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ESPEN Guideline

ESPEN practical guideline: Nutritional support for polymorbid medical inpatients

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SUMMARY

Background: Disease-related malnutrition in polymorbid medical inpatients is a highly prevalent syndrome associated with significantly increased morbidity, disability, short- and long-term mortality, impaired recovery from illness, and healthcare costs.
Aim: As there are uncertainties in applying disease-specific guidelines to patients with multiple conditions, our aim was to provide evidence-based recommendations on nutritional support for the polymorbid patient population hospitalized in medical wards.
Methods: The 2023 update adheres to the standard operating procedures for ESPEN guidelines. We undertook a systematic literature search for 15 clinical questions in three different databases (Medline, Embase and the Cochrane Library), as well as in secondary sources (e.g., published guidelines), until July 12th, 2022. Retrieved abstracts were screened to identify relevant studies that were used to develop recommendations (including SIGN grading), which was followed by submission to Delphi voting. Here, the practical version of the guideline is presented which has been shortened and equipped with flow charts for patients care.
Results: 32 recommendations (7× A, 11× B, 10× O and 4× GPP), which encompass different aspects of nutritional support were included from the scientific guideline including indication, route of feeding, energy and protein requirements, micronutrient requirements, disease-specific nutrients, timing, monitoring and procedure of intervention. Here, the practical version of the guideline is presented which has been shortened and equipped with flow charts for patients care.
Conclusions: Recent high-quality trials have provided increasing evidence that nutritional support can reduce morbidity and other complications associated with malnutrition in polymorbid patients. The timely screening of patients for risk of malnutrition at hospital admission followed by individualized nutritional support interventions for at-risk patients should be part of routine clinical care and multimodal treatment in hospitals worldwide. Use of this updated practical guideline offers an evidence-based nutritional approach to polymorbid medical inpatients and may improve their outcomes.
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Abbreviations

BI	Barthel Index
βHMB	β-hydroxy β-methylbutyrate
CG	Control Group
DRM	Disease-Related Malnutrition
EN	Enteral Nutrition
GLIM	Global Leadership Initiative on Malnutrition
HGS	Handgrip strength
IC	Indirect Calorimetry
IG	Intervention Group
LOS	Length Of hospital Stay
MDT	multidisciplinary team
MNA(-SF)	Mini Nutritional Assessment (Short Form)
MUST	Malnutrition Universal Screening Tool
NRS 2002	Nutritional Risk Screening 2002
NST	Nutrition Support Team
ONS	Oral Nutritional Supplement(s)
PICO	Population of interest, Interventions, Comparisons, Outcomes
PN	Parenteral Nutrition
QoL	Quality Of Life
REE	Resting Energy Expenditure
RCT	Randomized Controlled Trial
SF-12	1 Item Short Form Health Survey
SF-36	36-Item Short Form Health Survey
SGA	Subjective Global Assessment
SIGN	Scottish Intercollegiate Guidelines Network
SNAQ	Short Nutritional Assessment Questionnaire
TEE	Total Energy Expenditure
WG	Working Group

1. Introduction

As life expectancy increases and individuals acquire a variety of chronic illnesses, polymorbidity is becoming one of the greatest challenges facing many health services worldwide. Although there is no universally accepted definition of polymorbidity, some authors define it as being the co-occurrence of at least two chronic health conditions in the same person [1,2]. Lefevre et al. stated, "*we know, for example, how to educate a diabetic patient, a chronic bronchitis patient, and a hypertensive patient, but we do not know, in practical terms, how to educate a patient with all three diseases*" [3]. In this context, the current single-disease healthcare approach has been challenged [4]. Yet, recent large randomized controlled trials (RCT) have provided important new evidence showing that nutritional support can reduce morbidity and other complications in polymorbid patients. Therefore, there is a need for an up-to-date, evidence-based consensus on how to provide nutritional support for the polymorbid medical inpatient population and to strengthen recommendations that now have a solid evidence base for clinician decision making [5,6].

This guideline provides 32 practical and non-disease specific recommendations to guide clinicians treating polymorbid patients (flowchart overview, see Supplementary Fig. 1 and Table 1). Recent high-quality randomized controlled trials have provided increasing evidence that nutritional support can reduce morbidity and other complications, which is reflected by several A and B recommendation grades. The practical recommendations cover the most relevant aspects of nutrition support (screening, assessment, nutritional requirements, monitoring, and procedure of intervention) and provide a glimpse into the future, where individualization of nutritional therapy will become increasingly important. Nevertheless, this work also allowed gaps in the literature (areas with little or no evidence) to be identified which require further research.

2. Materials and methods

2.1. General methodology

The present practical guideline consists of 32 recommendations, it is based on the ESPEN guideline on nutritional support for polymorbid medical inpatients [7]. The original guideline was shortened by focusing the commentaries on the evidence and literature on which the recommendations are based on. The recommendations were not changed, but the presentation of the content was transformed into a graphical presentation. The original guideline was developed according to the standard operating procedure for ESPEN guidelines and consensus papers [8].

A comprehensive literature search was performed in July 2022. The search strategies used are presented the original guideline [9]. Existing evidence was graded according to the SIGN (Scottish Intercollegiate Guidelines Network) grading system. Recommendations were developed and graded into four classes (A/B/0/GPP) [10].

All recommendations were agreed in a multistage consensus process, which resulted in a percentage of agreement (%). The guideline process was funded both by ESPEN. For further details on methodology, see the full version of the ESPEN guideline [9] and the ESPEN standard operating procedure [8].

2.2. Pragmatic definition of polymorbidity for the current project

This guideline is based on clinical trials that investigate the effects of nutritional support on different outcomes. Because these population-based trials usually report an average number of comorbidities or number of drugs/medications, a pragmatic definition of the polymorbid medical inpatient population was established and does not differ from the original guideline:

- at least two co-occurring chronic diseases present in at least 50 % of the study population (in a few of the studies it is stated that x% of the study population suffers from disease A, y% of the study population suffers from disease B, and so on)

or, alternatively.

- a Charlson comorbidity index in the study population >1.5
- a mean number of diseases or drugs (medications) > 1.5

Full list of inclusion and exclusion criteria can be found in Table 2.

Table 1
Overview of covered topics and recommendations.

Topics	Recommendations
Screening for malnutrition risk and personalizing nutritional support	Recommendation 1 In polymorbid medical inpatients, a quick and simple nutritional screening method using a validated tool should be applied to identify malnutrition risk. Grade of recommendation B, Strong consensus 97 % agreement Recommendation 2 In patients at risk, a more detailed assessment should be performed and a treatment plan should be developed, to allow an early adequate nutritional therapy and to define quality outcome measures. B, 97 % Recommendation 3 The severity of acute-phase response should be used by clinicians as part of the criteria for selecting patients for nutritional screening, follow-up, and intervention. B, 100 % Recommendation 4 Specific nutritional biomarkers can be used to predict the response to nutritional support in polymorbid medical inpatients and therefore may help to personalize nutritional treatments. 0, 100 %
Nutritional support plan	**Definition of nutritional targets** **Energy/caloric target** Recommendation 5 Energy requirements in polymorbid medical inpatients can be estimated using indirect calorimetry (IC), a published prediction equation or a weight-based formula, although the accuracy of prediction equations in this population is low. 0, 100 % Recommendation 6 In the absence of IC, total energy expenditure (TEE) for polymorbid older patients (aged ≥65 years) can be estimated at approximately 27 kcal/kg actual body weight/day. REE can be estimated at 18–20 kcal/kg actual body weight/day with the addition of activity or stress factors to estimate TEE. 0, 100 % Recommendation 7 In the absence of IC, resting energy expenditure (REE) for severely underweight patients can be estimated at 30 kcal/kg actual body weight. 0, 96 % Recommendation 8 This target of 30 kcal/kg actual body weight in severely underweight patients should be cautiously and slowly achieved, as this is a population at high risk of refeeding syndrome. GPP, 100 % **Protein target** Recommendation 9 Polymorbid medical inpatients requiring nutritional support shall receive 1.1.5 g protein/kg of body weight per day as a cost-effective and highly efficient measure to prevent body weight loss, to reduce complications, to improve functional outcome and quality of life. A, 100 % Recommendation 10 For polymorbid medical inpatients at nutritional risk with impaired kidney function (eGFR <30 ml/min/1.73m2) who are not on kidney replacement therapy, a low amount of protein of 0.8 g protein/kg body weight/day should be targeted. B, 96 % **Micronutrient target** Recommendation 11 In polymorbid medical inpatients exclusively fed orally, an adequate intake of micronutrients (vitamins and trace elements) to meet daily estimated requirements should be ensured. GPP, 100 % Recommendation 12 In polymorbid medical inpatients exclusively fed orally, documented or suspected micronutrient deficiencies should be repleted. GPP, 96 % **Other specific targets** Recommendation 13 In polymorbid medical inpatients with pressure ulcers, specific amino-acids (arginine and glutamine) and βHMB can be added to oral/enteral feeds to accelerate the healing of pressure ulcers. 0, 92 % Recommendation 14 In polymorbid medical older inpatients requiring EN, EN formulas enriched in a mixture of soluble and insoluble fibers can be used to improve bowel function. 0, 96 % Recommendation 15 We cannot recommend the use of other disease-specific nutritional supplementation in polymorbid medical inpatients. 0, 100 %
Initiation of nutritional support	Recommendation 16 In polymorbid medical inpatients with reduced food intake and hampered nutritional status, at least 75 % of calculated energy and protein requirements shall be achieved in order to reduce the risk of adverse outcomes and mortality. A, 100 % Recommendation 17 Early nutritional support (i.e. provided in less than 48 h post hospital admission) compared to later nutritional support shall be performed in polymorbid medical inpatients, as mortality and adverse events are lower and lean body mass loss could be decreased and self-sufficiency could be improved. A, 100 % Recommendation 18 Underlying disease modifies the effect of nutritional therapy and should be considered when initiating nutritional support. B, 92 % **Oral Nutrition** Recommendation 19 In malnourished polymorbid medical inpatients or those at high risk of malnutrition who can safely receive oral nutrition, individualized provision of nutritional support via oral nutritional supplements (ONS) to reach energy and protein requirements shall be offered to improve their nutritional status, QoL and overall survival. A, 100 % Recommendation 20 In malnourished polymorbid medical inpatients or those at high risk of malnutrition, high protein nutrient specific ONS should be administered, when they may help maintain functional status and muscle mass, reduce mortality and improve QoL. B, 96 % Recommendation 21 In polymorbid medical inpatients who are malnourished or at high risk of malnutrition and can safely receive nutrition orally, ONS shall be offered as a cost-effective way of intervention towards improved outcomes. A, 100 % Recommendation 22 In polymorbid medical inpatients who are malnourished or at high risk of malnutrition, able to safely receive nutrition orally, and cannot tolerate or wish not to receive ONS, food fortification can be

Table 1 (*continued*)

Topics	Recommendations
	considered an effective way in order to reach relevant energy and protein targets and in improving nutritional intake. 0, 100 % **Enteral and parenteral nutrition** Recommendation 23 In polymorbid medical inpatients whose nutritional requirements cannot be met orally, EN before PN can be administered to ensure reaching nutritional goals. 0, 100 % Recommendation 24 In polymorbid medical inpatients whose nutritional requirements cannot be met orally, the use of EN may be superior to PN because of a lower risk of infectious, non-infectious complications and maintenance of gut integrity. 0, 100 %
Monitoring and continuation post-discharge	**Monitoring** Recommendation 25 While nutritional and functional parameters should be monitored to assess responses to nutritional support, functional indices may be more appropriate in assessing other clinical outcomes (i.e., survival, quality of life) in polymorbid medical inpatients and should be used for this purpose. B, 100 % Recommendation 26 In polymorbid medical inpatients there is an important possibility of drug–drug or drug–nutrient interactions that needs to be taken into account, therefore, a pharmacist-assisted management plan for any interactions should be established. GPP, 100 % **Continuation of nutritional support** Recommendation 27 In malnourished polymorbid medical inpatients or those at risk of malnutrition, nutritional support shall be continued after hospital discharge in order to maintain or improve body weight and nutritional status. A, 100 % Recommendation 28 In malnourished polymorbid medical inpatients or those at high risk of malnutrition, nutritional support should be continued post hospital discharge to maintain or improve functional status and quality of life. B, 100 % Recommendation 29 In polymorbid medical inpatients at high risk of malnutrition or with established malnutrition aged 65 and older, continued nutritional support post hospital discharge with either ONS or individualized nutritional intervention shall be considered to lower mortality. A, 96 % Recommendation 30 In polymorbid medical inpatients at high risk of malnutrition or with established malnutrition aged 65 and older, continued nutritional support post hospital discharge with either ONS or individualized nutritional intervention should be considered for more than two months in order to lower mortality/impact clinical course. B, 100 % **Organizational changes** Recommendation 31 Organizational changes in nutrition support provision like enriched menus should be implemented for polymorbid medical inpatients who are malnourished or at risk of malnutrition to improve intake and nutritional outcome. B, 100 % Recommendation 32 Organizational changes, particularly the establishment

(*continued on next page*)

Table 1 (*continued*)

Topics	Recommendations
	of a nutrition support team and the use of multidisciplinary nutrition protocols, should be implemented in polymorbid medical inpatients at risk for malnutrition. B, 100 %

ONS, oral nutritional supplements; EN, enteral nutrition; PN, parenteral nutrition; IC, indirect calorimetry; TEE, total energy expenditure; REE, resting energy expenditure; eGFR, estimated glomerular filtration rate; BCAA, branched chain amino acids, βHMB, beta-hydroxy-beta-methylbutyrat.

3. Results

3.1. Screening for malnutrition risk (Fig. 1, Fig. 2)

1) **In polymorbid medical inpatients, a quick and simple nutritional screening method using a validated tool should be applied to identify malnutrition risk.**

(R1, Grade B, Strong consensus 97 %)

Commentary

Polymorbid medical inpatients are at high risk of malnutrition. Several prospective cohort studies showed a prevalence of approximately 40–50 % in a hospitalized population of tertiary centers [11,12]. In a prospective observational cohort study, Lengfelder et al. were able to show higher odds for malnourished patients having a LOS of ≥3 days (2.38, 95 % CI, 1.45 to 3.88; $p < 0.001$) and for readmission within 30 days (2.28, 95 % CI, 1.26 to 4.12; $p < 0.006$) [13]. The same effect was shown by Li et al. in patients with community acquired pneumonia [14]. The latter also showed a significant increase in the prevalence of nutritional risk measured by the Nutritional Risk Screening 2002 (NRS 2002) within two weeks after admission (40.61 % vs. 48.93 %; $p = 0.036$).

Scoring systems for determining nutritional risk, such as NRS 2002 and the Mini Nutritional Assessment Short-Form (MNA-SF) link nutritional risk assessment to treatment by predicting that nutritional interventions will have a positive influence on variable outcomes [15–18]. Both of these tools are rapid, easily undertaken and show a high degree of content validity and reliability, thereby making them suitable in polymorbid medical inpatients including those patients with cognitive dysfunction [19,20].

2) **In patients at risk, a more detailed assessment should be performed and a treatment plan should be developed, to allow an early adequate nutritional therapy and to define quality outcome measures.**

(R2, Grade B, Strong consensus 97 %)

Commentary

If patients screen positive, diagnosis should be established according to GLIM criteria – the Global Leadership Initiative on Malnutrition (GLIM) proposes a two-step approach for the malnutrition diagnosis, which includes a validated screening and second, a detailed assessment with phenotypic and etiologic criteria for diagnosis and grading the severity of malnutrition [21]. This guideline did not focus specifically on the assessment and diagnosis with GLIM criteria in polymorbid medical inpatients but generally on assessments to identify pathogenic factors which should be used to develop a treatment plan.

In a controlled trial, Rypkema et al. demonstrated that a standardized, early nutritional intervention in older polymorbid medical inpatients at nutritional risk, determined by the MNA-SF, is effective and does not significantly increase hospital costs. The

Table 2
Inclusion and exclusion criteria.

Criteria	Inclusion	Exclusion
Patients characteristics	- Human adults aged ≥18 years	- Non human, ≤18 years, pregnant women
	- Patients hospitalized in acute care wards	- Patients admitted to critical/intensive care units - Surgical patients - Patients living on long-term care facilities - Outpatients - Patients receiving end of life care
	- Polymorbid inpatient population as defined by a) at least two co-occurring chronic diseases are present in at least 50 % of the study population Or b) mean number of diseases or drugs/medication or the Charlson comorbidity index in the study population as being more than 1.5 In case of uncertainties about the way comorbidities are reported, the trials' authors are contacted in to obtain more information; if contact is not possible, the WG makes a consensus decision about the inclusion/exclusion of the studies.	- Healthy population - Less than 50 % of the study population has two co-occurring diseases
Outcomes	Nutritional outcomes (e.g. weight, energy and protein intake) Clinical outcomes (e.g. mortality, infections) Patient-centered outcomes (e.g. quality of life) Healthcare resources use	
Language and year	English; no restriction on publication year	

intervention resulted in both a more pronounced weight gain (0.92 ± 0.27 kg in the IG (IG) vs. −0.76 ± 0.28 kg in the CG, $p < 0.001$) and a significant lower rate of nosocomial infections (23.6 % vs. 36.7 %, $p = 0.01$) [22].

In a prospective, non-randomized cohort study, Jie et al. found nutritional support was beneficial for polymorbid medical inpatients at nutritional risk as defined by the NRS 2002 [12]. The overall complication rate was significantly lower in the group with nutritional therapy than in the no-support group (20.3 % vs. 28.1 %, $p = 0.009$), primarily because of the lower rate of infectious complications (10.5 % vs. 18.9 %, $p < 0.001$). These effects were robust after multivariate adjustment.

3.1.1. Individualizing nutritional support

3) **The severity of acute-phase response should be used by clinicians as part of the criteria for selecting patients for nutritional screening, follow-up, and intervention.**

(R29, Grade B, Strong consensus 100 %)
Commentary

Inflammation is a key factor with several important metabolic effects on a cellular level (e.g., increase in insulin resistance leading to an inhibition of nutrition entering cells) and on different organs such as the brain (e.g., causing disease-related anorexia and reduced food intake), the intestines and on muscle (e.g., causing catabolism and sarcopenia) [23]. A double-blind randomized trial of nutritional supplementation published [24] by Gariballa et al., in 2006, including 445 polymorbid patients, concluded that the acute-phase response was strongly associated with poor nutritional status and worse clinical outcomes, particularly in older patients. Interestingly, recent data also suggest that inflammation modulates the response to nutritional treatment. A secondary analysis of EFFORT suggested that patients with CRP levels of ≥100 mg/L no longer responded to nutritional therapy, while patients with lower levels had a significant mortality benefit from nutritional support [25]. A similar association was also found for cancer patients, with a significantly extenuated response to nutrition in patients with high inflammation [26]. These findings may also explain differences in results of nutritional trials, depending on the clinical setting with several nutritional studies in the ICU setting or in patients with advanced cancer not showing significant benefits form nutrition in regard to clinical outcomes [23,27].

4) **Specific nutritional biomarkers can be used to predict the response to nutritional support in polymorbid medical inpatients and therefore may help to personalize nutritional treatments.**

(R32, Grade 0, Strong consensus 100 %)
Commentary

Finding specific nutritional biomarkers to predict the response to nutritional treatment is an emerging field in clinical research as not all patients show the same benefit from nutritional interventions [23] (e.g. patients with cachexia may show less response [23,28]).

Markers of inflammation have been shown to correlate with several malnutrition parameters and predict lack of response to nutritional treatment [25,29,30]. In a secondary analysis of EFFORT, unlike patients with lower CRP concentrations (≤100 mg/L), patients with high inflammation (CRP level >100 mg/L) did not respond to nutritional support [25]. Similarly, markers of chronic kidney dysfunction are associated with renal cachexia and weight loss, but patients with reduced kidney function show a particularly stronger response to nutritional treatment [5]. Albumin and prealbumin levels also have a strong prognostic value, but little correlation with nutritional response [31,32]. There are several studies looking at biomarkers of muscle strength and/or function with some suggesting that low muscle strength measured by HGS is a predictor for response [33] while others found sarcopenia to be a predictor of non-response in mixed populations [23,28].

Struja et al. used an untargeted proteomics approach to find predictive and prognostic metabolites – so far the metabolites had only little potential for phenotyping the malnutrition risk or treatment response [34]. Currently, no specific blood biomarkers of treatment response are used in routine clinical care.

4. Nutritional support plan

4.1. Definition of nutritional targets (Fig. 3)

4.1.1. Caloric target

5) **Energy requirements in polymorbid medical inpatients can be estimated using indirect calorimetry (IC), a published prediction equation or a weight-based formula, although the accuracy of prediction equations in this population is low.**

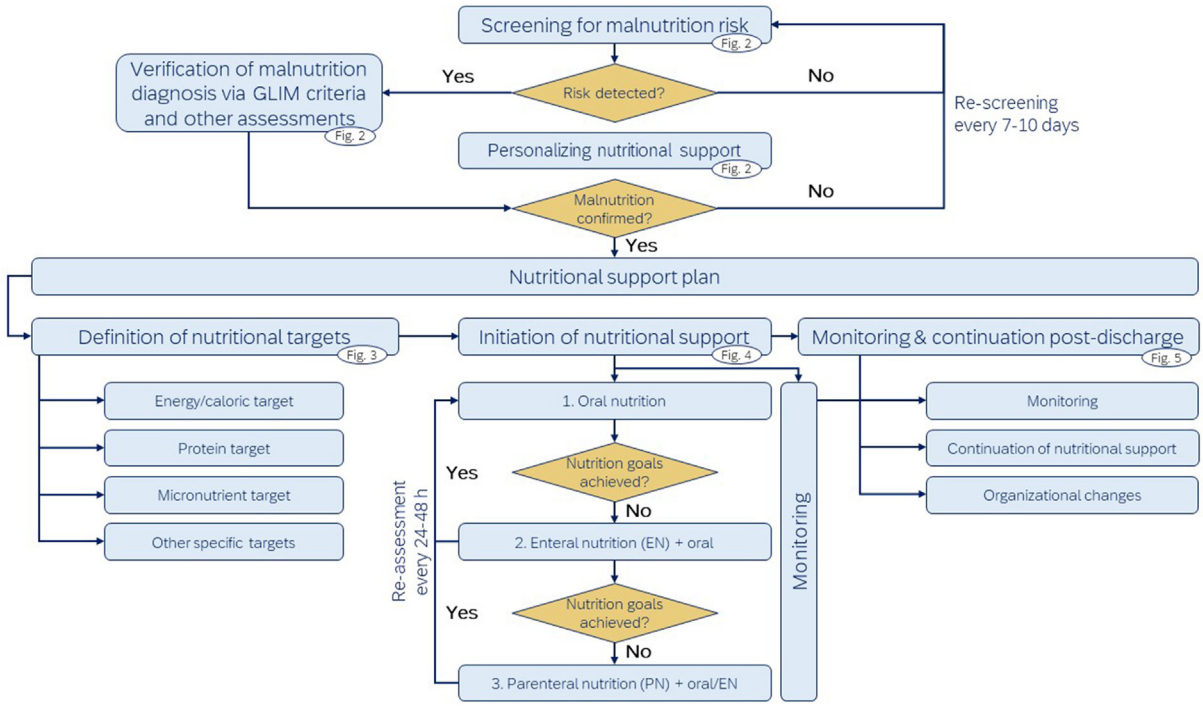


Fig. 1. Nutritional support for polymorbid medical inpatients. EN, enteral nutrition; GLIM, Global Leadership Initiative on Malnutrition; PN, parenteral nutrition.

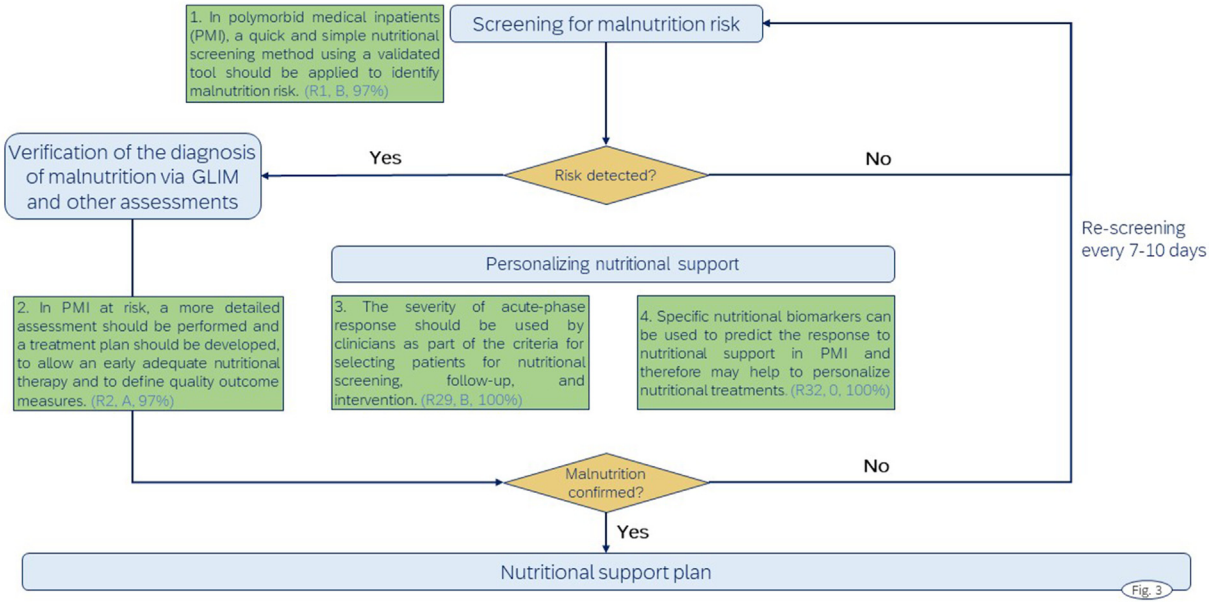


Fig. 2. Screening for malnutrition risk. GLIM, Global Leadership Initiative on Malnutrition; PMI, polymorbid medical inpatients.

(R8, Grade 0, Strong consensus 100 %)

Commentary

The estimation of energy requirements requires the determination of an individual's total energy expenditure (TEE) i.e., the sum of resting energy expenditure (REE), diet-induced thermogenesis and the energy expended during physical activity. The gold standard to measure REE is IC and for TEE the gold standard is doubly labelled water. However, these methods are rarely available in the clinical setting and require considerable expertise [35]. Practitioners therefore tend to rely on either published prediction equations (e.g. Harris-Benedict [36] or Ireton-Jones [37]) or weight-based formulae (e.g. 25–30 kcal/kg body weight/day).

In a study designed to evaluate the accuracy of prediction equations against IC in hospitalized patients demonstrated that no single prediction equation was accurate (within 90–110 % of measured REE). Another recent study conducted in 23 malnourished polymorbid, older hospitalized patients confirmed these results: the average REE predicted by the Harris–Benedict formula exceeded the REE measured by IC (after an overnight fast) on admission and at discharge by 29 % and 11 %, respectively,

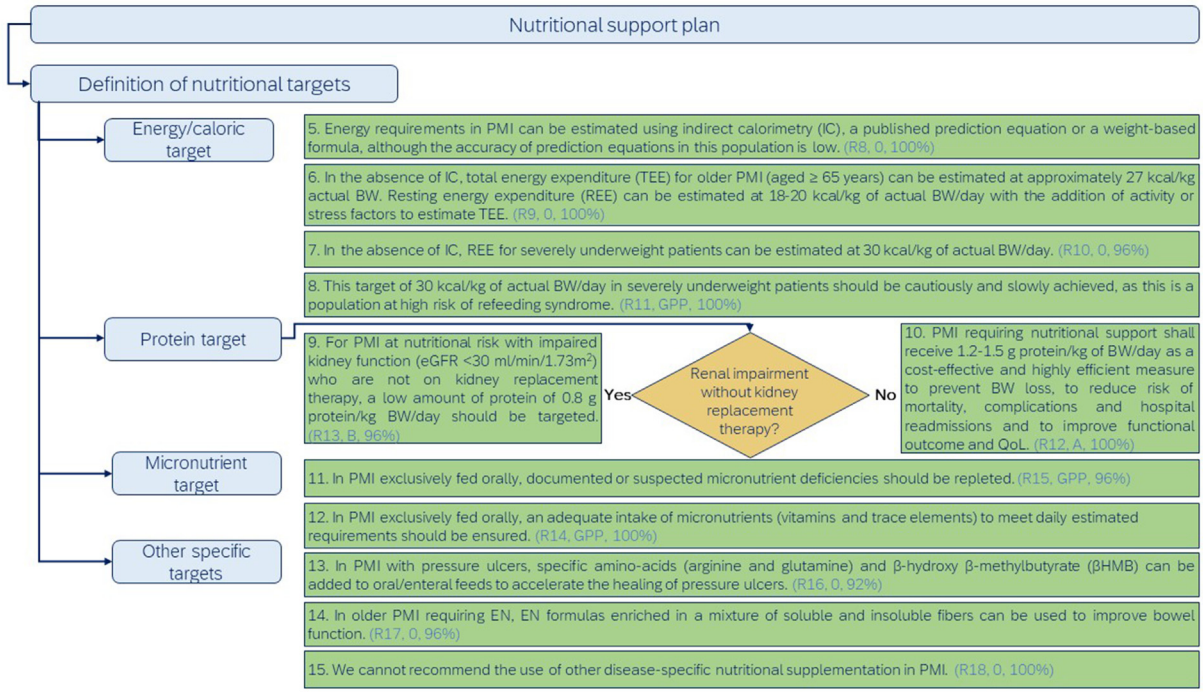


Fig. 3. Definition nutritional targets. β-HMB, β-hydroxy β-methylbutyrate; BW, body weight; eGFR, estimated glomerular filtration rate; EN, enteral nutrition; IC, indirect calorimetry; PMI, polymorbid medical inpatients; PN, parenteral nutrition; REE, resting energy expenditure; TEE, total energy expenditure.

suggesting that the Harris–Benedict formula is not accurate in this patient population [38].

Clinicians should be aware of the limitations of using precise numbers on weight-based formulae (or prediction equations) since in all studies there is considerable variation around the effect estimate. They should therefore only be used as a starting point when estimating requirements. In fact, this highlights the need for input from a suitable and experienced healthcare professional to adequately assess the nutritional needs of the patient, e.g., a dietitian.

6) **In the absence of IC, TEE for polymorbid older patients (aged ≥65 years) can be estimated at approximately 27 kcal/kg actual body weight/day. REE can be estimated at 18–20 kcal/kg actual body weight/day with the addition of activity or stress factors to estimate TEE.**

(R9, Grade 0, Strong consensus 100 %)

Commentary

In a review designed to determine the energy requirements of frail older people [39], including polymorbid patients, 33 studies (2450 subjects) were identified where REE was measured by IC in subjects aged 65 years or more and the results were compared with healthy older individuals. Only studies that measured REE by IC after a fast and at rest were considered eligible for inclusion in the review. The mean age was 73.0 ± 6.6 years, with no significant difference in BMI between the healthy and sick cohorts (25.6 ± 1.5 kg/m^2 and 25.2 ± 2.5 kg/m^2 respectively) and no differences in fat mass or fat-free mass. The weighted mean for the whole group was 20.4 kcal/kg actual body weight whereas the weighted mean for the polymorbid hospitalized older group was lower at 18.5 kcal/kg body weight. The mean TEE in sick older individuals was 27 ± 1.8 kcal/kg body weight and the weighted physical activity level in these patients was 1.36 ± 0.03 reflecting the relative physical inactivity of this population. The results of this review should be interpreted with caution since relatively few data were available in the sick older individuals (n = 248) compared with the healthy older individuals (n = 1970).

7) **In the absence of IC, REE for severely underweight patients can be estimated at 30 kcal/kg actual body weight.**

(R10, Grade 0, Strong consensus 96 %)

8) **This target of 30 kcal/kg actual body weight in severely underweight patients should be cautiously and slowly achieved, as this is a population at high risk of refeeding syndrome.**

(R11, Grade GPP, Strong consensus 100 %)

Commentary

In a study designed to determine the energy requirements of severely underweight hospitalized patients energy expenditure was measured by IC in 14 patients [40]. Mean BMI was 15.8 ± 1.8 kg/m^2 and mean age was 66.5 ± 13.9 years. In this study mean REE by IC was 1300 ± 160 kcal/day equating to 31.4 kcal/kg body weight. These results should be interpreted with caution since the sample size was very small. Furthermore, patients received continuous EN or PN during IC and thus measured energy expenditure included not only REE but also diet-induced thermogenesis.

The target of approximately 30 kcal/kg body weight in severely underweight patients may need to be achieved with caution, as this is a population at high risk of refeeding syndrome. The diagnostic criteria and the factors proposed for screening of refeeding syndrome have been proposed elsewhere [41].

4.1.2. Protein target

9) **For polymorbid medical inpatients at nutritional risk with impaired kidney function (estimated glomerular filtration rate [eGFR] <30 ml/min/1.73m^2) who are not on kidney**

replacement therapy, a low amount of protein of 0.8 g protein/kg body weight/day should be targeted.

(R13, Grade B, Strong consensus 96 %)

Commentary

In polymorbid medical inpatients with impaired kidney function, protein requirements should be lower [42]. Within EFFORT [43], protein targets of 1.2–1.5 g were lowered to 0.8 g/kg body weight/day for patients with eGFR <30 ml/min/1.73 m^2 according to earlier guidelines [7,44]. However, the degree of kidney impairment was a strong predictor for response to nutritional support and patients with eGFR of 15–29 L/min/1.73 m^2 receiving 0.8 g protein and those with 30–59 ml/min/1.73 m^2 receiving 1.2–1.5 g protein/kg body weight/day showed the strongest benefits on 30-day mortality (OR 0.37, 95 % CI 0.14 to 0.95 and 0.39, 95 % CI 0.21 to 0.75, respectively) [45]. This finding supports the concept of adjusting protein goals in polymorbid patients with renal conditions and impaired kidney function for eGFR and using targets from 0.8 g/kg body weight if eGFR is < 30 ml/min/1.73 m^2 and at 1.2–1.5 g with eGFR if ≥ 30 ml/min/1.73 m^2. Based on our search, there is a lack of trials comparing higher vs. lower protein targets in the polymorbid patient population with impaired kidney function. A recent critical review supported by the European Renal Nutrition Group of the European Renal Association (ERN-ERA) and ESPEN also recommends that renal status be prioritized in patients with advanced CKD (stages 4 and 5) [46] - however, they also conclude that patients with CKD need a personalized approach to prior renal or nutritional goals.

10) **Polymorbid medical inpatients requiring nutritional support shall receive 1.2–1.5 g protein/kg of body weight per day as a cost-effective and highly efficient measure to prevent body weight loss, to reduce risk of mortality, complications and hospital readmissions and to improve functional outcome and QoL.**

(R12, Grade A, Strong consensus 100 %)

Commentary

Protein targets of at least 1.0 g/kg body weight/day have been recommended in the past [7], e.g. supported by a high-quality RCT with 132 polymorbid patients. More recent and larger RCTs, such as the EFFORT trial including 2088 polymorbid patients, support a higher daily protein target of 1.2–1.5 g/kg body weight [43,47,48]. Compared to the usual care CG, odds for adverse outcomes and 30-day mortality were significantly lower in patients receiving individualized nutrition with these protein targets (OR 0.79, 95 % CI 0.64 to 0.97 and OR 0.65, 95 % CI 0.47 to 0.91 respectively), while functional status via BI, and QoL significantly increased - an intervention that was also cost-effective [48].

To reach high protein targets of 1.2–1.5 g/kg body weight, several strategies were used in recent trials and combined to respect patients individual preferences including ONS, protein-rich hospital menu, food fortification, and high-protein deserts and snacks [43,49,50].

Regarding combination of nutrition with exercise, one RCT of 47 malnourished polymorbid patients participating in a rehabilitation program on a geriatric ward, compared whey supplementation vs. no whey supplementation and demonstrated positive effects on daily protein intake (1.48 vs. 1.05 g/kg body weight) and muscle strength [49].

4.1.3. Micronutrient target

11) **In polymorbid medical inpatients exclusively fed orally, documented or suspected micronutrient deficiencies should be repleted.**

(R15, Grade GPP, Strong consensus 96 %)

Commentary

The need for micronutrient supplementation is often based on clinical assessment and in some cases estimated daily micronutrient requirements may temporarily exceed recommended daily intakes in order to account for depleted stores and/or increased utilization (particularly in patients who are exclusively fed orally) [51]. A study by Kilonzo et al. [52] on self-reported morbidity from infections in free-living patients (rather than inpatients) aged >65 years, randomized to receive either a daily vitamin and mineral supplement or placebo, found fewer QALYs per person in the supplemented group. This result is counter-intuitive; however, incomplete supplements not designed to replete micronutrient stores were used despite almost one third of the participants being judged at risk of micronutrient deficiency on recruitment. Daily micronutrient supplementation in free living individuals ≥60 years old did not improve incidence and severity of acute respiratory tract infections [53], although since the subjects were well-nourished they perhaps did not benefit from the supplementation. Another study of frail subjects in the community ≥65 years found a reduction in frailty with increased dietary intake but not with supplementation of only micronutrients [54]. However, the potential influence of increased micronutrient intake associated with the higher dietary intake in this study is unclear and the micronutrients-only group received estimated daily needs rather than repletion [55].

12) **In polymorbid medical inpatients exclusively fed orally, an adequate intake of micronutrients (vitamins and trace elements) to meet daily estimated requirements should be ensured.**

(R14, Grade GPP, Strong consensus 100 %)

Commentary

Polymorbid medical inpatients may be at risk of micronutrient deficiency due to decreased intake or greater utilization, which can compromise health and recovery from illness. Some studies suggest beneficial outcomes from supplementation of micronutrients like James et al. [56] or Schuetz et al. [5], although the specific role of micronutrient supplementation is still unclear. Just as micronutrients underprovision could compromise polymorbid medical inpatients so too could overprovision.

General micronutrient supplementation (provision of multivitamins rather than combined multivitamin and multi-trace element) appears to be common, and often based on financial cost of the supplement. However, if a subject may have general micronutrient depletion or generally increased micronutrient requirements then there is likely to be a need to provide trace elements as well as vitamins. Therefore, supplementation should aim to deliver a complete range of both multivitamins and multi-trace elements rather than multivitamins alone. Complete micronutrient supplementation to meet reference nutrient intakes or otherwise estimated daily requirements could be particularly important in polymorbid medical inpatients due to the potential for any deficiencies to affect multiple and already compromised organ systems [57]. ESPEN provides practical advice on micronutrient status affecting disease and vice versa, micronutrient provision and monitoring, and potential micronutrient deficiencies resulting from medicine administration such as vitamin B12 or iron with proton pump inhibitors, or thiamine with diuretic therapy [58]. No studies were identified that reported the supplementation of multivitamins (with or without trace elements) compared to no supplements in polymorbid medical inpatients exclusively fed orally.

4.1.4. Other specific targets

13) **In polymorbid medical inpatients with pressure ulcers, specific amino-acids (arginine and glutamine) and βHMB can be added to oral/enteral feeds to accelerate the healing of pressure ulcers.**

(R16, Grade 0, Strong consensus 92 %)

Commentary

Pressure ulcers are responsible for protein loss, hypermetabolism and hypercatabolism, and are often associated with malnutrition. This includes nutrient deficiencies that are critical to the different phases of wound healing (conditionally essential amino acids and antioxidant micronutrients). A RCT from Singapore that included 26 polymorbid patients hospitalized for more than two weeks [59] showed a marginal albeit significant effect of an arginine/glutamine/βHMB mixture on the healing of pressure ulcers (greatest improvement of viable tissues at two weeks in the IG, by 43 % vs. 26 %, $p = 0.02$). The amino acid mixture (14 g arginine, 14 g glutamine and 2.4 g calcium βHMB per day) was not part of a nutritional formula, but all patients were fed per recommendations for hypermetabolic and hypercatabolic patients (30–35 kcal and 1.2.0 g protein/kg body weight/day according to the stage of the ulcer). In another RCT from Hong Kong, 87 polymorbid malnourished older adults with pressure ulcers were randomized to receive or not the same mix of arginine/glutamine/βHMB for four weeks, besides an adapted nutritional support (at least 30 kcal and 1.2 g protein/kg body weight/day) [60]. A statistically significant reduction in pressure ulcer size ($p = 0.048$) and depth ($p = 0.002$) was observed in the IG while the Pressure Ulcer Scale for Healing (PUSH score) showed a significant improvement in the CG ($p < 0.001$).

Other positive studies have been published using an oral nutritional supplement enriched in arginine, zinc and antioxidants in patients outside the scope of these guidelines [61,62].

14) **In polymorbid medical older inpatients requiring EN, EN formulas enriched in a mixture of soluble and insoluble fibers can be used to improve bowel function.**

(R17, Grade 0, Strong consensus 96 %)

Commentary

Diarrhea and constipation are the most frequent complications of EN in hospitalized patients. A Belgian study of 145 older patients receiving enteral feeding [63] found positive effects of a formula enriched with 30 g fiber including 33 % insoluble (cellulose and hemicellulose A) and 67 % soluble (pectin, hemicellulose B, inulin) fiber (IG) vs. the CG, which received the same EN with no fiber. The frequency of stools was lower (4.1 ± 2.6 per week versus 6.3 ± 4.7 per week; $p < 0.001$) and the stool consistency higher in the IG (31 % had solid form stools in the IG vs. 21 % in the CG, and 2 % had liquid-watery stool in the IG vs. 13 % in the CG, $p < 0.001$); however, patients in the CG received more laxatives during the study period than patients in the fiber group. A global 4-week mortality of 24 % underlines the severity of the patients' conditions.

The effects on bowel function associated with the absence of detrimental metabolic effect argue for a recommendation for a first intention use of EN formulae enriched with a mixture of soluble and insoluble fibers (supposed to match the multiple sources of fibers in normal food). The same recommendation has been made in ESPEN's clinical nutrition and hydration guidelines in geriatrics [57].

15) **We cannot recommend the use of other disease-specific nutritional supplementation in polymorbid medical inpatients.**

(R18, Grade 0, Strong consensus 100 %)

Many specialized ONS/EN feeds have been developed for specific diseases that usually involve chronic/acute inflammation, specific micronutrient deficiency or specific metabolic disorders [64]. However, most studies were not conducted in identified hospitalized polymorbid patients, even though some of these patients may well be polymorbid, and the number of useable studies identified is extremely low. The scarcity of quality intervention studies in populations adequately described as polymorbid does not allow to recommend the use of other disease-specific nutrients. One of such prospective studies with negative findings was conducted in Japan in 50 patients with exacerbation of COPD [65]. They were randomized to receive either ONS with 1.1 g of eicosapentaenoic acid (EPA) or a comparable one without n-3 fatty acid during their hospitalization, both groups receiving a total of 30–35 kcal/kg/day. At discharge (after 12–13 days of supplementation in both groups), there was a non-significant increase in lean body mass index and skeletal muscle mass index in the EPA group compared with the CG (lean body mass index: +0.35 vs. +0.19 kg/m^2, $p = 0.60$, and skeletal muscle mass index: +0.2 vs. −0.3 kg/m^2, $p = 0.17$, respectively). The changes in skeletal muscle mass index were significantly correlated with the LOS in the EPA group, but not in the CG ($r = 0.53$, $p = 0.008$, and $r = -0.32$, $p = 0.31$, respectively).

4.2. Initiation of nutritional support (Fig. 4)

16) **In polymorbid medical inpatients with reduced food intake and hampered nutritional status, at least 75 % of calculated energy and protein requirements shall be achieved in order to reduce the risk of adverse outcomes and mortality.**

(R25, Grade A, Strong consensus 100 %)

Commentary

In polymorbid medical inpatients reduced food intake is associated with increased mortality and complications [66–69]. The EFFORT trial has demonstrated that reaching ≥75 % of estimated nutrition goals versus lower achievements led to significant lower risk of adverse events and mortality [5]. Supporting this finding in a meta-analysis from 2019, Gomes et al. [70] stratified trials by adherence to nutrition protocol and found that high adherence led to a more pronounced survival benefit. Whether the impact would be more pronounced if the IG had achieved 100 % cannot be answered by the data. Achieving 100 % of the targets should be strived for but is usually not realistic when patients are hospitalized and have either an exacerbation of one of their conditions or a current complication.

A prospective observational study [71], reported that patients with reduced food intake had a higher in-hospital mortality as well as 90-day mortality. Similar results were observed in a supportive study conducted in the critically ill population [72]. In a trial Li et al. found nutritional intake to be higher in patients with LOS of less than twelve days compared to patients with higher LOS [14]. However, a small sample size ($n = 40$) pilot RCT could not find a difference in readmissions within 30 days between the IG that reached 75 % of their nutritional goals and the CG that did not [73].

17) **Early nutritional support (i.e., provided in less than 48 h post hospital admission) compared to later nutritional support shall be performed in polymorbid medical inpatients, as mortality and adverse events are lower and lean body mass loss could be decreased and self-sufficiency could be improved.**

(R17, Grade A, Strong consensus 100 %)

Commentary

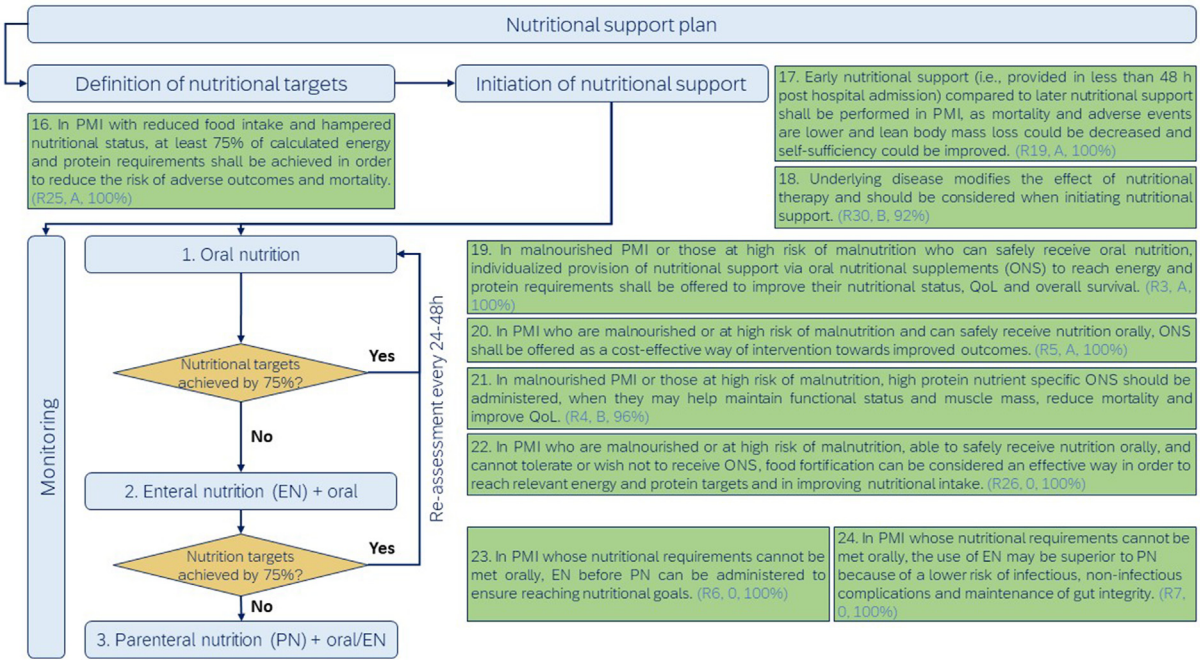


Fig. 4. Initiation of nutritional support. EN, enteral nutrition; ONS, oral nutritional supplements; PMI, polymorbid medical inpatients; PN, parenteral nutrition; QoL, quality of life.

The large EFFORT trial [5] addressed this question as the IG got their therapy initiated within 48 h. By 30 days, patients in the IG experienced 21 % less adverse clinical outcomes and 35 % lower mortality (adjusted OR 0.65 [0.47 to 0·91], p = 0.011).

A prospective RCT from Hegerová et al. [74] demonstrated that early nutrition support ONS (600 kcal, 20 g/day protein) added to the standard diet and exercise lead to no decrease in lean body mass compared to CG - an effect that persisted 3 months after discharge. Zheng et al. [75] compared early EN with "family managed nutrition" in a RCT of patients with acute stroke and dysphagia. Early nutrition support led to a significant lower infections rate and to a better National Institutes of Health Stroke Scale (NIHSS) score.

Using a nationwide inpatient database with 432,620 eligible patients hospitalized for acute heart failure after propensity score matching, Kaneko et al. showed that delayed initiation of feeding was associated with higher in-hospital mortality, longer LOS and higher incidence of pneumonia and sepsis when compared to earlier initiation of feeding [76].

Two studies addressed budget impact analysis applied to Colombian [77] and Mexican [78] population. Both found early nutritional support to be cost-effective (savings of 1351 $/patient in

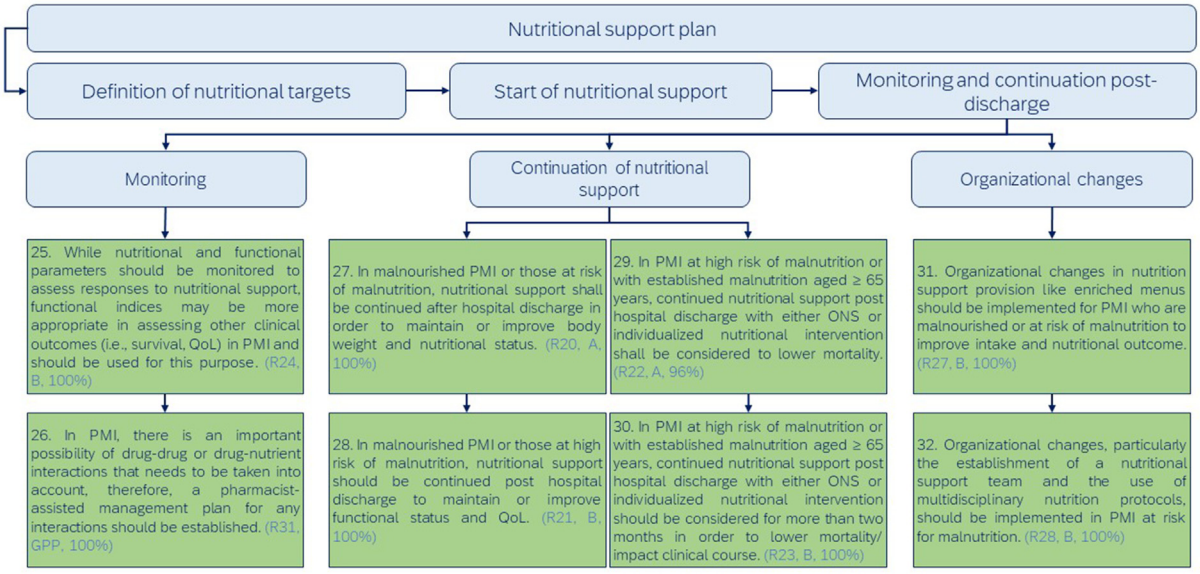


Fig. 5. Monitoring and continuation post-discharge. ONS, oral nutritional supplements; PMI, polymorbid medical inpatients; QoL, quality of life.

Colombia and 2505 $/patient in Mexico, mainly due to lower complications and readmissions.

18) **Underlying disease modifies the effect of nutritional therapy and should be considered when initiating nutritional support.**

(R30, Grade B, Strong consensus 92 %)

Commentary

There is strong evidence from large RCTs that polymorbid patients at risk for malnutrition benefit from nutritional support [79]. In a population-based cohort study of more than 110,000 patients, effect of nutritional support remained robust in subgroup analyses which stratified for main diagnoses and comorbidities, among others [80]. However, among medical patients, the effect of nutritional support may also depend on underlying disease. Mudge et al. identified diagnosis of infection or cancer to be associated with inadequate energy intake in patients aged 65 years or older [81]. A recent study by Bargetzi et al. found that kidney disease predicted response to nutritional treatment with lower eGFR showing stronger clinical benefit [45]. Similarly, patients with chronic heart failure have shown strong benefit from nutritional support. A survival benefit in chronic heart failure patients receiving nutritional support was found in a Spanish trial by Bonilla-Palomas et al. with 120 patients [82] and in secondary analysis of 645 patients from a randomized trial by Hersberger et al. [83]. Similar results were also found within the NOURISH study with a significant survival benefit associated with nutritional support [6]. Other conditions which may increase the effects of nutritional support are cancer [84], COPD [85] among others. However, it remains unclear how to implement these findings into clinical routine.

4.3. Oral nutrition

19) **In malnourished polymorbid medical inpatients or those at high risk of malnutrition who can safely receive oral nutrition, individualized provision of nutritional support via oral nutritional supplements (ONS) to reach energy and protein requirements shall be offered to improve their nutritional status, QoL and overall survival.**

(R3, Grade A, Strong consensus 100 %)

Commentary

Provision of ONS has been found to impact clinical outcome. Schuetz et al., in the EFFORT trial, reported a lower risk of adverse clinical outcome in the IG compared to controls (adjusted OR 0.79, 95 % CI 0.64 to 0.97, p = 0.023) and a lower risk of mortality (adjusted OR 0.65, 95 % CI 0.47 to 0.91, p = 0.011), with no statistically significant difference in side effects between both groups [86]. Similarly, improved survival, lower non-elective hospitalizations, improvements in functional status in medical inpatients receiving nutritional support was reported in the meta-analysis by Gomes et al. [70]. Gressies et al. confirmed these findings in 2022 by an updating and re-analyzing Gomes et al. for the polymorbid patient cohort only. The analysis again showed a significant reduction in mortality risk (OR 0.68; 95 % CI 0.51–0.91) (Fig. 6) and hospital readmissions (OR 0.64; 95 % CI 0.45–0.90) [87]. Hegerová el al. conducted a prospective RCT in 200 medical inpatients and found that the provision of ONS (with physiotherapy) increased the energy and protein intake without negatively affecting the hospital food consumption [74]. This supplementation resulted in significant preservation of muscle mass and increased independence (Barthel Index).

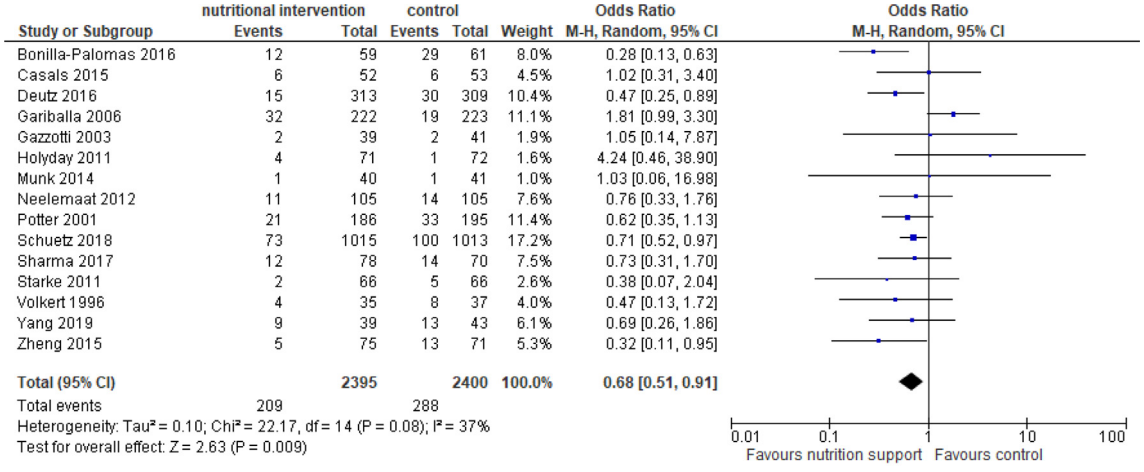
In EFFORT the positive effects of individualized nutritional support provided during hospitalization which were observed at 30 days, were not sustained at six months after discharge when nutritional support was discontinued [47].

20) **In polymorbid medical inpatients who are malnourished or at high risk of malnutrition and can safely receive nutrition orally, ONS shall be offered as a cost-effective way of intervention towards improved outcomes.**

(R5, Grade A, Strong consensus 100 %)

Commentary

Early detection and intervention against DRM has been shown to improve nutritional status and reduce complications during hospital stay and non-elective readmissions [6,88]. According to a retrospective cost-effectiveness analysis by Philipson et al., the provision of ONS resulted in a reduction in LOS of 2.3 days that subsequently decreased annual hospital costs by 4734 and reduced the readmission rate by 6.7 % [89]. The greatest benefit was seen among the most severely ill patients, underscoring the importance of providing nutritional support to those who need it most [90].



A Mantel-Haenszel random-effects model was used. Squares indicate mean values, with the size of squares reflecting the weight and the lines indicating 95% CIs. Diamonds indicate pooled estimates, with horizontal points of the diamonds indicating 95% CIs.

Fig. 6. Forest plot comparing nutritional intervention versus control for mortality in polymorbid medical inpatients [87].

The cost analysis of the EFFORT trial showed that nutritional support for polymorbid medical inpatients is a highly cost-effective intervention to reduce risks for ICU admissions and hospital-associated complications, while improving patient survival [91]. Confirming results were also reported in an economic analysis of Schuetz et al. [92] and a meta-analysis of RCTs on hospitalized patients at high risk of developing pressure ulcers, by Tuffaha et al. [93].

In line with these findings the economic evaluation of the NOURISH study concluded that the high protein βHMB ONS intervention was cost effective and positive in terms of survival [94] . Moreover, Ballesteros-Pomar et al. analysis proved the intervention to be cost effective, improved survival and marginally reduced cost of treatment [95].

21) **In malnourished polymorbid medical inpatients or those at high risk of malnutrition, high protein nutrient specific ONS should be administered, when they may help maintain functional status and muscle mass, reduce mortality and improve QoL.**

(R4, Grade B, Strong consensus 96 %)
Commentary

Several nutrient specific ONS have been tested for their effectiveness in improving outcomes in hospitalized patients. According to the NOURISH study, a multicenter RCT which included 652 malnourished inpatients, a high protein Hydroxy β-Methylbutyrate (βHMB) ONS may not yield a difference when compared with placebo on readmission rates, but may help with the maintenance of muscle mass during hospital stay and result in a significant decrease in post-discharge mortality (90-day mortality was 4.8 % in the IG vs. 9.7 % in the CG; RR 0.49, 95 % CI 0.27 to 0.90, p = 0.018) [6]. The effects of this ONS were also positive in a subgroup of patients with chronic obstructive pulmonary disease (COPD). Moreover, COPD patients receiving the high protein βHMB ONS showed an increase in handgrip strength (HGS) from discharge to 30 days (1.56 kg vs. −0.34 kg, p = 0.0413) and increased body weight (0.66 kg vs. −0.01 kg, p < 0.05) [96]. Improved functionality measured by HGS was also observed in other subgroup analyses from the NOURISH study, including patients with cardiovascular and pulmonary disease [85].

In addition, provision of ONS containing 995 kcal from macronutrients and covering 100 % of the RDA for healthy older adults in vitamins and minerals led to a lower incidence of depressive symptoms (p = 0.021) in older medical inpatients, with no other effect on their cognitive performance but with a significant positive effect on their self-reported QoL [97,98].

22) **In polymorbid medical inpatients who are malnourished or at high risk of malnutrition, able to safely receive nutrition orally, and cannot tolerate or wish not to receive ONS, food fortification can be considered an effective way in order to reach relevant energy and protein targets and in improving nutritional intake.**

(R26, Grade 0, Strong consensus 100 %)
Commentary

To reach nutritional goals different approaches can be used, especially because provision of nutritional support via ONS is often discontinued or not well tolerated by hospitalized patients [99,100] A Danish RCT [101] tested protein fortification of a novel energy dense menu supplementary to the standard hospital food service and could increase the food based nutrition intake of energy and protein beyond 75 % of calculated requirements. HGS and LOS were also reported but there were no differences to be observed, as expected when the study was not powered for such endpoints.

Another supportive study is a Dutch RCT [50] used protein-enriched familiar foods and drinks to improve protein intake in older hospitalized polymorbid patients. According to Mills et al.'s meta-analysis provision of energy or protein in the form of fortified foods or supplements in food items could be considered a cost-effective, well tolerated and effective way of improving nutrient intake in older inpatients [102]. A result that was confirmed in another meta-analysis by Morilla-Herrera et al. [103], but also the need of higher quality studies was stressed.

4.4. Enteral and parenteral nutrition

23) **In polymorbid medical inpatients whose nutritional requirements cannot be met orally, EN before parenteral nutrition (PN) can be administered to ensure reaching nutritional goals.**

(R6, Grade 0 − Strong consensus 100 %)
Commentary

Reaching energy goals in medical inpatients is important to prevent weight loss and the loss of muscle mass that may lead to poorer functional outcomes. However, in the acute care setting many obstacles may prevent patients from meeting their nutritional requirements orally. These obstacles include loss of appetite due to acute illness, delayed gastric emptying causing both nausea and early satiety, inability to swallow, and vomiting, among others. In these situations, the use of EN or PN can help increase nutritional intake until oral intake is sufficient [42,104]. Several randomized studies have compared the effect of nutritional support on outcomes of medical inpatients. A 2019 systematic review and meta-analysis on nutritional support in medical inpatients found significantly improved clinical outcomes in those receiving adequate nutritional support. The review included 27 RCTs from several countries comprising 6803 medical inpatients, and reported a 27 % reduction in mortality and non-elective hospital readmissions [70]. The review also found significantly higher energy and protein intake, as well as beneficial effects on weight when comparing nutritional support (including counseling and oral and enteral feeding) to CG patients.

24) **In polymorbid medical inpatients whose nutritional requirements cannot be met orally, the use of EN may be superior to PN because of a lower risk of infectious, non-infectious complications and maintenance of gut integrity.**

(R24, Grade 0, Strong consensus 100 %)
Commentary

Several trials found that the addition of either EN or PN to oral nutrition improves outcomes [105–107], but high-quality randomized studies comparing EN and PN head-to-head in the polymorbid medical inpatient setting are scarce. Observational evidence consists of one large, prospective, non-randomized study including patients at nutritional risk, that investigated the outcomes of patients receiving either EN or PN to patients without nutritional support [12]. Overall, the study found a significantly lower risk of overall complications and infectious complications associated with nutritional support (adjusted OR 0.54, 95 % CI 0.38 to 0.77), p < 0.001 and adjusted OR 0.42, 95 % CI 0.27 to 0.64, p < 0.001, respectively). When comparing patients receiving PN and EN within the nutritional support group, those receiving EN had significantly lower overall complication rates, as well as rates of infectious and non-infectious complications, compared to patients

without nutritional support ($p = 0.001$). However, no difference in the complication rates was found between patients with PN and patients with no nutritional support ($p = 0.29$).

Still, when also considering high-quality evidence from critical care [108] and in patients with pancreatitis [109] as well as observational evidence from polymorbid medical inpatients, there are several arguments for the use of EN as a first line therapy as compared to PN due to lower risks for infectious and non-infectious complications. An important physiological rational is also the prevention of intestinal mucosal atrophy by EN compared to PN [110].

4.5. Monitoring and continuation post-discharge (Fig. 5)

4.5.1. Monitoring

25) **While nutritional and functional parameters should be monitored to assess responses to nutritional support, functional indices may be more appropriate in assessing other clinical outcomes (i.e., survival, QoL) in polymorbid medical inpatients and should be used for this purpose.**

(R24, Grade B, Strong consensus 100 %)

Commentary

Limited evidence exists to answer this clinical question as most trials use nutritional and functional status as outcome rather than as monitoring tools. A secondary analysis from EFFORT supports the use of functional parameters to monitor nutritional support but also to guide initiation of it. Kaegi-Braun et al. illustrates that individualized nutritional support was most effective in reducing mortality in patients with low HGS. Furthermore, an incremental decrease of HGS by 10 kg resulted in doubling 30-d mortality in females and 50 % increase in 30-d mortality in males, reflecting the prognostic potential of HGS [33].

A cohort study by Ballesteros-Pomar et al. found that a higher HGS, but not muscle mass, was related to better QoL, less readmissions and lower mortality after adjusting for age, sex, and comorbidity [111]. However, another prospective observational study failed to show a significant association between HGS and 100-day mortality [112].

A study from 1995 [113] suggests that although nutrition therapy improves nutritional status and outcome, functional parameters are more robust prognosticators of outcome. Norman et al. [114] demonstrated that post-discharge dietary counseling plus ONS (IG) and dietary counseling (CG) improved body weight and body cell mass. However, HGS and peak flow improved only in the IG. By applying the reasoning used for the trial by Mendehall et al., it appears that Norman et al. confirm that functional parameters may be superior to nutritional parameters.

26) **In polymorbid medical inpatients there is an important possibility of drug–drug or drug-nutrient interactions that needs to be taken into account, therefore, a pharmacist-assisted management plan for any interactions should be established.**

(R31, Grade GPP, Strong consensus 100 %)

Commentary

Polymorbid medical inpatients often require multiple medicines to manage their comorbidities. Whilst this may be an essential approach, it carries several risks including potential 'drug–drug' and/or 'drug-nutrient' interactions and their associated consequences [115]. In a systematic review polypharmacy was significantly associated with malnutrition [116,117] and with sarcopenia [118], which could result in insufficiency of some electrolytes or micronutrients [119]. A recent meta-analysis from 2023, which included 29 studies, also demonstrated that sarcopenia is associated with a higher prevalence of polypharmacy and higher number of medications compared with individuals without sarcopenia [120]. Some interactions will be familiar including physical binding of drugs such as tetracyclines to the divalent and trivalent cations from milk or antacid preparations [121] or in many of the ONS and enteral formulas, which limits absorption from the gastrointestinal tract. Other interactions that may be less familiar include the potential for physical binding of ceftriaxone to calcium salts when both are given intravenously [122] or the effect of hydration status, which is commonly impaired in acute medical admissions [123], on drug enrichment [124]. Whilst some drugs have no specific requirement to be taken with or without food there can still be toxic potential if specific examples such as simvastatin are taken concurrently with grapefruit juice [125]. A description of pharmacokinetic interactions between food and drugs is available [126]. Advice on the complexities of all these potential interactions in polymorbid medical inpatients may be obtained from a pharmacist or pharmacologist.

5. Continuation of nutritional support

27) **In malnourished polymorbid medical inpatients or those at risk of malnutrition, nutritional support shall be continued after hospital discharge in order to maintain or improve body weight and nutritional status.**

(R20, Grade A, Strong consensus 100 %)

Commentary

For the present question, only interventions initiated in the hospital (and continued after discharge) were included. Many polymorbid patients leave the hospital malnourished, which increases the risk for functional decline, loss of independence, greater morbidity and risk of unplanned readmissions [127]. A recent meta-analysis also demonstrated that caloric intake but also protein intake was significantly higher in patients receiving nutritional support after hospital discharge [128], which is also confirmed by systematic reviews [129,130].

One study by Feldblum et al. which directly compared 6-month individualized nutritional support in hospital followed by three home visits after discharge showed that continued nutritional support in malnourished patients resulted in a significantly higher change in mean MNA score, compared to the CG [131]. Similarly, in a prospective RCT of 80 patients aged 75 years or more admitted for acute disease and at risk for malnutrition, a 60-day intervention with ONS resulted in maintained body weight and improved MNA scores, whereas CG patients continued to lose weight [132].

Similar results were obtained in other RCTs e.g. by Casals et al. [133] or Persson et al. [134] Confirming this, a sub-analysis of the NOURISH study showed an increase in nutrient intake in IG patients without decrease in dietary intake [55].

28) **In malnourished polymorbid medical inpatients or those at high risk of malnutrition, nutritional support should be continued post hospital discharge to maintain or improve functional status and QoL.**

(R21, Grade B, Strong consensus 100 %)

Commentary

Enhancing functional status post-discharge is crucial in preventing extended recovery, readmissions, or loss of autonomy. In one RCT conducted in malnourished adults, 3-month specialist ONS intervention resulted in a reduction in the number of falls [135], a significant improvement in functional limitations [136], and was neutral in financial cost [137]. In a study by Persson et al. treatment with liquid supplements and dietary advice for four months

resulted in an improvement of Katz's activities of daily living index, but not in QoL assessed by the SF-36 [134]. On the other hand, Casals et al. reported significantly improved QoL scores after six months of individualized nutritional support [138].

In malnourished patients who received ONS during their hospital stay and for three months post discharge, QoL assessed by the SF-36 was significantly improved in the IG patients compared to the CG patients [139]. HGS and peak expiratory flow increased after three months only in the intervention patients [114]. HGS was also significantly improved in the IG of malnourished patients after three months of nutrient adapted ONS in the NOURISH study [140].

A study which used multimodal nutritional approach showed a significant improvement in the 30 s chair rise test in the IG. The improvements in physical function were significantly higher in the IG but clinically relevant in both groups [141].

29) **In polymorbid medical inpatients at high risk of malnutrition or with established malnutrition aged 65 and older, continued nutritional support post hospital discharge with either ONS or individualized nutritional intervention shall be considered to lower mortality.**

(R22, Grade A, Strong consensus 96 %)

Commentary

One of the largest RCTs to date (NOURISH; n = 652) on in- and post hospital (=continued) nutritional support reported lower 90-day mortality in the IG receiving nutrient-adapted ONS twice a day for three months compared to the CG patients who received a placebo (4.8 % in the IG vs. 9.7 % in the CG, p = 0.018) [6]. A finding that is supported by Feldblum et al.'s study [131]. The PICNIC study of Bonilla-Palomas et al. initiated nutritional intervention in patients with heart failure at admission to hospital and continued for six months. At twelve months, the primary composite endpoint occurred in 27.1 % of the IG compared to 60.7 % of CG patients (HR 0.45, 95 % CI 0.19–0.62, p = 0.0004). Both mortality (HR 0.37, 95 % CI 0.19–0.72, p = 0.003) and readmission rates were lower in the IG patients (10.2 vs. 36.1 %, p = 0.001) [82]. The benefits of the nutritional intervention persisted at 24 months [142,143].

Also two recent systematic reviews and meta-analyses [128,144] concluded that mortality was significantly lowered in patients with nutritional support which was continued after hospital discharge (OR 0.63, 95 % CI 0.48 to 0.84, p = 0.001) and (OR 0.72 95 % CI 0.57 to 0.91, p = 0.006).

Only one study studied the impact of three-month nutritional support on long-term mortality and revealed no differences in mortality at year one and four between groups [145].

30) **In polymorbid medical inpatients at high risk of malnutrition or with established malnutrition aged 65 and older, continued nutritional support post hospital discharge with either ONS or individualized nutritional intervention should be considered for more than two months in order to lower mortality/impact clinical course.**

(R23, Grade B, Strong consensus 100 %)

Commentary

The ideal duration of post discharge nutritional intervention varies. However, most RCTs on interventions with ONS spanned three months [6,114,135–137,139], while individualized nutritional support was usually provided for longer periods (four month [134], or six months [82,131,138,146]). While readmission rates were not reduced after three months in one of the largest trials [6] in geriatric patients [147] or in older patients [148], it was significantly reduced after six months of nutritional intervention in several trials [82,131,146] but not all [141]. A recent meta-analysis also showed that interventions which lasted >60 days had a stronger effect on mortality (OR 0.53 95 % CI 0.38 to 0.75) than trials with shorter durations of the intervention (OR 0.85 95 % CI 0.64 to 1.13, p for subgroup difference: 0.04) [144].

A longer duration of nutritional treatment is also necessary to improve QoL in older adults [149]. Neelemaat et al. argue that while they were able to show an effect on functional limitations after three months, the length of nutritional support might not have been sufficient to show an effect on QoL [137] which is similar to the results in the trial of Munk et al. [141].

6. Organizational changes

31) **Organizational changes in nutrition support provision like enriched menus should be implemented for polymorbid medical inpatients who are malnourished or at risk of malnutrition to improve intake and nutritional outcome.**

(R27, Grade B, Strong consensus 100 %)

Commentary

The organization of nutritional support in hospitals requires a multi-disciplinary approach involving catering, nursing, finance, and therapy services. Changes to the organization for inpatients may improve outcomes: these include the use of nutritional healthcare assistants [150], targeted education for dietitians and the multidisciplinary team (MDT) to improve early use of ONS [151], food fortification [152], introduction of nutritional screening [153] and technological innovations used to facilitate timely referral to the Nutrition Support Team (NST) [154]. Despite these general studies, a systematic review of non-randomized studies showed that improvements are not consistently demonstrated [155]. Therefore, it is important to consider the specific impact of organizational changes on polymorbid medical inpatients. A single-blinded RCT [101,156] demonstrated that the use of a protein fortified menu was effective in increasing protein intake of IG but however did not change energy intake, LOS or HGS. The CG received the standard hospital menu.

A pilot, controlled trial compared a modified hospital menu, including higher energy and protein choices, to the standard hospital menu [157]. There was no difference in patients' weight, HGS, functional independence or LOS. However, energy and protein intake were higher in the IG.

A further, prospective controlled trial [22] demonstrated that applying an early multi-disciplinary intervention protocol led to a significant weight gain in IG, without a change in LOS or the development of pressure ulcers. In addition, the IG developed fewer hospital acquired infections.

32) **Organizational changes, particularly the establishment of a NST and the use of multidisciplinary nutrition protocols, should be implemented in polymorbid medical inpatients at risk for malnutrition.**

(R28, Grade B, Strong consensus 100 %)

Commentary

A cohort study reported the impact of multiple nutrition improvement initiatives on a one-day record of intake of estimated energy and protein requirements (>75 % of requirements) [158]. The number of patients achieving adequate energy and protein intake increased significantly from pre-intervention to post-interventional. It is suggested that this increase in intake was primarily a consequence of introducing the hot breakfast option. Dietary intake also improved via nutrition improvement initiatives

over seven years by Young et al. on three medical wards [159]. Phased initiatives included the introduction of assisted mealtimes, nursing assistant to help with nutrition administration/feeding assistance and additional education for nurses, dietitians and the wider MDT.

In another mealtime study, trained volunteers assisted patients for one year [160]. The authors reported that although their intervention released time for nursing staff, they found no positive effect on dietary intake, which is a similar finding to Roberts et al. [158].

A cohort study [161] demonstrated the impact of an NST on the management of patients requiring PN. After a structured training program for nurses led by the NST, catheter-related sepsis rates decreased in PN patients from 71 % pre-NST to 29 % in their first year ($p = 0.05$).

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Disclaimer

This guideline has been developed with reasonable care and with the best of knowledge available to the authors at the time of preparation. They are intended to assist healthcare professionals and allied healthcare professionals as an educational tool to provide information that may support them in providing care to patients. Patients or other community members using this guideline shall do so only after consultation with a health professional and shall not mistake this guideline as professional medical advice. This guideline must not substitute seeking professional medical and health advice from a health professional.

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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 with legitimate interest upon request to the ESPEN executive.

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Appendix A. Supplementary data

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