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# Malnutrition

# Prevalence, screening and outcome in hospitalised children in Europe: a prospective multicentre cohort study

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# 1. List of abbreviations

| | |
|---|---|
| BMI | Body mass index |
| CDC | Centers for Disease Control and Prevention |
| DRM | Disease-related malnutrition |
| DXA | Dual-energy X-ray absorptiometry |
| ESPEN | European Society for Parenteral and Enteral Nutrition |
| FTT | Failure to thrive |
| HCG | Hellenic growth charts |
| HFA | Height-for-age |
| LOS | Length of hospital stay |
| MAM | Moderate acute malnutrition |
| MUAC | Mid-upper arm circumference |
| NCHS | National Centre for Health Statistics |
| NRS | Nutritional Risk Score |
| NST | Nutritional screening tool |
| PediSMART | Pediatric Digital Scaled Malnutrition Risk Screening Tool |
| PNRS | Simple Pediatric Nutritional Risk Score |
| PNST | Pediatric Nutritional Screening Tool |
| PYMS | Paediatric Yorkhill Malnutrition Score |
| SAM | Severe acute malnutrition |
| SDS | Standard deviation score |
| SGNA | Subjective Global Nutritional Assessment |
| STAMP | Screening Tool for the Assessment of Malnutrition in Paediatrics |
| $STRONG_{KIDS}$ | Screening Tool for Risk of Impaired Nutritional Status and Growth |
| TSFT | Triceps skin fold thickness |
| UNICEF | United Nations Children's Fund |
| WFH | Weight-for-height |
| WHO | World Health Organisation |

## 2. List of publications

The present thesis comprises two published research articles:

**Publication I**: Hecht C, Weber M, Grote V et al. Disease associated malnutrition correlates with length of hospital stay in children. *Clinical Nutrition* 2015;34(1):53-9. doi:10.1016/j.clnu.2014.01.003

**Publication II:** Chourdakis M, Hecht C**,** Gerasimidis K et al. Malnutrition risk in hospitalized children: use of 3 screening tools in a large European population. *Am J Clin Nutr.* 2016 May; 103(5):1301 – 10. Doi: 10.3945/ajcn.115.110700. Epub 2016 Apr. 2016

# 3. Introduction

## Disease-related malnutrition

Disease-related malnutrition (DRM) is a highly prevalent condition in a large number of European hospitals and is associated with increased healthcare costs [1-4]. It affects individuals across various life stages including early infancy, childhood and adolescence [5]. DRM is found in 6 - 37% of hospitalised children, depending on the chosen criteria and reference values [6, 7]. Recently, Freijer et al. performed a cost-of-illness analysis showing that DRM in paediatric Dutch patients in non-academic hospitals is associated with an increase of 80 million euros in annual hospital costs [4]. Task forces around the world have gathered data and experience and have summarised evidence into guidelines [5, 8-11]. Over the last years mandatory screening for DRM in hospitalised children was introduced in several countries, including the Netherlands and France [12]. The overall goal of nutrition societies is to ensure that screening for DRM becomes an integral part of routine nutritional practice [11].

## Malnutrition – Underweight

The United Nations Children's Fund (UNICEF) remarks that although the word 'malnutrition' is commonly used to refer to undernutrition, however, it technically also encompasses overnutrition [13]. Malnutrition can be due to insufficient macro- and micronutrient intakes due to environmental settings or excessive consumption of unhealthy products [14] or it can be a result of chronic disease [15]. Three months are recommended to be used as a cut-off to classify the duration of malnutrition as acute (< 3 months) or chronic (3 months and longer) [14]. The origin can include an underlying pathophysiology and/or inflammatory process [16]. Knowledge of the aetiology of malnutrition is highly important for specific treatment of the causes in addition to any symptoms [16]. However, DRM is often hard to detect and to diagnose at the onset since DRM is mostly subtle and indefinable [17]. Nutrition support must be appropriate to the pathology, pharmacology and management of the underlying cause [18]. Ethical and legal aspects have to be taken into account to determine if a nutrition intervention, therapy or counselling is necessary and supportive [17].

In the past, undernutrition was associated with developing countries and overnutrition with developed countries [11]. Today many parts of the world experience a double burden of malnutrition [5, 19]. The definition of malnutrition is of interest for clinicians, coders and administrators for recordkeeping and billing purposes [20]. During the last three decades, the

clinical description and perspective of malnutrition has evolved [11]. A wide variety of definitions is used, depending on personal views, medical settings and disciplines [14, 21]. Lochs et al. introduced several clinical terms and definitions in the field of nutrition with regard to the ESPEN (European Society for Parenteral and Enteral Nutrition) Guidelines on Enteral Nutrition [22]. Malnutrition was defined as a state of nutrition in which a deficiency, excess or imbalance of energy, protein or other nutrients causes measurable adverse effects on body shape, size, composition, function or clinical outcomes [22]. ESPEN places the main focus on undernutrition, which was defined as a state resulting from lack of uptake or intake of nutrition leading to altered body composition (decreased fat free mass and body cell mass) leading to diminished physical and mental function and impaired clinical outcome from disease [23]. A few years ago, a new definition of paediatric malnutrition (undernutrition) was proposed by Mehta and colleagues: "… an imbalance between nutrient requirements and intake, resulting in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes." [14]. This definition takes into account that growth and development are of major concern in paediatrics. However, until summer 2017 no modifications were made to malnutrition diagnoses codes of the International Classification of Diseases, 10th Revision [12]. In a recent ESPEN consensus report one core concept of clinical nutrition was defined as malnutrition/undernutrition, which includes DRM with (e.g. cachexia) and without inflammation, and malnutrition/undernutrition without disease, e.g. hunger-related malnutrition [24]. Pathophysiology of the individuals is unfortunately not addressed in this categorisation [16].

In clinical trials investigating malnutrition, frequently used endpoints are morbidity, mortality, length of hospital stay (LOS) and cost efficacy [17]. Successful treatment of undernutrition should result in substantial clinical improvements for patients and considerable cost savings to health care systems and society [17]. Efficacy of treatments and benefits for the patients have to be characterised in well-designed trials. Weight gain and LOS could serve as outcome.

In the context of this thesis, the focus is secondary (due to underlying disease) DRM in paediatrics, which is defined by underweight. Evaluation of undernutrition in neonates and micronutrient deficiencies are beyond the scope of this research.

## Malnutrition in paediatrics

Malnutrition in infants, children and adolescents has even more serious consequences on the progression of the disease and long-term health than malnutrition in adults [25, 26]. Body stores are finite at young ages and several homeostatic and metabolic processes are still

limited [27]. The prompt identification and treatment of DRM in paediatrics is essential and yet more complex than for adults, as growth needs to be considered [19, 28]. In healthy young children, energy needs per kg body weight are about three times higher than in adults [27]. In diseased children, estimated average increases in energy reach 120 - 170%, and in critically ill paediatric patients, energy needs can reach up to 200% [27]. In addition, malnutrition and growth faltering during early childhood induce lasting damage at later stages of life, including cognitive abilities, body composition and body height [14, 29].

In scientific literature, documentation of the relationship between malnutrition in hospitalised children and outcome (e.g. length of hospital stay and complication rates) is limited [30, 31]. The evidence-base demonstrating to which extent malnourished paediatric patients will benefit from nutritional intervention is also inadequate [14]. According to previous studies, and depending on the method of assessment, DRM affects up to 24% of paediatric patients in Europe [6]. Potential reasons for this high prevalence include a lack of adequate diagnostic strategies and a lack of targeted nutritional care in paediatrics [21]. Equipment for anthropometric measurements is often inadequate, measurements are seldomly performed in a reliable way and collected data are frequently misinterpreted [5, 32]. A standardised approach to the recognition and diagnosis of paediatric malnutrition is lacking [11]. Available criteria are numerous, inconsistent and not based on firm evidence [11, 14, 21, 33].

## Diagnostic measures and criteria for malnutrition in children

Anthropometry measures the anatomical changes associated with nutritional status. Weight is a very valuable tool in paediatric practice within growth assessment, particularly when combined with length or height in growth charts [23]. Mid-upper arm circumference (MUAC) is a useful surrogate for weight when weighing is impossible [11, 14, 34]. It can be combined with triceps skin fold thickness (TSFT) to derive useful correlates of muscle and fat mass [23]. Chronic malnutrition may, in addition to the anthropometric changes in acute malnutrition, be characterized by stunting (decreased height velocity) [14]. Currently, several different anthropometric indices for malnutrition in children are used, which do not correlate with each other and identify different groups and numbers of patients as malnourished [6, 35].
Becker et al. recently published a consensus statement aiming to identify a basic set of indicators that can be used to diagnose and document undernutrition in the paediatric population aged 1 month to 18 years [11]. The choice of the cut-off values used to identify the status of (normal versus abnormal) and risk for (low versus high) malnutrition is of great influence for the results. Thus, the prevalence of malnutrition (based on underweight) varies according to the criteria applied [21]. Currently, the criteria used show great variation (summarised in Table 1).

Whereas Waterlow and Gomez defined three groups of malnutrition (mild, moderate and severe) other authors stayed with two or one group only. Waterlow proposed a classification for malnutrition based on a "rather arbitrary choice of groupings" [36] and chose percentiles of weight-for-height (WFH) based on the Gomez classification [37]. Gomez had shown the influence of the degree of malnutrition based on weight and the "Boston standard" (reference tables of weight-for-age derived from children in Boston from 1930 to 1956) on mortality. Both classifications, which were initially applied to infants and young children only, are nowadays often used in paediatric patients up to 18 years of age. Over the last several years, standard deviation scores (SDS) are increasingly used over percentile values [11, 28].

**Table 1: Currently used criteria for malnutrition based on underweight (modified after Chourdakis [26])**

| Criteria | Malnutrition grade | | |
|---|---|---|---|
| | Mild | Moderate | Severe |
| **Acute Malnutrition** | | | |
| Gomez [37] | 75 - 90% WFA[a] | 60 – 74% WFA[a] | < 60% WFA[a] |
| Waterlow [36] | 80 - 90% WFH[a] | 70 - ≤ 80% WFH[a] | < 70% WFH[a] |
| Tanner [38] | | < 5th percentile WFH | |
| Olsen [33] | | Weight and BMI for age < 5th percentile | |
| WHO [39] | | < -2 to -3 SDS WFH | < -3 SDS WFH |
| Ling (WHO) [40] | | < -2 to -3 SDS BMI | < -3 SDS BMI |
| **Chronic malnutrition** (short stature as potential marker) | | | |
| WHO [39] | | < -2 SDS HFA | |
| Olsen [33] | | Length for age < 5th percentile | |

[a]of the median of the gender specific reference values; BMI: Body mass index, HFA: Height-for-age, SDS: Standard Deviation Score, WFA: Weight-for-age, WFH: Weight-for-height, WHO: World Health Organisation

Currently, the most commonly used criteria are the World Health Organisation (WHO) cut-offs, which define moderate acute malnutrition (MAM) as WFH < -2 to -3 SDS, severe acute malnutrition (SAM) as WFH < -3 SDS and stunting as height-for-age (HFA) < -2 SDS, which

is a sign of chronic malnutrition [39, 41]. Olsen pointed out that in developed countries WFH references for children aged > 5 years of age are less available than age-specific body mass index (BMI) references, which is the case for e.g. WHO standards [11, 33]. It is difficult to find reliable reference data for WFH SDS for children older than 5 years. Therefore BMI < -2 SDS is often used as a simple proxy for defining malnutrition due to feasibility [40].

Mei et al. compared BMI and WFH data of children aged 2 - 19 years who participated in the NHANES III survey (National Health and Nutrition Examination Survey, US population) [42]. They concluded that BMI and WFH had a similar predictive value for low body fat, based on TSFT (n = 11096) and percentage of body fat or total body fat measured by dual-energy X-ray absorptiometry (DXA). The DXA data (n = 920, 3 - 19 years of age) were derived from pooled data sets of children in the United States, Italy and New Zealand. Olsen compared seven clinically-used criteria (including Waterlow and Gomez criteria) for failure to thrive (FTT) in a large Danish cohort aged 2 - 11 months and found poor agreement among them [33]. Of interest, less than half of the infants identified by the Waterlow criterion as malnourished had a weight < 5$^{th}$ percentile, but all had a BMI < 5$^{th}$ percentile.

As stated above, the choice of the criterion and of the reference influences the assessed prevalence of and risk for malnutrition [21]. Fernandez et al. wrote that cut-off values might even require adapting to reference values in order to maintain diagnostic accuracy [34]. Reported and used references are, for example, the international WHO standards, the Centers for Disease Control and Prevention (CDC) references or national ones [6]. Silveira et al. compared the National Centre for Health Statistics (NCHS), CDC and WHO growth charts in Brazilian children aged 0 - 5 years [43]. Despite the documented strong agreement, they recommend WHO charts for the detection of malnourished children, due to their high sensitivity. However, the WHO growth standards differ from national references [44, 45]. They are based on anthropometric data collected from 1994 to 2003 in Brazil, Ghana, India, Norway, Oman and USA and a good choice for international, multi-centre settings. For national or single centre settings, national references could be the better and more representative choice depending on the date of data collection.
Data presented in this thesis have been compared to the WHO growth standards [39] because data collection was performed in a multi-country setting.

## Nutritional risk screening

The primary objective of screening is the early detection of a condition at a stage when treatment is less expensive, more effective, or both [46]. Global performance of nutritional screening on admission in all patients, using a validated nutritional screening tool (NST), is of high importance and should be standard of practice [47]. The screening results can give the

direction to applying specific nutrition therapy shortly after admission [12]. Therefore, it is necessary to increase the awareness of health care professionals for this topic and to provide clear strategies and concepts. Nutrition therapy should aim to prevent malnutrition rather than being used as a therapeutic intervention once DRM has already developed, and has negatively impacted the paediatric patients [48].

The foundation of any nutritional care plan is the identification of patients at nutritional risk [49]. A good screening instrument, however, should not only be simple, rapid and easy to carry out by admitting staff. It should also meet content validity, predictive validity and reliability and should lead to appropriate and explicit action [50]. Patients found to be at nutritional risk should undergo a detailed assessment, including history, examination, bedside tests and relevant laboratory tests. Based on screening and assessment results, a nutrition management and monitoring plan should be developed. Nutrition support should be considered in patients thought to be malnourished or at risk of malnutrition.

The ideal tool for screening and assessing malnutrition in paediatrics is still debated in the scientific literature [51]. The first tool to be found in paediatric literature is the Reilly Nutritional Risk Score (NRS) [52]. However, evidence to support the use of the NRS is insufficient [53]. Within the last decade, further paediatric malnutrition risk screening tools have been developed and validated [51, 54]. The earlier ones, including the Subjective Global Nutritional Assessment (SGNA) and the Simple Pediatric Nutritional Risk Score (PNRS) are more a detailed assessment, time-consuming and necessary data cannot be collected within one day [55-57]. Thus, they are too complicated for use in daily clinical practice [21]. Some other tools address specific patient groups with specific nutritional needs such as for example a risk-based classification system for individuals with cystic fibrosis [58] or cancer [59]. Simpler tools have been proposed recently and are currently used, including the Paediatric Yorkhill Malnutrition Score (PYMS) [60-62], the Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP) [63, 64] and the Screening Tool for Risk Of Impaired Nutritional Status and Growth ($STRONG_{KIDS}$) [31]. Those three tools are quickly filled out and can therefore be applied within one day after admission. A validation study in Belgium reported that the actual time needed for the completion of $STRONG_{KIDS}$ was 3 minutes [46]. PYMS, STAMP and $STRONG_{KIDS}$ have been developed and applied in different hospital settings. Performance of the tools strongly depends on the growth charts and SDS applied. For example, it makes a great difference whether WHO-CDC vs. UK-WHO charts and WFH vs. BMI SDS are used when applying the PYMS tool [65]. The most recently developed tools are the Pediatric Digital Scaled Malnutrition Risk Screening Tool (PediSMART) [66] and the Pediatric Nutritional Screening Tool (PNST) [67].

Testing the clinical performance of a NST against an appropriate benchmark is important. Van Bokhorst-de van der Schueren and colleagues performed a systematic review of

screening tools for the hospital setting in adults and the elderly addressing the question "Does one size fit all?"[68]. They came to the conclusion that no single screening or assessment tool is suitable for satisfactory nutrition screening as well as predicting poor nutrition related outcome. Two recent reviews of paediatric NST concluded that all compared tools present with advantages and disadvantages [53, 69]. So far there is no adequate evidence to choose one NST over another for the general paediatric population [70].

## ESPEN Research network grant project

In 2009 Prof. Dr. med. Berthold Koletzko and colleagues drafted the basic concept for the project "Malnutrition and Outcome in Hospitalised Children in Europe" and successfully acquired the ESPEN Research network grant. All network partners had already participated in smaller studies on nutrition and nutritional assessment or in large European multi-centre studies. They were experienced in the field of paediatric clinical malnutrition such as detection and treatment in routine daily practice. The aim of the project was to characterize the prevalence of DRM on admission in hospitalised children across Europe. In addition, the effects of malnutrition in paediatric patients on relevant outcomes, such as LOS (primary outcome) and days with infectious complications (fever, antibiotic use), vomiting and diarrhoea should be assessed. A further goal was to compare feasibility, sensitivity and specificity of previously proposed paediatric screening tools and to characterize the prevalence of patients at risk for malnutrition based on the applied tools. To our knowledge, this was the first large-scale, European study on paediatric DRM. It was a cross sectional study with longitudinal elements (duration of hospital stay; days with infection). In contrast to adult medicine, this field of paediatric research had advanced very little due to lack of funding. Few data were available in European patient populations and the association between DRM and outcome has only been studied in scattered areas [25]. Published studies have used a wide variety of measures and criteria, and therefore the opportunity for meta-analysis is limited. The data and outcome of the ESPEN project with its large European cohort aimed at adding strength and evidence for nutrition interventions in paediatrics [71].

## DRM in hospitalised children: from scientific evidence to hospital practice

The extensive ESPEN cohort study contributed valuable scientific evidence in the field of paediatric DRM. The results obtained reinforce the need of having paediatric nutrition teams and help accelerating the process of including screening as part of hospital quality of care criteria (personal communication with Prof. Frederic Gottrand (France) and Prof. Raanan Shamir (Israel) August 2017). The published data was used as evidence to support future

grants and to initiate further international research within the European paediatric population including the United Kingdom, Israel, France, Croatia and The Netherlands. The publication “Disease associated malnutrition correlates with length of hospital stay in children” is one of the most highly cited papers published in Clinical Nutrition in the year of publication (personal communication with Prof. Dileep Lobo, Chair Scientific Committee ESPEN 2017). Obviously, the interest in paediatric DRM in is growing.

A tool with good diagnostic validity identifies the majority of patients you want to treat (sensitivity). Equally important is the good positive predictive value, which strongly depends on the specificity (i.e. 1- false positive rate). As already discussed, currently, there is no reference method for nutritional risk to compare to. BMI SDS was chosen as the best standard for undernutrition in our European setting.

Sensitivity (proportion of patients with BMI < -2 SDS that have been categorised in the high-risk group) was highest for PYMS (91%), followed by STAMP (77%) and lowest for $STRONG_{KIDS}$ (45%). Consequently, false negative rate (number of patients with BMI < -2 SDS that have not been categorised in the high-risk group) was highest for $STRONG_{KIDS}$ (55%) and lowest for PYMS (9%). Positive predictive value (number of high risk patients with BMI < -2 SDS) was comparable low for all three NST (PYMS 22%, STAMP 19%, $STRONG_{KIDS}$ 23%). PYMS and STAMP both use anthropometric values (BMI, weight and height centiles) as components of the risk score. As there appear to be unavoidable statistical issues relating these two NST to BMI, associations with MUAC as well as with TSFT were explored additionally. MUAC and TSFT served as surrogate markers of undernutrition, which unlike BMI, are not contained in PYMS and STAMP. None of the NST was both sensitive and reasonably specific for identifying anthropometric depletion.

HFA is an indicator of duration on undernutrition (chronicity). In terms of patients with HFA < -2 SDS positive predictive value was highest for $STRONG_{KIDS}$ ($STRONG_{KIDS}$ 19%, STAMP 14%, PYMS 8%). False negative rate was nearly equally high for PYMS (74%) and $STRONG_{KIDS}$ (73%). Consequently, sensitivity was highest for STAMP (STAMP 42%, $STRONG_{KIDS}$ 27%, PYMS 26%). HFA sensitivity is low, because height is affected after a variable time of poor weight gain. In acute malnutrition (accompanying acute disease or decompensation of chronic illness) WFA is more sensitive, even if it might over-diagnose undernutrition. Because of this overdiagnosis, WFH or BMI are better indexes than HFA for the purpose of this study. The higher prevalence of stunting secondary to genetic, syndromic or neurologic disease is another important aspect that is relevant to tertiary hospitals in developed countries. It is evident that 58-74% of children with stunting have an adequate WFH stature and thus mistakenly do not belong to “high risk” category. However, the purpose of screening is to categorise inpatients according to the degree of likelihood of

suffering or being at risk of malnutrition rather than offering confirmatory diagnosis which should follow on and be carried out by the dietetic/medical team.

A screening tool has to be as sensitive as possible. However, the resources and the capacity of the health system to cope with the implications of confirmatory diagnosis required for large number of test positive children must be taken into account. In situations where there is a low prevalence of undernutrition and limited number of false positives, this would not be a problem. Identification and selection of a valid tool should be the starting block in the clinical implementation of routine screening for malnutrition in a hospital.

Our European data are in line with a recently published study among hospitalised children in the United States [72]. The US study showed paediatric DRM to be associated with longer LOS, lower quality of life, higher infection rates and an increased risk for complications [12]. Moreover, the reported prevalence of undernutrition found in our study corresponds with other European data, which indicate that roughly one in every ten hospitalised children suffers from undernutrition [73, 74]. Our findings also agree with the conclusions of the three reviews on NST mentioned before [53, 68, 69]. One NST which is applicable to heterogenous settings (e.g. residential, ambulatory/outpatient, acute care) in different paediatric hospitals all over Europe might not be achievable. Another recent systematic review provides a well-structured overview of the search for a consensus on paediatric NST in various disease-specific settings [51]. The authors conclude that further research should focus on performing large multi-centre studies comparing the currently existing tools rather than creating new tools. Creation of new NST seems needless and will most likely not lead to new insights [68]. Further studies comparing various existing NST within one patient population might be more constructive. A guide on how to assess clinical performance of a NST was published several years ago [60]. Milani et al. showed that acquisition of anthropometric measurements and assessment of growth in paediatric inpatients by nursing staff can be improved with the introduction of a screening tool [75].

In a publication on the accuracy of NST in assessing the risk of undernutrition in paediatrics the authors underlined that the choice of the cut-off values will strongly influence sensitivity and specificity of the NST [53]. According to a recent review, WHO growth standards have a wide range of application, can be used for growth assessment of the majority of hospitalised infants and are used in over 50% of all countries worldwide [43, 76]. This is of special interest for the conduction of clinical projects with a multi-centre multi-country setting.

In the last decade, paediatric malnutrition gained increased interest within nutritional societies and experts worldwide [6]. The French Paediatric Society recommends to assess each child with a BMI < -2 SDS for further signs of clinical malnutrition [77]. It is generally

agreed that identification and treatment of malnutrition should be a core competency for paediatricians and related health care professionals [9, 47].

An Italian study described associations between NST score and serum albumin [78]. In Romania good agreement between WHO malnutrition classification and $STRONG_{KIDS}$ was found when adding low serum protein level to the tool [7]. However, it has to be ensured that the NST score is rapid and should not be delayed due to pending biochemical parameters. One step to enforce the evidence of future studies on DRM could be the use of BMI < -2 SDS as criterion and the WHO standard as reference. A harmonised approach would lead to comparable results and therewith strengthen the power of the findings.

Additionally, in future research projects, it is important to focus in parallel on the subsequent step: how to translate the gained evidence best into clinical practice. A lot of field work needs to be done in the years to come as malnutrition is still often unrecognised and underestimated from the health-care staff [74]. Health-care staff members still tend to perceive DRM as an outcome rather than a medical condition [5]. One interesting approach was performed by Beer et al. [79]. Based on current developments in literature, they implemented a malnutrition identification program within a large tertiary care children's hospital and assessed 522 admitted children. The program comprised a tool for dieticians that guided them on how to put all applied criteria into practice. Evaluation of the program showed that awareness and diagnosis of malnutrition increased strongly within one year after implementation. This result underlines that clinical teams need to be trained to monitor, record and interpret the nutritional status on a regular, systematic basis. Also Gerasimidis et al. published several years ago that good training of the staff during implementation period of a NST enhances compliance [60] as well as the collection of the impression of the end users (nurses, dieticians etc.) [62]. The end users need to understand the merit of nutritional screening [70] and to be convinced that it is worth applying NST.

As we are still looking for the holy grail in the field of NST, best practice is to test various tools at various hospitals and settings and decide what NST is best in each respective environment. Nutritional screening and intervention in primary care settings might decrease the need for a costlier hospitalisation [80]. In a small Israeli study population STAMP was validated for ambulatory use in paediatrics [81]. The authors concluded, that the use of the NST helped to identify children in need of nutritional intervention and raised clinician's awareness to nutritional status in general. Cheirakaki et al. applied PYMS and STAMP, that were completed based either on the WHO criteria for underweight or on the Hellenic growth charts (HCG) [82]. For their setting, two hospitals in Athens, PYMS combined with HCG performed best. Also Lestari et al., who conducted a study in Indonesia, were in favour of PYMS [83]. In contrary, two Spanish studies found STAMP to be the tool of choice [84, 85].

Other studies in Belgium, Italy and Romania used and validated the $STRONG_{KIDS}$ Tool [7, 46, 78]. Also, in a study in New Zealand $STRONG_{KIDS}$ performed best [86].

Next to the transfer from evidence to practice challenges and pitfalls in practice have to be evaluated. Over the last several years, nutritional screening has been increasingly performed in paediatric inpatients, but a large number of malnourished children still remain undiagnosed and untreated. Table 2 presents barriers to nutrition screening on different levels.

**Table 2: Challenges for the implementation of nutritional screening into routine practice (modified after Agarwal [5])**

| |
|---|
| **Management level** |
| Lack of clearly defined responsibility |
| Lack of sufficient personnel capacity |
| Lack of awareness, low priority |
| Seldom mandatory and/or supported |
| **Health-care personnel level** |
| Lack of awareness and training |
| Inadequate<br>• time (due to competing priorities)<br>• instruments (weighing scales, height measurements)<br>• training and education (regarding the use of the tools) |
| Perception that the tool is “too complex” or “too complicated” to use |
| Confusion between screening and assessment |
| Preference for other parameters to determine nutritional status such as biochemical markers |
| Prioritising medical treatment over nutritional support |
| **Patient and parent level** |
| Prioritising medical treatment over nutritional support |
| Cultural and/ or educational differences |

A large, nationwide survey in Belgian secondary-level hospitals showed that lack of training and awareness among staff is one general reason [70]. In paediatrics, a deficit of validated protocols for screening, assessment and treatment are still an issue, as well as the enduring use of inconsistent criteria for malnutrition. Despite increasing awareness of the importance of nutritional support during the last two decades, organised nutritional screening, assessment und management is still not fully established in clinical practice [70].

In conclusion, effective and early detection and treatment of DRM in paediatric patients should be key priorities. They should become the mutual interest of doctors, hospital administration and health authorities represented in collaboration with and appreciation for

nutritional teams. Improved organisation of nutritional screening, assessment and therapy will most likely have both clinical and economics benefits in the hospital service. Efficacy of nutritional therapies has to be explored in future studies. The newly formed ESPEN Special Interest Group in Paediatric Clinical Nutrition [87] might be the leading task force to achieve this goal in the subsequent years.

# 4. Objectives and author's contribution

The present thesis comprises two published research articles which are both derived from data collected within the framework of the ESPEN Research network grant project. The overall contribution of the author to the project and the two articles is described as follows:

- **ESPEN Network Grant project - project management and study coordination:** Preparation of the study protocol, application to the local ethical committee, registration at ClinicalTrials.gov, preparation of the agreements governing the joint conduct of the clinical trial between the sponsor and the trial sites in collaboration with the legal department, budget responsibility, planning and conduction of the training workshop in Munich, development and preparation of the case report forms and the standard operating procedures and organisation of study meetings

- **Data collection, data management and data analysis:**
  Data collection at the coordinating centre in Munich, coordination of the global data monitoring (collection and source data) and global data review for data quality check, major part of the data entry (copies of the CRFs of all centres were sent to Munich for data entry), major part of data management and statistical analysis (with support of Weber M and Grote V)

The key objectives of this work are to:

- Characterise the prevalence of paediatric malnutrition at hospital admission in Europe
- Determine the effect of paediatric malnutrition on selected outcomes
- Check proposed paediatric screening tools against each other
- Compare the screening tools and their predictive value on outcomes

In summary, the results of the present publications indicate that:

- the overall prevalence of paediatric malnutrition at hospital admission was 7%, with a higher prevalence in infants (10.8%) and toddlers aged 1 - 2 years (8.3%).
- paediatric malnutrition is associated with selected outcomes: longer LOS, lower quality of life and increased frequency of vomiting and diarrhoea.
- the use of applied paediatric screening tools (PYMS, STAMP, $STRONG_{KIDS}$) cannot be recommended for assessing nutritional risk in routine clinical practice due to small agreement between the tools.
- all three tools showed a predictive value on LOS and on body composition.

**Publication I**: Hecht C, Weber M, Grote V et al. Disease associated malnutrition correlates with length of hospital stay in children. Clinical nutrition 2015;34(1):53-9. doi:10.1016/j.clnu.2014.01.003

**Contribution of Hecht C:**
Drafting and preparation of the manuscript, coordination of co-authors' intra-group reviews and communication, conclusion and discussion, revision of the manuscripts and integration of reviewers' comments towards publication.

In a large European paediatric cohort of 2567 inpatients from 14 hospitals in 12 countries a BMI < -2 SDS was present in 7% of the study participants at hospital admission. BMI and WFH < -2 SDS had a good level of agreement (97%), but BMI showed a higher prevalence of severely malnourished children (2.1% vs.1.5%). Low BMI (-2 to -3 SDS, < -3 SDS) was correlated with a longer LOS (1.3 days and 1.6 days; respectively), lower quality of life (total score ≥4 in 15.1% malnourished vs. 6.4% well-nourished children, $p < 0.001$) and increased frequency of vomiting (26% vs.14%; $p < 0.001$) and diarrhoea (22% vs. 12%, $p < 0.001$).

**Publication II:** Chourdakis M, Hecht C**,** Gerasimidis K et al. Malnutrition risk in hospitalized children: use of 3 screening tools in a large European population. Am J Clin Nutr. 2016 May; 103(5):1301 – 10. Doi: 10.3945/ajcn.115.110700. Epub 2016 Apr. 2016

**Contribution of Hecht C:**
First drafting and preparation of the manuscript, coordination of co-authors input, discussions within the writing group, answering of reviewers' comments including additional statistical analysis.

The identification and classification of risk of malnutrition varied between the three applied tools PYMS, STAMP and $STRONG_{KIDS}$, with an agreement of only 41%. A positive association was found between high malnutrition risk (PYMS: 25%; STAMP: 23%; $STRONG_{KIDS}$: 10%) and LOS (1.4, 1.4 and 1.8 days longer, respectively) and a reverse association was found between body composition (MUAC and TSFT) and nutritional risk status.

# 5. Abstract

Background

Disease-related malnutrition is often not directly identifiable and it is seriously underestimated in affluent societies. In European, hospitalised children, a prevalence of 6 – 30% is reported. This wide range is due to the lack of harmonised diagnostic criteria. Various anthropometric indices classify different patient groups as malnourished. In industrialized countries, an association between malnutrition and important clinical variables e.g. length of hospital stay (LOS) in paediatric patients was reported for few studies with small cohorts only. Similarly, there is no clear evidence for the use of nutritional screening tools (NST) to define the risk for malnutrition in paediatrics.

Objectives

Within the framework of a large European cohort study, we performed selected anthropometry in hospitalised children and evaluated the following NST which were previously reported in the literature: “Paediatric Yorkhill Malnutrition Score” (PYMS), “Screening Tool for the Assessment of Malnutrition in Paediatrics” (STAMP) and “Screening Tool for Risk of Impaired Nutritional Status and Growth” ($STRONG_{KIDS}$). We aimed to indicate the prevalence of underweight and stunting and possible associations with relevant outcomes (LOS and complications rates). In addition, we evaluated how the three NST compared with and were related to anthropometric measures and clinical variables.

Methods

Between February 2010 and July 2011, a total of 2567 hospitalised patients aged one month to 18 years were included in a prospective multi-centre nutrition study at 14 hospitals across 12 European countries. The three NST were applied during a structured interview within 24 hours after admission and standardised anthropometric measurements (weight, standing height or supine length, mid-upper arm circumference (MUAC) and triceps skin fold thickness (TSFT)) were performed. Patients were classified into different nutritional risk groups based on calculated NST scores. Body mass index (BMI), weight-for-height (WFH) and height-for-age (HFA) were defined, translated into standard deviation scores (SDS, WHO reference) and grouped according to cut-offs. Tool based nutritional risk groups and SDS based nutritional status groups were compared with and were related to LOS (primary outcome), MUAC, TSFT, frequency of gastrointestinal complications (vomiting and diarrhoea) and infection rates (fever and antibiotic use), weight change during stay and quality of life (QOL).

Results

Median age of all study participants was 4.7 years, 45% were female. During hospital stay (median 4.0 days) 12.3% of the patients got nutritional support. We found a BMI < -2 SDS in 7% of study participants at hospital admission, including 2% of children with severe malnutrition (BMI < -3 SDS). Prevalence was higher the younger the children were (toddlers 8.3% and infants 10.8%). Underweight (BMI < -2 SDS) and/or stunting (HFA < -2 SDS) was present in 13.4% of examined patients. QOL was lower in patients with low BMI and diarrhoea and vomiting was more frequent (22% vs. 12% and 26% vs. 14%; $p < 0.001$, both). LOS was longer in moderate (BMI -2 to -3 SDS) and severe (BMI < -3 SDS) malnourished children (1.3 days longer CI 95: 1.01, 1.55; $p = 0.04$ and 1.6 days CI 95: 1.27, 2.10; $p < 0.001$). For PYMS data from 86% of the children was available for analysis, for STAMP and $STRONG_{KIDS}$ it were 84% and 81%, respectively. The results of risk classification had only an overall agreement of 41% between the three NST. Patients categorised as high risk (PYMS: 25%; STAMP: 23%; $STRONG_{KIDS}$: 10%) showed a longer LOS than patients at low risk (PYMS and STAMP: 1.4 days longer; $STRONG_{KIDS}$: 1.8 days; $p < 0.001$). Thereby, a BMI < -2 SDS was found in 22% of the PYMS high risk patients and a HFA < -2 SDS in 8%; for STAMP and $STRONG_{KIDS}$ high risk patients results were 19% and 14% or rather 23% and 19%, respectively. False negative rate (proportion of patients with BMI < -2 SDS that have not been categorised in the high risk group) was highest for $STRONG_{KIDS}$ (55%), followed by STAMP (23%) and lowest for PYMS (9%).

Conclusion

In this heterogeneous group (age, underlying diagnosis) of well-nourished and malnourished paediatric hospital patients, we found a correlation between nutritional status and clinical outcome, namely higher complication rates, considerably reduced QOL and longer LOS. The observational nature of the present study cannot establish causality. However, the data might be important evidence to underline the adverse effect of malnutrition on clinical outcomes in European paediatric patients. None of the three tested NST is of exclusive superiority of the others. Results varied between the tools and a remarkable number of children with subnormal anthropometric measures were not identified by all three NST. Based on the collected data no choice for recommendation could be made. The choice which tool should be used depends on the clinical setting, the hospital population and the country-specific regulations. It is important to develop a system, that suits the specific needs and circumstances.

The demonstration of a correlation between the degree of risk for DRM and relevant outcomes (LOS) will hopefully lead to wide implementations of evidence-based nutritional interventions in paediatric patients. Thereby, collaboration with and appreciation for

nutritional teams is of great importance. Efficacy of nutritional interventions has yet to be demonstrated in future studies.

# 6. Zusammenfassung

Hintergrund

Krankheitsbedingte Mangelernährung ist oft nicht unmittelbar zu erkennen und wird in unserer Überflussgesellschaft erheblich unterschätzt. Bei hospitalisierten Kindern in Europa wurde eine Häufigkeit von 6 - 30% berichtet. Diese große Spannweite beruht vor allem auf dem Fehlen einheitlicher diagnostischer Kriterien für Mangelernährung. Verschiedene anthropometrische Indizes definieren unterschiedliche Patientengruppen als mangelernährt. Pädiatrische Daten zum Zusammenhang zwischen Mangelernährung und wichtigen klinischen Zielgrößen z.B. Länge des Krankenhausaufenthalts („length of stay", LOS) wurden bislang für Industrieländer nur in wenigen Studien mit kleinen Fallzahlen beschrieben. Ebenso gibt es in der Pädiatrie keine klare Datenlage zum Einsatz von Screening-Werkzeugen („nutritional screening tools", NST) für die Risikoabschätzung der Mangelernährung.

Ziele

Im Rahmen einer großen, europaweiten Kohortenstudie wurden bei hospitalisierten Kindern definierte anthropometrische Messungen durchgeführt und folgende in der Literatur beschriebene NST evaluiert: „Paediatric Yorkhill Malnutrition Score" (PYMS), „Screening Tool for the Assessment of Malnutrition in Paediatrics" (STAMP) und „Screening Tool for Risk of Impaired Nutritional Status and Growth" ($STRONG_{KIDS}$). Es galt die Häufigkeit von krankheitsbedingtem Untergewicht und Kleinwuchs, sowie mögliche Auswirkungen dieser auf relevanten Endpunkte (LOS, Komplikationsraten), zu erfassen. Zudem wurden die drei NST untereinander bezüglich der Einordnung der Patienten in die verschiedenen Ernährungsrisiko-Gruppen verglichen und die Ergebnisse mit anthropometrischen Messungen und klinischen Variablen in Beziehung gesetzt.

Methoden

Zwischen Februar 2010 und Juli 2011 wurden 2567 stationäre Patienten im Alter zwischen 1 Monat und 18 Jahren aus 14 Kliniken von 12 europäischen Ländern in die prospektive multizentrische Studie aufgenommen. Die drei NST kamen während eines leitfadengestützten Interviews innerhalb von 24 h nach Krankenhausaufnahme zum Einsatz und es wurden standardisierte anthropometrische Messungen (Gewicht, Größe/Länge, Oberarmumfang (OAU) und Trizeps-Hautfalte (THF)) durchgeführt. Basierend auf den NST Daten wurden Punkte berechnet und die Patienten anhand dieser in Risikogruppen eingeteilt. Zudem wurden Körper-Masse-Index (BMI), Gewicht-zu-Größe-Index und Größe-zu-Alter-Index gebildet, in „standard deviation score" (SDS, WHO Child Growth Standards) übersetzt

und kategorisiert. NST basierte Ernährungsrisiko-Gruppen und SDS basierte Ernährungsstatus-Gruppen wurden miteinander verglichen. LOS (primärer Endpunkt), OAU, THF, Häufigkeit von gastrointestinalen Komplikationen (Erbrechen und Durchfall), Infektionsraten (Fieber und Antibiotikagabe), Gewichtsveränderung während des Klinikaufenthalts und Lebensqualität wurden mit den Gruppen in Beziehung gesetzt.

Ergebnisse

Das Alter der Studienteilnehmer betrug im Median 4,7 Jahre, 45% waren weiblich. Während des Krankenhausaufenthaltes (Median 4,0 Tage) erhielten 12,3% der Patienten eine ergänzende Ernährung. Bei Krankenhausaufnahme wiesen 7% der Studienteilnehmer einen niedrigen BMI (< -2 SDS) und 2% der Kinder ein sehr starkes Untergewicht (BMI < -3 SDS) auf. Die Prävalenz von Untergewicht war umso höher, je jünger die Kinder waren (1-2 jährige Kleinkinder 8,3% und Säuglinge 10,8%). Untergewicht (BMI < -2 SDS) und/oder Kleinwuchs (Körperlänge < -2 SDS) lagen bei 13,4% der untersuchten Patienten vor. Die Lebensqualität war bei Patienten mit vermindertem BMI geringer, wobei Erbrechen und Durchfall in dieser Patientengruppe vermehrt auftraten (22% vs. 12% und 26% vs. 14%; jeweils $p < 0.001$). Der Klinikaufenthalt war bei moderat (BMI -2 bis -3 SDS) und schwer (BMI < -3 SDS) mangelernährten Kindern im Vergleich zu den normal ernährten Kindern verlängert (1,3 Tage länger CI 95: 1,01 - 1,55; $p = 0,04$ und 1,6 Tage länger CI 95: 1,27 – 1,10; $p < 0,001$).
Für PYMS waren Daten von 86% der Kinder zur Auswertung verfügbar, für STAMP und $STRONG_{KIDS}$ waren es jeweils 84% und 81%. Die Ergebnisse zur Klassifizierung des Mangelernährungsrisikos zeigten beim Vergleich der drei NST lediglich eine Übereinstimmung von insgesamt 41%. Patienten, die sich in den Hochrisikogruppen befanden (PYMS: 25%, STAMP: 23%, $STRONG_{KIDS}$: 10%) waren gegenüber solchen mit einem geringen Risiko durch einen längeren LOS gekennzeichnet (PYMS und STAMP jeweils 1,4 Tage länger; $STRONG_{KIDS}$: 1,8 Tage länger; $p < 0,001$). Dabei hatten von den mittels PYMS identifizierten Hochrisiko-Patienten 22% einen BMI < -2 SDS und 8% einen niedrigen Größe-zu-Alter SDS (< -2); im Fall des STAMP und $STRONG_{KIDS}$ waren es jeweils 19% und 14% bzw. 23% und 19%. Die falsch-negativ Rate (Anteil der Patienten mit einem BMI < -2 SDS, die nicht der Hochrisikogruppe zugeordnet wurden) war bei $STRONG_{KIDS}$ (55%) am höchsten, gefolgt von STAMP (23%) und am niedrigsten für PYMS (9%).

Schlussfolgerungen

In dieser heterogenen Gruppe (Alter und zugrundeliegende Diagnose) von normal- und mangelernährten stationären pädiatrischen Patienten konnten wir eine Korrelation zwischen Ernährungsstatus und klinischen Zielgrößen zeigen (gehäufte Komplikationen, deutlich eingeschränkte Lebensqualität und verlängerte Verweildauer). Aufgrund des beobachtenden Designs der Studie kann keine Kausalität herbeigeführt werden. Die Daten können jedoch

eine wichtige Evidenz darstellen, welche die negative Auswirkung von Mangelernährung auf klinische Zielgrößen bei pädiatrischen Patienten in Europa unterstreicht. Keiner der drei evaluierten NST ist von herausragender Überlegenheit. Die Ergebnisse variierten zwischen den NST und eine erhebliche Anzahl an Kindern mit subnormalen anthropometrischen Messungen wurde von allen drei NST nicht erfasst. Basierend auf den erhobenen Daten kann keine Empfehlung für die Anwendung eines NST ausgesprochen werden. Die Wahl des richtigen NST hängt vom klinischen Bereich, den Patientengruppen und den landspezifischen Vorschriften ab. Es ist wichtig einen Leitfaden zu generieren, der den speziellen Bedürfnissen und Umständen entspricht.

Der Nachweis der Korrelation zwischen dem Grad des Risikos für Mangelernährung und relevanten Zielgrößen (LOS) sollte zukünftig zu umfassendem Einsatz evidenzbasierter Ernährungsintervention bei pädiatrischen Patienten führen. Dabei spielt die Zusammenarbeit mit und steigende Bedeutung von Ernährungsteams eine wichtige Rolle. Die Wirksamkeit der Ernährungsintervention muss in zukünftigen Studien gezeigt werden.

## 7. Publication I

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Original article

# Disease associated malnutrition correlates with length of hospital stay in children☆

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SUMMARY

*Background & aims:* Previous studies reported a wide range of estimated malnutrition prevalence (6–30%) in paediatric inpatients based on various anthropometric criteria. We performed anthropometry in hospitalised children and assessed the relationship between malnutrition and length of hospital stay (LOS) and complication rates.

*Methods:* In a prospective multi-centre European study, 2567 patients aged 1 month to 18 years were assessed in 14 centres in 12 countries by standardised anthropometry within the first 24 h after admission. Body mass index (BMI) and height/length <−2 standard deviation scores (SDS, WHO reference) were related to LOS (primary outcome), frequency of gastrointestinal (diarrhoea and vomiting) and infectious complications (antibiotic use), weight change during stay (secondary outcomes) and quality of life.

*Results:* A BMI <−2 SDS was present in 7.0% of the patients at hospital admission (range 4.0–9.3% across countries) with a higher prevalence in infants (10.8%) and toddlers aged 1–2 years (8.3%). A BMI <−2 to ≥−3 SDS (moderate malnutrition) and a BMI <−3 SDS (severe malnutrition) was associated with a 1.3 (CI95: 1.01, 1.55) and 1.6 (CI95: 1.27, 2.10) days longer LOS, respectively ($p = 0.04$ and $p < 0.001$). Reduced BMI <−2 SDS was also associated to lower quality of life, and more frequent occurrence of diarrhoea (22% vs 12%, $p < 0.001$) and vomiting (26% vs 14%, $p < 0.001$).

*Abbreviations:* HFA, height/length for age; SDS, standard deviation scores; BMI, body mass index; LOS, length of hospital stay; MUAC, mid upper arm circumference; TSFT, triceps skin fold thickness; ICD, international classification of diseases; IQR, interquartile ranges.

☆ Part of the data previously presented at ESPGHAN (Stockholm) and ESPEN (Barcelona) congresses 2012.

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*Conclusion:* Disease associated malnutrition in hospitalised children in Europe is common and is associated with significantly prolonged LOS and increased complications, with possible major cost implications, and reduced quality of life.
This study was registered at clinicaltrials.gov as NCT01132742.


## 1. Introduction

Diseases increase the risk of malnutrition in infants and children. Malnutrition is induced by many childhood diseases, e.g. Crohn's disease[1] or cystic fibrosis,[2] and many others. However, it is not possible to distinguish clearly between severity and chronicity of disease and nutritional status which interact. The prevalence of disease associated malnutrition in hospitalised children in Europe has been reported to range from 6% to 30%.[3,4] This wide variation appears mainly due to the inconsistency of criteria used for defining disease associated malnutrition in paediatric patients.[3] Several different anthropometric indices have been used, which identify different groups and proportions of patients as malnourished.[4,5] The most frequently used criteria for acute malnutrition are the WHO cut-off weight for length/height (WFH) <−2 standard deviation scores (SDS) or alternatively body mass index (BMI) <−2 SDS. Height/length for age (HFA) <−2 SDS is suggestive of stunting and used as a marker of chronic malnutrition in developing countries but also in children with chronic illness.[6]

In adults, adverse effects of disease associated malnutrition defined by anthropometry, and benefits of nutritional intervention on clinical outcomes have been documented.[7] In contrast, the relation between malnutrition in children and outcomes, e.g. length of hospital stay (LOS), has only been reported in a limited number of small paediatric studies.[8,9] Our study aimed at assessing the prevalence of disease associated malnutrition (BMI < −2 SDS) in hospitalised children across Europe and to investigate the possible impact on length of hospital stay and on complication rates.

## 2. Material and methods

### 2.1. Definitions

Malnutrition in this context is defined as underweight only, defined by BMI < −2 SDS. The French Paediatric Society recommends the cut-off BMI < −2 SDS or below the third centile for protein-energy malnutrition screening in children.[10] In developed countries WFH standards are less available than age specific BMI standards.[11,12] For the calculation of the prevalence of malnutrition and it's relation to length of hospital stay the degree of malnutrition was classified as moderate (≥−3 to ≤ −2 SDS) and severe (<−3 SDS). Patients with stunted height, which can be a marker of chronic malnutrition, were classified using height for age (HFA) < −2 SDS. WFH < −2 SDS was investigated for reason of comparison in children <5 years of age as this is the upper limit for WHO tabulation for WFH. A previous cross-validation study in Brazil showed that the performance of BMI and WFH in predicting underweight in children aged 2–19 years was similar.[13]

### 2.2. Study design

This prospective European multi-centre cohort study was supported by a Network Grant of the European Society for Clinical Nutrition and Metabolism (www.espen.org). Patients admitted to general paediatric and surgery paediatric wards in collaborating centres aged 1 month to 18 years, with an expected hospital stay exceeding 24 h, and not enrolled in the present study during previous admissions, were eligible for study participation. Preterm infants (<37 weeks gestational age) during the first 12 months of life and infants <1-month of age were excluded per protocol, since anthropometric assessment criteria for older patients were expected to be inadequate for these patients. Children admitted to intensive care and day hospital care were not eligible, because data collections were expected to be difficult to achieve without major interference with patient care, and outcomes were expected to be rather different than in patient populations hospitalised on general paediatric wards. Patients with cerebral palsy or genetic syndromes were not excluded per protocol. Participating patients were assessed by standardised anthropometry within the first 24 h after admission.

The primary outcome measure was length of hospital stay (LOS) in days. Secondary outcome measures were frequency of infectious complications (number of days with temperature >38.5 °C, and days with antibiotic use), number of days with vomiting and with diarrhoea, and percent weight loss per hospital day (based on the difference between admission weight and discharge weight in % of admission weight and LOS).

Fourteen tertiary hospitals in 12 countries recruited patients between February 2010 and July 2011. We aimed at a recruitment of 220 newly admitted eligible patients from each country, i.e., about 220 patients from each of the centres in Munich (Germany), Zagreb (Croatia), Petah Tikvah (Israel), Milan (Italy), Lille (France), Oxford (England), Glasgow (Scotland), Cluj-Napoca (Rumania), Thessaloniki (Greece) and Copenhagen (Denmark). In addition we aimed at recruiting about 110 patients from each of the two centres in the Netherlands (Rotterdam and Groningen) and in Poland (two hospitals in Warsaw). Recruitment phase per centre started on the day when the first patient was recruited and lasted until the predetermined number of subjects who fulfilled all inclusion criteria had been achieved at this site. Within this period information on age, gender and attended ward (surgical/general) was collected of all patients admitted to the participating wards in the respective centre (in Glasgow this was not permitted by the local research ethics committee). Recruitment phases varied between 3 and 30 weeks per centre (~1.8 recruited patients per day) depending on the number of assessors and predetermined number of subjects. The study protocol was reviewed and approved by the local research ethic committees at all centres. A prerequisite for participation was a signed informed consent by parents or caregivers and agreement to an age-adapted consent form by those patients sufficient with understanding.

### 2.3. Methods

This study was performed according to good clinical practice (GCP) criteria as far as they could be applied to a cohort study. The case report form for data documentation was developed and tested during a pilot phase at the Dr. von Hauner Children's Hospital in Munich, Germany during February to April 2010 in a group of 100 patients. For the subsequent main study, each study centre appointed at least one but not more than three assessors to collect all data at their study site. A training workshop was held in March 2010 at Munich to establish standard operating procedures and

harmonized approaches among all centres. Prior to starting recruitment, each centre tested the procedures on a 'pilot day' at the respective site.

All anthropometrical measurements were performed in duplicate within 24 h after admission. Mean values were calculated and used for data analysis. Hydration status (dehydration, normal hydration, edema/ascites) and time of last meal/drink were additionally recorded by the assessor. Weight and supine length in infants (nude) or standing height in children (with minimal clothing) were measured using calibrated standard equipment (digital scales, infantometer or stadiometer). BMI was calculated as weight (kg)/[length or height (m)]$^2$. For all children with a LOS $\geq$4 days the last measured weight before discharge was obtained from the hospital patient chart whenever this was available.

Information on demographic and medical data (gender, age, date of admission, main ethnic background (Caucasian, African, Asian, other), chronic disease (yes/no), elective admission, number of hospital stays during the last 12 months and nutritional support) was documented during a structured interview with the patient and/or the parents/caregivers, which was performed after the anthropometric measurements. For children 2 years of age or older a score for quality of life was obtained (cf. Supplementary Material): information about sensation and perception (ability to hear, see and speak), mobility, self-care and pain was gathered during this interview, with a score of 0–4 for each element. A lower total score indicates a better quality of life. The diagnosis leading to admission and any underlying chronic disease (lasting three months or more) were coded according to the International Classification of Diseases (ICD-10 Version 2010). Further outcome data including length of stay, the number of days with temperature >38.5 °C, the presence of diarrhoea and/or of vomiting, nutritional support and antibiotic use were recorded after discharge based on the hospital record.

To ensure data quality, 14 local reviewers not involved in the ESPEN Network project compared a randomly selected 5% sample of the case report forms from each site to hospital patient charts. ABBYY FlexiCapture 10 (ABBYY Europe GmbH, Munich, Germany), a module for direct text recognition, was used for converting data from paper documents into an electronic database with built-in plausibility checks (e.g. a predetermined range of plausible values for length and weight in relation to age and gender that could only be overcome after answering a specific question).

### 2.4. Statistical analysis

Age- and gender-specific SD-scores were calculated using WHO reference data: WHO growth reference study data were used for children aged 0–≤5 years (http://www.who.int/childgrowth/software/en/) and further age-adequate WHO reference data were used for patients aged >5–18 years (http://www.who.int/growthref/en/). BMI SD-scores could be calculated for children aged 1 month to 18 years. The calculation of WFH SD-scores was confined the children 0–<5 years of age due to the lack of reference data for older children. Therefore the comparison between WFH and BMI for assessing malnutrition could only be provided for children <5 years of age ($n$ = 1229).

Data are presented as medians with interquartile ranges (IQR: 25th and 75th percentiles). Baseline characteristics between groups were compared using Fisher's exact test or Pearson's chi$^2$-test for categorical data. Non-normally distributed continuous data were compared using the Wilcoxon rank sum test or Kruskal–Wallis tests for more than two categories. Kaplan–Meier curves were estimated to describe differences in LOS with regard to nutritional status. To assess the impact of malnutrition on LOS a zero truncated poisson regression model was calculated using robust variance estimation with clustering by study center.[14] Unadjusted and adjusted estimates are reported. Data management and statistical analyses were carried out with the software package R 2.13.2 (The R Foundation for Statistical Computing, Vienna, Austria) and Stata 12.1 (StataCorp LP, College Station, TX).

## 3. Results

### 3.1. Patient characteristics

During the study period 9055 of all 11,453 patients (33% surgical and 67% general) consecutively admitted to the participating wards fulfilled the inclusion criteria and were eligible for study participation. Due to limitations regarding the parental language or periods of absence from the ward during the first 24 h after admission (of parents [16%], patients [18%] or assessors [65%; on weekends or due to too many patients newly admitted to address all within the first 24 h]) 5952 patients were not available for recruitment. Parents of another 536 children did not agree to participate. Thus, a total of 2567 patients (20% surgical and 80% general) were enrolled into the study. Study participants were significantly younger than all eligible hospital patients (Wilcoxon test, $p \leq 0.001$), with a median age of 4.7 years (IQR: 1.4–11.1 years) vs. 5.3 years (IQR: 1.6–11.7 years), respectively. Gender was not significantly different between eligible and enrolled children. Most included participants were admitted from home (91.7%) and were of Caucasian origin (91.2%). A total of 44.9% of the study population were female, 43.9% were electively admitted and 44.8% had an underlying chronic disease. Some 11.8% had received nutritional support prior to admission. Further characteristics of the study population are shown in Table 1. Predominant reasons for hospital admission were diseases of the respiratory (ICD 10 – J) or digestive (ICD 10 – K) system (Suppl. Table 1). Dehydration was present in 130 children and edema/ascites was found in 34 children.

### 3.2. Prevalence of malnutrition

Weight and length/height were measured in 2543 (99%) and 2415 (94%) patients, respectively. The criterion BMI < −2 SDS was applied to all subjects with available BMI data ($n$ = 2410, 94% of all subjects) and resulted in a prevalence of malnutrition of 7% ($n$ = 167), with 5% of the participants being moderately malnourished (BMI < −2 to ≥ −3 SDS) and 2% being severely malnourished (BMI < −3 SDS).

BMI and WfL < −2 SDS each classified 7.6% ($n$ = 93) of the subgroup of 1229 patients aged 1 month to 5 years as being malnourished. Both criteria agreed in 97% of the patients.

**Table 1**
Demographic characteristics of the study population.

| Demographic characteristics | Total $N$ = 2567 | Surgical $N$ = 511 (20%) | Paediatric $N$ = 2056 (80%) |
|---|---|---|---|
| Age groups | | | |
| 31 days–0.9 years | 484 (18.9%) | 97 (19.0%) | 387 (18.8%) |
| 1–1.9 years | 312 (12.2%) | 54 (10.6%) | 258 (12.5%) |
| 2–5.9 years | 630 (24.5%) | 125 (24.5%) | 505 (24.6%) |
| 6–12.9 years | 689 (26.8%) | 138 (27.0%) | 551 (26.8%) |
| 13–17.9 years | 452 (17.6%) | 97 (19.0%) | 355 (17.3%) |
| Female | 1152 (44.9%) | 225 (44.0%) | 927 (45.1%) |
| Caucasian | 2340 (91.2%) | 456 (89.2%) | 1884 (91.6%) |
| Admission[a] | | | |
| Elective | 1126 (43.9%) | 350 (68.5%) | 776 (37.7%) |
| Acute | 1441 (56.1%) | 161 (31.5%) | 1280 (62.3%) |
| Chronic disease | 1143 (44.6%) | 223 (43.6%) | 920 (44.7%) |

[a] Chi$^2$-test, comparison between surgical and paediatric patients, $p < 0.001$.

### 3.3. Demographic aspects

The distribution of underweight and stunted height among different demographic groups is shown in Table 2. Acutely admitted children and non-Caucasian children were more likely to be malnourished. The prevalence of malnutrition was significantly higher in children with an underlying chronic disease. There was no difference of malnutrition prevalence according to gender.

Across countries the percentage of malnutrition ranged from 4.0% to 9.3% ($Chi^2$-test, $p = 0.277$) (Suppl. Table 2).

### 3.4. Clinical diagnosis

A high prevalence of BMI $< -2$ SDS ($>10\%$) was found in patients hospitalized because of diagnosed mental and behavioural disorders (ICD 10 − F), patients with diseases of the digestive system (ICD 10− K) and those with endocrine, nutritional or metabolic diseases (ICD 10 − E) (Suppl. Table 1). Dehydration was present in 12 children with a BMI $< -2$ SDS (7.1%) whereas edema/ascites was not present at all.

### 3.5. Primary outcome: length of hospital stay

Median LOS was 4 days (IQR: 3–7 days), with a longer LOS (5 days) both for infants up to one year and for children aged 13 years or older (Kruskal–Wallis test, $p = 0.031$). No death occurred during hospital stay. Moderately and severely malnourished patients had a longer LOS (Kaplan–Meier estimates, Fig. 1). The number of participants per group (no, moderate, severe malnutrition) decreased with longer LOS and thus the uncertainty of the estimates increased (broader confidence bound at longer LOS). The median LOS was 5 days (IQR: 3–8.25 days) in moderately malnourished patients and 7 days (IQR: 3–10 days) in severely malnourished patients. More of the well-nourished patients (BMI $\geq -2$) were discharged during the first 4 days after hospital admission; therefore the curve of these patients drops faster than of those with moderate and severe malnutrition. The effect estimates in Table 3 show that disease associated malnutrition still affects LOS after adjustment for age, gender, chronic disease status and centre. Moderately malnourished children stayed 1.3 days longer in the hospital than their well-nourished peers, and severely malnourished patients stayed 1.6 days longer than their well-nourished peers. There was no indication that the effect of the nutritional status differed according to the chronic disease status, i.e. that malnourished children who were chronically ill would have stayed longer in the hospital than other children ($p$ value for interaction = 0.604).

The comparison of BMI and WFH $< -2$ SDS showed that moderately malnourished children <5 years of age stayed 1.4 days (CI95: 1.08–1.74, $p = 0.010$) and 1.2 days (CI95: 0.99–1.41, $p = 0.058$) longer than children with a higher SD-score, respectively. In severely malnourished children <5 years of age the prolonging effects were 1.6 days (CI95: 1.21–2.17, $p = 0.001$) for BMI $< -3$ SDS and 1.4 days (CI: 0.90–2.25, $p = 0.130$) for WFH $< -3$ SDS.

**Table 2**
Prevalence of malnutrition and demographic aspects ($n = 2410$).

| | Underweight[a] $n$ (%) | $p$[b] | Stunting[c] $n$ (%) | Sum $n$ (%) |
|---|---|---|---|---|
| Total group | 167 (7%) | | 193 (7.9%) | 322 (13.4%) |
| Moderate (−2 to −3 SDS) | 120 (5%) | | 133 (5.5%) | 241 (10.0%) |
| Severe (<−3 SDS) | 47 (2%) | | 60 (2.5%) | 97 (4.4%) |
| Age groups | | | | |
| 31 days–0.9 years | 49 (10.8%) | <0.001 | 44 (9.7%) | 79 (17.4%) |
| 1–1.9 years | 24 (8.3%) | | 31 (10.7%) | 49 (17.0%) |
| 2–5.9 years | 24 (4.1%) | | 52 (8.8%) | 73 (12.4%) |
| 6–12.9 years | 45 (6.9%) | | 42 (6.4%) | 81 (12.4%) |
| 13–17.9 years | 25 (5.8%) | | 24 (5.6%) | 40 (9.3%) |
| Sex | | | | |
| Female | 67 (6.1%) | 0.188 | 81 (7.4%) | 136 (12.5%) |
| Male | 100 (7.6%) | | 112 (8.5%) | 186 (14.1%) |
| Ethnic background | | | | |
| Caucasian | 142 (6.5%) | 0.005 | 164 (7.4%) | 280 (12.7%) |
| Non-caucasian | 25 (11.8%) | | 29 (13.7%) | 42 (19.9%) |
| Admission | | | | |
| Acute | 100 (7.9%) | 0.038 | 103 (7.6%) | 184 (13.7%) |
| Elective | 67 (5.7%) | | 90 (8.3%) | 138 (12.9%) |
| Chronic disease | | | | |
| Yes | 99 (9.2%) | <0.001 | 123 (11.4%) | 195 (18.1%) |
| No | 68 (5.1%) | | 70 (5.3%) | 127 (9.6%) |
| Ward | | | | |
| Surgical | 33 (7.1%) | 0.897 | 33 (7.1%) | 59 (12.7%) |
| General | 134 (6.9%) | | 160 (8.9%) | 263 (13.5%) |

[a] Defined as body mass index <−2 standard deviation scores (SDS).
[b] $Chi^2$-test; comparison between the malnourished and not malnourished patients.
[c] Defined as height/length for age <−2 SDS.

### 3.6. Secondary outcomes

A higher percentage of malnourished children experienced diarrhoea (22% vs. 12%, $p < 0.001$) and vomiting (26% vs. 14%, $p < 0.001$) than well-nourished patients (Table 4). The median period of vomiting was significantly longer in the malnourished than in the well-nourished group (2 days vs. 1 day, Wilcoxon test, $p = 0.006$). No relationship was found between malnutrition and the period of diarrhoea.

The last measured weight before discharge was collected in 938 patients, with a minimum of 4 days between weight measurement at admission and before discharge. Of those, 23% ($n = 217$) lost weight (0.4 ± 0.4% of admission weight per day), whereas 77% ($n = 721$) gained weight (0.5 ± 0.5% of admission weight per day) or showed no weight change (total change less than 1% from admission weight). Of all children who lost weight 3.7% had a total loss of more than 5%. Within the group of patients already malnourished at admission this percentage was 6.8%.

### 3.7. Quality of life

All four questions were completed for 99% of the children ≥2 years of age ($n = 1746$). Within this subgroup BMI was available for

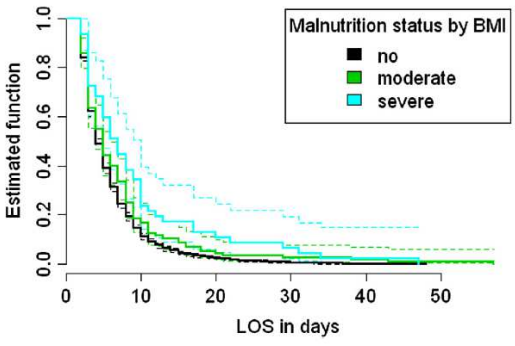


**Fig. 1.** Kaplan–Meier curves (with 95% confidence bounds; dotted lines) for length of stay of severe (<−3 SDS BMI, $n = 47$), moderate (<−2 to −3 SDS BMI, $n = 120$) or not malnourished patients ($n = 2243$). They show the probability that a patient stays for a time period (in days) in the hospital.

**Table 3**
Effects for nutrition status on LOS of a zero truncated regression with robust variance estimation by centre.

| Normal | Model 1[a] | | Model 2[b] | | Model 3[c] | |
|---|---|---|---|---|---|---|
| | – | | – | | – | |
| Moderate | 1.23 (0.97,1.57) | 0.082 | 1.26 (1.02, 1.56) | 0.034 | 1.25 (1.01,1.55) | 0.040 |
| Severe | 1.63 (1.27,2.11) | <0.001 | 1.57 (1.20, 2.03) | <0.001 | 1.63 (1.27,2.10) | <0.001 |

Effect on length of hospital stay (LOS) with CI 95 and *p*-value for children with BMI ≥ −2 SDS (normal), BMI < −2 SDS and ≥ −3 SDS (moderate malnutrition) and BMI ≤ −3 SDS (severe malnutrition).
[a] Model 1: Unadjusted ($n = 2410$).
[b] Model 2: Age, sex, chronic disease status and centre adjusted ($n = 2406$).
[c] Model 3: Age, sex, chronic disease and centre adjusted and additionally interactions between centre and chronic disease status ($n = 2406$); superior model according to AIC and BIC.

1644 patients of which 94 were classified as malnourished. Most patients (92%) indicated a good regular quality of life at time of admission with a score of 0–3. Within the malnourished patients 15.1% had a total score ≥4 indicating non optimal quality of life, whereas for the well-nourished group this was 6.4% (Fisher's exact test, $p < 0.001$) (Table 5).

### 3.8. Nutritional support

Of all participants, 11.8% ($n = 302$) received enteral and/or parenteral nutrition support prior to admission (6.9% ($n = 176$) oral supplements, 4.9% ($n = 127$) tube feeding and 0.6% ($n = 15$) parenteral nutrition) and 12.3% ($n = 314$) during their hospital stay (6.2% ($n = 158$) oral supplements, 6.1% ($n = 157$) tube feeding and 0.8% ($n = 20$) parenteral nutrition). Close to 80% of the children who already received nutritional support prior to admission continued to receive support during their hospital stay ($n = 229$). Children who received nutritional support during their hospital stay or prior to admission had a high prevalence of malnutrition of 17.9% and 15.4%, respectively. They were also more likely to be of stunted height with a percentage of 23.4% and 23.8%, respectively. Overall, 25.2% of the malnourished children received nutritional support prior to admission and 30.5% received support during their hospitalisation, with a median LOS of 6 days (IQR: 3–11 days).

### 3.9. Stunting

Shunting (length/height < −2 SDS), was present in 7.9% of the study population, with a higher prevalence of 11.4% in patients with an underlying chronic disease. Overall, 63.7% ($n = 123$) of all stunted children had an underlying chronic disease. The highest percentage of stunting (10.7%) was found in children aged 1–2 years (Table 2). The prevalence decreased with increasing age to 5.6% in children 13 years or older ($Chi^2$-test, $p = 0.030$). There were no differences between genders and for the type of admission (acute or elective). The prevalence of short stature varied widely between countries (Suppl. Table 2). It was most prevalent in children with endocrine, nutritional or metabolic diseases (ICD 10 – E).

Stunted children did not have a longer LOS than non-stunted children (Wilcoxon test, $p = 0.772$). Stunted children did not have significantly more episodes of fever (21% vs. 19% $Chi^2$-test, $p = 0.5921$) or diarrhoea (15% vs. 13% $Chi^2$-test, $p = 0.436$), and they did not receive more antibiotics (40% vs. 37% $Chi^2$-test, $p = 0.460$). However, stunted children vomited more frequently (21% vs. 14% $Chi^2$-test, $p = 0.016$) and received more nutritional support (35% vs. 10% $Chi^2$-test, $p < 0.001$) during their hospital stay, while 34% received nutritional support prior to admission. Lower quality of life was indicated by a higher total score (Table 5).

Overall, either BMI < −2 SDS or HFA < −2 SDS was present in 13.4% of the patients, whereas both low BMI and low HFA combined was found in 1.6% of the patients.

## 4. Discussion

This multi-centre cohort study shows that disease associated malnutrition occurs frequently on paediatric wards in Europe and is associated with longer LOS and other adverse outcomes, with implications for the patients' quality of life. Malnutrition and stunting in European hospitalised children is associated with chronic underlying diseases, especially in those with disorders of the digestive, neurocognitive, endocrine and metabolic system.

The appreciation of nutritional teams and the importance of malnutrition need to be strengthened in paediatric hospitals. Nutritional teams are the task force for assessment and management of disease associated malnutrition that still occurs in an unacceptable high number of patients. The prevalence might be even higher in the overall admitted population due to a possible recruitment bias against sicker and against non-Caucasian children.

Less than one third of the underweight patients received nutritional support during hospital stay; eighty percent of those already got support prior to this hospital admission. The benefits of nutritional intervention not only on gain in BMI SD-score or height for age but also for improvement of the patient's quality of life[15] and functional outcomes should be assessed further to convince hospital administration, health authorities and young doctors about their accountability to support nutritional interventions. Our study cannot establish causality but it offers hints for studies to explore this association with a prospective intervention approach and it underlines the importance of disease associated malnutrition and its possible implications in the paediatric population.

The rate of weight loss in our studied population was similar to the findings of Hulst et al.[9] where weight loss was present in 35% of the patients with a hospital stay of 4 days or longer. Poor nutritional intake, pain and severity of disease were previously discussed as potential reasons for loss of body weight during hospital stay.[16] We found weight loss during hospital stay in well- and malnourished children. Loss of body weight in the hospital is not favourable and underlines the importance of the nutritional team.

The strengths of our study are the large number of centres and participants and the prospective design. Due to the training prior to the recruitment, data collection and measurements were performed with great consistency. Furthermore, the assessment of quality of life is a new element in studies concerning hospital related malnutrition.

But the multicentre, multi-country character of the study also introduces variations. Body weight and size were compared to an

**Table 4**
Occurrence of secondary outcomes among malnourished and not malnourished paediatric patients.

| Outcome | Occurrence *n* (%) | | *P*-value[b] |
|---|---|---|---|
| | Not malnourished ($n = 2235$) | Malnourished[a] ($n = 167$) | |
| Fever | 428 (19%) | 42 (25%) | 0.074 |
| Use of antibiotics | 831 (37%) | 75 (45%) | 0.057 |
| Diarrhoea | 275 (12%) | 37 (22%) | <0.001[c] |
| Vomiting | 308 (14%) | 43 (26%) | <0.001[d] |

[a] Defined as body mass index <−2 standard deviation scores.
[b] $Chi^2$-test.
[c] $p = 0.008$ after excluding the malnourished children with present dehydration ($n = 12$).
[d] $p < 0.001$ after excluding the malnourished children with present dehydration ($n = 12$).

**Table 5**
Quality of life score in children ≥ 2 years of age.

| Score | 0 | 1 | 2 | 3 | 4–9 | 10–15 |
|---|---|---|---|---|---|---|
| BMI[a] < −2 SDS[c] ($n = 94$) | 50 (53.2%) | 15 (16.0%) | 7 (7.4%) | 4 (4.2%) | 14 (14.9%) | 4 (4.2%) |
| BMI ≥ −2 SDS ($n = 1550$) | 1042 (67.2%) | 199 (12.9%) | 135 (8.7%) | 75 (4.8%) | 81 (5.2%) | 18 (1.2%) |
| HFA[b] < −2 SDS[d] ($n = 115$) | 50 (43.5%) | 13 (11.3%) | 11 (9.6%) | 6 (5.2%) | 26 (22.6%) | 9 (7.8%) |
| HFA < −2 SDS ($n = 1532$) | 1045 (68.2%) | 201 (13.1%) | 131 (8.6%) | 73 (4.8%) | 69 (4.5%) | 13 (1%) |

[a] Body mass index.
[b] Height/length for age.
[c] Fisher's exact test; comparison between the malnourished and not malnourished patients; $p < 0.001$.
[d] Fisher's exact test; comparison between patients with and without stunting; $p < 0.001$.

international reference to characterise the heterogeneous study population. Disease was coded according to the International Classification of Diseases, but still variation was large making meaningful subgroup analysis difficult. As expected median LOS varied within centres which had to be considered when fitting the regression model.

LOS has been criticized as an outcome measurement influenced by many non-nutritional factors. However, LOS is related to adverse effects of under-nutrition such as infections, gastrointestinal complications and impaired organ function.[17,18] We found an association between reduced BMI and LOS in a large group of hospitalised children across Europe which persists after adjustment for age, gender and chronic disease, despite different hospital discharge policies in different countries. LOS was 1.3 days longer for children with a BMI < −2 SDS, leading to a markedly increased cost of hospital treatment in the malnourished group.

In children with diarrhoea and vomiting, e.g. gastroenteritis patients, dehydration can be present and may mimick malnutrition. However, children with a BMI <−2 SDS without reported dehydration experienced diarrhoea and vomiting more often. In some patient groups, e.g. children with stunted height, oncology patients or patients with ascite or edema arm anthropometry might be a good alternative to BMI.

Prevalence rates of malnutrition based on a low BMI were very different among centres in the different countries. These data are not necessarily representative for the respective countries and may be influenced by the particular patient characteristics of the participating hospitals.

Joosten and Hulst[19] stressed the importance of the reference choice when interpreting prevalence rates of malnutrition, which may have important clinical implications.[20] We choose to use the WHO growth standards because they represent an international reference. This choice may have influenced the reported malnutrition prevalence. However, the differences from previous studies and between centres are small and strengthen the generalisability of our findings.

We consider the use of BMI based on WHO references a suitable and feasible choice to assess the global nutritional status and its association to length of hospital stay in this mixed hospital population aged 1 month to 18 years in developed countries.[10,12] The investigation of the subgroup <5 years of age showed that the use of the more conventional measure of WFH SDS found similar prevalence rates.

BMI was not available in 6% of the participants in this study because of disease or other reasons. These patients were included because this study also investigates the value of three previously proposed malnutrition risk screening tools. In these patients it is important for the nutritional team to work with other parameters such as weight for age, arm anthropometry or bioelectrical impedance analysis.

Further limitations to our study included the dependence on the parents' agreement on study participation which involves the risk of recruitment bias. Parents of adolescents were less likely to be available for consent within the first 24 h after admission than parents of young children who stayed more often with their children in the hospital. Thus the study population was younger than the overall hospital population. As in previous studies, malnutrition prevalence was highest in the youngest patients.[21] Of importance, we experienced that parents of severely ill children often declined study participation and critically ill children admitted to the intensive care were excluded per protocol. Both groups have a high risk for malnutrition. The proportion of non-Caucasian children could be underestimated because of exclusion due to refusal or language barriers and difficulties in communication. As included non-Caucasian children were more likely to be malnourished the prevalence of disease associated malnutrition might be higher in the admitted hospital population. A further limitation of our study is the high number of missed patients due to the absence of patients, parents or assessors. As the assessors did not work on the wards on a regularly basis and as they had to cover more wards it was not feasible be present on all wards within 24 h after each admission. They consecutively approached all patients they could reach within the first 24 h after admission.

In conclusion, disease related malnutrition in hospitalized children is frequent and is associated with prolonged length of hospitalisation, other outcomes and lower quality of life with a presumed increased cost of health care. Therefore effective and early detection and treatment of disease associated malnutrition are key priorities. They should become the common interest of hospital administration, doctors and health authorities represented in collaboration with and appreciation for nutritional teams.

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**Statement of authorship**

CH contributed to writing the study protocol, coordinated the study, participated in its conduction, performed the data entry, management and analyses and drafted the manuscript. MW and VG participated in the design of the study, the sample analyses and helped with the statistical analyses. BK conceived of the study, participated in its design, contributed to writing the study protocol and helped to draft the manuscript. RS, JH, KJ, HK, JK and HS participated in the initial part of study design, contributed in the sample collection, data interpretation and analysis and revised the draft of manuscript. KO (Warsaw study centre), JR (Lille study centre) and AVR (Oxford study centre) were responsible for data acquisition (measurements, questionnaires completion and study records). FG (Lille study centre) and TK-L (Thessaloniki study centre) coordinated and supervised the study conduction and participated in data interpretation and analysis. ED was responsible for data acquisition in Thessaloniki study centre and revised the manuscript.

SK (Zagreb study centre), CH (Petah Tikvah study centre), PBS (Oxford study centre), KG and DF (Glasgow study centre) coordinated and supervised the study conduction. KG commented on the original draft. TN was responsible for data acquisition in the Zagreb study centre and participated in data interpretation and analysis. LD and PP were responsible for study conduction and data acquisition in Milan study centre. AP contributed to the sample collection and was responsible for data acquisition in Warsaw study centre.

All authors read and approved the final manuscript.

## Conflict of interest

There is no conflict of interest from authors related to this study.

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## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.clnu.2014.01.003.

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**Supplementary Table1**

**Supplementary Table 1**

Diagnosis leading to hospital admission ordered by prevalence of underweight (< -2 SDS BMI)

| ICD 10 chapters (n = 2406) | Underweight[a] n (%) | Stunting[b] n (%) | Sum n (%) |
|---|---|---|---|
| Mental & behavioural (n = 44) | 5 (11.4 %) | 0 (0.0 %) | 5 (11.4 %) |
| Digestive (n = 244) | 25 (10.3 %) | 21 (8.6 %) | 41 (16.8 %) |
| Endocrine/nutritional/metabolic (n = 130) | 13 (10.0 %) | 24 (18.5 %) | 31 (23.8 %) |
| Infectious & parasitic (n = 142) | 13 (9.2 %) | 9 (6.3 %) | 20 (14.1 %) |
| Pregnancy, perinatal period… (n = 210) | 17 (8.1 %) | 26 (12.3 %) | 37 (17.6 %) |
| Respiratory (n = 408) | 32 (7.8 %) | 28 (6.8 %) | 54 (13.2 %) |
| Eye & ear (n = 46) | 3 (6.5 %) | 4 (8.7 %) | 7 (15.2 %) |
| Other (n = 472) | 27 (5.7 %) | 44 (9.3 %) | 64 (13.6 %) |
| Injury & poisoning (external) (n = 93) | 5 (5.4 %) | 2 (2.1 %) | 7 (7.5 %) |
| Neurological ( n = 131) | 7 (5.3 %) | 10 (7.3 %) | 15 (11.5 %) |
| Genitourinary (n = 131) | 7 (5.3 %) | 5 (3.8 %) | 12 (9.1 %) |
| Neoplastical & haematological (n = 153) | 8 (5.2 % | 6 (3.9 %) | 13 (8.5 %) |
| Musculoskeletal (n = 85) | 4 (4.7 %) | 6 (7.6 %) | 8 (9.4 %) |
| Circulatory (n = 65) | 1 (1.5 %) | 5 (7.7 %) | 5 (7.7 %) |
| Dermatological (n = 52) | 0 (0.0 %) | 3 (5.7 %) | 3 (5.7 %) |

[a]defined as body mass index < -2 standard deviation scores

[b]defined as height/length for age < -2 standard deviation scores

**Suppl. table 2 revision**

**Supplementary Table 2**

Prevalence rates of underweight, stunting, the sum of both and LOS in 12 European countries, ordered by prevalence of underweight

| Country | Underweight[a] n (%) | Stunting[b] n (%) | Sum n (%) | LOS[c] Median (IQR[d]) [days] |
|---|---|---|---|---|
| England | 5 (4.0 %) | 13 (10.2 %) | 16 (12.5 %) | 3 (2-5) |
| Poland | 9 (4.1 %) | 12 (5.4 %) | 20 (9.0 %) | 6 (3-10) |
| Greece | 10 (4.7 %) | 17 (8.1 %) | 26 (12.3 %) | 5 (3-7) |
| Croatia | 12 (5.5 %) | 4 (1.8 %) | 16 (7.3 %) | 6 (3-9) |
| The Netherlands | 13 (6.2 %) | 14 (6.7 %) | 23 (11.0 %) | 5 (3-9) |
| Italy | 14 (6.4 %) | 15 (6.8 %) | 24 (11.0 %) | 7 (5-9) |
| France | 22 (7.9 %) | 26 (9.2 %) | 44 (15.8 %) | 4 (3-6) |
| Germany | 18 (8.3 %) | 22 (10.2 %) | 36 (16.7 %) | 4 (3-7) |
| Scotland | 15 (8.7 %) | 17 (9.8 %) | 30 (17.4 %) | 3 (2-4) |
| Denmark | 9 (8.7 %) | 6 (5.8 %) | 13 (12.6 %) | 4 (3-7) |
| Romania | 20 (9.2 %) | 27 (12.4 %) | 39 (17.9 %) | 5 (3-8) |
| Israel | 20 (9.3 %) | 20 (9.3 %) | 35 (16.4 %) | 6 (3-9) |

[a]Defined as body mass index < -2 standard deviation scores

[b]Defined as height for age < -2 standard deviation scores

[c]Length of hospital stay

[d]Inter quartile ranges

**Suppl. Quality of life questionnaire**

Espen Network Study "Child Nutrition and Outcome" Patient-ID

**Regular quality of life (for children two years and older)**

SENSATION

- ☐ Able to see, hear and speak normally for age.
- ☐ Ability to see, hear and speak is delayed/limited due to learning difficulty.
- ☐ Requires equipment to see or hear or speak.
- ☐ Sees, hears, or speaks with limitations even with equipment.
- ☐ Blind, deaf, mute.

MOBILITY[1] (show GMFCs illustration sheet)

- ☐ GMFCS Level I: Able to walk, bend, lift, jump and run normally for age.
- ☐ GMFCS Level II: Walks, bends, lifts, jumps or runs with some limitations but does not require help.
- ☐ GMFCS Level III: Requires mechanical equipment (such as canes, crutches, braces, or wheelchair) to walk or get around independently.
- ☐ GMFCS Level IV: Requires the help of another person to walk or get around and requires mechanical equipment as well.
- ☐ GMFCS Level V: Unable to control or use arms and/or legs.

SELF-CARE

- ☐ Eats, bathes, dresses, and uses the toilet normally for age.
- ☐ Eats, bathes, dresses, and uses the toilet independently with difficulty.
- ☐ Requires mechanical equipment to eat, bathe, dress, or use the toilet independently.
- ☐ Requires the help of another person to eat, bathe, dress, or use the toilet.

PAIN

- ☐ Free of pain and discomfort.
- ☐ Occasional pain and discomfort without disruption of normal activities.
- ☐ Frequent pain and discomfort.
- ☐ Frequent pain, frequent disruption of normal activities. Discomfort requires prescription narcotics for relief.
- ☐ Severe pain. Pain not relieved by drugs and constantly disrupts normal activities.

[1] Palisano R., Rosenbaum P., Walter S., Russell D., Wood E., Galuppi B., Development and reliability of a system to classify gross motor function in children with cerebral palsy.Dev. Med Child Neurol 1997 Apr; 39:214-223.

3

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# Malnutrition risk in hospitalised children: use of three screening tools in a large European population

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Running title: Risk for malnutrition in hospitalised children

# Malnutrition risk in hospitalised children: use of three screening tools in a large European population°

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46

47 Abbreviations:

48 **BMI**: body mass index; **ESPEN**: European Society for Clinical Nutrition and Metabolism;
49 **HFA**, height for age; **IQR**: interquartile ranges; **LOS**: length of hospital stay; **MUAC**: mid
50 upper arm circumference; **PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening
51 Tool for the Assessment of Malnutrition in Pediatrics; **STRONG$_{KIDS}$**: Screening Tool for
52 Risk Of Impaired Nutritional Status and Growth; **TSFT**: triceps skin fold thickness.

53

54 Trial registration:

55 This study was registered at clinicaltrials.gov as NCT01132742

56

57 **Abstract**

58 **Background:** Several malnutrition screening tools have been advocated for use in pediatric
59 inpatients.

60 **Objective:** This study evaluated how three popular pediatric nutrition screening tools
61 (Pediatric Yorkhill Malnutrition Score-PYMS, Screening Tool for the Assessment of
62 Malnutrition in Pediatrics-STAMP and Screening Tool for Risk of Impaired Nutritional
63 Status and Growth-STRONG$_{KIDS}$) compare and relate to anthropometry, body composition
64 and clinical parameters in patients admitted to tertiary hospitals across Europe.

65 **Design:** The three screening tools were applied in 2567 inpatients in 14 hospitals in 12
66 European countries. Classification of patients into different nutritional risk groups was
67 compared between tools and related to anthropometry and clinical parameters (e.g. length of
68 stay, LOS; infection rates).

69 **Results:** A similar rate of completion of the screening tools for each tool was achieved
70 (PYMS 86%, STAMP 84%, STRONG$_{KIDS}$ 81%). Risk classification differed markedly
71 among tools, with an overall agreement of 41% between the tools. Children categorized at
72 high risk (PYMS 25%, STAMP 23% and STRONG$_{KIDS}$ 10%) had a longer LOS compared to
73 children at low risk (1.4, 1.4 and 1.8 days longer, respectively, $p<0.001$). Among high-risk
74 patients identified with PYMS, 22% had a low (<-2 SD) body mass index (BMI) and 8% a
75 low height-for-age (HFA). For STAMP the respective percentages were 19% and 14% and
76 for STRONG$_{KIDS}$ 23% and 19%.

77 **Conclusion:** Identification and classification of malnutrition risk varies among the pediatric
78 tools used. A considerable portion of children with subnormal anthropometry was not
79 identified with all tools. The data obtained do not allow recommending using any of these
80 screening tools for clinical practice.

81

82 **Key words**

83 Nutritional screening, malnutrition, hospitalized children, PYMS, STAMP, $STRONG_{KIDS}$

84

## Introduction

Malnutrition screening has been advocated as part of patients' standard care (1-3). This is because malnutrition upon admission or deterioration of the nutritional status during hospitalisation has been associated with prolonged hospital stay and adverse outcomes (e.g. increased rates of complications such as infections) although causality in these associations remains to be explored (4-7). Early identification of nutritional risk followed by an appropriate nutritional management was proposed as part of routine clinical practice (8). The "*Guidelines for nutrition screening*" by the European Society for Clinical Nutrition and Metabolism (ESPEN) provide recommendations for adult patients but do not address pediatric patients (9). Screening tools for assessing malnutrition risk for adults have been available for many years (9-11). However similar pediatric tools have only recently been developed and were only tested in small cohorts of hospitalized children (5, 7, 12-14). These tools consist of questions related to the patient's history and measurements or clinical estimation of body size to assess the risk of poor nutritional status (15). They aim to screen all inpatients and identify those missed during routine admission and whose disease outcome would improve or would not deteriorate from tailored nutritional intervention. However, there is a lack of sufficient data on the predictive value of such pediatric screening tools on outcome and objective indices of malnutrition in large multicentre studies, and of comparative evaluation of the various tools. Addressing these aspects may direct health professionals on their decision to select the most suitable nutritional screening tool.

We compared the risk scoring of three previously proposed pediatric nutrition screening tools, i.e. the Pediatric Yorkhill Malnutrition Score (PYMS) (16, 17), the Screening Tool for the Assessment of Malnutrition in Pediatrics (STAMP) (13) and the Screening Tool for Risk Of Impaired Nutritional Status and Growth ($STRONG_{KIDS}$) (5) in a large multi-centre study in children admitted to hospitals across Europe. In addition we explored the agreement among

the tools (concurrent validity) and the relation of risk scores to anthropometry and body composition measurements as well as clinical parameters, such as hospital length of stay (LOS).

It is arguable which could be the best outcome measure for the assessment of the effect of using a screening tool as it is somewhat controversial as to whether such screening tools should predict anthropometry or clinical outcome. Therefore, in this study we aimed to explore the association of the scores provided by the tools with both subnormal BMI and with length of hospital stay (LOS).

## Subjects and methods

### *Study design and subjects*

This prospective European multi-centre cohort study enrolled patients from February 2010 to July 2011 in 14 centres in 12 countries (Zagreb, Croatia; Copenhagen; Denmark, Lille, France; Munich, Germany; Thessaloniki, Greece, Petah Tikvah, Israel; Milan, Italy; Rotterdam and Groningen, the Netherlands; Warsaw, Poland; Cluj-Napoca, Romania; Oxford, England and Glasgow, Scotland). Patients (1 month to 18 years old) admitted to pediatric and pediatric surgery wards with an anticipated length of stay >24 hours were eligible to participate. They were consecutively invited to participate whenever data collection was possible within the first 24 hours after admission. Patients attending the accident and emergency department of the day care unit were excluded.

We excluded children admitted to intensive care because of the limited feasibility to perform detailed anthropometry on the day of admission in critically ill children. To identify children at risk of malnutrition in this group of patients is redundant, since all of these children are -by the nature of their critical illness (e.g. unconscious hence unable to eat)- at

high risk of malnutrition and therefore should receive respective attention of the medical and dietetic staff. The principle of screening is to identify those at risk who might go missed, and to refer to the clinical team. We also excluded children admitted to day hospital care because their expected LOS was shorter than 24 hours. Patients with cerebral palsy or genetic syndromes were not excluded per protocol. Details about the recruitment and the protocol have been previously published by Hecht el al (18).

*Methods*

Patients were assessed by a set of questions considering nutritional risk, and measurements of anthropometry and body composition were all performed within the first 24 hours after admission. The assessors were a multidisciplinary team including research nurses, dietitians, medical students and nutritionists. A training workshop to harmonise recruitment and standardise anthropometry and data collection among the different centres was held in March 2010 at Munich, Germany.

Demographic and medical data together with a questionnaire for nutritional status were collected during a structured interview with patients and (when required) their caregivers. The questionnaire integrated the 4 items of the PYMS tool (16, 17), the 3 items of the STAMP tool (13) and the 4 items of the STRONG$_{KIDS}$ screening tool (5) and sorted them by item content. For each patient, the steps of each tool were completed by the same investigator in the same order. The total score for each screening tool was computed during the analysis of the data. The 28 assessors were encouraged not to add the scores for each tool during data collection to avoid bias by the knowledge on categorization in a screening tool. Only the treating physicians and dietitians, and not the assessors, decided on whether or not to start

nutritional support during hospitalisation. This decision was taken according to normal routine procedures and was not by any means influenced by the study data.

Important characteristics of PYMS (1, 16, 17), STAMP (13, 19), and STRONG$_{KIDS}$ (5, 19) are reported in **Supplemental Table 1.** PYMS and STAMP include anthropometry (BMI vs. weight and height, respectively); STRONG$_{KIDS}$ includes a subjective clinical assessment of nutritional status. Total scores for each tool were computed for those age groups for which the tools were validated: PYMS was completed for patients aged 1 to 16 years, STAMP for patients aged 2 to 16 years and STRONG$_{KIDS}$ for patients aged 1 month to 18 years. For the comparison of the three tools, only children aged 2-16 years were considered, since patients within this age range account as eligible for screening by all three tools.

Data on height, weight, mid upper arm circumference (MUAC) and triceps skin fold thickness (TSFT) were collected. Methods have been described previously by Hecht el al (18). Clinical parameters, including LOS as primary outcome and frequency of infectious complications (number of days with temperature >38.5° C and number of days with antibiotic use) were derived from hospital records after discharge.

The total score and classification of malnutrition risk (low, medium or high) was determined for each study participant and screening tool. The scores obtained by the three screening tools were then related to anthropometry, body composition and outcome data. For the cross-tabulation of risk classification between the tools we decided to group the classification of malnutrition risk into two rather than three categories (i.e. "high": vs. "medium+low") as children allocated in the high group category are the ones that need to be further referred for assessment to the dietetic and clinical team.

179 The study protocol was accepted by the local research/medical ethic committees of each
180 participating centre. Prior to participation informed written consent was obtained by parents
181 and their caregivers (whenever required).

182

183 *Statistical analysis*

184 Risk scores were cross-tabulated within the three screening tools, and agreement rates
185 were computed (concurrent validity). The Cohen's kappa statistic test was applied to describe
186 the level of agreement between the two tools (20) taking into account the agreement occurring
187 by chance. Baseline characteristics between groups were compared using Fisher's exact test
188 or Pearson's $chi^2$-test for categorical data. Linear regression analysis was applied separately
189 for gender to adjust the association of risk for malnutrition with TSFT and MUAC for age,
190 chronic disease and centre. Residuals were checked for normal distribution. In clinical
191 practice a substantial intervention (e.g. referral to a dietitian) will only occur in children with
192 a high-risk score. Therefore in all data analysis except for the random coefficient model, low
193 and medium risk patients for each screening tool were combined and presented as one group
194 versus the high-risk patients.

195 Age- and gender-specific BMI and WFH SD-scores were calculated using the WHO
196 reference data: WHO growth reference study data were used for children aged 1 month to ≤5
197 years (http://www.who.int/childgrowth/software/en/) and further age-adequate WHO
198 reference data were used for patients aged >5-18 years (http://www.who.int/growthref/en/).
199 MUAC and TSFT SD-scores based on WHO reference data were limited to patients aged 3
200 months to 5 years.

201 Multilevel mixed-effects Poisson regression was used to accommodate the general
202 dependence of LOS on the centre of the patient and the existing differences in severity and

type of chronic diseases between centres. Thus, centre was included as a random effect while additionally allowing varying effects by chronic disease status. The association of each nutritional risk classification by PYMS, STAMP and $STRONG_{KIDS}$ with LOS was tested including age, sex and chronic disease status as confounders. An interaction between chronic disease status and nutritional risk classification was also tested.

Furthermore, the percentages of children with suboptimal skinfolds or MUAC and suboptimal BMI who were correctly identified or misclassified at high risk of malnutrition by each tool were calculated and compared to each other. Also the percentage of children classified at high risk despite a normal MUAC, TSFT or BMI was compared among the three tools. In order to have the same children included for each tool, only children aged 2-5 years were included for the analysis of SD-scores for MUAC and TSFT.

Data management and statistical analyses were carried out with R 2.13.2 (*The R Foundation for Statistical Computing; Vienna, Austria*) and Stata 12.1 (StataCorp LP, College Station, TX).

## Results

*Patient characteristics*

A total of 2567 patients (median age 4.7 years; IQR: 1.4, 11.1 years) were enrolled into the study (80% general and 20% pediatric/surgical patients). Nearly half of the study population were females (44.9%), 44.8% had an underlying chronic disease and were electively admitted (18). Most study participants were of Caucasian origin (91%) and were at home prior to admission (91%). Nutritional support prior to admission was administered to 11.8% of the study population. During the hospital stay nutritional support was given to 12.3% of the participants (6.2% oral supplements, 6.1% tube feeding and 0.8% parenteral

227 nutrition, with few overlaps), of whom 76% were already receiving it prior to their admission.
228 Some 20% of children who received nutritional support prior to admission were not allocated
229 to a nutritional support regime after admission, according to hospital data.

230 Median length of hospital stay was 4 days (IQR: 3, 7 days). A BMI <-2 SDS was present
231 in 7.0% of the study population at hospital admission, whereas for HFA<-2 SDS this was the
232 case for 7.9% of the participants.

233

234 *Completion of the screening tools*

235 As each of the three screening tools were developed for different age ranges, the number
236 of eligible children these could be applied to varied among them. Some 933 patients were
237 either <2 or ≥16 years and therefore STAMP could not be completed. Similarly, for 621
238 participants aged either <1 or ≥16 years PYMS could not be applied. In total, PYMS was
239 completed for 1664 (86% of the children in the targeted aged group: *1–16 years*), STAMP
240 was completed for 1374 study participants (84% of children in the targeted aged group: *2–16*
241 *years*), and STRONGKIDS was completed for 2089 (81% of the children in the targeted aged
242 group: *1 month –18 years*). For almost half of the study group (1258 children, 49%) all three
243 tools have been completed. The completion rates of each individual component of the three
244 tools are listed in **Table 1.** As the researchers occasionally found it challenging to respond to
245 some of the steps of the individual tools, a numbers of screens were left incomplete.

246

247 *Malnutrition risk classification*

248 The classification of malnutrition risk of the assessed children by the three screening tools
249 shows a substantial variation among the different tools (**Figure 1**). The risk classification

250 distribution varied markedly also within and between countries (**Figure 2**). Overall the
251 proportion of high risk patients ranged between 5-51% (PYMS: 15-51%, STAMP: 9-51% and
252 $STRONG_{KIDS}$: 5-30%). The greatest difference between the proportions of high-risk patients
253 based on the 3 screening tools within one centre was 32% (Greece).

254 For the 1258 patients in whom all three tools were completed, the distribution of risk
255 classification according to the three screening tools is shown in **Supplemental Figure 1.** In
256 more detail, in this subgroup of 1258 patients the different tools categorized 10%
257 ($STRONG_{KIDS}$) to 22% (STAMP and PYMS) of children in the high-risk group. In total only
258 87 participants (7% of all patients with three completed tools) were jointly rated as at high
259 risk for malnutrition from all three tools. Less than half of the patients (41%) were classified
260 at the same risk level for malnutrition with the use of the three different tools. This percentage
261 increased to 74% when children with low and medium risk were group together and
262 compared to the high risk group. The agreement between the tools, accounting for statistical
263 chance, was fair to moderate. (20)

264 Pairwise comparison resulted in 55% agreement for PYMS with STAMP ($\kappa$=0.31, CI:
265 0.28, 0.35) and 58% PYMS with $STRONG_{KIDS}$ ($\kappa$=0.33, CI: 0.29, 0.37). The greatest degree
266 of agreement was found between STAMP and $STRONG_{KIDS}$ (60%, $\kappa$=0.37, CI: 0.33, 0.40).
267 This agreement increased to 74% when a combined classification "*low+medium*" versus the
268 "*high*" risk group was used. Pairwise comparison between tool pairs resulted in approx. 80%
269 agreement and is shown in **Table 2** (PYMS vs. STAMP: *moderate agreement*, PYMS vs.
270 $STRONG_{KIDS}$: *fair agreement*, and STAMP vs. $STRONG_{KIDS}$ : *fair agreement*) (21).

271

*Clinical characteristics of patients in the three risk groups for each tool*

Characteristics of children within the risk groups of each screening tool are described in **Table 3**. The proportion of patients with an underlying chronic disease was higher for patients identified with high risk vs. medium or low risk for STAMP (75% vs. 53% or 36%) and STRONGKIDS (89% vs. 48% or 30%). With the use of PYMS patients with a chronic disease were equally classified into the three risk categories (48% vs. 49% or 48%). The administration of nutritional support both prior to admission or during the hospital stay was higher for patients identified with high risk vs. medium or low risk for all three tools. Additionally, high-risk patients identified with all three tools experienced fever more frequently and were prescribed more antibiotics than medium-risk-patients and low-risk-patients.

LOS increased from low to high-risk patients as identified by all three tools (**Table 3**). This was also supported by the effect estimates of the multivariate regression analysis taking age, sex, chronic disease and centre into account (**Table 4**).

*Risk categorization and anthropometry*

Mean SD-scores for either BMI or HFA were significantly different between the 3 risk groups within each tool. (**Table 3** and in more details in **Supplemental Table 2**). Additionally, a considerable number of children with low BMI (<-2SD) were not picked up as high-risk (and were categorized either in the low or in the medium risk category) by the three tools. **Table 5** displays relevant differences among the 3 tools for the group of children (n=1253) who completed all three tools and had BMI data available.

MUAC and TSFT were measured in 2263 (88%) and 2094 (82%) study participants respectively. Linear regression results for all three screening tools showed a significant relationship between malnutrition risk and MUAC for both sexes after adjustment for age,

296 chronic disease and centre. SD-scores for MUAC and TSFT for patients ≥ 2 years and ≤ 5
297 years of age in relation to the risk groups of each screening tool can be found in **Table 6**.

298

299 **Discussion**

300 The aim of all three screening tools is to identify children at risk of malnutrition on
301 admission to select patients for further evaluation and potential intervention. However, there
302 are differences concerning the use of these tools, as they were designed for application by
303 different users (pediatricians, nurses etc.) and in different age groups (5, 13, 17). Additionally,
304 PYMS and STAMP include anthropometry, while $STRONG_{KIDS}$ focuses on identifying
305 children at nutritional risk on admission by visual inspection of body habitus alone.

306 This study found marked differences in the number of patients who could be screened by
307 the three tools. Also the scores and classification of malnutrition risk among children varied
308 substantially according to the tool used. Few smaller studies conducted previously have
309 looked into the agreement in nutritional risk classification using PYMS, STAMP and
310 $STRONG_{KIDS}$, and also found this to be modest (19, 22-24). Lack of agreement may be
311 explained by the fact that the tools are different, albeit containing similar steps. While several
312 components within the tools are similar, there are discrepancies in scoring, duration of recall
313 history and approaches to assess body size.

314 By definition (item 1) PYMS was expected to categorize all children with a BMI <-2SD
315 into the high risk category. However, this was not the case for a low number of children (7
316 out of 96) with suboptimal BMI not identified correctly by PYMS. This is likely to be
317 explained by discrepancies in the values of low BMI threshold ($<2^{nd}$ centile), between the
318 WHO growth charts, we used to analyse the data, and the UK-WHO adapted version cited on
319 the original PYMS form.

320 In this study, we assessed the discriminant validity of the screening outcomes of each
321 tool against body composition and explored their ability to predict adverse clinical outcomes.
322 For each tool we found a reverse association between malnutrition risk with body
323 composition and a positive one with LOS. In particular, children scored at high risk for
324 malnutrition, for each tool, stayed longer in the hospital and had lower mean MUAC and
325 TSFT values than the patients with low or medium risk. It should be emphasized that
326 sensitivity and cut off points of MUAC are still debatable, and MUAC might be a more
327 valuable tool in assessing markedly malnourished children. However, it is often considered
328 useful in the clinical assessment and follow-up of patients.

329 The association between the risk score classification and LOS was strongest with
330 STRONG$_{KIDS}$. It is, however, unclear how much of this association is explained by disease
331 severity and how much is attributed to the effect of malnutrition.

332 It is arguable which would be the best benchmark assessing the value of a screening tool.
333 Amaral et al (3) and Kyle et al (25) found a significant association between the screening
334 score of nutrition risk screening tools and LOS in adults, but they stated that LOS is also
335 influenced by many non-nutritional factors. However, adverse effects of malnutrition and the
336 influence of the underlying disease interact and both affect LOS, which should be considered
337 when assessing associations of risk scores and secondary outcomes such as fever or use of
338 antibiotics.

339 We think that it is important that the tools would agree in the detection of the high risk
340 patients including those with a subnormal BMI, HFA and skinfold thickness measurements,
341 which was not the case in this study. We consider as high-risk patients those who need to be
342 referred to a more detailed assessment and are more likely to need nutritional intervention.
343 Moreover, screening tools are also aiming to identify children at risk of deterioration of
344 malnutrition risk due to an acute medical insult despite normal anthropometry at hospital

admission. This encompasses a large proportion of children admitted in acute settings in developed countries and intervention and prevention of weight loss is probably as important as correction of weight loss and growth catch up in those children who are already malnourished (26).

Strengths of our study are its multicentre setting and the large number of participants from different countries. To our best knowledge this is the first study that compares three different screening tools in a large pediatric population. We used one growth reference (the WHO growth standard) for all children and thereby excluded the variation between different country specific growth charts. However, we did not use disease specific growth charts, as available, for example, for cerebral palsy patients, because these are only available for a few selected diagnoses and have generally not been based on pan-European patient populations.. We also acknowledge that our study may have suffered from a sample selection bias as some children who were severely sick may have not joined the study. Additionally a substantial number of children were on nutritional support at study entry which most likely reflects the profile of patients who regularly attend the highly specialised hospitals which participated in this study. A further potential limitation of this study is the fact that we did not perform full nutritional assessment as a reference for the comparison of the screening scores (1, 17). Moreover, with our data we could not account for the effect of disease groups or severity on the association between malnutrition risk and clinical outcome. The power to detect nutrition-associated infections is limited by the generally short LOS of the patients included in the study, which reflects current clinical practice. Large differences were found between countries, which may reflect differences in population characteristics or clinical practice. Furthermore, our study evaluated the screening tools in the specific study population enrolled, and extrapolation of results to other populations may be done cautiously.

369 While for all three tools significant associations were observed between high risk of
370 malnutrition with increased LOS and suboptimal anthropometry, the agreement among tools
371 to classify the same patients at the same risk of malnutrition was modest. While screening
372 tools have potential in enhancing clinicians' awareness on the importance of nutritional status
373 of pediatric patients (1, 23), raising awareness amongst health care professionals alone is not
374 a sufficient justification for establishing an additional investigation in patients. Rather, a
375 reasonable prediction of the risk of malnutrition or of outcome with a good sensitivity and
376 specificity is expected, as a prerequisite for clinical routine use of a screening tool.

377 While $STRONG_{KIDS}$ is not based on anthropometric measurements, the authors
378 describing $STRONG_{KIDS}$ also advocate measuring weight and height as part of assessing
379 nutritional status on admission after the initial risk screening. PYMS or STAMP are based on
380 anthropometry and thus detect the large majority of children with abnormal anthropometric
381 measures (26, 27). However, the use of these tools may be at the expense of too many
382 children being categorized as high risk. Other aspects need to be considered too, such as the
383 clinical performance and impact of any selected tool on current health care resources (e.g.
384 staff workload, practicality).

385 Identification and classification of risk of malnutrition varied among tools and countries.
386 The agreement between s tools was modest, a finding which partially might be attributed to
387 the absence of and a consensus definition and agreed measurements of malnutrition. Based on
388 these findings, no firm conclusions can be drawn about the superiority of one tool over the
389 other tool. Beyond diagnostic validity, we recommend that the selection of the most
390 appropriate tool, for routine use on hospital admission, will further depend on its clinical
391 performance, the availability of and impact on health care resources.

392

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403

404 **Statement of authorship**

405 MC wrote the manuscript, coordinated intragroup reviews and communication, helped with
406 the statistical analyses and drafted the manuscript. CH contributed to writing the study
407 protocol and first draft of the manuscript, coordinated the study, participated in its conduction,
408 and performed the data entry, management and analyses. KG, participated in the initial part of
409 study design, contributed in the sample collection and coordinated intragroup reviews and
410 communication. KJ, TKL, HK, JK, CL, RS, HS and JH participated in the initial part of study
411 design, contributed in the sample collection, were responsible for data acquisition, data
412 interpretation and analysis. BK conceived of the study, participated in its design, contributed
413 to writing the study protocol and helped to draft the manuscript. MC, CH, KG, KJ, BK and
414 JH commented on the first and subsequent drafts. All authors read and approved the final
415 manuscript.

416

## CONFLICT OF INTEREST

The authors hereby declare that the article is original, is not under consideration for publication anywhere else and has not been previously published. Authors declare no potential or actual personal, political or financial interest in the material, information or techniques described in the paper. However, Jessie Hulst, Koen Joosten and Konstantinos Gerasimidis and Diana Flynn have been involved in the development of STRONGKIDS and PYMS, respectively.

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**Table 1:** Scoring of screening tool items for the group of children aged 2-16 years (N=1724) who completed all tools (N = 1258) expressed as N (%)

| | **Scores of children completing ALL tools n = 1258** *(%)* | | | | **Children aged 2-16 years n = 1724** *(%)* | |
|---|---|---|---|---|---|---|
| **ITEMS**[1] | **0** | **1** | **2** | **3** | **Total Assessed** | **Not assessed according to original tool questions** |
| **Item 1: Current nutritional condition**[2] | | | | | | |
| PYMS (0-2) | 1152 (*92*) | | 106 (*8*) | | 1538 (*89*) | 186 (*11*) |
| STAMP (0-1-3) | 967 (*77*) | 169 (*13*) | | 122 (*10*) | 1474 (*85*) | 250 (*15*) |
| $STRONG_{KIDS}$ (0-1) | 1031 (*82*) | 227 (*18*) | | | 1607 (*93*) | 117 (*7*) |
| **Item 2: Weight loss**[3] | | | | | | |
| PYMS (0-1) | 1036 (*82*) | 222 (*18*) | | | 1568 (*91*) | 156 (*9*) |
| STAMP (NA) | | | | | | |
| $STRONG_{KIDS}$ (0-1) | 1027 (*82*) | 231 (*18*) | | | 1633 (*95*) | 91 (*5*) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Item 3: Reduced intake**[4] | | | | | | |
| PYMS (0-1-2) | 1004 (*80*) | 228 (*18*) | 26 (*2*) | | 1633 (*95*) | 91 (*5*) |
| STAMP (0-2-3) | 913 (*73*) | | 317 (*25*) | 28 (*2*) | 1633 (*95*) | 91 (*5*) |
| $STRONG_{KIDS}$ (0-1) | 861 (*68*) | 397 (*32*) | | | 1633 (*95*) | 91 (*5*) |
| **Item 4: Underlying disease**[5] | | | | | | |
| PYMS (0-1-2) | 994 (*79*) | 255 (*20*) | 9 (*1*) | | 1509 (*88*) | 215 (*12*) |
| STAMP (0-2-3) | 670 (*53*) | | 324 (*26*) | 264 (*21*) | 1529 (*89*) | 195 (*11*) |
| $STRONG_{KIDS}$ (0-2) | 893 (*71*) | | 365 (*29*) | | 1515 (*88*) | 209 (*12*) |

[1] Possible scores are put in parentheses and for each item differ for each tool

Risk classification according to total scores differs between the tools:

**low risk:** PYMS: 0 points, STAMP: 0-1 points, $STRONG_{KIDS}$: 0 points

**medium risk:** PYMS: 1 point, STAMP: 2-3 points, $STRONG_{KIDS}$: 1-3 points

**high risk:** PYMS: 2-7 points, STAMP: 4-9 points, $STRONG_{KIDS}$: 4-5 points

[2]**Item 1:**

PYMS: Is the BMI below the cut-off value shown in the BMI Scoring Guide?

STAMP: Use a growth chart or the centile quick reference tables to determine the child's weight and height measurements.

STRONGKIDS: Is the patient in a poor nutritional status judged by subjective clinical assessment?

[3]**Item 2:**

PYMS: Has the child lost weight recently?

STRONGKIDS: Is there weight loss or poor weight gain (infants <1 year) during the last few weeks/months?

[4]**Item 3:**

PYMS: Has the child had a reduced intake (including feeds) for at least the past week?

STAMP: What is the child's nutritional intake?

STRONGKIDS: Is one of the following items present: excessive diarrhoea (≥5/day) and/ or vomiting (>3/day), reduced food intake during the last few days, pre-existing nutritional intervention or inadequate nutritional intake due to pain?

[5]**Item 4:**

PYMS: Will the child's nutrition be affected by the recent admission/condition for at least the next week?

STAMP: Does the child have a diagnosis that has any nutritional implication?

STRONGKIDS: Is there an underling illness with risk for malnutrition or expected major surgery?

**PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening Tool for the Assessment of Malnutrition in Pediatrics; **STRONGKIDS**: Screening Tool for Risk Of Impaired Nutritional Status and Growth.

**Table 2:** Cross-tabulation of risk classification between PYMS, STAMP and STRONGKIDS

| | | Risk for malnutrition | | |
|---|---|---|---|---|
| | | low + medium | high | |
| agreement 82% ( n=1308) | | **STAMP** | | |
| **PYMS** | low + medium | 897 | 121 | κ= 0.47 (CI: 0.42, 0.53) |
| | high | 118 | 172 | |
| agreement 83% ( n = 1318) | | **$STRONG_{KIDS}$** | | |
| **STAMP** | low + medium | 990 | 32 | κ= 0.39 (CI: 0.33, 0.45) |
| | high | 187 | 109 | |
| agreement 81% (n = 1490) | | **PYMS** | | |
| **$STRONG_{KIDS}$** | low + medium | 1088 | 249 | κ= 0.35 (CI: 0.28, 0.42) |
| | high | 39 | 114 | |

**PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening Tool for the Assessment of Malnutrition in Pediatrics; **$STRONG_{KIDS}$**: Screening Tool for Risk Of Impaired Nutritional Status and Growth.

**Table 3:** Characteristics of children within the risk groups of each screening tool

| | PYMS (1–16y) N=1664 | | | STAMP (2–16y) N=1374 | | | STRONGKIDS (1m–18y) N=2089 | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Low N=943** | **Medium N=305** | **High N=416** | **Low N=512** | **Medium N=547** | **High N=315** | **Low N=915** | **Medium N=968** | **High N=206** |
| Median age (y) (95% IQR) | 7.4 (3.6, 11.3) | 5.8 (3.0, 11.3) | 4.4 (2.0, 9.9) | 8.3 (4.7, 12.0) | 7.8 (4.1, 12.0) | 7.6 (3.8, 12.3) | 5.1 (1.3, 11.2) | 4.4 (1.4, 10.6) | 6.3 (1.9, 12.6) |
| Age groups (%) | | | | | | | | | |
| 31 days – 0.9 y | 0 | 0 | 0 | 0 | 0 | 0 | 21 | 18 | 15 |
| 1 – 1.9 y | 12 | 13 | 24 | 0 | 0 | 0 | 10 | 14 | 10 |
| 2 – 5.9 y | 30 | 37 | 34 | 34 | 39 | 41 | 23 | 26 | 24 |
| 6 – 12.9 y | 40 | 32 | 29 | 49 | 41 | 38 | 29 | 26 | 27 |
| 13 – 17.9 y | 18 | 18 | 13 | 17 | 20 | 21 | 17 | 17 | 24 |
| Female (%) | 44 | 50 | 43 | 46 | 45 | 43 | 44 | 45 | 44 |
| Caucasian (%) | 92 | 93 | 90 | 94 | 91 | 92 | 92 | 91 | 88 |
| Acute admission (%) | 45 | 54 | 65 | 52 | 48 | 53 | 48 | 62 | 58 |

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| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Chronic disease (%) | 48 | 49 | 48 | 36 | 53 | 75 | 30 | 48 | 89 |
| Surgical (%) | 20 | 21 | 17 | 16 | 21 | 19 | 25 | 15 | 20 |
| BMI- SDS (mean, SD) | 0.52 (1.23) | 0.28 (1.14) | -0.77 (1.58) | 0.46 (1.17) | 0.15 (1.23) | -0.30 (1.85) | 0.42 (1.25) | -0.04 (1.37) | -1.19 (1.61) |
| HFA-SDS (mean, SD) | 0.15 (1.37) | 0.19 (1.43) | -0.19 (1.54) | 0.38 (1.25) | 0.02 (1.29) | -0.34 (1.62) | 0.37 (1.31) | 0.04 (1.38) | -0.86 (1.97) |
| Nutritional support (%) Prior admission | 6 | 11 | 24 | 1 | 9 | 26 | 1 | 11 | 54 |
| Nutritional support (%) During hospitalization | 5 | 12 | 25 | 1 | 9 | 27 | 2 | 11 | 56 |
| LOS (median (IQR), days) | 4 (3, 6) | 5 (3, 8) | 5 (3, 9) | 4 (3, 7) | 4 (3, 7) | 5 (3, 8) | 4 (3, 7) | 4 (3, 7) | 6 (3, 10) |
| Secondary outcomes (%) | | | | | | | | | |
| Fever (%)[1] | 10 | 21 | 29 | 10 | 17 | 19 | 13 | 23 | 23 |
| Use of antibiotics (%)[2] | 28 | 44 | 44 | 28 | 33 | 41 | 28 | 43 | 44 |

[1] At least one event-day of fever



[2] At least one event-day of antibiotics

**PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening Tool for the Assessment of Malnutrition in Pediatrics; **STRONG$_{KIDS}$**: Screening Tool for Risk Of Impaired Nutritional Status and Growth. **BMI**: body mass index; **SDS**: standard deviation score; **HFA**: height for age; **LOS**: length of stay.

Percentages and median (IQR) are reported for the total number of children in the risk groups of each screening tool.



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**Table 4:** Relationship between LOS and nutritional risk classification using a random coefficient model[1] (95% CI), P-value

| | **PYMS** *(N=1669)* | **STAMP** *(N=1379)* | **STRONG$_{KIDS}$** *(N=2089)* |
|---|---|---|---|
| **Low risk** | - | - | - |
| **Medium risk** | 1.11[2] *< 0.001* (1.05, 1.18) | 1.08 *0.005* (1.02, 1.14) | 1.19 *< 0.001* (1.14, 1.24) |
| **High risk** | 1.38 *< 0.001* (1.32, 1.45) | 1.37 *< 0.001* (1.29, 1.46) | 1.82 *< 0.001* (1.72, 1.93) |

[1] Adjusted for Age, sex and chronic disease status and taking the dependence within centres into account while

[2] Comparison to low risk category, i.e. medium risk patients stayed 1.11 days longer in the hospital than the low risk patients scored by PYMS.

**PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening Tool for the Assessment of Malnutrition in Pediatrics; **STRONG$_{KIDS}$**: Screening Tool for Risk Of Impaired Nutritional Status and Growth; **LOS**: length of stay.

**Table 5:** BMI SD-scores within the risk groups of three malnutrition risk screening tools (for the 1253 out of 1258 completing all tools)

| BMI | **PYMS** (2–16y) N=1253[1] | | | **STAMP** (2–16y) N=1253[1] | | | **STRONG$_{KIDS}$** (2-16y) N=1253[1] | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Low** N= 757 | **Medium** N=222 | **High** N= 274 | **Low** N= 485 | **Medium** N= 494 | **High** N= 274 | **Low** N=575 | **Medium** N=550 | **High** N=128 |
| Mean *(SD)* | 0.50 ( 1.25) | 0.23 ( 1.16) | -0.78 ( 1.55) | 0.45 ( 1.18) | 0.14 ( 1.23) | -0.27 ( 1.88) | 0.53 ( 1.26) | 0.05 ( 1.39) | -0.88 ( 1.50) |
| ≥ -1SDS | **687** | 190 | 147 | **437** | 410 | 177 | **518** | 434 | 72 |
| <-1 to ≥-2 SDS | 66 | **30** | 67 | 42 | **75** | 46 | 49 | **88** | 26 |
| < -2 SDS | 4 | 2 | **60** | 6 | 9 | **51** | 8 | 28 | **30** |
| % of BMI <-2SD **NOT** categorized in the high-risk group | 9.1% *(6/66)* | | | 22.7% *(15/66)* | | | 54.6% *(36/66)* | | |



[1] All children with completion of the tool and BMI.For 5 children no BMI could be calculated due to length value missing.

**PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening Tool for the Assessment of Malnutrition in Pediatrics; **STRONG$_{KIDS}$**: Screening Tool for Risk Of Impaired Nutritional Status and Growth; **SD**: standard deviation; **BMI**: body mass index.



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**Table 6:** MUAC and TSFT SD-scores for children ≥2 and ≤5 years old within the risk groups of three malnutrition risk screening tools

| | **PYMS** | | | **STAMP** | | | **STRONG$_{KIDS}$** | | |
|---|---|---|---|---|---|---|---|---|---|
| **MUAC** | N=407[1] | | | N=389[1] | | | N=401[1] | | |
| | low | medium | high | low | medium | high | low | medium | high |
| Mean *(SD)* | 0.52 *(1.17)* | 0.24 *(1.18)* | -0.27 *(1.13)* | 0.44 *(1.15)* | 0.31 *(1.11)* | -0.21 *(1.33)* | 0.67 *(1.13)* | 0.17 *(1.29)* | -0.81 *(1.16)* |
| ≥ -1SDS | 197 | 75 | 82 | 119 | 149 | 69 | 156 | 173 | 19 |
| <-1 to ≥-2 SDS | 13 | 12 | 16 | 10 | 18 | 13 | 5 | 27 | 9 |
| < -2 SDS | 4 | 0 | 8 | 1 | 1 | 9 | 0 | 7 | 5 |
| **TSFT** | N=382[2] | | | N=361[2] | | | N=365[2] | | |
| | low | medium | high | low | medium | high | low | medium | high |
| Mean *(SD)* | 1.13 *(1.22)* | 0.85 *(1.12)* | 0.42 *(1.33)* | 0.96 *(1.23)* | 0.88 *(1.15)* | 0.75 *(1.50)* | 1.09 *(1.23)* | 0.87 *(1.30)* | 0.34 *(1.32)* |
| ≥ -1SDS | 192 | 81 | 84 | 117 | 150 | 70 | 140 | 178 | 23 |
| < 1 to ≥2 SDS | 8 | 2 | 10 | 7 | 4 | 8 | 7 | 9 | 3 |
| < -2 SDS | 0 | 1 | 4 | 1 | 2 | 2 | 0 | 4 | 1 |

[1] All children with completion of the tool and MUAC (e.g. PYMS and MUAC)

[2] All children with completion of the tool and TSFT (e.g. PYMS and TSFT).



**PYMS**: Pediatric Yorkhill Malnutrition Score; **STAMP**: Screening Tool for the Assessment of Malnutrition in Pediatrics; **STRONG$_{KIDS}$**: Screening Tool for Risk Of Impaired Nutritional Status and Growth; **SD**: standard deviation; **MUAC**: mid upper arm circumference; **TSFT**: triceps skin fold thickness

**Figure 1:** Malnutrition risk classification based on the 3 screening tools expressed as percentages of the total number of assessed children for each tool.

**Figure 2:** Prevalence of malnutrition risk in different countries using the different screening tools.

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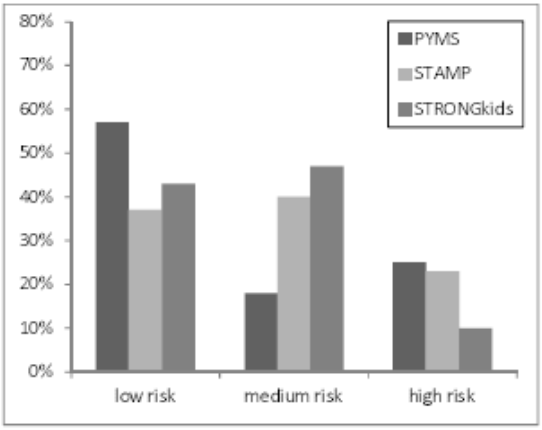

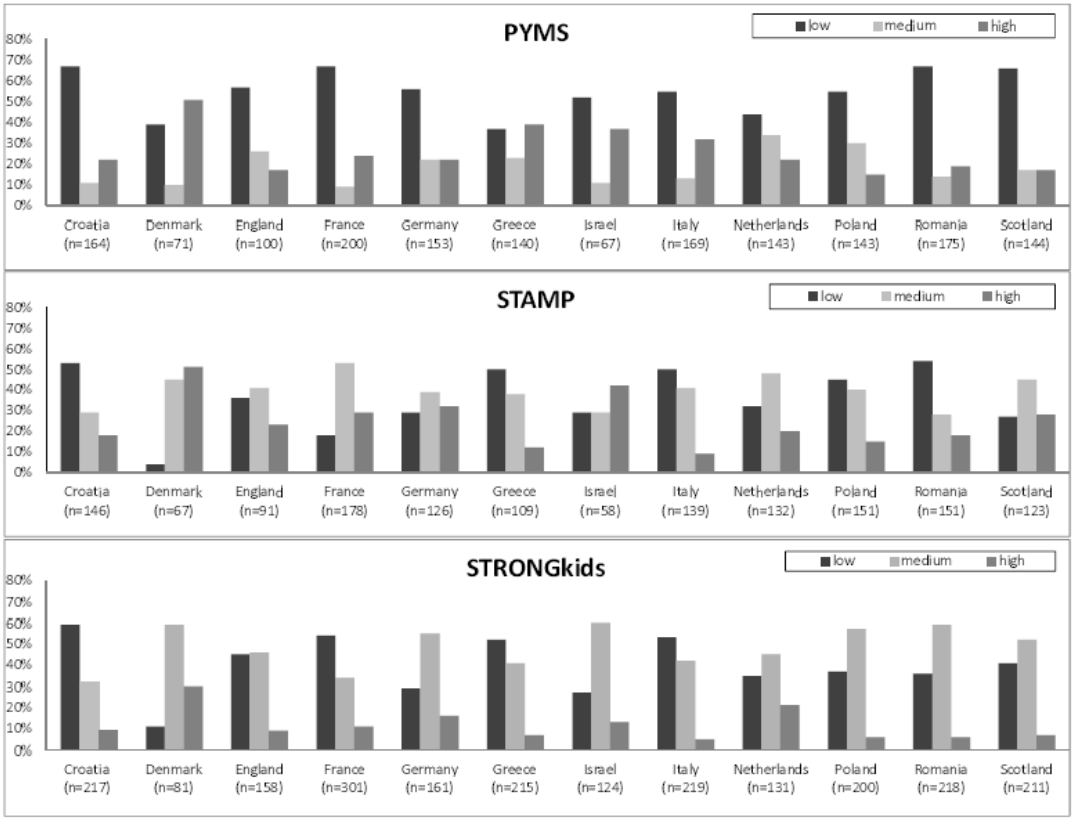


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