A practical approach to identifying pediatric disease-associated undernutrition: a position statement from the ESPGHAN special interest group on Clinical Malnutrition.

Jessie M. **Hulst**[1, 2], Koen **Huysentruyt**[1,3], Konstantinos **Gerasimidis**[4], Raanan **Shamir**[5], Berthold **Koletzko**[6], Michail **Chourdakis**[7], Mary **Fewtrell**[8], Koen F. **Joosten**[9] on behalf of Special Interest Group Clinical Malnutrition of ESPGHAN.

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1. Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, Ontario, Canada;
2. Department of Pediatrics & Department of Nutritional Sciences, University of Toronto, Toronto, Canada
3. Department of Pediatric Gastroenterology, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium
4. Human Nutrition, School of Medicine, Dentistry and Nursing, University of Glasgow, New Lister Building, Glasgow Royal Infirmary, Glasgow, UK
5. Institute of Gastroenterology, Nutrition and Liver diseases, Schneider Children's Medical Center, Petah Tikva, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.
6. LMU - Ludwig-Maximilians-Universität Munich, Div. Metabolic and Nutritional Medicine, Department Paediatrics, Dr von Hauner Children's Hospital, LMU University Hospitals, Munich, Germany.
7. School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece.
8. UCL Great Ormond Street Institute of Child Health, UCL, London, United Kingdom.

9. Department of Pediatrics and Pediatric Surgery, Erasmus Medical Center- Sophia Children's Hospital, Rotterdam, the Netherlands.

Corresponding author

Jessie M. Hulst

Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Room 8260 Black Wing, 555 University Avenue, Toronto, Ontario, Canada, M5G 1X8. Tel: +1 (416) 813-7654. Ext 203565; email: jessiehulst@sickkids.ca

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ABSTRACT

Disease-associated undernutrition (DAU) is still common in hospitalized children and is generally accepted to be associated with adverse effects on disease outcomes; hence making proper identification and assessment essential in the management of the sick child. There are however several barriers to routine screening, assessment, and treatment of sick children with poor nutritional status or DAU, including limited resources, lack of nutritional awareness, and lack of agreed nutrition policies. We recommend all pediatric facilities to 1) implement procedures for identification of children with (risk of) DAU, including nutritional screening, criteria for further assessment to establish diagnosis of DAU, and follow-up, 2) assess weight and height in all children as a minimum, and 3) have the opportunity for children at risk to be assessed by a hospital dietitian.

An updated descriptive definition of pediatric DAU is proposed as "Undernutrition is a condition resulting from *imbalanced nutrition* or *abnormal utilization of nutrients* which causes clinically meaningful adverse effects on tissue function and/or body size/composition with subsequent impact on health outcomes." To facilitate comparison of undernutrition data, it is advised that in addition to commonly used criteria for undernutrition such as z-score < -2 for weight-for-age, weight-for-length, or BMI < -2, an unintentional decline of ≥ 1 in these z-scores over time should be considered as an indicator requiring further assessment to establish DAU diagnosis. Since the etiology of DAU is multifactorial, clinical evaluation and anthropometry should ideally be complemented by measurements of body composition, assessment of nutritional intake, requirements, and losses, and considering disease specific factors.

What is known

- Various definitions and criteria for diagnosing disease-associated undernutrition (DAU) exist that lead to inconsistencies and confusion in research and clinical practice.
- Assessment of body size, body composition and weight/growth changes over time are fundamental in assessment of nutritional status of sick children.

What is new

- A new definition for pediatric DAU is proposed: “Undernutrition is a condition resulting from *imbalanced nutrition* or *abnormal utilization of nutrients* which causes clinically meaningful adverse effects on tissue function and/or body size/composition with subsequent impact on health outcomes.”
- Recommendations for written hospital policies for identification of children with (risk of) DAU, including an algorithm for nutritional screening, criteria for further assessment to establish diagnosis of DAU and its causes, and follow-up are provided.

INTRODUCTION

Undernutrition is common in children admitted to hospital and is associated with adverse effects on disease outcome (1-5). It is generally accepted that undernutrition should be prevented, or, if present, promptly identified and treated. **Table 1** provides a recent overview of cross-sectional studies reporting on the prevalence of acute or chronic undernutrition, based on weight and height z-scores and internationally accepted threshold values. However, in clinical practice, anthropometric measurements are frequently not obtained from children when they are seen in outpatient clinics or admitted to hospital and, even when obtained, they may not be plotted on growth charts or used to assess nutritional status and growth, hence missing the opportunity to influence patient management and improve patient care (6). Definitions and criteria for diagnosing undernutrition are variable, leading to inconsistencies and confusion in research and clinical practice. In recent years, several nutrition screening tools (NST) have been developed, with the aim of identifying children who are likely to already be undernourished or considered at risk of becoming so. However, there are shortcomings with the approaches used to test such tools, their use in routine clinical practice is variable (7), and their role in improving nutritional status or clinical outcome has not yet been tested.

The aim of this position paper is to:

(1) review the definitions and criteria of disease-associated undernutrition (DAU) in the paediatric population;

(2) consider methods currently used to identify undernutrition or risk of undernutrition, including their strengths, limitations and practical issues;

(3) provide recommendations for current practice, pending further evidence and acknowledging limitations of available data;

(4) suggest future research directions and priorities.

This manuscript focusses on pediatric DAU, including underweight, suboptimal linear growth and altered body composition as well as deficiencies of one or more micronutrients. We do not discuss primary undernutrition due to food insecurity or parental neglect in young children. This position paper does not refer to undernutrition in community settings of low-medium income countries. The management of undernutrition is outside the scope of this position paper. A systematic literature search as well as expert discussions informed the content of this paper. The systematic search strategy for original research studies on nutritional screening and assessment tools in hospitalized children was based on a previously published search strategy (8). The search was last updated in September 2019, but any leading publications identified by the authors since the last update were also included. The search strategy is included in **Supplementary document 1**.

1. Defining undernutrition

Several terms are used in parallel to describe undernutrition (**Table 2**), therefore agreed definitions are important. Furthermore, various cut-off values for anthropometric parameters and criteria have been used to classify acute and chronic undernutrition. In 1956, Gomez introduced a classification of malnutrition based on weight below a specified percentage of median weight for age (WFA) (9). In the 1970s, Waterlow introduced a classification based on weight for height (WFH) and also recommended the use of standard deviation scores (SD score) (10), which have also been used since 1995 by the World Health Organization (WHO) (11). In 2013, Mehta et al proposed a broad framework for defining undernutrition which extends beyond acquisition of anthropometric measurements (12). In this framework the concepts of etiology and chronicity, mechanism and pathogenesis of undernutrition and its relationship with inflammation and functional outcome were incorporated.

In 2014 the American Society for Parenteral and Enteral Nutrition (ASPEN) and the Academy of Nutrition and Dietetics also proposed a set of diagnostic indicators to be used to identify pediatric undernutrition

based on the availability of either a single anthropometric data point or two or more data points, and categorized undernutrition in three subgroups (mild, moderate and severe). When only a single data point is available, mid upper arm circumference (MUAC) z-scores can also be considered in addition to z-scores for WFH, BMI for age, and height for age (HFA). When two or more anthropometric data points are available, weight gain velocity, weight loss, deceleration in WFH z-score and the adequacy of nutrient intake were determined to be primary indicators (13).

More recently, health care professionals who routinely assess and treat children with DAU identified ongoing weight loss, increased energy or nutrient losses, increased requirements, low intake and a high-risk condition as the most important clinical indicators through an international survey of 693 pediatric gastroenterologists and dietitians (14). These items are also frequently used in the currently available nutritional screening tools as described below.

In 2015 the European Society of Clinical Nutrition and Metabolism (ESPEN) provided a consensus-based minimum set of criteria for the diagnosis of malnutrition in adult patients to be applied independent of clinical setting and etiology, and subsequently the core nutritional concepts were defined (15, 16). It was stated that in adult patients identified by screening as at risk of malnutrition, the diagnosis of malnutrition should be based on either a low BMI (<18.5 kg/m^2), or on the combined finding of weight loss together with either reduced BMI (age-specific) or a low fat free mass (FFM) index using sex-specific cut-offs (16). However, this adult definition cannot be used in children because the cut-offs for BMI and FFM indices are dependent on age and gender and therefore need to account for growth and biological variation with age and gender; this essentially requires the use of z-scores for weight, height and body composition instead of set values. Previously an alternative approach was suggested using international cut-offs to define thinness in children and adolescents based on BMI at age 18 (17), but as these cut-offs would still vary by age there is no real practical benefit. Moreover, it is now generally accepted and customary to use z-score values for WFA, WFH, BMI including their changes over time.

In addition, in comparison to adults, access to reliable body composition methods estimating FFM (which is incorporated in the adult ESPEN criteria) is limited in pediatrics and the ability to use body composition z-scores has been hampered by the lack of reliable body composition reference data from healthy children.

Proposed new definition of undernutrition

Considering the previous definitions of undernutrition, the following components need to be considered to develop a new definition: body composition and growth velocity, determination of malnutrition risk factors and health outcomes. The ESPGHAN SIG in Clinical Malnutrition therefore proposes to define pediatric DAU as follows: "Undernutrition is a condition resulting from *imbalanced nutrition* or *abnormal utilization of nutrients* which causes clinically meaningful adverse effects on tissue function and/or body size/composition with subsequent impact on health outcomes.

Etiology and pathophysiology of disease associated undernutrition

Causes of imbalanced nutrition and by extension of DAU, can be multifactorial and include suboptimal intake, the effect of systemic inflammatory response, malabsorption, increased nutrient losses, and altered energy/nutrient metabolism or often a combination of these factors (see **Figure 1** child factors and disease factors). The mechanisms of DAU are closely related to the underlying disease. Mehta et al. have incorporated these mechanisms in their broad framework defining undernutrition (12). They highlighted the role of inflammation which can affect energy expenditure, alter nutrient utilization and metabolism, and can promote muscle catabolism, for example in conditions associated with a chronic systemic inflammatory response such as inflammatory bowel disease and cystic fibrosis but also in the acute phase inflammatory response in critical illness. Inflammatory cytokines play a critical role in this process. Pro-inflammatory cytokines including tumor necrosis factor-α (TNFα), IL-1β and IL-6 have been

implicated in development of nutritional cachexia and sarcopenia in cancer (18) and severe acute malnutrition (19).

2. How to identify undernutrition

Since the etiology of DAU is multifactorial, it is not feasible to use a single anthropometric parameter to adequately assess the nutritional status of all patients. Clinical evaluation and anthropometry should be complemented by other measures, depending on the clinical condition and the questions arising in the individual patient, for example assessment of dietary intake, body composition, laboratory biomarkers, and environmental conditions. Such measurements and information aim to globally assess nutritional status, risk factors predictive of future deterioration of nutritional status and the short-term and long-term consequences of undernutrition.

Selection of an appropriate method to assess the nutritional status of a patient depends on:

1. The purpose for which an evaluation is performed, with different approaches applied for screening purposes (identification of patients needing further assessment) as opposed to diagnostic assessment (i.e., the identification of patient with undernutrition)
2. The type of undernutrition the clinical team wants to identify, e.g., wasting, stunting, underweight, weight loss, altered body composition, or micronutrient deficiencies (see **Table 2**)
3. The availability of resources and staff available to carry out the assessment
4. Issues around practicality, user- and patient acceptance of the method

Table 3a gives an overview of the characteristics of various available methods for nutritional assessment and describes their aim, benefits, limitations, and practicality.

Body size, composition and growth velocity

Assessment of body size, composition and growth velocity are fundamental to the assessment of the nutritional status of sick children. Recent literature on the frequency of anthropometry acquisition for routine clinical use suggests that this is opportunistic though, particularly in patients with chronic illness and those unable to bear weight; albeit they are likely to be at increased nutrition risk. Measurement of height and weight should be performed on every hospital visit or as minimum at hospital inpatient admission. Subjective visual evaluation of weight, height measurements or body habitus tends to be inaccurate, imprecise and cannot be used interchangeably with measured anthropometry (20). Measured serial anthropometric values should always be plotted on growth charts and evaluated by the clinical team and in the context of the clinical scenario.

Assessment of WFH or BMI for age below a set threshold are indicative, but not necessarily diagnostic of acute undernutrition (see **Table 3b** for recommended anthropometric criteria indicative of moderate-severe acute undernutrition). Threshold values for the assessment of severe and moderate acute and chronic undernutrition have been proposed by the WHO for use in low-medium income countries and the same thresholds are often used in clinical practice in more affluent societies. Short stature might be a valid screening method for assessment of chronic undernutrition in the community of low-medium income countries, but its positive predictive validity in healthcare settings of more affluent societies may be confounded by factors independent of nutrition, such as the effects of the disease on linear growth. This is particularly the case in children with genetic syndromes and in those with chronic inflammatory conditions, where an activation of the pro-inflammatory cascade can interfere directly or indirectly with bone and pubertal development (21).

In patients with genetic syndromes affecting biological growth potential such as Down's syndrome or Ulrich-Turner Syndrome, the use of disease specific growth charts might be considered advantageous. However, many of the disease specific growth charts have been developed with relatively small sample

sizes, malnourished children may have been included in some of these charts and there is a large variation in how a syndrome can affect normal development as for example in the case of mild compared with severe cerebral palsy. Therefore they do not necessarily reflect the optimal growth pattern of children with specific conditions and assessments of nutritional status in such population need to be complemented with other methods, including body composition. (22)

As growth faltering is perhaps the strongest predictor of poor nutritional status, serial measurements of weight and height are preferable for use in assessing the nutritional status of a sick child. Short-term variations of weight and height trajectories are physiological and to be expected and should be distinguished from sustained faltering of growth over a prolonged period. In adults, involuntary weight loss is a sensitive predictor of poor nutritional status or underlying diseases, but in growing children not only weight loss but also absent or slow weight gain may indicate DAU.

While growth charts help visualize weight, height and WFH (or BMI) trajectory over time, knowledge about normal weight gain (**Table 3c**) especially, can be useful to set goals in treatment of sick hospitalized children who are recovering, i.e., set a goal for target weight and appropriate time for re-evaluation of nutritional status after nutritional intervention.

Different practical dynamic definitions have been used to define significant weight loss over time, but there is limited consensus on which criteria are best to use (23). For identification of failure to thrive (FTT) in children up to 2 years of age , O'Brien et al. proposed using a decrease across two major centile channels or a decrease beneath the second centile on standardized growth charts for at least 3 months (to exclude weight loss secondary to an acute illness)(24). ASPEN guidelines have recommended ≥5%, ≥7.5% and ≥10% weight loss to define respectively mild, moderate and severe malnutrition for children aged ≥2 years (13). Previously, criteria were published for failure to thrive necessitating immediate nutritional intervention (23): a) inadequate growth or weight gain for >1 month in a child <2 y of age; b) weight loss or no weight gain for >3 months in a child >2 y of age; c) change in WFA z-score >-1 SD in 3 months for

children <1 y of age on growth charts and; d) change in WFH z-score >-1 SD in 3 months for children ≥ 1 y of age on growth charts. The NICE guidelines on faltering growth specify criteria for infants according to birthweight i.e., a current weight <2nd centile for age whatever the birthweight, a fall across 1 or more, 2 or more, or 3 or more centile weight spaces if birthweight was <9th centile, between 9th-91st centile, or >91st centile respectively (26) (see Table 3b). In addition, in a child >2 years with concern about faltering weight or linear growth it is recommended to use of BMI <2nd centile and <0.4th centile to be suggestive of either undernutrition or small build, and probable undernutrition that needs assessment and intervention respectively (26). Overall, a clear definition linked with measurable clinical outcomes is still lacking but one should rely on a percentage of weight loss or a decline of z-score over time. Overall, within the ESPGHAN SIG on Clinical Malnutrition there is consensus that a decline of ≥ 1 z-score (WFA or WFH/BMI) over time must be considered as growth faltering and a red flag requiring further assessment to establish diagnosis for undernutrition and its causes.

Supplemental Tables 1 and **2** provide practical scenarios for different age groups and sex to interpret changes in weight over time expressed as absolute weight (kg), % weight and z-scores for weight for age Z-score (WAZ) and how they relate to each other.

Linear growth can be estimated by segmental measurements i.e. knee-heel length, tibia length, ulnar length, in patients who are unable to bear weight making accurate length measurements unfeasible (27). It is recommended to interpret segmental measurements in relation to reference charts for these specific measurements rather than using them to estimate actual height in individual patients because of error associated with prediction equations (28). MUAC and skinfold measurements of the arm and subscapular regions are useful and practical clinical tools to identify those patients with low fat and/or lean muscle stores despite normal anthropometry. They might not be popular for routine screening purposes but should complement the assessment of patients with suboptimal weight and/or height measurements or

in children where standard anthropometry is difficult to obtain reliably i.e., in case of contractures.

Body composition assessment

Pediatric patients with chronic, mainly inflammatory, conditions may manifest low lean body mass with or without normal or even increased fat stores, often termed as sarcopenia. Therefore, whole body composition assessment may be helpful in guiding appropriate medical and nutritional interventions and interpret anthropometry. In adult patients, suboptimal body composition has been associated with adverse clinical outcomes, such as in the case of sarcopenia and fall risk in the elderly, risk of mortality in cancer cachexia, poorer lung function in cystic fibrosis (29), and response to biologic agents in patients with inflammatory bowel disease(30). In contrast, there is currently limited evidence to advocate for the benefit of detailed body composition in relation to outcome prediction and management of pediatric patients (31, 32). Although there are several association studies, there is paucity of intervention studies to show benefit of body composition in improving patients' clinical outcomes or improving other aspects of their care.

Several caveats need to be considered with measurements of body composition in clinical practice; they are listed in Table 3a. Overall, it is important to interpret the results of body composition assessment in relation to other patient parameters such as weight, height, disease state, mobility, and physical activity in order to use the information for a patient-tailored nutritional advice and interventions.

Dietary intake assessment & feeding history

Dietary intake assessment is complementary to any approach used to assess the nutritional status of a patient. Unfortunately, all currently available methods suffer from a large degree of inaccuracy and imprecision (33) (Table 3a). Screening questions on recent changes of usual dietary intake should accompany assessment of undernutrition and can be applied by all health professionals in routine hospital

admission. In contrast, detailed dietary assessment requires dietitians, clinical nutritionists or appropriately trained staff, equipment and dietary analysis software. During hospitalization, it is recommended that food and fluid intake records should be kept in those patients at risk of undernutrition and as indicated by the treatment team.

A feeding history can complement the nutritional assessment of a child by questions regarding feeding conditions and setting (e.g., family, outdoor), potential stress around mealtimes, and observations of the feeding behavior in the clinical setting or at home (e.g., based on a video recording). Mealtimes that consistently take longer than 30 minutes, or mealtimes that are being perceived as very stressful by the patient or the caregivers should prompt further evaluation and potentially intervention. A history of repetitive respiratory infections, increased congestion or a "gurgly voice" at mealtimes, especially in neurologically impaired children, are suggestive of swallowing disorders and should prompt an additional work-up.

Biomarkers

There are currently no valid biomarkers to assess protein-energy status. Serum measurements of albumin and pre-albumin are known acute phase reactants perturbed independently of body nutrient stores by systemic inflammatory response, hepatic function, intestinal and renal losses, and fluid balance. These issues make them unsuitable as nutritional biomarkers. A recent systematic review confirmed that they remain normal in calorically restricted individuals without inflammatory conditions until severe extreme starvation becomes obvious (34).

Direct measurements of micronutrients or their functional biomarkers in blood are the standard clinical approach to diagnose deficiencies. However, similar to albumin and pre-albumin, micronutrient levels in plasma may be influenced by other factors such as systemic inflammation and the synthesis and turnover of transporting proteins (35), e.g., ferritin for iron, retinol binding protein for vitamin A or plasma

lipoproteins for vitamin E. The Committee on Nutrition of ESPGHAN has recently published a Position paper on assessment and interpretation of micronutrient status in sick children including the mainstream direct and indirect biomarkers used to assess adequacy of body micronutrients (35). They recommend the use of a decision tree to evaluate vitamin and trace element status particularly taking into account the presence of a systemic inflammatory response or low albumin which makes measurements of plasma micronutrients difficult to interpret. Instead, healthcare professionals should aim at assessing plasma measures of micronutrients when the systemic inflammatory response has resolved (e.g., normal levels of CRP). Functional biomarkers of micronutrient deficiencies (e.g., glutathione peroxidase in selenium) can ascertain true micronutrient deficiencies but these are not available for all micronutrients or available in routine practice. Future research may enhance diagnostic tools by using system biology or omics techniques as biomarkers of body micronutrient status and function (35).

Can nutritional screening tools benefit the detection of pediatric undernutrition?

The purpose of nutritional screening is to identify individuals who are at risk for undernutrition, who need further nutritional assessment, and may likely benefit from nutritional intervention which would potentially influence outcome. Nutritional risk is usually determined based on a combination of measurements and assessments including as minimum anthropometry and brief dietary intake assessment. Patients at nutritional risk may not already be undernourished but the disease and/or its treatment increases their risk of becoming so. Disease and its treatment can adversely influence appetite or intake and nutrient absorption and can increase energy expenditure and nutrient losses. If the effects of disease on nutritional status are prolonged this can lead to onset of undernutrition. According to ESPEN guidelines, screening tools embody the following 4 main principles: (1) current nutritional status, (2) recent changes, (3) expected or anticipated decline and (4) severity of the disease (36).

Currently several nutritional screening tools have been proposed for this purpose in a general population of children admitted to the hospital (25, 37-42). These screening tools have different aims in their use (43). An overview of the currently available screening tools, together with an analysis of their principal components and aims of use is presented in **Table 4.**

Recently, the use of three most cited screening tools in the literature (PYMS, STAMP and STRONGkids) was evaluated in a large European population (2567 children from 14 hospitals across 12 European countries) in relation to anthropometric measurements, body composition and clinical outcome parameters (7). There was an overall agreement in risk classification of only 41% between the tools. Classification of children as high risk ranged rather widely from 10-25% depending on the tool used. For all three tools, an association between the risk score classification and length of hospital stay was found. On the basis of the findings, it could not be concluded that any one tool was superior, which was similar to the conclusion of a systematic review of smaller studies published just prior to this (8), and more recent larger systematic reviews (44, 45). Most studies on pediatric nutrition screening tools focus on a mixed population of hospitalized children (46). Depending on the hospital structure and resource availability, there might be an interest in testing existing validated tools or developing new ones dedicated to specific disease populations (47-55) or age groups (56, 57), but prior to this the performance of existing tools should be explored. Ideally screening tools would be helpful if they lead to early assessment and appropriate nutritional intervention of patients, have a high sensitivity and specificity in identifying children that suffer or are likely to develop DAU, and contribute improving short- and long-term outcome, i.e., a decrease in length of hospital stay, postoperative complications and infections, and earlier functional recovery (muscle mass, endurance) and better neurocognitive outcome, respectively. Hard evidence from intervention studies is lacking. An association between a high nutrition risk score and greater hospital expenses and fever/infection has been reported in two Asian studies (52, 58). Overall, the ESPGHAN SIG in Clinical Malnutrition is supportive of the routine use of nutritional screening tools in

mixed population of hospitalized children upon admission to increase awareness about the importance of considering nutritional status and risk of malnutrition and to identify children who need further review by a dietitian; we are neutral about the choice for a particular screening tool as this depends on the setting, population, and available resources.

Barriers to adequate nutritional screening, assessment, and care in clinical practice

It is known that besides difficulties directly related to disease or patient status, there are also several barriers related to hospital care practices and resources that prevent optimal nutritional screening, assessment and care in hospitals, and themselves may contribute to poor nutritional care practices during hospital admission (see **Figure 1**) (59). These hospital-related barriers can be divided into three overarching categories:

A. *Personnel & resources related barriers*: Lack of personnel or time to obtain anthropometric measurements or perform screening, and dietitians or nutrition teams to provide nutritional care have been acknowledged as important barriers in previous research (6, 60). Patient electronic health records and integration of growth curves and nutritional screening questions in them may help identifying patients in need for referral to nutrition/dietetic team (41, 61).
B. *Lack of nutritional awareness:* In recent surveys low staff awareness and acknowledgement on the role of nutrition as important in patient care (14, 62), limited nutritional education (59) and professional training of health care professionals on nutrition (63, 64) were listed among the most important reasons associated with suboptimal nutritional screening and assessment practice.
C. *Lack of agreed policies and protocols on nutritional screening, assessment and treatment.* In contrast to other aspects of patient care for which clear policies and established protocols exist and are followed, in nutritional care similar frameworks and standards do not exist across hospitals in Europe (65-69). It is important that hospital policies are in place to clearly dictate

whose responsibility nutritional care in a hospital setting is, including practices around screening, standard measurements and further nutritional assessment, catering, provision of specialised nutritional support and intake monitoring.

3. Conclusions and recommendations for current practice

Conclusions

- Despite a relatively high prevalence of undernutrition in children treated or admitted to hospital, awareness of undernutrition remains low;
- A new definition for disease-associated undernutrition is proposed: Undernutrition is a condition resulting from *imbalanced nutrition* that causes clinically meaningful adverse effects on tissue function and/or body size/composition with subsequent impact on health outcomes. Causes of *imbalanced nutrition* can be multifactorial such as suboptimal intake, inflammation, malabsorption, increased nutrient losses, and altered energy/nutrient metabolism or a combination of these factors;
- Various methods for assessment of nutritional status are available with different aims, benefits, practical issues and limitations, which will guide the selection of the most appropriate method for use in each specific setting;
- Pediatric nutritional screening tools have been shown to relate to actual nutritional status or risk of deterioration of nutritional status but it is still unknown whether using screening tools improve short- and long term outcome;
- Multiple barriers, including disease- and hospital-related factors and lack of awareness and nutritional training, play a role in the lack of routine screening, assessment and treatment of children with disease associated undernutrition or poor nutritional status.

Recommendations

1. All facilities providing health care for children should develop and implement a written policy and protocol for identification of children with (risk of) undernutrition appropriate for the setting and should have management pathways with appropriate staffing and resources in place for such patients;
2. Weight and height measurements should be performed in all patients, plotted (as WFA, HFA and BMI/WFH) on an appropriate reference chart and interpreted in light of previous measurements and the clinical presentation for all inpatient and outpatient children;
3. In children where weight or height measurements are not feasible, alternative measurement methods should be performed (MUAC, segmental lengths) and be complemented with measurements of body composition including skinfold thickness;
4. Adequate, well-maintained and regularly calibrated equipment should be used for anthropometric assessment and made available in all inpatient and outpatient settings;
5. Identification of children with nutritional risk should be facilitated by considering recent nutritional intake, requirements and losses, and disease related factors and should be done, in addition to evaluating anthropometric measurements. The method for achieving this can be chosen depending on the patients' characteristics, setting and resources;
6. Electronic medical records may be used in order to facilitate the collection, interpretation and auditing of the nutritional parameters and therefore the overall nutritional assessment and nutritional care process;
7. At minimum, sick children at nutrition risk should have the opportunity to be reviewed and cared for by a hospital dietitian.

Considering these recommendations, **Figure 2** provides a proposed general algorithm for nutritional

screening, assessment and follow-up of nutritional status in children, which can be further adapted based on local or national guidance and resources. Using this algorithm will quickly identify undernourished children, and those at risk for nutritional deterioration. To achieve optimal practice, the establishment of a team approach involving multiple health care providers (e.g., nutrition nurse, dietitians, gastroenterologist, speech and language therapist, psychologist, gastrostomy nurse, and parenteral nutrition nurse) depending on the local situation is advised. Moreover, it is of utmost importance to incorporate a general process for implementation and auditing of such an algorithm, to assign clear responsibilities to health care providers and to provide feedback to health care personnel (65).

Although sufficient evidence for broad introduction of multidisciplinary nutrition support teams in pediatrics is lacking, such teams can be considered in order to promote and change nutritional practice, to help overcome the various barriers such as education and training of health care personnel, and to perform continuous auditing and evaluation of outcome. (70)

4. Suggestions for future research directions and priorities

Despite increased attention on pediatric malnutrition, a decrease in the prevalence of malnutrition in hospitalized children has not been noted in the past decades (Table 1). Moreover, practices in nutritional care in hospitals remain largely unchanged. Future research should focus more on health-related outcome parameters as primary endpoints including functional outcome parameters, quality of life and well-being. Nutritional intervention studies are needed next to demonstrate improvement in clinical and health related outcomes, and health care costs in patients with DAU. These studies can be focused on the evaluation of the effect of specific nutritional interventions, or the application of a nutritional care pathway/algorithm including screening, assessment, treatment and prevention of DAU.

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Figure legends

Figure 1. Multifactorial causes of imbalanced nutrition or abnormal utilization of nutrients which can lead to disease-associated undernutrition.

Figure 2.

Proposed general algorithm for nutritional screening, assessment, and follow-up of nutritional status in hospitalized children.

BMI = body mass index; HFA =height for age; P3 = third centile; WFA = weight for age; WFH =weight for height. Figure adapted from (65)

Figure 1.

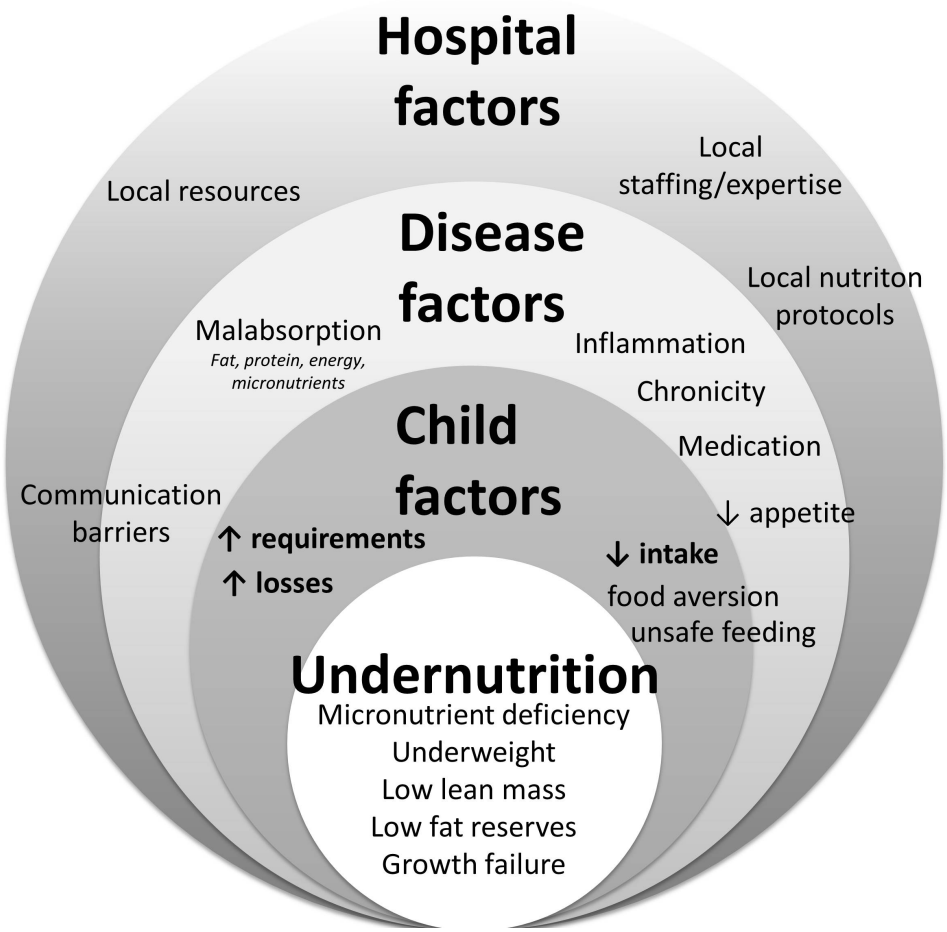
Hospital factors
Local resources
Local staffing/expertise
Local nutriton protocols
Disease factors
Malabsorption
Fat, protein, energy, micronutrients
Inflammation
Chronicity
Medication
Child factors
Communication barriers
↑ requirements
↑ losses
↓ appetite
↓ intake
food aversion
unsafe feeding
Undernutrition
Micronutrient deficiency
Underweight
Low lean mass
Low fat reserves
Growth failure

Figure 2.

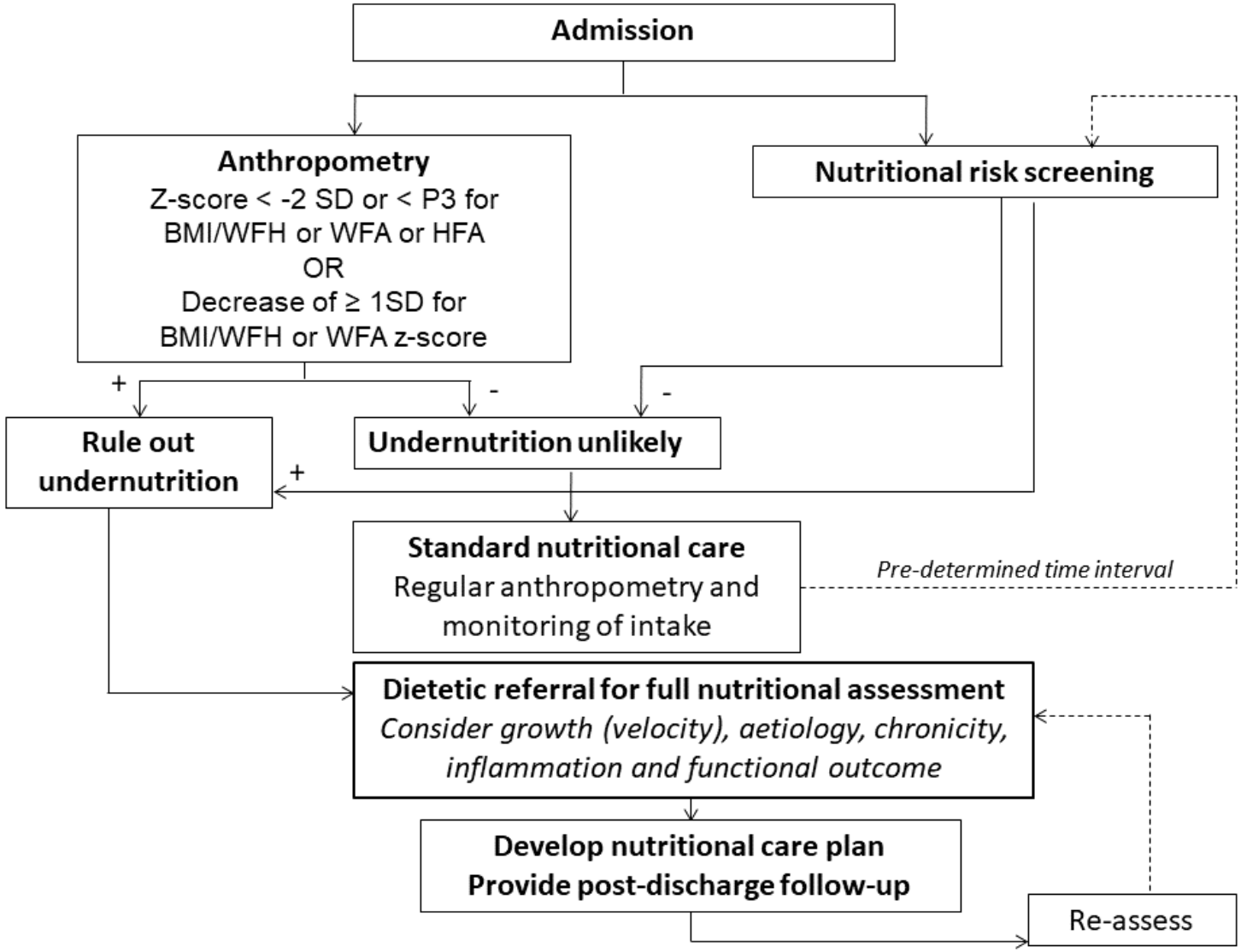
Admission
Anthropometry
Z-score < -2 SD or < P3 for
BMI/WFH or WFA or HFA
OR
Decrease of ≥ 1SD for
BMI/WFH or WFA z-score
Nutritional risk screening
+
-
-
Rule out undernutrition
Undernutrition unlikely
+
Standard nutritional care
Regular anthropometry and monitoring of intake
Pre-determined time interval
Dietetic referral for full nutritional assessment
Consider growth (velocity), aetiology, chronicity, inflammation and functional outcome
Develop nutritional care plan
Provide post-discharge follow-up
Re-assess

Table 1. Prevalence of undernutrition in the last 12 years in hospitalized children in the European setting.

Author	Country	N	Population	Underlying/ chronic disease (%)	Acute (%)	Chronic (%)
Campanozzi 2009 (71)	Italy	496	Grade I pathology	0	BMI <-2 SD: 10.2	
Joosten 2010 (4)	Netherlands	424	Pediatric + surgical	29	WFH <-2 SD: 11.0	HFA <-2 SD: 9.0
Huysentruyt 2013 (72)	Belgium	379	Pediatric + surgical	11.1	WFH <-2 SD: 9.0	HFA <-2 SD: 7.7
Sissaoui 2013 (73)	France	923	Pediatric + surgical	56	WFH <-2 SD: 11.9	WFH and HFA <-2 SD: 2.5
Pichler 2014 (74)	UK	93	Pediatric + surgical		WFH <-2 SD: 22.0	HFA <-2 SD: 17.4
Hecht 2015 (3)	Europe	2410	Pediatric + surgical	44.8	BMI <-2 SD: 7.0 WFH <-2 SD: 7.6	HFA <-2 SD: 7.9
Lezo 2017 (75)	Italy	1790	Pediatric + surgical	58.8	BMI <-2 SD: 13.2	HFA <-2 SD: 17.3
Beser 2018 (76)	Turkey	984 (2-18y*) 1513 (all**)	Pediatric + surgical	47.5	BMI <-2 SD: 9.5*	HFA <-2 SD: 16.6**
Lara-Pompa 2020 (31)	UK	152	Pediatric + surgical	N/A	WFA <-2 SD: 8.5 BMI <-2 SD: 4.2 LM <-2 SD: 16.9%	HFA <-2 SD: 13.6%

WFH: weight for height; WFA: weight for age; HFA: height for age; BMI: body mass index; LM: lean mass. Table adapted from (65, 77).

Table 2. Existing definitions of nutritional status.

Terms used to define nutritional status	**Description**
Malnutrition (78)	Malnutrition refers to deficiencies, excesses, or imbalances in a person's intake of energy and/or nutrients, and includes undernutrition (wasting, stunting, underweight), inadequate vitamins or minerals, overweight, obesity, and resulting diet-related non-communicable diseases.
Undernutrition (our proposed definition)	Undernutrition is a condition resulting from *imbalanced nutrition* or *abnormal utilization of nutrients* which causes clinically meaningful adverse effects on tissue function and/or body size/composition with subsequent impact on health outcomes (our proposed definition). Causes of *imbalanced nutrition* or *abnormal utilization of nutrients* can be multifactorial such as suboptimal intake, inflammation, malabsorption, increased nutrient losses, and altered energy/nutrient metabolism or a combination of these factors.
Wasting (78)	Wasting or thinness indicates in most cases a recent and severe process of weight loss, which is often associated with acute starvation and/or severe disease. However, wasting may also be the result of a chronic unfavourable condition (WHO). Wasting is also known as low weight-for-height

Stunting (78)	Stunted growth reflects a process of failure to reach linear growth potential as a result of suboptimal health and/or nutritional conditions. Stunting is also known as low height-for-age (WHO).
Underweight (78)	Underweight means low weight-for-age (WFA); WFA reflects body mass relative to chronological age. A child who is underweight may be stunted, wasted, or both as it is influenced by both the height of the child (height-for-age) and his or her weight (weight-for-height), and its composite nature makes interpretation complex (78).
Failure to thrive*(12)	Term used to describe children who are not growing as expected
Faltering growth*(12)	Decline in *z* score for individual anthropometric measurement (e.g., a decrease of more than 1 SD) as the indication of faltering growth
Cachexia (79)	A multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that can be partially but not entirely reversed by conventional nutritional support It is characterized by maladaptive responses to negative energy balance and can be caused by diverse medical conditions. The precise pathophysiological mechanism has not been described in children.
Sarcopenia (80, 81)	Sarcopenia is a condition which is characterized in adults by loss of skeletal muscle mass, reduced muscle strength or physical performance. There is an absence of childhood sarcopenia definitions due to lack of consensus on assessments methods for body composition and muscle strength.

Protein-energy malnutrition	The term protein-energy malnutrition (PEM) applies to a group of related disorders that include marasmus, kwashiorkor, and intermediate states of marasmus-kwashiorkor.
Kwashiorkor	Also called protein malnutrition or edematous malnutrition, condition caused by severe protein deficiency with adequate energy intake. Most common in some developing regions of the world where babies and children have a diet that lacks protein.
Marasmus	A form of severe malnutrition characterized by energy deficiency in all forms, including protein.

*no consensus definition with regard to specific anthropometrical criteria.

Table 3a. Characteristics of various commonly used methods for assessment of nutritional status.

Assessment method	**Aims**	**Practical issues**	**Limitations**
Weight	Indicator of acute undernutrition	• Routine measurement • Needs plotting on growth chart (z-score) and interpretation by health care professional	• Can be affected by hydration status, organomegaly, devices, edema/ascites. • No distinction between FM and LBM
BMI (calculated as weight/ height^2) Weight-for-height (WFH) Weight-for-length (WFL)	Indicator of acute undernutrition	• Routine measurement • Needs plotting on growth chart (z-score) and interpretation by health care professional	• Can be normal in case of stunting • Can be affected by hydration status, organomegaly, devices, edema/ascites. • No distinction between FM and LBM • Twofold range of variation in fatness for a given BMI value in individual children • Needs accurate height measurement which may be difficult to obtain in certain conditions

Height	Indicator of chronic undernutrition	• Routine measurement • Needs plotting on growth chart (z-score) and interpretation by medical team • Interpretation of z-score dependent on choice of reference • Accuracy dependent on user's error and measurement device used.	• Can be affected by other factors than nutrition - disease/chronic inflammation, genetic syndromes
Segmental measures (TL, KHL)	Indicator of linear development of extremities; proxy of linear growth	• Can be used in child unable to bear weight or child with contractures • Knemometer or caliper needed • Needs plotting on specially designed growth charts (82-84)	• Available equations for estimating height/length available but margin of error up to 10 cm • Not recommended to use calculated height based on segmental measures for calculation of BMI
SGNA (5, 85)	Abbreviated subjective nutritional assessment incorporating	• Needs trained health care professionals	• Subjective • Time consuming

	measurements, functional capacity, and physical exam		
MUAC	• Composite indicator of FM and LBM • Identify patients with low LBM	• Can complement nutritional assessment in patient with suboptimal weight and/or height measurements • Reference standards available • Can be used for routine screening purpose • Measurements should be plotted on charts or expressed as z-scores • Widely used in LMIC with absolute cut-off values • Quick & simple	• Estimation of LBM content doable but limited accuracy if applied to individual sick patients • Changes may reflect shifts in fluid compartment rather than changes in LBM or FM in patients with hydration anomalies and fluid shifts
Skinfolds	• Indicator of local subcutaneous fatness	• Can complement nutritional assessment in patients with suboptimal measurements of W and/or H	• Interpretation limited by significant inter- and intra-observer variability • Measurement difficult in case of edema

(i.e., triceps, biceps, subscapular)	• Identify patients with low subcutaneous FM	• Reference standards available • Not popular for routine screening purpose • Measurements should be plotted on charts or expressed as z-scores • Quick • Needs training	• May underestimate fat stores in children with more central fat distribution
BIA	Estimation of body water; derives FM and FFM using hydration constants.	• Possible at bedside • Non-invasive • Quick & simple	• Interpretation difficulties: various sample-based equations with W and H needed • Accuracy and precision limited in individuals • Fasting, hydration level, body posture and ambient temperature, can affect results • Validation limited
DEXA	Assess body composition (FM, LBM, BM)	• Precise • Accurate • Reference standards available	• Not bedside • Requires specialized equipment and trained staff

		• Provides information about bone density	• Expensive • Results are machine and software specific, so limited comparison possible. • Limited use in young children (movement artifacts) • Reference data for children < 4 y not readily available.
ADP (86)	Measures body volume and calculates body composition using Archimedes principle (FM, FFM)	• Precise • Accurate • Quick • Possible in children aged 0-18y	• Not routine • Not bedside • Requires specialized equipment and trained staff • Expensive
Grip strength	• Assessment of upper handgrip muscle strength	• Quick & simple • Possible at bedside • Low cost	• Limited feasibility in children < 6 years of age • No standardized method available for use in children

	• Potential proxy for whole-body muscular strength (87) • Potential proxy for FFM (88)	• Results influenced by body position, dynamometer used, hand dominance, number of assessments. • Reference values available (88-90)	• Influenced by disease severity
Dietary intake assessment - Prospective methods: weighted food diaries - Retrospective methods: dietary recalls	Assessment of food and fluid intake for estimating nutrient intake	• Complements nutritional assessment • Requires RDs, clinical nutritionists or appropriately trained staff. • Not routine	• Large degree of inaccuracy and imprecision in per subject assessments. • Prospective methods are laborious and time consuming for patients and RDs • Retrospective methods have large bias for individual assessment

Feeding history & observation	Assessment of feeding condition, safety, duration, and stressors around mealtime	• Abnormalities can guide further assessment (i.e., swallow study) and management • May need video equipment	• Time consuming • Need OT or SLT if observation is included

ADP=air displacement plethysmography, BIA = Bioelectric impedance analysis, BIVA = Bioelectric impedance vector analysis; CP= cerebral palsy, DEXA = dual energy x-ray absorptiometry, H = height , FFM = fat free mass, FM = fat mass, L= length, LBM = lean body mass, LMIC = low and middle income countries; MUAC= mid upper arm circumference, OT= occupational therapist, RD= registered dietitian, SIR = systemic inflammatory response.

Table 3b: Recommended anthropometric parameters indicative for moderate-severe acute undernutrition.

Indicative anthropometric parameters for moderate-severe acute undernutrition*	
IN CASE OF A SINGLE MEASUREMENT *According to our recommendation (adapted from WHO, (13, 26):* • WFA z-score <-2 (infants) • WFH/WFL z-score <-2 • BMI z-score <-2 (age ≥ 2 years) • MUAC z-score <-2	***IN CASE OF SERIAL MEASUREMENTS*** *According to our recommendation*: **All ages:** Deceleration in WFA/WFH/WFL/BMI z-score: decline of ≥1 SD *According to NICE guidelines (26)*: **Infants:** • A fall across **≥** 1 weight centile spaces, if BW was < 9th centile • A fall across **≥** 2 weight centile spaces, if BW was 9th - 91st centiles • A fall across **≥** 3 weight centile spaces, if BW was > the 91st centile • Current weight < 2nd centile for age, whatever the BW *According to consensus statement Academy of Nutrition and Dietetics/ ASPEN (13):* • Weight gain (<2 y of age): <50% of the norm for expected weight gain. • Unintended weight loss (2-20 years): ≥7.5% usual BW** • Deceleration in WFH/WFL z-score: decline of ≥2 SD#

**Clinical diagnosis of undernutrition entails more than fulfilling these criteria; A child who has an anthropometric parameter below these threshold values needs to be considered to have acute moderate-severe undernutrition and further review is needed to make the diagnosis of undernutrition or to disregard it.*

ASPEN= American Society of for Parenteral and Enteral Nutrition, BMI= body mass index, BW = body weight, MUAC= mid upper arm circumference, WFA = weight-for-age, WFH = weight-for-height, WFL=weight-for-length.

***Note: no specifics provided about time frame; the extend of weight loss needs to be assessed in light of baseline status of the patient.*

[#]Note: no specifics provided about time frame; a smaller decline in z-scores could also be indicative of undernutrition.

Table 3c: Practical guide on normal weight gain at different ages for interpretation of serial measurements over time (91, 92).

Age	Weight
0-1 year	
• 0-3 months	30 g/day
• 3-6 months	20 g/day
• 6-12 months	10 g/day
1-3 years	2.25 kg/year
4-9 years	2.75 kg/year
10-18 years	5-6 kg/year

Table 4. Aims, availability of validation studies, and components of available pediatric nutrition screening tools intended for mixed patient groups on admission to hospital.

Screening tool	Need for anthropometric measurements	Tied to action plan	Predict outcome without intervention	Validation studies in different populations	Accounts for current nutritional status	Accounts for weight loss/recent changes	Accounts for anticipated decline/ reduced intake	Accounts for disease severity
NRS (38)	Yes	Yes	No	No	Yes	Yes	Yes	Yes
PNRS (37)	No	Yes	Yes	No	No	No	Yes	Yes
STAMP (25)	Yes	Yes	No	Yes	Yes	No	Yes	Yes
PYMS (39)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
$STRONG_{kids}$ (40)	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
PeDiSMART (41)	Yes	Yes	No	No	Yes	Yes	Yes	Yes
PNST (42)	No	Yes	No	Yes	Yes	Yes	No	No

PNSS (93)	Yes	Yes	Yes	No	Yes	No	Yes	Yes

NRS: Nutrition Risk Score; PNRS: Pediatric Nutritional Risk Score; STAMP: Screening Tool for the Assessment of Malnutrition and Growth; PYMS: Paediatric Yorkhill Malnutrition Score; STRONG$_{kids}$: Screening Tool for Risk on Nutritional Status and Growth; PeDiSMART: Pediatric Digital Scaled Malnutrition Risk screening Tool; PNST: Pediatric Nutrition Screening Tool; PNSS: Pediatric Nutrition Screening Score. Table adapted from (43)