normal range [25].

We found eight studies among the guidelines assessing REE in groups of malnourished or at-risk medical inpatients with various acute illnesses (acute renal failure [26], cancer [27,28], ulcerative colitis [29], acute pancreatitis [30], alcoholic hepatitis [31,32], congestive heart failure [33]). Among them, we found six studies (four observational studies [27–30] and two non-randomized trials [31,32]), in which REE was measured by indirect calorimetry and compared to the value predicted by Harris-Benedict formula. The formula failed to accurately predict REE in all studies. In addition, of the eight studies extracted, four non-randomized trials showed an increase REE of 42% [26], 55% [29], 6% [30], and 18% [33] for inpatients, compared to healthy controls.

If recommendations given by ESPEN for energy intakes are different for each disease type, indirect calorimetry is invariably suggested as the method of choice to determine energy targets.

Because the total energy expenditure of malnourished or at-risk patients hospitalized in medical wards varies largely among this heterogeneous group, REE should be individually measured by indirect calorimetry to enable an accurate calculation of the energy requirements. However, when this method cannot be used, we suggest calculating REE with the body weight-adjusted Harris-Benedict formula as long as clinical judgement and experience is also used to determine the final caloric targets.

*Question 4. In malnourished or at-risk medical inpatients, do increased protein intakes result in improved outcomes, when compared with usual care?*

Protein needs are generally increased in case of illness and hospitalization as a compensation for higher protein breakdown and to limit loss of total body protein mass and malnutrition [34].

A total of six studies from the selected guidelines met our selection criteria and were included. One observational study of eight ulcerative colitis patients suggested that intakes of at least 1.4 g/kg BW/d are necessary to achieve nitrogen equilibrium [29]. In another small sample of six HIV patients, parenteral feeding supplying at least 1.2/kg BW/d of protein enabled patients to reach a positive nitrogen balance [35]. Of four studies conducted on individuals with liver disease [36–39], two studies (one observational of 37 patients [36] and one non-RCT of eight patients [37]) showed that patients receiving hospital diet providing 1.2 g of protein/kg BW/d achieved positive nitrogen balance. Improved physical condition was also found in the small

non-RCT [37]. One RCT of 36 patients found that oral diet providing 1.5 g of protein/kg BW/d had no effect on mortality, complications, or nutritional status [38]. The fourth study, an RCT of 64 patients from 1985 showed that protein supplementation of 65 g/day resulted in a positive nitrogen balance, but higher complication rates and no effect on mortality [39]. It is however impossible to assess the amount of protein per kilogram of BW that those patients received. Consistent with our findings, most selected guidelines recommend higher protein intakes (at least 1.2 g/kg BW/d). If malnutrition is diagnosed, including in elderly individuals, the ESPEN recommended protein intakes are further increased to 1.2 to 1.5 g protein/kg BW/d.

Intakes of protein increased to at least 1.2 g/kg BW/d should be provided to correct or prevent protein malnutrition in malnourished or at-risk medical inpatients. More studies are needed to draw conclusions about the clinical benefits of increased protein intake and optimal amounts to treat different diseases.

Detrimental effects of high protein consumption on kidneys have been demonstrated [40]. Defining the protein targets of patients with or at risk of DRM and with altered kidney function is challenging, particularly for elderly patients, whose protein needs are further increased, creating a paradox difficult to handle for clinicians. Interestingly, soy-based proteins might be less harmful for kidneys [41], although their use is still controversial and requires more RCTs to be implemented safely [42].

No study from the ESPEN guidelines for acute renal failure patients met our inclusion criteria because a large majority was performed on intensive care patients. Based on the recommendations found in ESPEN guidelines and clinical judgement, we suggest lowering the protein intake to 0.8 to 1 g/kg BW/day for at-risk or malnourished medical inpatients with acute and chronic renal failure without renal replacement therapy.

#### *Micronutrients and other nutrients requirements*

*Question 5. In malnourished or at-risk medical inpatients, does the supplementation of vitamins, minerals, and/or other nutrients (e.g. n-3 fatty acids and branched amino-acids) result in improved outcomes, when compared with usual care?*

Electrolytes and vitamins deficiencies are common in patients with or at-risk of DRM with acute diseases requiring hospitalization in medical wards [43]. Furthermore, overfeeding of those patients can result in refeeding syndrome, also creating or worsening micronutrient deficiencies. Providing patients with supplementation (such as multivitamin, multimineral, or micronutrient supplements) might help prevent or correct existing deficiencies. Due to their anti-inflammatory properties, n-3 fatty acids supplementation might also be beneficial in some hospitalized patients.

We found two studies investigating micronutrient supplementation in medical inpatients with or at risk of DRM. Both were recent RCTs studying acute pancreatitis patients for the effects of high-dose vitamin C and vitamin C in combination with selenium and n-acetylcystein, respectively. The first study was performed on 84 patients and showed increased recovery rate, improved cellular immune function as well as reduced rate of complications and LOS in the intervention group [44]. In the second study of 43 patients, vitamin C, selenium, and n-acetylcystein treatment did not improve organ function, mortality, and LOS and did not reduce oxidative stress [45]. Three other RCTs investigated the effect of n-3 fatty acids supplementation in oncology patients. In one study of 200 patients from 2003, supplementation resulted in weight gain, increased lean body

mass, and improvement of QoL [46]. None of the two other RCTs of 60 and 30 patients conducted in 2003 and 1998, respectively, reported beneficial effects on weight and functional status [47,48]. Additionally, no effect could be detected on appetite, nausea, tiredness, overall sensation of well-being, caloric intake, lean body mass [47], or survival rates [48] on supplemented patients.

The supporting evidence regarding vitamins, minerals, or other nutrients' supplementation on outcomes is limited to particular groups of patients (pancreatitis and cancer) and nutrients (vitamin C and n-3 fatty acids). It is therefore difficult to extrapolate those findings to general medical inpatients. Based on recommendations found in most selected guidelines, we suggest supplementing malnourished or at-risk medical inpatients with multivitamins and multiminerals to reach the recommended dietary allowance for micronutrients, thereby correcting or preventing deficiencies. Patients fed with enteral nutrition are addressed in question 7. Furthermore, an individual assessment of patients is needed in order to specifically correct out-of-norm values of micronutrients. No recommendations for supplementation with other nutrients (e.g. n-3 fatty acids) can currently be made based on available evidence.

#### *Additional oral supplementation*

*Question 6. In malnourished or at-risk medical inpatients, does additional oral supplementation (e.g. oral nutritional supplements (ONS) and fortified meals) result in improved outcomes, when compared with standard care?*

We identified five studies that explored the effect of ONS in at-risk or malnourished medical inpatients (elderly with various acute illnesses) and one in patients hospitalized for an acute exacerbation of COPD.

In a Cochrane review from 2002, the subgroup analysis of “unwell” (n = 1623) or “undernourished” (n = 854) elderly patients demonstrated beneficial effects of ONS on mortality reduction [49]. In a subsequent meta-analysis from the same author published in 2006 [50], supplementation of undernourished hospitalized elderly individuals reduced mortality and complications, improved nutritional status, but had no effect on LOS. Three other studies (RCTs) consistently found nutritional intake improvements and overall status of hospitalized elderly patients who received ONS [51–53]. Two of those studies [51,53] additionally reported improved functional status, and one also showed reduced risk of mortality, but no difference in LOS [51].

In a RCT conducted in 33 COPD patients, supplementation with ONS or extra snacks in addition to the hospital diet resulted in increased forced vital capacity, protein, and energy intakes, but no significant changes were observed in other functional and nutritional parameters.

None of these RCTs have analyzed data based on both protocol analysis and intention to treat analysis. Among the RCTs included in the systematic reviews, some studies reported that participants were excluded from the analysis because they felt unable to take the supplements, but the analysis of outcomes on an intention to treat basis was overall deficient. Poor compliance with ONS treatments may limit their effectiveness, although this is a parameter that is not always assessed. Moreover, other nutritional interventions such as serving smaller and fortified meals or between-meal snacks may also help improving the nutritional intakes of hospitalized patients, particularly in the elderly [54,55].

Given these findings and that the geriatric population represents a large proportion of patients hospitalized in medical

wards, as well as the consistent recommendations among selected guidelines, ONS should be used in addition to hospital meals ideally adapted to individual preferences to meet nutritional requirements and improve outcomes of malnourished or at-risk medical inpatients. Fortification of meals and providing patients with between-meal snacks should be at least equally part of the strategy to supplement intakes.

#### *Route, monitoring, and reassessment*

*Question 7. In malnourished or at-risk medical inpatients able to consume food orally, does enteral tube feeding result in improved outcomes when compared with oral nutrition?*

Oral feeding constitutes the most physiological route of feeding to correct DRM, but it is not always sufficient to treat DRM and improve outcomes, especially in cases of acute illness.

The supporting evidence we found to determine the preferred way of feeding malnourished or at-risk medical inpatients is limited to one RCT [56] conducted in acute pancreatitis patients where only one outcome (pain relapse following oral or enteral refeeding) was measured and no difference was found between both groups [56]. No data addressing the question of how long oral nutrition should be implemented before starting enteral tube feeding were found within the selected ESPEN guidelines.

All selected guidelines recommend oral nutrition as the first route of feeding for nutritional therapy of malnourished or at-risk patients who are able to ingest food. When the nutritional requirements cannot be met via this route during the recommended 5 to 7 d (according to the majority of the guidelines, although this period can be extended to 8 wk in chronic infectious diseases), enteral tube feeding is recommended. In most guidelines, the recommended route of feeding is a nasogastric tube or a percutaneous endoscopic gastrostomy, for example, when long-term tube feeding is required.

Based on ESPEN recommendations, on the observation that body weight stabilizes in patients able to reach 75% of their nutritional needs [57] and on our own clinical experience rather than on supportive data, enteral tube feeding, ideally maintaining some oral food intake, should be implemented in medical inpatients with or at-risk of DRM who could not reach 75% of their energy and protein targets (or consume more than 75% of the food served daily) within 5 d of oral feeding and for whom clinical judgment predicted that oral nutrition would not be sufficient to improve nutritional intakes. Intakes should be reassessed every 24 to 48 h.

Depending on how long enteral tube feeding is foreseen, both nasogastric tube and percutaneous endoscopic gastrostomy are possible routes. Unless enteral tube feeding provides more than 1500 kcal/d, a multivitamin and micronutrient supplementation is needed to cover micronutrient needs.

*Question 8. In malnourished or at-risk medical inpatients who are not able to consume sufficient food, does parenteral nutrition result in improved outcomes when compared with enteral nutrition?*

One meta-analysis compared enteral with parenteral nutrition in 263 medical inpatients with acute pancreatitis [58]. Enteral nutrition resulted in reduced incidence of surgical interventions and LOS, but no effects on mortality or non-infectious complications were observed.

The recommendations provided in all selected guidelines state that in patients with an intact gastrointestinal tract,

parenteral nutrition should be seen as a last resource when patients cannot be fed sufficiently orally or enterally.

Although supportive evidence is missing, we also recommend starting parenteral nutrition with a minimal oral or enteral feeding when possible, if oral and/or enteral nutrition is not possible or if at least 75% of energy and protein targets have not been reached during the 5 d after the beginning of enteral nutrition. Intakes should be reassessed every 24 to 48 h.

## Discussion

The procedures for detecting and treating DRM suggested in the present study should not be considered as providing robust recommendations such as those developed in validated guidelines (ESPEN or from other societies) for several reasons:

1. Our suggestions were developed using evidence extracted from selected current ESPEN disease- and medical specialty-specific guidelines (Table 1). Therefore, we relied on the studies identified and included by the authors of those guidelines rather than conducting a new systematic search of the literature, with the possibility that several studies potentially relevant to answering our clinical questions might have been missed. Moreover, the guidelines used as a source of evidence were updated for the last time at least 6 y ago, which consequently resulted in the extraction of studies published until 2007. Studies conducted later than this were therefore not captured and not used as evidence behind our questions.

2. The methodological quality and potential biases of the studies we extracted from the selected guidelines were not reassessed and were not taken in consideration when analyzing their results. This may have led to over- or underestimation of the effects of the interventions on the analyzed outcomes.

3. Due to limited evidence found to answer our questions, the procedures we suggest are not only based on published studies, but also take in consideration the recommendations given in the ESPEN guidelines we selected, as well as expert opinions, based on the clinical experience of the members of our working group.

4. Although the procedures suggested in this report are intended to apply to any medical inpatient independent of underlying disease, they do not exempt clinicians from identifying particular groups of patients for which an adaptation is needed to ensure optimal, clinically and ethically sound nutritional support, such as in the management of acute pancreatitis or patients in terminal conditions. A uniform nutritional strategy suitable for all medical inpatients might also lack from precision and might lead to a less sensitive effect compared to a more targeted approach. Yet, due to the growing challenges of older and frail medical inpatients, a pragmatic and integrated approach may still be needed.

## Conclusion

Although this work differs from validated guidelines, we were able to develop and provide practical and simple guidance to detect existing DRM as well as those patients at-risk of developing DRM and implement nutritional therapy in the heterogeneous population of medical inpatients. Our suggestions are summarized in Table 2 and also graphically represented in the form of a user-friendly nutritional algorithm (Fig. 1), which is currently used to provide nutritional therapy in medical wards of several Swiss hospitals as part of a large multicenter RCT.

While this RCT includes the heterogeneous medical inpatient population receiving nutritional therapy according to the herein

described practical procedures, it should be noted that particular subgroups of patients requiring a specific nutritional therapy approach are excluded from the trial (e.g., pancreatitis, terminal patients), in accordance with the previously acknowledged limitation of this study.

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## Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.nut.2016.01.019>.

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