Evaluation of a New Infant Nutrition Screening Tool (Infant Paediatric Yorkhill Malnutrition Score) and its applicability in Iran as compared to the United Kingdom

Shamsi Afiat Milani

BSc and MSc in Nutrition sciences

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University of Glasgow
United Kingdom

Author's declaration

I hereby declare that the work contained within this thesis is original and my own work and has not been submitted for any other degree at the University of Glasgow or any other institution, except where due acknowledgment is made in the thesis.

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Without the infants and their care givers who participated, this study would have been impossible and I thank them. I hope this will have contributed at least in some way to reducing malnutrition in paediatric inpatients.

Dedicated to my eldest brother

Mahmoud Milani

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ABBREVIATION LIST

BCM	Body Cell Mass
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
DXA	Dual – energy x- ray absorptiometry
ECW	Extra-Cellular Water
ESPEN	European Society of Parenteral and Enteral Nutrition
FFM	Fat Free Mass
FM	Fat Mass
FTT	Failure to Thrive
GP	General Practitioner
HFA	Height for Age
HV	Health Visitor
ICW	Intracellular water
LM	Lean Mass
LMI	Lean Mass Index
LOS	Length of stay
MRI	Magnetic Resonance Imaging
MUAC	Mid Upper Arm Circumference
PYMS	Paediatric Yorkhill Malnutrition Score
SES	Socioeconomic status
SGNA	Subjective Global Nutritional Assessment
STAMP	Screening Tool for the Assessment of Malnutrition in Paediatrics
STRONGkids	Screening Tool Risk on Nutritional status and Growth
TBW	Total Body Water
TSF	Triceps skin-fold
UK	United Kingdom
WFA	Weight for Age
WFH	Weight for Height
WHO	World Health Organization
DGH	District General Hospital
TPH	Tertiary Paediatric Hospital

ABSTRACT

A high prevalence of malnutrition has been reported in paediatric inpatients both in developed and developing countries, using various methodology and criteria. According to national and international guidelines, all inpatients should be screened for risk of malnutrition on admission using a validated screening tool. However, because of the lack of universally accepted definition for malnutrition, there is no consensus on the measures and methods to use for nutritional screening. There is controversy concerning the validity, reliability and practicality of existing paediatric nutrition screening tools**.** Moreover, current paediatric screening tools have not been designed and validated for infants.

The study aimed to

1) Validate a novel malnutrition screening scheme for infants - the Infant Paediatric Yorkhill Malnutrition Score (iPYMS) and compare its utility in different hospital settings, in UK and Middle East, Iran
2) Compare the usefulness of various anthropometric measures to predict malnutrition in infants
3) Determine the factors that correlated with malnutrition in hospitalised infants
4) Explore the use of body composition measures in sick infants

The Paediatric Yorkhill Malnutrition Score (PYMS) had already been developed in Glasgow for use in children admitted to hospital. It utilized four elements that were reported as recognized predictors of the past, present or future nutrition risk. An audit was carried out at the beginning of the PhD course and aimed to evaluate the effect of PYMS on collection of anthropometric measurements in the wards**.** Findings suggested that introduction of a screening tool improved the acquisition of anthropometry by nursing staff, but their utilization by medical staff remained poor.

Method

The Infant Paediatric Yorkhill Malnutrition Score (iPYMS) was developed by the research team. The score encompasses 4 rated steps that similar to those used for older children: weight $<2^{nd}$ and 9^{th}centile was used as opposed to BMI, and 3 elements concerning the history of nutritional issues. A score of 1 classifies a patient at medium risk and ≥2 or ≥3 indicates high risk. Infants were studied at admission to two tertiary children's hospital, 210 (0-12 months) in

Glasgow, UK and 187 (1-12 months) in Tabriz, Iran. Convenience sampling was used to recruit equal number of patients in each risk group. Four researchers recruited the samples for the UK cohort and one for the Iran cohort.

The diagnostic accuracy and validity of iPYMS in both cohorts were assessed by comparing the iPYMS nutritional risk with the Paediatric Subjective Global Nutritional Assessment (SGNA) that determine malnutrition risk and mean skinfolds z-scores (triceps and subscapular) below <-2SD as the benchmark for low fat stores and acute/chronic malnutrition. Discriminant validity was assessed using body composition and anthropometry measurements, with the hypothesis that infants at high risk of malnutrition will have lower fat and possibly lean mass compared with those at low risk.

Results

More infants in Iran (32%) were rated as high risk for undernutrition than UK (7%). The diagnostic performance of iPYMS improved with the cut-off ≥ 3, more so in Iran than the UK. In Iran, only, infants who were classified as being at high risk of malnutrition had longer hospital stay. Infants in the iPYMS moderate and high risk groups all had significantly lower mean SD-score for anthropometry. After excluding patients scored high risk based only on low weight z-score (≤-2 SD), the differences in weight and BMI z-scores remained significant. In Iran 76% infants with raised iPYMS had mean skinfolds <-2SD, but only 5% in the UK. The UK infants may thus not actually be malnourished. They may be ill and just at risk of malnutrition.

The first step of iPYMS (weight below <9th or 2nd centile) was a strong predictor of malnutrition risk, more so in Iran; in the Iranian cohort, 91% and in the UK 70% of infants above the high risk threshold of ≥ 3 scored as high risk due to the weight below <9th or 2nd centile.

ROC Analysis either with SGNA or sum skinfolds z-score as the main outcomes illustrated that admission weight and growth velocity had almost the same predictive value in predicting malnutrition risk. This suggests that weight velocity is no improvement on weight alone as a predictor of malnutrition.

Current breast feeding was found to be an independent predictor of malnutrition in Iran. Socioeconomic factors were weak predictors of malnutrition in this population.

There is a lack of validated and suitable methods to assess body composition in infants. To determine whether analysing bio-electrical impedance data is practical in our young age range

population, this was compared to skinfolds thicknesses and how the two measures of body composition varied relative to SGNA. The WHO standard for skinfolds only starts at 3 months, excluding nearly one third of infants in the Iran cohort and half in the UK**.** An iPYMS skinfold reference was thus generated using the iPYMS dataset for the UK cohort, as this was a population with low rates of malnutrition risk who had skinfolds levels mainly within the WHO range beyond age 3 months. In Iran, most high SGNA risk infants (72%) had low skinfolds, but in UK there was no association. Iranian infants had much lower mean lean and fat than the UK infants. Fat measured by BIA varied by SGNA rating risk group with both cohorts, but lean differed between risk groups only for Iran cohort.

Conclusion

Malnutrition was common in this tertiary children's hospital in Iran. iPYMS might perform well in this setting and could be used by health professionals to identify infants with malnutrition. In contrast, in the UK, iPYMS would mainly identify infants at risk of malnutrition, because of the low prevalence of under-nutrition. On the other hand, we found that weight alone (the first component of iPYMS) is a robust predictor of malnutrition risk. Therefore iPYMS may not add any advantage over the simple measurement of weight alone to identify infants at risk of malnutrition. This is essential where there are limited resources.

Studies should be continued to explore a suitable and appropriate gold standard to test the validity of the tools particularly in low prevalence settings as well as the resources and cost of the introducing the tool in clinical practice. Any screening tool for malnutrition can only be considered effective if it results in early intervention and improved clinical outcomes, so the effectiveness of iPYMS needs to be explored in future intervention studies.

INTRODUCTION

The risk of malnutrition in paediatric inpatients is thought to be high worldwide. International guidelines state that all inpatients should be screened for malnutrition on admission to hospital using a validated screening tool. Although recent effort has gone into developing appropriate nutritional screening tools for children on admission, such tools are not useful for infants as they have not been validated in this age group. The overall aim of this thesis was to evaluate a novel malnutrition screening scheme for infants - the Infant Paediatric Yorkhill Malnutrition Score (iPYMS), to discover how well it distinguishes infants who are well-nourished from those undernourished, or at risk of undernutrition. Furthermore, this thesis explored the utilization of iPYMS in two diverse hospital settings; one in the UK, and the other in the Middle East (Iran). Additionally, this study evaluated the use of bioelectrical impedance in the measurement of body composition in sick infants, and explored correlates and predictors of malnutrition in sick infants.

This thesis will be presented into five main parts:

1. Literature review: This is an introduction to the subject studied, reviewing the existing literature regarding the understanding of the definition of malnutrition, as well as issues associated with methods of assessing and screening malnutrition risk in paediatrics inpatients. A number of methods and tools have been drawn on the basis of existing literature (Chapter 1).

2. Background of PYMS project and an initial audit: The (Paediatric Yorkhill Malnutrition Score) PYMS project is described briefly to provide a background of the current research reported in this thesis, followed by an initial audit published as a research paper in the Journal of Human Nutrition and Dietetics, 2013, entitled 'Acquisition and utilisation of anthropometric measurements on admission in a paediatric hospital before and after the introduction of a malnutrition screening tool' (Chapter 2)**.**

3. Overall methods: General methods and procedures used for both cohorts UK and Iran are described in this chapter, however detailed methods used for the validation of iPYMS (see Chapter 4), the measurement and generation of the body composition values (Chapter 6),

and the identification of predictors and correlates of malnutrition (Chapter 5) are described elsewhere in this thesis.

4. The main findings of the research: the main findings for two different settings (UK and Iran) presented in this thesis are organised into three chapters: 1) Validation Chapter, containing the results of the validation of iPYMS versus SGNA and also STRONGkids versus SGNA; 2) Body Composition Chapter assesses the body composition data in terms of methodological aspects, and; 3) Predictors and Correlates Chapter presents the predictors and correlates of malnutrition. For each chapter (excluding the correlates chapter), the findings obtained from both the UK and the Iranian cohort are compared for the research questions of interest (Chapter 4-6).

5. Discussion: A general discussion of the research findings is presented in Chapter 7.

CHAPTER ONE

LITERATURE REVIEW

1.1 Growth and nutrition

1.1.1 Normal nutritional status

Normal nutritional status can be supported by a standard pattern of growth and body composition. However, although nutrient intake may be different for each child, a healthy child will follow an individual growth curve. A child should meet the sufficient requirements of nutrients in order to sustain the potential optimum growth and health. The effect of adequate nutrition on growth and health is considered particularly important in infants, who have high-nutrient requirements in order to overcome their enhanced susceptibility to infections, increased requirements for rapid growth and relatively inefficient metabolism (United Nations Children Funds, UNICEF, 2013).

1.1.1.1 Growth

Infancy is considered the most important period of the child's growth. After birth, an infant normally loses about 5 - 10% of his or her birth weight. However, by approximately age 2 weeks, an infant should start to gain weight and grow quickly. By age 4 - 6 months, an infant's weight should be double the birth weight. During the second half of the first year of life, growth is not as rapid. It is often assumed that growth velocity - the rate of weight gain between two ages – will be the same for all children of a particular age. However, due to the phenomenon of regression to the mean, on average, light infants tend to have a higher expected velocity than heavier infants (Wright et al., 1994; Cole, 1995).

Growth charts describe the pattern of growth and its variability that is evident in a population at a given time point, but they do not assume that any particular level of growth is optimal. By plotting values of weight and height/length on growth charts (WHO growth standards) at any age, a child can be compared relative to others of the same age and sex to assess growth and nutritional status. Based on longitudinal data (serial measurements from the same child), from early childhood onward, the majority of children do not cross up or down far through the centiles but tend to track roughly along a given centile, indicating that the growth trajectory is individually genetically-determined. Thus, whether a child is large or small at any given time point, centile crossing gives an indication of a clinical growth abnormality. On this basis,

growth charts are used in clinical monitoring to detect individual abnormalities in growth trajectory and also any pathological changes due to disease (Wells, 2014).

1.1.1.2 Body composition

Although body composition can be described in several ways, the most common definition of body composition refers to the proportion of fat and fat free mass in the body. Fat mass (FM) refers to body fat, incorporating both essential fat, which is necessary for optimal health and includes fat in the bone marrow and cell membranes and, non essential or storage fat, including subcutaneous adipose tissue and visceral fat, used mostly as energy stores when the body is in need. On the other hand, fat free mass (FFM) indicates the lean tissues that maintain the body (protein, water, bone). Lean body mass incorporates FFM plus essential fat. Percent body fat (% BF) standard exist for different sexes and ages. Regarding diseases associated with malnutrition, the percent body fat may decrease below the average standard (Fusch et al., 2013).

The amount and proportion of body fat and fat free mass components varies greatly in children from birth to age 10 years. FFM is indicative of the muscle and bone content of the body, whilst FM indicates the main energy store, which peaks during infancy and declines thereafter (Fomon et al., 1982, Maynard et al., 2001). There is little normative data regarding the body composition of children (Wright, 2008a), and even less for infants (Butte et al., 2000; Fomon and Nelson, 2002). A prospective study of body composition during the first 2 years of life revealed that FFM was higher in boys than girls between 15 days and 18 months, and percent FM was significantly higher in girls than in boys at 6 and 9 months (Butte et al., 2000). Reference data (percentile reference curves and standardized z-scores) generated for triceps and subscapular skinfold thicknesses for US children, illustrated similar median subscapular skinfold thicknesses in white and black children (Addo and Himes, 2010). Furthermore, reference norms for a FFM and FM index in a large population of healthy Japanese children (Nakao and Komiya, 2003), and body fat reference curves for healthy Turkish children and adolescents (Kurtoglu et al., 2010) have been developed. Recently, Wells et al. (2012) have developed comprehensive reference data for body composition of children aged 4-23 years using the 4-component (4-C) model as gold standard, and a variety of simple reference techniques. They have now constructed body composition growth charts and standard

deviation scores for different measures. It is noted that this approach could greatly enhance the use and evaluation of body composition measurements (fat and fat free mass) in routine clinical practice for individual patients (Wells et al., 2012). Simultaneously, Weber et al (2013) generated reference data for fat mass index (FMI) and lean mass index (LMI) in children and adolescents drawn from a large representative sample of the US population using the method of dual-energy X-ray absorptiometry (DXA). However, these data did not include young children and therefore cannot be useful for infants as a reference data.

As outlined earlier, infants are constantly growing and the proportion of body fat and fat free mass components varies considerably in this age range, and also in some disease states (Sullivan et al., 2006; Wright et al., 2008a).

Considering the evidence based limitations of BMI in definition of nutritional status and risk, assessment of body composition has been recommended as an alternative approach. Wright et al. (2008a) reported that important variations in nutritional status were detected using lean and fat mass index derived from BIA that would not be detected using anthropometry alone. They illustrated that children with chronic disabling conditions as a group were very short and had low to average BMI, whilst using BIA they had low lean z scores but average to high fat z scores. Wright et al. (2008a) noted that the children with BMI below the second centile had fat indices ranging from below the second to above the 50^{th} centile, whilst children on the 50^{th} centile for BMI had fat scores ranging from -3 to +3SD. Furthermore, a very recent study evaluated the effects of population ancestry and LM on BMI, %BF, and FMI, reporting that the use of percentiles and z-scores for FMI and LMI in children and adolescents (national reference data of US population) provides a more accurate assessment of adiposity than BMI and % BF, by allowing for the independent assessment of FM and LM compartments (Weber et al., 2013). This procedure led to an overdiagnosis of excess adiposity amongst subjects when BMI was used, and to an underdiagnosis of excess adiposity amongst individuals with high LM when %BF was used (Weber et al., 2013). Thus, the measurement of body composition may be important in the identification, and the appropriate management of malnutrition in young children, particularly in clinical settings. However, there is a lack of a validated and suitable method to assess body composition in infants (Demerath and Fields, 2014)

Body composition models

Body composition models divide the body into two compartments (2-C model) or multiple compartments. In the two compartment model (the simplest and most common model), the body is divided into the fat and fat-free mass compartments. This model was originally used particularly for the assessment of body fatness, which is derived by subtracting FFM from body weight to obtain FM, and is expressed as a percentage of body weight. Thus, the FFM compartment was used only in the calculation of the FM value rather than used as a separate value (Ellis, 2007). If the water content of FFM is regarded as constant and FM is anhydrous, the measurement of total body water (TBW) can be used to derive FFM and FM (Kushner et al., 1992).

The multiple-compartment models divide FFM into its various components. The body can be defined as a 3-component model (3-C model) made up of FM, TBW and dry FFM (protein and minerals). If the mineral content (M) or total body protein (TBP) is also measured, then the body can be viewed as a 4-component model (4-C model). All of these measurements rely on certain assumptions. 3- and 4-C models measurements have more rigorous theoretical bases. However, they are more difficult to perform, expensive and require access to techniques that are not universally available (Norgan, 2005) and not always practical for paediatric use (Reilly, 1998).

Considering the 2-C model (based on the assumption of a constant composition of FFM) is the simplest, least expensive and invasive model and does not require skilled technical expertise, it can be used in the current investigation to assess the body composition of infants on admission to the hospital.

1.1.1.3 Dietary requirements for growth

UNICEF highlights the nutritional requirements for the pregnancy and early childhood noting that "From a life-cycle perspective, the most crucial time to meet a child's nutritional requirements starts during pregnancy, ending with the child's second birthday. During this time, the child has increased nutritional needs to support rapid growth and development and to overcome enhanced susceptibility to infections and sensitivity to biological program" (United

Nations Children Funds, UNICEF, 2013). A child's nutrient needs thus correspond with the changes in growth rates.

According to the World Health Organization (WHO) recommendations, an infant should be exclusively breastfed (breast milk only, with no water, other fluids, or solids) for 6 months, introducing complementary feeding by 6 months of age and continued breastfeeding for two years of age (Hoddinott et al., 2008).

An infant needs more energy in relation to size than a preschooler or school-age child. However, determining energy requirement based on the child's body weight is not appropriate, as it may result in taking extra energy and consequently, increase the risk of becoming overweight. However, the estimation of energy requirements using child body composition (fat and lean mass) can be preventive of over-consumption, as energy expenditure for lean mass is obviously higher than that for the fat mass. This method of estimation also takes into consideration the change of FM and FFM during periods of growth and as a result of some medical conditions (Wells, 2003).

1.1.2 How nutritional status impacts on health and well being

Nutritional status in children has been considered an indicator of health and well-being at the individual and population levels (Zemel et al., 1997). Malnutrition is increasingly recognized as a cause of potentially lifelong functional disability (Pelletier et al 1995; Black et al, 2013). The major nutrition challenges faced today include dealing the burden of undernutrition affecting those individuals living in conditions of poverty and deprivation, and preventing nutrition-related chronic diseases that are the main causes of disability globally. This challenge requires a life-course perspective, as effective prevention starts before birth and continues at each stage of life. Hence, it is proposed that in order to meet the global nutrition challenges for optimal human health and well-being in the new millennium, some actions should be addressed, namely; using the term ‘malnutrition in all its forms as a description that encompasses the full spectrum of nutritional disorders when interacting with policy makers and members of the public developing integrated prevention and control strategies for infant, child and adult undernutrition, and nutrition- related chronic disease throughout the lifecycle to achieve life-long health, and; reconsidering the concept of dietary quality and optimal

growth, particularly in relation to life-long health. In practice 'adequate food' should consider not only quantity of energy, but also overall diet quality (Uauy et al., 2009).

1.1.3 How under-nutrition impacts on growth and body composition

1.1.3.1 Impacts of undernutrition on growth

A child who is extremely under-nourished cannot develop and grow, because the dietary requirements are not available. When there is a deficiency in energy intake with or without other nutrients, the body initially loses, or fails to acquire fat stores (FM), which is reflected by weight loss, weight faltering, and wasting. If the deficiency persists, height velocity and acquisition of lean mass is affected, causing slow growth and stunting. If it persists severely, it causes catabolism and other metabolic and immune disturbances which may lead to death. This suggests that there are a range of under-nutrition syndromes comprising wasting, nutritional stunting, and weight faltering although they may not characterise the same clinical conditions, but all of them are indicative of different potential symptoms of under-nutrition (Wright and Garcia, 2012).

In particular, under-nutrition (weight faltering) in the first few months of infancy is associated with adverse effects. It has been demonstrated that children who are undernourished in infancy remain lighter and shorter than their peers at childhood (Black et al., 2007; Ud Din et al., 2013). Data from the Avon Longitudinal Study of Parents and Children (ALSPAC) indicates that although infants with early weight faltering catch up in weight by 2 years, height gain remained disproportionally slow (Ud Din et al., 2013). A study from the ALSPAC also reported that infants with weight faltering later in infancy remained shorter and lighter throughout childhood. In fact, the pattern of growth later in childhood depends on when weight faltering occurs in infancy (Ud Din et al., 2013). Similarly, growth patterns from developing countries demonstrated that linear growth faltering begins early in life and continues through at least preschool years (Shrimpton et al., 2001; Victora et al., 2010). Moreover, data from long-term follow-up studies in low and middle-income countries have illustrated that lower birth weight or small size at birth and childhood stunting were linked with short adult stature, reduced lean body mass and diminished intellectual functioning (Victora et al., 2008). Thus, growth deficits encountered during infancy may never be

completely overcome and may be linked to long-term stunting (Dewey and Begum, 2011) and possible metabolic effects in adulthood (Eriksson et al., 2002).

Wright and Garcia (2012), using more detailed measures, criteria and analysis in affluent countries with low prevalence of malnutrition, discovered that growth and body composition patterns in childhood can still be influenced by under-nutrition (defined as weight faltering and low BMI) occurring in infancy. The authors found that infants with both weight faltering and a low BMI went on to be shorter as children, but those with either sustained weight faltering or low BMI alone did not and they suggested that they were probably not undernourished (Wright and Garcia, 2012).

Clinical syndromes of child under-nutrition

Wasting

Wasting is predominantly occurs in the developing world. According to the WHO (2009) recommendations, wasting or severe acute malnutrition in infants and children should be identified by the criterion of BMI or weight-for-height/length below -3 SD score demonstrating that their body stores are significantly reduced (WHO, UNICEF, 2009). This approach is likely to be fairly efficient in the identification of acute malnutrition where the prevalence of undernutrition is high. However, the diagnostic value of low BMI and its clinical implication is very little known in more prosperous settings (Wright and Garcia, 2012).

Stunting

Stunting, defined as low height-for-age, is considered an important indicator of malnutrition in the undernourished populations. However, where there are low rates of undernutrition, short stature is more likely to be genetic or caused by organic disease (Wright and Garcia, 2012). Thus it is considered as a marker of chronic malnutrition in developing countries, but also as an indicator of chronic illness (WHO Technical Report, 1995).

In settings where stunting is highly prevalent, wasting (weight-for-height) underestimates the burden of malnutrition (Ruel et al., 1995; Simkiss, 2011). Although stunting and wasting have tended to be assessed separately, there is a growing movement to consider both conditions together (Emergency Nutrition Network - ENN, 2014).

The pathogenesis of stunting

Linear growth failure in childhood is the most prevalent form of undernutrition globally, representing a major public health priority (UNICEF, WHO, World Bank, 2012). Despite the high global prevalence of stunting, the pathogenesis underlying linear growth failure is poorly understood. For this reason, the most controllable pathways for effective interventions to promote healthy growth remain unclear (Piwoz et al., 2012; Prendergast et al., 2014a; Andrew et at., 2014; ENN, 2014). In a study of Zimbabwean children, there was evidence of chronic inflammation very early in life (by 6 weeks of age). Levels of inflammatory markers (e.g. CRP) were persistently higher in stunted than in non-stunted infants, and were associated with the level of maternal inflammation at birth, suggesting one potential common mechanism linking antenatal and postnatal growth failure (Prendergast et al., 2014b).

Consequences of the stunting syndrome

Martorell and Zongorne in their review argue that stunting is associated with increased risk of later disease and premature death, possibly via the mechanism of increased risk of the metabolic syndrome (Martorell and Zongrone, 2012). They describe stunting as an 'intergenerational cycle of poverty' whereby stunted women tend to have smaller babies and live in economic circumstances that tend to lead to further undernutrition. The WHO pointed out as long ago as 1995 that stunting is likely to limit the productivity of whole communities due to its association with reduced cognition and lifetime attainment, making it the most effective marker of inequality in childhood health (WHO Technical Report, 1995).

Failure to thrive (weight faltering)

Wright and Garcia (2012) argued that failure to thrive – usually seen in wealthy societies and more precisely defined as weight faltering – can be considered one of the undernutrition syndromes. They noted that observing the trajectory of slow weight gain in clinical practice is one of the procedures to identify weight faltering in younger children (Wright and Garcia, 2012). They argue that this growth pattern does usually reflect undernutrition because those children who are weight faltered in infancy, have slow weight gain in the early weeks of their life and also show a recovery pattern after 1 year of age (Wright et al., 1998).

1.1.3.2 Impacts of under-nutrition on body composition

Mild and moderate malnutrition lead to weight loss and mobilization of body fat, and thus a consequent decrease in subcutaneous adipose tissue, whilst lean body mass diminishes with severe malnutrition at a slower rate. In severe and acute malnutrition, subcutaneous fat is markedly reduced, and protein catabolism leads to muscular wasting resulting in impaired function of the skeletal and immune system (Torun and Viteri, 1988). In chronic malnutrition, there is a persistent deterioration of body composition, to which the individual has adapted by balancing the energy expenditure to intake. This balance is lost when the individual is faced with an infection (James, 1987). There have been major advances in conceptual models relating anthropometry to body composition, which provide insight into the physiological mechanisms represented by anthropometry (WHO Technical Report, 1995).

The importance of the effect of disease on body composition has also been highlighted. Diseases have multiple impacts on body composition and may influence FFM and/or FM components to a different extent. In some diseases, both components change in the same direction, whereas in others, the change in FFM and FM may occur conversely and in this case, a child might even maintain a normal weight despite having alterations in body composition. For example, anorexia affects both components of weight (low FM and FFM) (Wells, 2003). In contrast, chronic lung disease has a deviating effect of body composition components, enhancing FM whilst decreasing FFM (Kyle et al., 2006). Thus, improving understanding of these patterns will enhance determination of energy requirements which should ideally be based on lean size, as lean mass rather than weight increases the total energy expenditure. Addressing this area could have a marked influence on clinical outcomes in the longer term (Wells, 2003). Furthermore, undernutrition leads to inflammatory activity and consequently to abnormal body composition. In the majority, undernutrition is accompanied by varying degrees of inflammation, and a decrease in intracellular water (ICW) to extracellular water (ECW) ratio, with an expansion of ECW and reduction of ICW (Barac-Nieto et al., 1978). Moreover, both undernutrition and inflammatory activity lead to an inadequate host response following acute disease, and to diminished mobility (Soeters et al. 2008). In cachexia, the clinical symptoms consist of loss of FFM as well as fat tissue mass, caused by a negative nutrient balance and inflammatory activity (Soeters et al., 2009). Body

composition considerations are therefore important in determining the most suitable method of nutritional assessment, particularly amongst children in clinical settings (Zemel et al., 1997; Wells, 2003).

1.1.3.3 Impact of undernutrition on function

Malnutrition has an effect on the function and recovery of every organ system (Saunders and Smith, 2010). Saunders argues that the most significant symptom of malnutrition is weight loss due to loss of fat and muscle mass (Saunders and Smith, 2010). One description for this finding is reductive adaptation. Insufficient dietary intake, not meeting the body requirements, leads to using reserves in tissue, adipose and bone and produces changes in body composition, loss of functional capacity and metabolic state (Jackson, 2003). Thus, the malnourished state incorporates changes in body composition and function, which should be assessed to diagnose and grade malnutrition (Soeters et al., 2009). Regarding practical applications, more measurements of function are needed such as measurements of muscle function and handgrip strength, and immune and cognitive functions (Meijers et al., 2010).

1.1.4 How illness relates to nutritional status

The relationship between child nutrition and disease tends to be bidirectional; illness can impair nutritional status and poor nutrition can increase the risk of disease (Figure 1.1). Malnutrition-associated disease occurs more commonly and rapidly, with increased disturbing effects in children compared to adults (Briassoulis et al., 2001). Disease may worsen the nutritional status by increasing nutritional requirement due to metabolic response to an inflammatory process, fever, or infection. Dietary intake may be reduced due to anorexia, vomiting, pain, inability to take food, or difficulties in swallowing. There also are increased nutritional losses due to the disease process, drug-nutrient interactions, or diarrhoea. The consequent malnutrition results in impaired tolerance to any underlying medical condition, increasing susceptibility to infection, and prolonging recovery from the disease (Ghirshan, 1999).

Nutritional status of infants and children is worsened by many childhood diseases, for example Crohn's disease (Gerasimidis et al., 2011) or cystic fibrosis (Scaparrotta et al., 2012). Under-

nutrition in childhood has a potentiating effect on common infectious diseases, such as pneumonia and diarrhoea. In turn, explicit and subclinical infections, and inflammation (especially in the gut), alter nutrient intake, absorption, secretion, diversion, catabolism and expenditure (Jones et al, 2014).

Jackson noted that changes in cytokines, glucocorticoids, insulin and insulin-like growth factors lead to decline in appetite which results in reduced dietary intake as the most crucial factor in disease related malnutrition (Jackson, 2003). According to Elia and Green's report another risk factor for losing weight and being undernourished can be malabsorption due to intestinal failure or abdominal surgery. While, it was thought that increased energy expenditure was major cause of malnutrition associated disease, recent evidence based studies contradict this idea indicating that in many diseases, the total energy expenditure is generally less than in normal health due to reducing the physical activity (Elia, 1995; Green, 1999).

Immune function is also affected in the acute malnourished state. Impaired cytokine and phagocyte function can increase the risk of infection (Green, 1999; Stratton et al., 2003). If the nutritional requirements are not adequately met, these are worsened over the course of illness. Lean tissues are also catabolised to provide energy substrates for wound and inflammatory reactions (Briassoulis et al., 2001). When patients with chronic protein energy malnutrition become acutely ill, considerable loss of lean body mass and fat occurs. If the recovery from the underlying disease is prolonged, then the under-nutrition may worsen and compromise survival. Malnourished patients who have undergone surgery may also have delayed wound healing (Green, 1999; Stratton et al., 2003).

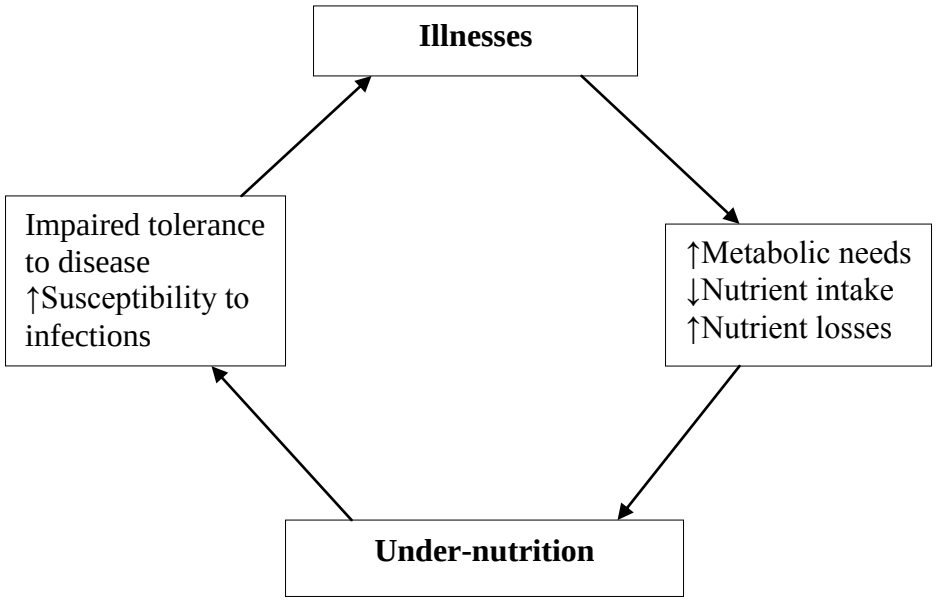

Figure 1.1: Relationship between illnesses and under-nutrition

1.1.4.1 Hospital-acquired malnutrition

Hospital-acquired malnutrition refers to nutrient imbalance acquired during hospitalisation, and can occur with or without pre-existing malnutrition. A child's nutritional status often deteriorates after admission to the hospital, resulting in longer duration of hospital stay and increased risk of complications. A number of studies have assessed the effect of hospitalisation on the nutritional status of children. Rocha et al. (2006) evaluated the nutritional status of 203 children under 5 years old on admission as well as on discharge. They noted that, 51.6% of 186 children lost weight during their stay in hospital, with most lost by those with prolonged hospital stays. Children who had malnutrition on admission (18.7%, 18.2% and 6.9% for weight for age (WFA), height for age (HFA) and weight for height (WFH) respectively) remained malnourished on discharge, and 9.2% of well-nourished children developed mild malnutrition by the time they were discharged. Similarly**,** another study illustrated that children with mild clinical condition and a BMI z-score < -2 SD on admission had a mean BMI decrease at the end of their hospital stay, which was significantly higher than in children who were in a better nutritional state at admission (Campanozzi et al, 2009). In this study risk factors for hospital-acquired malnutrition were reported as being less than 2 years of age, a duration of hospital stay > 5 days, fever, and abdominal pain. In Hulst

et al. (2010) study, children with moderate or high risk score had longer hospital stay compared to those with low risk, although, unlike Campanozzi et al. study, Hulst and colleagues reported that WFH SD-score between admission and discharge increased significantly greater in high risk children compared to those at moderate and low risk. More recent studies (Huysentruyt et al., 2013a; Hecht et al., 2014) have also reported a high incidence of hospital-acquired malnutrition using anthropometric measurements. In these studies, longer hospital stay significantly increased the risk of hospital-acquired malnutrition, while patients with more frequent occurrence of diarrhoea and vomiting (Hecht et al., 2014) had a higher risk of malnutrition.

Although in most of the studies that indicate an association between malnutrition and negative clinical outcomes such as increased length of hospital stay, it is difficult to find out the effect of disease severity in the association between poor nutrition and clinical outcomes. Association studies looking at correlation only as the reason that children at high risk of malnutrition stay longer such as that of Hecht et al.(2014), may be also due to them being more sick.

The nutritional status of children thus may be compromised in the course of their hospitalisation, and this hospital acquired malnutrition is associated with increased risk of adverse clinical events. However, it must be remembered that although nutritional status may be compromised by illness, there might be a reverse causation whereby a longer hospital stay is caused by illness rather than nutritional status. However, the only way about to test this difference is a nutritional trial intervention study.

1.2 Nutritional assessment

1.2.1 Limitations and advantages of different methods/measures and definitions of malnutrition

Although in recent years more effort has been put into introducing screening and assessment of nutritional state in routine clinical practice, no complete agreement exists on the optimal way to perform nutritional risk screening and to assess nutritional status. Various methods are used, leading to different outcomes both on an individual and population level. This is largely

due to the lack of agreement regarding the definition and assessment of nutritional state. Hence, methods and measurements need to be further developed, tested, and validated. Common methods and measures assessing nutritional status of children are described later this section.

1.2.1.1 Anthropometric measurements

Anthropometry, such as weight and length/height must be measured carefully and accurately using appropriate and well-calibrated instruments, in order to assess the growth and nutritional status of children. Measurements over time are also essential for children with chronic illness to determine whether the frequently of inadequate height or altered growth patterns are likely to result from nutritional or non-nutritional factors (Bear and Harris, 1997). However, there is substantial controversy concerning the most useful measurement, and inconsistency in the anthropometric parameters and statistical measures used to characterise the individual nutrition state.

Weight

Weight for age z-score is the easiest criterion to assess nutritional status in children. However, it does not distinguish between present and long- malnutrition. Underweight (low WFA) is, therefore, a combined measure of stunting (low HFA) and wasting (low WFH) (Carlson and Wardlaw, 1990). Weight measurement is particularly useful in infants under one year of age in whom length measurement is difficult to accurately record. However, weight measurement fails to differentiate tall, thin children from those who are short with adequate weight (Gorstein et al., 1994).

In clinical settings, serial measurements of weight in younger children are used to identify growth faltering. Olsen et al. noted that grow faltering, which is defined based on falling below a low centile is likely to over-select infants with low birth weight rather than those with poor weight gain after birth. Although it is rational to select the children on the basis of a fall down the centile chart, this procedure tends to over-identify larger infants who are declining towards the mean (Olsen et al., 2007). In this case however, measures of conditional change in weight SD score adjusted for the baseline centile position can be useful (Cole, 1995; Wright et al., 1994).

Obtaining precise serial weight measurements is also demanding in paediatric inpatients, and the movement of seriously ill children for weight measurements is difficult (Spence et al., 2003**).** The measurements may also not be accurate as there may be fluid retention (Taylor and Dhawan, 2005) or extra weight due to dressing and other equipments.

Length/height

A height-for-age value indicates long-term nutritional status as compared to weight, this parameter responds slowly to changes in negative nutritional status. It is essential to measure recumbent (known as supine) length for infants and children younger than 2 years, and standing height for those older than 2 years. Children are susceptible to stunting (low height-for-age) in response to any prolonged or severe illness, or impaired nutrition during the rapid growing period, especially during the first two years of life. Height-for-age fails to differentiate between heights deficit due to past events and height deficits that are a result of a chronic and ongoing events, which is important to consider in the management of children (Ojo et al., 2000). Height/length for age < -2 SD is suggestive of stunting and is used as a marker of chronic malnutrition in both developing countries and in children with chronic illness (WHO Tech Rep Ser, 1995).

Weight-for-Height (WFH)

Weight for height/length is not age-specific measure; and age does not need to be known for it to be determined. As the measure most likely to identify children with critically reduced stores, it is used to identify wasting. It is calculated as the child's weight divided by the expected weight for the same height/ length in children of reference population. According to WHO criteria (WHO Technical Report, 1995), SD-scores <-2 for weight-for-height/length describes acute malnutrition (wasting). The weight-for-height index has been suggested as providing valid criterion for the identification and treatment of severe acute malnutrition in infants and children using the cut-off of SD scores <-3 (Isanaka et al., 2009 and WHO, UNICEF, 2009). A reason for the choice of this cut-off is because these children have a higher weight gain when receiving a therapeutic diet compared to other diets, which results in faster recovery. Furthermore, in a well-nourished population there are practically no children below -3 SD score (<1%) (WHO, UNICEF, 2009). Although weight-for-height can be used for the screening of acute malnutrition, its diagnostic value is limited when attempting to identify

children in the early stages of undernutrition, or patients at risk of deterioration in nutritional status as the result of a medical condition. In this case, history of some relative signs such as current appetite, food intake, retention in the body (by asking about symptoms of diarrhoea and vomiting), and severity of disease provide a wider picture of current energy balance and the risk of nutritional deterioration. The combination of these signs along with anthropometric measurements provides a better estimation of nutritional deterioration risk compared to anthropometry alone. Weight for height/length is limited as although the relationship between WFH varies with age, age is not adjusted for when using weight for height/length.

Body Mass Index (BMI)

BMI is calculated as weight in kilograms divided by height in metres squared, and is used to express weight adjusted for height. BMI varies with age in children and it should be interpreted with age and gender specific reference values (Cole et al., 2000) or standard deviation scores. BMI cut-offs have been suggested as criteria for defining thinness in children and adolescents (Cole et al., 2007). The 17 kg/m^2 thinness cutoff is close to the −2 SD cutoff for wasting.

Both WFH and BMI are limited due to their inability to distinguish between FM and LBM, particularly at the lower end of the range (Maynard et al., 2001). The use of BMI as a proxy of adiposity is especially problematic in the paediatric population, because the relative contributions of FM and LBM to body weight vary by age, sex, and population ancestry. Annual increases in BMI from mid-childhood onwards are mostly due to increases in LBM rather than an increase in FM (Wells, 2000; Maynard et al., 2001), and differences in BMI percentiles indicate differences in FM only for high percentiles of BMI (Demerath et al., 2006). Body composition differs by population ancestry as well, as it has been shown that black people have a higher LMI than white people (Nelson and Barondess, 1997; Schutte, et al., 1984; Ellis et al, 2000; Foster et al., 2012). The failure of BMI to account for the independent contributions of FM and LBM may lead to misclassification of adiposity status when applied to individuals (Ellis et al., 1999; Weber, 2013).

Mid upper arm circumference (MUAC)

MUAC is the circumference of the left upper arm, measured at the mid-point between the tip of the shoulder and the tip of the elbow using a simple and non-stretched tap. It is a compound

measure of muscle, fat, and bone. It has been used as an alternative index of malnutrition in rapid nutritional surveys when weight and height measurement are not feasible (WHO Technical Report, 1995). MUAC changes little during the early years. It is a simple and accurate measurement. WHO standards for MUAC-for-age show that in a well nourished population, there are very few children aged 6–60 months with a MUAC less than 115 mm. Children with a MUAC less than 115 mm have a highly elevated risk of death compared to those who are above this value. Thus it is recommended to increase the cut-off point from 110 to 115 mm to define severe acute malnutrition (SAM) with MUAC. The prevalence of SAM, (i.e. numbers of children with SAM), based on weight-for-height below -3 SD of the WHO standards are very similar to those based on a MUAC cut-off of 115 mm (WHO, UNICEF, 2009). Regarding patients with fluid shifts and edema, MUAC may be a better indicator than WFH in the classification of acute malnutrition (Myatt et al., 2006).

Overall, there is no single anthropometric measure to assess the nutritional status of children comprehensively. Wright and Garcia note that although some individual thresholds and measures of anthropometry are used to identify undernutrition in children in wealthy societies, they are not well-specific, because a single measurement fails to give a precise diagnosis and just functions as a warning indication (Wright and Garcia, 2012). The validity of individual anthropometric parameters may vary based on the population of children. Hence, it is suggested that a combination of measurements obtained by a trained individual alongside other clinical parameters should guide nutrition assessment in children (Mehta et al., 2013).

1.2.1.2 Definition of malnutrition

1.2.1.2.1 Challenges in defining malnutrition

Although attempts to define and assess malnutrition go back many decades, there is still a lack of consensus on the definition of malnutrition. Many aspects influence the definition of malnutrition, such as the use of different criteria (due to the lack of validated criteria) and cut-off points for assessment of undernutrition in children. Additionally, assessment is often conducted using differing measurements (including new measurements) and there are variations in reference populations for specific countries, particularly in response to the new WHO growth standards. In addition, researchers sometimes refer to specific medical conditions and syndromes (Joosten et al., 2010, 2011), and at times also use different

metabolic and physiological aspects, diminished function, and different syndromes to define and measure malnutrition (Soeters et al., 2008). These many aspects have considerably complicated the provision of a definition of malnutrition.

1.2.1.2.2 Recent attempts to define malnutrition

Recently, an interdisciplinary paediatric malnutrition definitions workgroup (American Society for Parenteral and Enteral Nutrition - A.S.P.E.N.) proposed a comprehensive definition of malnutrition based on available evidence and multidisciplinary consensus in the group. Accordingly, paediatric malnutrition (undernutrition) is defined as "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" (Mehta et al., 2013).

According to the ESPEN consensus reports (Lochs et al., 2006), malnutrition is ‘‘a state resulting from a lack of uptake or intake of nutrition leading to altered body composition, decreased fat free mass but specifically body cell mass and diminished function’’. On the other hand according to WHO criteria (WHO Technical Report, 1995) SD scores <-2 for weight-for-height and height-for-age respectively describe acute and chronic malnutrition. WHO has also used BMI to describe malnutrition in terms of thinness, which reflects body composition and function (WHO Multicentre Growth Reference Study Group, 2006a; Cole et al., 2007).

Waterlow et al. in 1972 suggested the terms ‘wasting’ or ‘acute’ for a deficit in weight for height, and ‘stunting’ or ‘chronic’ for a deficit in height for age. By so doing, the severity of wasting and stunting can be graded into four categories (establishing cut-off points for normal, mild, moderate, and severe) by calculating weight as a percentage of the reference median weight for height, and height as a percentage of the reference median height for age. Use of this system showed that 80% of median weight for height and 90% of median height for age in undernourished populations are useful classification limits for identifying malnourished children. In 1977, Waterlow et al. developed this scheme, recommending methods of classification using centiles and standard deviation scores which they hoped might be widely acceptable and thus enable international comparisons. The use of centiles and standard

deviations from the mean instead of percentage deviations from the median is statistically more appropriate. However, percentage deviations are easier to understand. There are also other disadvantages in using the centiles method; extremes of variation are less easy to characterize than in the standard deviation method. As a large number of children in developing countries are outside the range of the reference population, they cannot be classified accurately by centile or plotted on growth charts to monitor longitudinal changes. Therefore Waterlow recommends that for an undernourished population, standard deviation scores are used instead of percentage deviation from the median. In this classification scheme -2SD unit should also be included for both height for age and weight for height. Furthermore, - 2SD weight for height is approximately equal to 80% of the median weight for height and 90% of median height for age. Therefore if below -2SD is needed in order to classify, it could be done in units of -0.5 or -1SD. This was shown in the WHO study (Duggan et al., 2010) which noted that a SD score for weight for height between -2 and -3 can be considered as moderate malnutrition and a SD score below-3 as severe malnutrition. This classification is used widely and internationally.

Joosten (2010) defines malnutrition as a nutritional state which results from deficiency or an excess of energy, protein or other nutrients, leading to an adverse effect on tissue and body form and function, presenting a measurable clinical outcome. A similar definition has been proposed by Soeters et al., 2009, whilst considering different underlying malnutrition syndromes, including pathogenetic factors. Soeters et al. suggested that malnutrition is caused by disturbances in nutrient balance and inflammatory activity, which leads to changes in body composition (loss of FFM and fat tissue mass) and diminished function. According to Soeters et al., changes in body composition and function should be assessed to diagnose and grade malnutrition.

Meijers et al. (2010) summarises experts' opinions on elements of the definition and development of malnutrition. According to this study, a definition of malnutrition should include at least three elements: deficiency of energy, deficiency of protein, and a decrease in FFM. However, function and inflammation are also suggested as important in defining malnutrition. Furthermore, Meijers et al. state that for diagnostic purposes, most experts include weight loss, BMI, and no nutritional intake. However, they give no consensus on the cut-off points for these elements.

Wright and Garcia (2012) define child undernutrition as "a condition that represents a net energy deficit, with or without other nutrient deficiencies, but the manifestations of that deficit will vary depending on severity, duration and age of onset". They suggest that there is unlikely to be a single gold standard method to diagnose children with undernutrition. Various measures and thresholds should be used depending on the underlying prevalence of malnutrition and what can be measured reliably. According to Wright and Garcia, in wealthy societies, a decline in weight with low BMI centile or wasting is strong enough, as long as they are combined. This then should influence the clinical algorithms followed by measuring body composition (using measure of skinfolds/DXA/BIA).

Despite the variety of above definitions, there is no complete agreement concerning the most appropriate definition of the term 'malnutrition' (Table 1.1), it can be described as a deficiency, excess or imbalance of energy and nutrients, resulting in a measurable adverse effect on growth, body composition, function and clinical outcomes. Although malnutrition includes both undernutrition and overnutrition, this term predominately refers to 'undernutrition', as in this thesis. The most important descriptions of malnutrition incorporate causes and how it can be measured, and is classified by the type, severity, and consequences – the clinical outcomes. Figure 1.2 illustrates the main components of malnutrition.

Clinical outcomes

As already discussed, in definition of malnutrition, it is fundamental that beside anthropometric parameters, other clinical outcomes such as lean body mass measurements, muscle strength, frequency or severity of acquired infection, recovery period and length of hospital stay must be taken into account to reach a reliable diagnose.

Finally, it is emphasised to provide a practical classification scheme for paediatric malnutrition, the definition should incorporate chronicity, etiology, and severity of malnutrition. The classification of chronicity and severity can be done by applying the anthropometric criteria - whilst the impact of malnutrition on growth, body composition and functional outcomes and also its association with inflammation should be considered.

Table 1.1: Various definitions and criteria used for malnutrition

Authors and published year	Criteria used	Working model
Waterlow 1977	Low SD scores of height-for-age and weight-for-height for chronic and acute malnutrition	Suggest the terms 'wasting' for a deficit in weight for height, and 'stunting' for a deficit in height for age
WHO Technical Report 1995	Low weight-for-height as acute and height-for-age as chronic malnutrition	Describe malnutrition only in terms of thinness, underweight and overweight
WHO Multicentre Growth Reference Study group, 2006 Cole et al. 2007	BMI/WFH	Describe malnutrition only in terms of thinness, underweight and overweight
Lochs et al. (ESPEN reports) 2006	Body composition (decreased FFM but specifically BCM)	Lack of uptake or intake of nutrition leading to altered body composition and diminished function
Soeters et al. 2009	Changes in body composition (loss of FFM and fat tissue mass) and function	Disturbances in nutrient balance and inflammatory activity, which leads to changes in body composition and diminished function
Joosten 2010	Tissue, body form, function and clinical outcome	Deficiency or an excess of energy, protein or other nutrients, leading to an adverse effect on tissue and body form and function and a clinical outcome which will be measurable
Meijers et al. 2010	Weight loss and BMI. No consensus on the cut-off points for these elements	Definition of malnutrition should include at least three elements: deficiency of energy; deficiency of protein; and decrease in fat-free mass. function and inflammation are also important
Wright and Garcia 2012	In affluent societies: combination of both, decline in weight or BMI centile and wasting, followed by measuring body composition	Define child undernutrition as a net energy deficit, with or without other nutrient deficiencies
Mehta et al. 2013	Weight, height/length, skinfolds, mid upper arm circumference z-scores	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

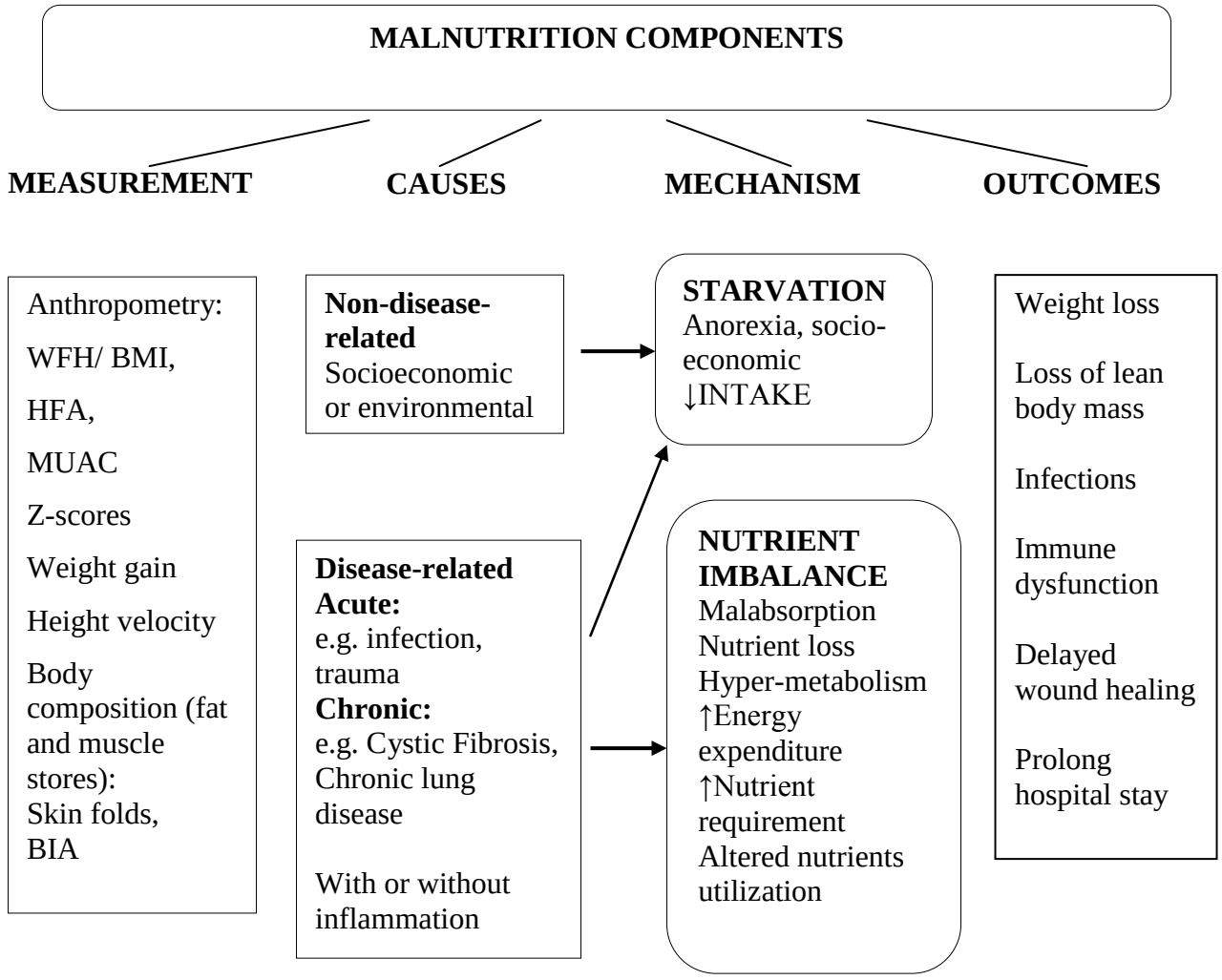

Figure 1.2: Main components of definition malnutrition in hospitalized children

1.2.1.3 Nutritional intake (dietary history)

Assessment of dietary intake is used to estimate the adequacy of nutrient intakes in population subgroups. Food–frequency questionnaire (FFQ) and 24-hour dietary recall are commonly used methods to assess nutritional intake (Bornhorst et al., 2014). Dietary Reference Intakes (DRIs) may be used to assess whether diets provide enough nutrients to meet requirements. However, the assessment of food intake is challenging and prone to errors, especially when concerning children (Livingstone and Robson, 2000; Cullen et al., 2008), and incorrect information may mislead the estimation of nutritional status as well and mislead nutritional interventions.

Alongside the increase of dietary requirements, the reduction of dietary intake is one of the main causes of undernutrition in hospitalised patients. Therefore, the subjective assessment of dietary intake is included in nutritional assessment and screening tools, such as the Subjective Global Nutritional Assessment (SGNA). Such tools include questions concerning detailed dietary intake of the child, and is often regarded as time-consuming, and may be unreliable. In clinical practice, screening methods include assessment of dietary intake as a percentage of normal intakes. If individuals are able and willing to report objectively their intake over the past weeks and months, a dietary history can be a valuable accessory to nutritional assessment. However, this is often impossible (Soeters et al., 2008).

Moreover, assessing the energy requirements of patients with acute and chronic disease is more complex than for those in good health. Requirements for specific nutrients and of energy can fluctuate significantly in response to different diseases, and at different stages and severity of the same disease. Requirements also depend on levels of inactivity and the presence of prior malnutrition. Although it was previously thought that the energy requirements of a number of severe acute diseases were increased (Elia, 2005; Elia, 1995), it is now realised that this is not usually the case and for most conditions, the overall energy requirement is normal or decreased (Elia and Stratton, 2011; Elia M, 2005). In addition, it can be hard to assess dietary intake reliably and accurately over a period of days or week (Elia and Stratton, 2011).

1.2.1.4 Clinical signs

One of the most necessary components of clinical examination is nutritional assessment. Since in clinical settings, where anthropometric measurement can't be easily and precisely done, these assessments are usually used to identify malnutrition risk in paediatric inpatients. However, there is decisions based on clinical judgment alone as a subjective assessment may not be valuable in identifying of malnutrition without considering the anthropometry (Cross et al., 1995) as an objective measures of nutritional status (Hartman et al., 2012). Cross et al (1995) measured the ability of three experienced childcare professionals to grade the nutritional status of patients of varying ages and nutritional status, comparing clinical examination with anthropometry, noting that assessors were uniformly consistently poor at detecting severe malnutrition and assessing the nutritional status of infants in the absence of

anthropometric measurements. Thus, the reproducibility in clinical assessment of nutritional status is weak, even amongst senior paediatricians, especially in the more severely malnourished. Clinical evaluation of nutritional status alone is inadequate for accurate assessment, and anthropometry is essential (Sullivan, 2010).

Although clinical signs of possible nutritional disorders, such as abnormal skin or hair conditions, can be assessed on medical examination of the child, these symptoms are rare as they appear only after a prolonged period of nutrient deficiency. Medical records can also be reviewed from a nutritionist's point of view, which includes looking for a history of anaemia, recurrent infections, chronic constipation or diarrhoea, food intolerances or allergies, and pica. Additionally, prenatal maternal weight gain, birth weight, early feeding problems and practices, growth pattern, and laboratory data are also important (Bear and Harris, 1997).

1.2.1.5 Biochemical measures

Serum biomarkers have been used to evaluate the nutritional status, during hospital admission (Ferrie and Allman, 2013). Serum biomarker such as albumin, transferrin, measured as part of routine blood tests are used as objective criteria. Although, nutrition-related serum biomarkers have been used to assess the degree of malnutrition in the critically ill children to assess the degree of malnutrition in intensive care unit, current medical literature has not supported any association between nutrition related serum biomarkers and clinical outcomes in critically ill children (Ong et al., 2014). It is suggested that There are no robust and specific biochemical screening measures for assessment of undernutrition.

1.2.1.6 Measuring Body Composition

Knowledge concerning body composition in childhood is important to better define nutritional status and growth and nutritional needs, particularly amongst children who may have special nutritional requirements as a result of disease and medical conditions, or in those at a high risk of malnutrition (Zemel et al., 1997; Norgan, 2005; Ellis, 2007). Measuring body composition has been a constant challenge, and no standard method is accepted to measure body compartments accurately and precisely (Wells and Fewtrell, 2006a).

Anthropometry and BMI are usually used in the assessment of body fat. However, there are limitations with these tests. Although BMI has been adopted as a measure of fatness, energy stores and energy undernutrition (WHO Multicentre Growth Reference Study Group , 1995), this value does not differentiate between fatness and lean mass (Wells, 2006b). BMI does not measure fat directly in children, and its relationship with body fatness and the risk of subsequent related disease is not actually known (Wright et al., 2008). Moreover, low BMI can reflect a low lean mass rather than low fat store (Burnham et al., 2005). Although in healthy adults and children, BMI, originally an index of morbidity risk, correlates well with fatness (Reilly, 2006), its diagnostic value to differentiate fat from lean mass is questionable, particularly in a diseased state. Thus, BMI is considered a poor proxy for body fatness (Piers et al., 2000) and is non-specific indicator of body composition (Wellens et al., 1996; Prentice, 2001). BMI-based assessments of nutritional status may be under-estimating children's fatness (Wells et al., 2002). Additionally, it is noted that there are differences in body composition for the same BMI value in different population groups (Deurenberg et al., 1999, 2003; Rennie et al., 2005; Stone et al., 2008), making it difficult to use BMI to predict risk in all types of population.

1.2.1.6.1 Methods used for measuring body composition

There are a variety of techniques available, and acceptable, for paediatric use. The most commonly used is the measurement of whole-body compartments, using either the 2-C techniques (FM and FFM) which include densitometry and hydrometry, or the 3-C (FM, LBM, and bone) model (Norgan, 2005). For example, a stable isotope used in the research setting effectively measures the size of TBW in infants and children (Schoeller et al., 1980). TBW measurements can be used to estimate FFM using age appropriate hydration factors (Fomon et al., 1982), which estimate the fraction of the TBW in FFM. FM and percent body fat can then be calculated once the FFM is determined. Despite being expensive and labour intensive, this technique is not invasive for children. Another technique is dual- energy x-ray absorptiometry (DXA), which measures three compartments of the body (bone, lean and fat mass). DXA is based on the principle that bone, lean tissue, and fat attenuate x-rays differently. This new body composition measurement technique is becoming increasingly available for clinical use, and has a high level of precision, distinguishing it from other techniques. However, it must be noted that DXA is not as accurate when measuring the

extremely obese. Using DXA, remarkable abnormalities in body composition were found in children at the time of diagnosis of coeliac disease (Barera, 2000). Although this technique is non-portable, relatively expensive in terms of capital costs and requires specialist staff, the non-invasive and time-efficient nature of DXA means it is commonly used as reference method in validation studies (Reilly et al., 2010; Gerasimidis et al., 2014).

As measurements of body composition are mostly made in the field or clinical setting, practical, cheap, safe and validated methods of body composition assessment appropriate for these settings are necessary. The most commonly used field techniques are skinfold thickness (SFT) and bio-impedance analysis (BIA) (Norgan, 2005).

1.2.1.6.1.1 Skinfold thickness (SFT)

SFT measurements exhibit many characteristics of a good method used in large scale and routine clinical practice (Norgan, 2005). This measurement is simple, quick, acceptable, inexpensive, portable, and appropriate for use in most age groups, including young children and infants. However SFT measurement may have low precision (Oppliger et al., 1987), as they are prone to inter-observer error and require well-trained personnel. Furthermore, SFT may cause discomfort in young children. In large scale studies, prediction of body fatness is often made from anthropometric measurements, including BMI and SFT. However, these techniques applied to measure body compartments (FFM, FM, SFT) are not well validated and do not precisely characterize body fat or muscle mass (Wang et al., 2000). Furthermore, these techniques may be at risk of a high degree of both intra- and inter-observer variation (Jebb et al., 1993; Piers, 2000), and these methodological errors during the collection of raw data may affect the accuracy of the prediction. Intra-observer and inter-observer error are low compared to between-subject variability, but in obese children accuracy and precision are poorer (Wells and Fewtrell, 2006). Additionally although, SFT measurements are reliable in the assessment of groups or populations, they may not be reliable in the estimation of body composition of individuals (Piers, 2000). Thus, it is essential to standardise this method and train the participating staff in order to decrease measurement error regarding intra-observer variation (Stomfai et al., 2011; WHO Multicentre Growth Reference Study Group, 2006b).

The best use of SFT data is as raw values, which represents reliable indices of regional fatness. Using SFT to predict body composition involves two predictions. Firstly, raw measurements are used to predict a body component using regression equations and secondly, this value is converted to final body composition data using further theoretical assumption. Prediction equations certainly confound accurate raw values with predictive error. Thus, for assessment of fatness, it is better to leave skinfolds in raw form or standard deviation score (SDS), which are reliable indices of regional fatness, than to make a prediction of total FM. For assessment of total FFM, an approach based on skinfold equation is particularly inappropriate, as no index of this component of weight is directly measured during SFT measurements (Wells and Fewtrell, 2006).

Triceps SFT is one of the most valuable anthropometric and inter-measures of nutritional status, providing a good indication of energy reserves and correlating well with total body fat stores (Zemel et al. 1997). Subscapular SFT is a good measure of fat stores, and may be less sensitive to short-term fluctuations in nutritional status (WHO technical report, 1995). The combination of the triceps and subscapular skinfolds has been used for calculating the sum of skinfolds (or mean z-score) for nutritional assessment, which should be more robust than using them singly. Reference data is now available for children and infants regarding SFT measurements, but only from age 3 months (WHO Child Growth Standards, Methods and development, 2007).

A combination of skinfold and arm circumference measurements in the assessment of body composition may define body fat with greater precision (Bear and Harris, 1997). For instance, a child may be underweight for height but still have adequate fat stores, particularly if LBM is reduced because of an underlying medical problem.

When mid upper arm circumference is combined with the triceps skinfold measurement, upper arm muscle and fat stores can be estimated (Frisancho et al., 1981). Mid-arm muscle circumference (MAMC) may be calculated from MUAC and triceps skin fold (TSF) using the formula MAMC = MUAC – (TSF × 0.314). These measures may give some idea about muscle mass and FM of the body. However, body composition cannot be assessed in detail with anthropometry alone. A recent validation study was conducted to compare different field methods (anthropometry - skinfold measured at two-six sites and foot-to-foot bioelectrical

resistance) for estimating body FM with a reference value derived by a 3-C model (as reference method) in children aged 4-10 years from four different European countries. This study revealed that the best predictions were given by combining skinfold and circumference measurements. This study showed that when combining circumference and skinfold measurements, estimations of FM can be obtained with a limit of agreement of 1.91 kg in normal weight children, and of 2.94 kg in overweight and obese children (Bammann et al., 2013). However, these are still rather wide limits and crude estimates.

Skinfold measurement must be interpreted carefully in small children, as small variations can account for the difference between the 5^{th} and 50^{th} percentiles (Bear and Harris, 1997). Moreover, skinfold thickness can also be confounded by child's length (Midorikawa et al., 2011). For example, when using fat thickness × height, the accuracy of predicting total FM from skinfold thickness in Japanese children, was higher than that using only the sum of SFT obtained from the triceps and subscapular sites without involving the length factor.

1.2.1.6.1.2 Bio-electrical impedance analysis

Bio-electrical impedance analysis (BIA) is commonly used to estimate body composition and is widely accepted as a field and bedside technique. It is simple, quick, cheap, and non-invasive, but less accurate and requires transformation (as above) before application. BIA has better reproducibility than skinfolds, which makes it more appropriate for large studies with multiple measures (Norgan, 2005).

When a weak alternating electrical current is passed through the body, the body's resistance to the current is inversely proportional to its hydrated tissue mass, adjusted for body length (Foster and Lukaski, 1996). Thus, the measured resistance can be converted to an estimate of FFM, and used with the 2-C model to calculate FM. TBW is the main component of FFM, and can be estimated using the formulas shown, as it is proportionate to lean mass ($Height^2/z$):

$TBW = Height^2/z$ *resistivity constant

Lean mass = TBW *hydration constant

BIA has been promoted as an alternative technique for patients when overhydration is not present (Kyle et al., 2004), however patients with severe malnutrition may be over hydrated or dehydrated, posing an issue for using BIA to assess body composition. Moreover, the

estimation of body composition using BIA in acutely dehydrated subjects is likely to be unreliable (Dal Cin et al., 1992). Despite these limitations, carefully performed measurements are valuable indicators of changes in body compartments in the individual patient (Soeters et al 2008).

Computation of BIA data

BIA (using the equations of Lukaski et al., 1986 and Segal et al., 1988 and Heitmann, 1990) provided inaccurate estimates of FFM both at the individual and group level when compared to estimates from deuterium dilution (DD) method. Although the risk of error was less at group level than at an individual level, it was found to be significant in both cases. However, when using the Heitmann equation (1990) to analyse BIA (as the bias from the revised equations of Heitmann was small and non-significant) in combination with measures of SFT and MUAC, the estimates of FFM generated both for individuals and groups were improved (Piers et al., 2000).

It is known that FM and FFM vary with height, but there is no commonly used method of adjusting FFM for height. In the assessment of fatness, FM is usually expressed as a percentage of total weight. FFM has only been used in the calculation of the FM without considering it as a separate value (Wells, 2003; Ellis, 2007). Fat percentage may vary with changes in FFM, which is particularly important in childhood as FFM varies significantly with maturation (Fomon et al., 1982; Maynard et al., 2001). Thus, a child with a low FFM may have a high fat percentage, despite a normal or even low FM (Wells and Cole, 2002). To overcome this weakness, Wright et al. (2008a) developed a new method of manipulating BIA in the assessment of nutritional status in children, based on lean and fat indices adjusted for body size. This method illustrated important variations in nutritional status (as high, average or low fatness and leanness independently) that would not be detected using anthropometry alone (BMI), and can better identify children at risk of being underweight or obesity in field and clinical settings, particularly where variation in FFM is of importance.

As stated above TBW, can be estimated using formulas as it is proportionate to lean mass ($Height^2/z$). However, two regression constants derived from population validation studies are required for this:

$TBW = Height^2/z$ *resistivity constant

Lean mass = TBW *hydration constant

BIA determines the electrical impedance of body tissues, which provides an estimate of TBW that is converted to an estimate of FFM, with assumed constant values for the hydration of lean tissue with age. Different BIA models have been used among various age groups and it requires population specific validation equations. There is a lack of information on hydration of fat-free tissue in different populations of children (Wells et al., 2009). The above constants were obtained using the constants derived from other studies in the same age range. The values for resistivity and hydration constants combined (0.6/0.776=0.77) give very similar values to Deurenberg's estimate (Deurenberg et al., 1989) in a sample of children aged 11-16 years.

An alternative, simplified approach to analysing BIA data (Wells et al., 2007) has been proposed for expressing weight, height and impedance data as an index, all adjusted for size by dividing by height². This approach does not require population specific validation equations. Wells pointed out that as:

$$Lean\ mass\ \alpha\ Height^{2}/z,$$

then lean mass divided by height² (Lean index)

$$Lean\ index\ \alpha\ 1/z$$

This then allows calculation of a sort of fat index using linear regression of Lean index against BMI for the whole cohort to derive a fat residual (the residual variation in BMI not explained by lean mass) as follows:

$$Fat\ residual = BMI - (1/z \times B + C),$$

where B and C represent the regression constant and intercept respectively. This method of interpreting BIA data requires no population derived constants and simply produces a ranking of individuals in terms of LMI.

Wells's study showed that the index 1/*R* (1/impedance) was a highly significant predictor of LMI, and may be particularly valuable as an index of LMI when used in combination with skinfold measures of fatness. It suggested that clinical trials, based on samples with close age and sex, including children under 2 years old, can benefit from this simplified approach where the aim is to identify either trends in relation to other variables or differences between groups (Wells et al., 2007).

Both of these two methods (Wells et al., 2007; Wright et al., 2008a) have considered FM and FFM separately to assess the nutritional status of children using lean and fat indices adjusted for body size, but the advantage of the simplified method is that it does not require population derived constants, which are not available for infants. Overall, these methods have been applied in children or young adults in order to establish a logical and proper use of BIA data in assessment of nutritional status (Wells et al., 2007; Wright et al., 2008a). However, there is a lack of studies that have used BIA in this way to assess the nutritional status of infants.

1.2.2 The complexity of assessing nutritional wellbeing in infants

1.2.2.1 Body composition methods for use in infancy

Considering the lack of an accurate and simple method of assessment and reference data for body composition of infants, the use and interpretation of body composition measurements (FM and FFM) has been limited in this age group. Although recently, a few simple validated methods (Wright, et al., 2008a, Wells et al., 2007) and a reference data (Wells et al., 2012) have been developed for children, these have been established for older children and do not include data for infants. Skinfold reference data (WHO reference) are now available for infants, but only from the age of 3 months. Such limitations have been caused due to a lack of using body composition data as an indicator of nutritional status of infants, particularly in clinical setting and at an individual level.

The various means of assessing nutritional status and definition of malnutrition have been outlined in this review. It is not only necessary that a consensus is reached regarding how malnutrition should be defined, but also it is fundamental that an agreement is made on an appropriate set of measurements to assess and to diagnose malnutrition.

1.3 Nutrition screening tools

1.3.1 Why develop a screening tool?

As already outlined, due to the adverse effects of malnutrition-associated disease on child growth, health, and well-being, the assessment of nutritional status of hospitalised children is very important for establishing appropriate management. However, it is not possible for all

children admitted to the hospital to be assessed for full nutritional status. Nutrition screening is applied as a simple and quick procedure, with the aim to identify children who are already malnourished or at risk of developing malnutrition (Corish, 1999). Such children are then referred to a dietician or nutrition specialist for more detailed nutritional assessment. Nutritional intervention can be therefore initiated early for children who are identified as being at risk of malnutrition to prevent adverse consequences. The nutrition screening process aims to make an early identification of patients who require a more detailed assessment and formulation of an early individualised management plan. Thus, the importance of early identification and early treatment has led the development a number of nutrition screening tools.

1.3.1.1 Prevalence of malnutrition in hospitalised children

The prevalence of malnutrition and the risk of developing under-nutrition have been consistently reported as high in hospitalised children (Joosten and Hulst, 2011; Huysentruyt et al., 2013b). However, it remains mostly unrecognized and untreated (Pawellek et al. 2008; Huysentruyt et al., 2013a). Malnutrition occurs in both developed and developing countries; however the factors influencing nutritional status differ markedly between the developing world and industrialized nations. In developed countries, undernutrition most often occurs in association with chronic disease, psycho-social disturbance, and medical and surgical conditions. In contrast, in the developing world it is frequently a result of socioeconomic and environmental factors which lead to stunting of the physical and mental development of the majority of children (Grover and Ee, 2009). Thus, children admitted to hospitals in developing countries may already be malnourished, as indicated in a study in Kenya, where sixteen percent of children admitted to a rural hospital had severe wasting (Allen and Lagunju, 2007). However, the interpretation of the factors resulting malnutrition in the societies that are somewhat in the economic transition state are more complicated.

1.3.1.1.1 Current issues concerning the interpretation of prevalence of malnutrition

The use of new WHO child growth chart

The WHO Growth Reference Study Group conducted a longitudinal study between 1997 and 2003 to establish the new child growth charts in healthy, breast-fed children from 6 countries,

including Brazil, Ghana, India, Norway, Oman, and the USA (WHO Multicentre Growth Reference Study Group, 2006a). It is likely that the prevalence of under or overweight is affected by introducing the new charts. Juliusson et al compared the new WHO standards to the national growth curves of Belgian and Norwegian children, and argued that the proportion of children with malnutrition differed from the expected norm. The pattern of breastfed children in both countries was more compatible with the national standards than the WHO one (Juliusson et al., 2011). Many other studies which have attempted to compare the new WHO standards with previous standards have obtained similar results to those discussed by Juliusson et al. For instance, cross-sectional data from longitudinal studies in India, Peru, and Vietnam indicated that using WHO standards, a higher proportion of children were stunted and fewer children classified as underweight in all 3 countries (Fenn and Penny, 2008). Similar evidence has been provided by a prospective birth cohort study in Gabonese children, which reported that when using the new WHO standards, a higher proportion of 3-month-old infants were underweight compared with previous child growth charts/references (CDC or NCHS) (Schwarz et al., 2008). The conclusion can be drawn that the prevalence rate of underweight children in countries that adopt the new WHO charts will be different from the CDC, the NCHS, and national references.

Depending on the reference growth curves, the prevalence of malnutrition varies (Joosten et al., 2010). The WHO Growth Reference Study Group conducted a longitudinal study between 1997 and 2003 to establish the new child growth charts in healthy, breast-fed children from 6 countries, including Brazil, Ghana, India, Norway, Oman, and the USA (WHO Multicentre Growth Reference Study Group, 2006a). It is likely that the prevalence of under or overweight is affected by introducing the new charts. Juliusson et al explored that in comparing the new WHO standards to the national growth curves of Belgian and Norwegian children, the proportion of children with malnutrition are highly deviated from the norm. The pattern of breastfed children in both countries was more compatible with the national standards than the WHO one (Juliusson et al., 2011). Many other studies which have attempted to compare the new WHO standards with previous standards have obtained similar results to those discussed by Juliusson et al. For instance, cross-sectional data from longitudinal studies in India, Peru, and Vietnam indicated that using WHO standards, a higher proportion of children were stunted and fewer children classified as underweight in all 3 countries (Fenn and Penny, 2008). Similar evidence has been provided by a prospective birth cohort study in Gabonese

children, which reported that when using the new WHO standards, a higher proportion of 3-month-old infants were underweight compared with previous child growth charts/references (CDC or NCHS) (Schwarz et al., 2008). The conclusion can be drawn that the prevalence rate of underweight children in countries that adopt the new WHO charts will be different from the CDC, the NCHS, and national references.

Criteria choice

The prevalence of malnutrition also depends on the criteria adopted (Joosten and Hulst, 2008). Various definitions and criteria are used to describe the prevalence of malnutrition (Table 1.2). In Europe, the prevalence of malnutrition in hospitalised children has been reported to range from 6% to 30% (Joosten and Hulst, 2008; Pawellek et al. 2008). This wide disparity appears mostly due to the inconsistency of criteria used for defining disease-associated malnutrition in paediatric patients. Very recently, a prospective multi-centre European study in 12 countries, reported that, using the criterion of BMI< - 2SD, malnutrition was shown in 7.0% of the patients at hospital admission, with a range 4.0 - 9.3% across countries (Hecht et al., 2014). According to WHO criteria, acute malnutrition or wasting is determined using WFH standard deviation (SD) scores or BMI, whilst HFA SD scores are commonly used for chronic malnutrition. The likelihood of malnutrition is defined using a cut-off point of < -2 SD score (WHO Tech Rep, 1995).

Wright and Garcia (2012) have looked at this issue more capably and noted that "in the absence of a gold standard for diagnosis, the prevalence of child under-nutrition in community studies in affluent societies mainly depends on the measure, threshold and the growth reference used, as well as age." The authors explored how different syndromes of wasting, stunting and failure to thrive can be overlapped, reflecting true under-nutrition. They revealed that children who had both weight faltering and low BMI in infancy show growth and body composition patterns later in childhood that is suggestive of previous under-nutrition. Older children showed less overlap. Wright and Garcia concluded that while low individual measures are useful for identifying under-nutrition where under-nutrition is common, they will cause overdiagnosis when in it is rarer and they argued that under-nutrition might be better identified using both a decline in weight or BMI centile and wasting.

The use of specific references for specific medical conditions

Using disorder-specific growth charts (available for some genetic disorders such as Down syndrome) helps differentiate between normal growth for children with specific conditions and alterations in growth rate due to poor nutrition (Bear and Harris, 1997).

1.3.1.2 Trends in child's under-nutrition in the community

The reduction of infant and young child malnutrition is essential to the achievement of the Millennium Development Goals (MDGs) and nutrition is at the top of the global development agenda. The latest prevalence estimates of stunting and underweight amongst children under five years of age worldwide suggest that there has been a decrease since 1990 (UNICEF, WHO, World Bank, 2012). In 2011, 26% of children under five years of age were stunted (HEA<-2SD), a 35% decrease from 1990. 16% of children under five years of age were underweight (WFA<-2SD) – a 36% decrease from 1990. 8% of children under five were wasting (WFH/L<-2SD) – a 11% decrease from 1990. Although the prevalence of stunting and underweight amongst children under five years of age worldwide has decreased since 1990, overall progress is insufficient (UNICEF, WHO, World Bank, 2012).

Unlike the high prevalence of malnutrition in developing countries, the prevalence of malnutrition in the community based studies in affluent societies has been reported to be very low. A review of twelve studies regarding the prevalence of undernutrition in affluent countries demonstrated that using the second percentile (- 2 SD), the prevalence of wasting and stunting tends to be in the range of 1-4%, which is roughly the proportion of healthy children expected to be below that threshold (Wright and Garcia, 2012).

1.3.1.3 Changes in prevalence of malnutrition in hospitalised children

The prevalence of malnutrition in hospitalised children has not changed significantly (Sullivan, 2010). Although comparisons between studies regarding the prevalence of malnutrition are somewhat confounded by the use of different definitions of malnutrition, the accretion of published data indicates the existence of malnutrition amongst hospitalised children (Table 1.2). For example, Moy et al. in 1990 reported that 14% of 273 children in Birmingham Children's Hospital, UK, were severely wasted, with a further 20% being

considered to be ‘at risk’ of severe nutritional depletion. Similarly, Pawelleck and colleagues in 2008 found that 24.1% of 475 consecutive admissions to a Children’s Hospital in Munich, Germany, were malnourished according to the Waterlow criteria. Moreover, Joosten et al. in 2010 have shown that nearly one in five children in the Netherlands are malnourished on admission to hospital. Thus, malnutrition is still an unrecognized and untreated problem in the hospital settings. However, as outlined earlier it should be noted that the reported prevalence of malnutrition in hospital are assessed using anthropometric measurements only, in children who may exhibit disordered growth and body proportions due to disease. Therefore, the figures from such studies may not be reflective of the true rate of malnutrition in the hospital.

Table 1.2: Prevalence of malnutrition and risk of under-nutrition in hospitalized children using different criteria

Authors	Published year	Study population	Criteria used	Prevalence of malnutrition (definition)	Risk of future malnutrition
De Moraes Silveria et al.	2008	426 children, 1 months -12 yr, general paediatric hospital, Brazil	WFA, WFH, HFA, BMI <5 yr: WHO/2006 standards , >5 yr: NCHS reference	WFA: 18% WFH: 10% HFA: 21% BMI: 15% (z-score ≤-2)	Not assessed
Pawelleck et al.	2008	475 children, Dr von Hauner Children's Hospital in Munich, Germany	Waterlow criteria	6.1% (WFH≤80th centile) 24.1% at high risk (WFH≤90th centile)	
Joosten et al.	2010	424 children, 1 month – 18 yr, 44 hospitals, Netherland	WFH, HFA (WHO reference)	11% acute, 9% chronic, overall 19% (z scores ≤-2)	54% at moderate risk, 8% at high risk based on STRONGkids score
Aurangzeb et al.	2012	150 children, 0 – 18 yr, Australia	WHO criteria, as above	4.5% wasted, 8.9% stunted (SD scores ≤-2)	47.8% at high risk based on NRS score
Husentruyt et al.	2013b	368 children, 1 month – 16 yr, Belgium	WFH, HFA (Belgium reference)	8.7% acute, 7.9% chronic (SD scores ≤-2)	45% at moderate risk, 7.6% at high risk based on STRONGkids score
Hecht et al.	2014	2567 children, 1 months –18 yr, 14 centres in 12 countries (Multi-centre European study)	BMI and WFH <-2 SDS (WHO reference)	7.0% (Range 4.0-9.3% across countries) (BMI<-2 SD)	Not assessed
Baxter et al.	2014	322 children, 1 months –19 yr, Hospital for Sick Children in Toronto, Ontario	WFH, HFA (WHO reference)	6.9 % acute, 13,4% chronic (SD scores ≤-2)	Not assessed

1.3.1.4 The need to screen for risk of malnutrition in hospitalised children

Although the risk of malnutrition in hospitalised children is high, it is not necessarily recognized. Both malnutrition and disease severity can affect outcomes such as prolonged hospitalisation, complicated rate, slowing of growth, and increased susceptibility to various infections. As an important part of routine admission procedure and early detection of the risk for malnutrition among hospitalised children, the screening for nutritional risk and status is thus considered essential for earlier management and prevention of those negative outcomes and adverse effects of hospitalisation. Quality Improvement Scotland has published standards for food, fluid and nutritional care, which state that all patients should be screened for under-nutrition on admission, and periodically during their stay at hospital (NHS QIS, 2003). Whilst a vast number of malnutrition screening tools have been developed for adults (Green and Watson, 2005), few reliable screening tools have been validated in children, particularly infants.

1.3.1.5 Criteria for choosing a screening tool

As aforementioned, screening tools basically identifies patients who require more a detailed assessment and subsequently, an individualised management. It should be simple, rapid and easy to screen patients (Corish, 1999). Screening tool should be reliable, applicable and acceptable by patients and users (Cochrane and Holland, 1971). It is designed for specific age groups and purpose. It is essential that the screening tool has demonstrated its qualities, is fit for purpose and appropriate agreement is reached regarding compliance/ acceptability and the practicality of the tool before it is implemented (Elia et al., 2012).

The qualities of a tool are discussed in terms of key characteristics relating to its validity and reliability (Burden et al., 2001). The validity of a screening tool is tested by its ability to give a true measure of a patient's degree of risk. It includes two main components: sensitivity (the ability to detect risk when really present) and specificity (the ability to produce negative results where the patient is not at risk). In other words, the validity of a nutritional screening tool represents how precise the tool is in identifying the patients with or at risk of becoming malnourished on admission to hospital. A screening tool also should be reliable, producing

consistent results when is used by different people such as nursing staff, dietitians or clinicians.

Validity and gold standard

Different types of validities have been considered to assess the suitability of screening tools for clinical use, including criterion, concurrent, predictive and discriminant validity. However, assessing the validity of screening tools in the absence of both a universally agreed definition of malnutrition, and a gold standard (Meijers et al., 2010; Joosten and Hulst, 2014) has been of controversial debate.

The use of one tool to judge the relative merits of another tool can be misleading, as different tools have been designed for diagnostic, prognostic or both purposes (Elia and Stratton, 2011). For example, to test the concurrent validity, the extent of agreement between different tools is considered for comparison of the quality of the tools. However, one tool cannot be compared with another tool to judge for its utility. In some studies, the validity of the tool has been assessed by comparing all the tools tested with one tool, such as SGNA (Wonoputri et al., 2014), a full nutritional assessment (Gerasimidis et al., 2010; McCarthy et al., 2012), the presence of a nutritional intervention (Ling et al., 2011), or finally, anthropometric criteria (Hulst et al., 2010) as the 'gold' or reference standard. The ones, who are classified by reference standard as being malnourished, but as well-nourished by the tool tested, are considered as misclassified. Thus, in the lack of any proved 'gold' standard, the sensitivity and specificity analysis have resulted in the use of many different reference standards and consequently, very different results.

Moreover, in some studies, greater importance has been attached to how well screening tools predict the clinical outcomes, without considering nutritional interventions. Raslan et al. noted that clinical outcome during hospital stay is considered the most efficient criterion of the screening tool (Raslan et al., 2010). However, other criteria can be also important. Elia and Stratton argued that screening tools cannot be expected to predict clinical outcomes. Nutritional interventions as well as observed outcomes are essential to adequately assess these tools (Elia and Stratton, 2011).

Thus, the evaluation of the suitability of a screening tool for clinical use must consider many factors, but ideally its use would be tested as a randomized intervention, though no study has yet reached this step.

1.3.2 What are the advantages of simple measurement in identification of malnourished children?

Simple measurements, such as anthropometry, can be considered as beneficial due to good reproducibility, and the fact that it provides an easy and basic procedure for the identification of children who are malnourished. The application of such measurements are also suitable in settings where the prevalence of severe malnutrition is high. Simple objective measurement is likely to be associated with better inter-rater agreement than a more complex tool, which may consider subjective measures that require decisions about vague issues. Moreover, simple measurement can be applied for the diagnostic purpose of malnutrition, particularly in hospital settings where there are limitations in terms of resources, nutritionists or a dietetic team. Simple measurements are valuable in the early detection and treatment of severe acute malnutrition. It is thus emphasized that in all children, weight and height measurements and the subsequent interpretation of such measurements using appropriate growth charts should be performed routinely in the hospital setting.

However, whilst simple measurements such as anthropometric measurements provide information about the current nutritional status of a child, they will not identify those at risk of developing malnutrition in future. It is for this purpose that various screening tools have been developed.

1.3.3 Current nutrition screening tools for hospitalised children

1.3.3.1 Clinician Delivered Specialist Assessment tools

Recently a variety of nutritional screening tools have been developed for assessment of nutritional status of children in hospital settings. Sermet-Guadelus et al. (2000) developed a Simple Paediatric Nutritional Risk Score (PNRS) to identify children at risk of malnutrition during hospitalisation. In this study 296 children were evaluated for nutritional risk in the first two days after admission and it was found that a weight loss of more than 2% of most

recently recorded weight was related to 50% reduced food intake as well as pain, and the severity of the pathologic conditions. Secker and Jeejeebhoy (2007) developed the Subjective Global Nutritional Assessment (SGNA) screening tool, and tested its validity to identify children who are at a high risk of nutrition-related complications and prolonged hospital stay. The evaluation of 175 children with abdominal surgery comprised history of child's current height and weight, parental heights, dietary intake, frequency and how long they had been symptomatic, functional capacity and nutrition-associated physical examination. These items together led to a global assessment of the patient's nutritional status. SGNA successfully divided children into three groups (well-nourished, moderately malnourished, and severely malnourished) with significantly different mean values for various anthropometric measures. The tools described by Sermet-Gaudelus et al. and Secker and Jeejeebhoy are able to identify children at risk of malnutrition during hospitalisation. However, both mentioned tools are too complex and take too long to complete to be used in clinical practice**.** The tool developed by Sermet-Gaudelus et al. takes 48 h after admission to be completed**.** The SGNA is also rather complex, as further details related to the history of the child have to be obtained. Furthermore, healthcare staffs are often reluctant to implement a time-consuming tool.

1.3.3.2 Short, nurse-delivered tools

McCarthy et al. (2008 and 2012) developed the Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP) at Manchester Children's Hospital, which refers to a combination of measurements of weight and height, with two additional questions on disease risk and intake. This tool was deemed reliable when compared to a nutritional assessment by a registered paediatric dietician. However, STAMP was also found to be time-consuming and complex to use, with nurses being unwilling to plot growth and BMI centile charts whilst using it during the pilot scheme.

Another tool, the Paediatric Yorkhill Malnutrition Score (PYMS) has been developed by Gerasimidis et al. (2010) to help nursing staff identify undernutrition in children on admission to hospital. The PYMS outlines four stages, each of which bears a nutrition risk score, and the combined score corresponds to overall undernutrition risk of the patient. This tool was evaluated via four questions which consider the BMI value (using wheel and look up table not plotting), recent weight loss, decreased intake the previous week, and the expected nutritional

state one week after admission. Full dietetic assessment was used as the reference standard to assess the validity of this tool, classifying children as low, medium, or high malnutrition risk. Gerasimidis et al. (2010) noted that 47% of children scored as being at high risk of malnutrition by the nurse-rated Paediatric Yorkhill Malnutrition Score were identified as being at the same risk on the full dietetic assessment (true positive). It was found that the PYMS screening tool is an acceptable screening tool for identifying children at risk of malnutrition without producing unmanageable numbers of false-positive cases. Gerasimidis et al. (2011) also assessed the performance of PYMS by auditing completion rates, yield, and impact on dietetic workload via the evaluation of dieticians' feedback. It was reported that PYMS is feasible for use by paediatric staff, indicating a high yield of patients at risk of malnutrition without requiring significant increases in staffing levels or workloads. However, this tool is not suitable for nutritional screening of infants, as it has not been designed for this age group.

Finally, Hulst et al. (2010) developed a simple tool for assessing nutritional risk, called STRONGkids (Screening Tool Risk on Nutritional Status and Growth), which was performed and tested in a nationwide study on 424 children with a median age of 3.5 years (31d-17.7 years), admitted to 44 hospitals in the Netherlands. This tool consists of four items; high risk of disease; nutritional intake and losses; weight loss or poor weight gain, and; subjective clinical assessment. The four questions in this tool can be completed shortly following admission, and the nutritional risk can be assessed fairly imminently. STRONGkids predicted that 57% of the children were at moderate risk, and 8% were at high risk of developing malnutrition, whilst the prevalence of malnutrition based on the weight and length measurements was 19%. This study noted a significant relationship between a high-risk score, a negative SD score in weight-for-height, and a prolonged hospital stay. The tool was successfully applied to 96% of the children included in the Dutch hospitals, although representation of this cohort is unclear. It seems that use of the STRONGkids tool will help to raise clinicians' awareness of nutritional risks, and might help them in early detection of children at risk, enabling their introduction of the appropriate intervention referral system. However, there is a lack of measuring inter-rater variability that can test the sensitivity or specificity of the STRONGkids tool.

1.3.3.3 Consideration of the different aspects of current nutrition screening tools

Although all the screening tools described above have been developed for use in hospitalised children, they have been designed for various purposes and comprised different components. Furthermore, in the lack of an accepted gold standard for the assessment of the nutritional status of children, the qualities of those tools have been evaluated using different gold or reference standards. Additionally, the issues regarding their applicability in routine clinical settings are considered the most crucial debate. Thus, the nutritional screening tools currently available for hospitalised children are reviewed in this thesis to consider each of the following issues; purpose, components, validity and reproducibility, and, limitations and applicability.

1.3.3.3.1 Purpose

According to European Society of Parenteral and Enteral Nutrition (ESPEN), " the purpose of nutritional screening is to predict the probability of a better or worse outcome due to nutritional factors and whether nutritional treatment is likely to influence this" (Kondrup et al., 2003). Elia and Stratton in their review noted that, nutrition screening tools are designed for a number of purposes, but all broadly relate to identifying individuals in need of intervention (Elia and Stratton, 2011).

While this is true for all the too shown in Table 1.3, SGNA, STAMP and PYMS also assess nutritional status. And PNRS, PYMS and STRONGkids aim to predict future clinical state. However, there is a lack of tools designed to predict the effects of nutritional interventions in patients. Furthermore, none of these screening tools were designed to predict the clinical effects of nutritional interventions in paediatric patients, which would effectively prove the true outcome of malnutrition risk, and thus the effectiveness of these tools.

Table 1.3: Patient characteristics and aim of the screening tools

Tools	Population/setting number and age	Aim		
		Identify nutritional status	**Identify need for nutritional intervention**	**Predict clinical outcome without nutritional intervention**
PNRS Sermet-Gaudelus et al. 2000	Medical/surgical 296 children >1 month-18yr		×	×
SGNA Secker and Jeejeebhoy 2007, 2012	Surgical 175 children >1 month-18yr	×	×	
STAMP McCarthy et al**.** 2008, 2012	Medical/surgical 110 children 2–17 yr	×	×	
PYMS Gerasimidis et al**.** 2010, 2011	Medical/surgical 247 children 1-16 yr	×	×	×
STRONGkids Hulst et al. 2010	Medical/surgical 423 children >1 month-18yr		×	×

PNRS: Paediatric Nutrition Risk Score; SGNA: Subjective Global Nutritional Assessment; STAMP: Screening Tool for the Assessment of Malnutrition in Paediatrics; PYMS: Paediatric Yorkhill Malnutrition Score; STRONGkids: Screening Tool for Risk of Impaired Nutritional Status and Growth.

1.3.3.3.2 Components

According to ESPEN guidelines in 2003, "screening tools are designed to detect protein and energy undernutrition and/or to predict whether undernutrition is likely to develop or worsen under the present and future conditions of the patient". They specify four main principles of screening tools as follows:

1) "How is the actual condition now?" Body composition is affected by patient's clinical and nutritional state. Current condition can be described using measurements of height and weight which allows BMI to be calculated.

2) “Is the condition stable?” Recent weight loss found through patient's history or medical records is used to indicate instability.
3) “Will the condition worsen?” This assesses the length of time and likely extent of decrease food intake which may lead to worsening.
4) “Will the disease process speed up nutritional deterioration?” The nature of the individual disease may increase nutritional requirements due to the stress metabolism which can lead to a poor nutritional status.

The first three are considered in all tools, but the 4^{th} one is specific to the hospital setting. Each variable must be given a score in every screening tool and the degree of the risk is consequently calculated (Kondrup et al., 2003).

The components of each paediatric nutritional screening tools can be considered according to these four main principles laid out by ESPEN (Kondrup et al., 2003). As shown in Table 1.4, the PYMS, SGNA and STRONGkids include all these 4 items in their tool. Whereas anthropometric measurements are used to define actual nutritional status by PYMS and STAMPS, subjective clinical assessment is the basis of SGNA and STRONGkids. The STRONGkids tool has been considered to be more time-effective than STAMP due to the exclusion of weight and height measurements (Ling et al., 2011). However, some may consider this as its disadvantageous (Sullivan, 2010; Hartman et al., 2012). Paediatricians may believe that they can recognize a malnourished child but the facts do not always agree with this. Reproducibility in the clinical assessment of nutritional status was reportedly poor in a study carried out by Cross et al (1995), especially in the assessment of the more severely malnourished children. Clinical evaluation of nutritional status alone is inadequate for accurate assessment and anthropometry is important (Sullivan, 2010). Both STRONGkids and STAMP consider the impact of disease on nutritional deterioration and, unlike PYMS, have included a list of underlying diseases. The PNRS and SGNA have included additional items (pain for PRNS and gastro-intestinal symptoms, parental height and functional capacity for SGNA).

Table 1.4: Comparison of the components of each paediatric screening tools based on four main principles of a screening tool according to ESPEN

Tools	Current nutritional status (criteria used)		Weight loss	Reduced intake	Disease severity	Additional items
	Objective	Subjective				
PNRS				×	×	Pain assessment
SGNA		×	×	×	×	gastrointestinal symptoms, Functional capacity, Parental height
STAMP	×			×	×	Using a list of underlying disease
PYMS	×		×	×	×	
STRONGkids		×	×	×	×	Using a list of underlying disease

PNRS: Paediatric Nutrition Risk Score; SGNA: Subjective Global Nutritional Assessment; STAMP: Screening Tool for the Assessment of Malnutrition in Paediatrics; PYMS: Paediatric Yorkhill Malnutrition Score; STRONGkids: Screening Tool for Risk of Impaired Nutritional Status and Growth.

1.3.3.3.3 Validity and reproducibility

The characteristics of an ideal screening tool and possible issues concerning the current paediatric nutritional screening tools have been described earlier. As summarized in Table 1.5, various methods have been used to evaluate the performance of each of these screening tools.

Different evaluations of validity have been done for each tool, but they usually assessed predictive validity (prediction of outcomes) and criterion validity (sensitivity, specificity). STAMP (McCarthy et al., 2012) and PYMS (Gerasimidis et al., 2010 and 2011) tool assessed sensitivity, specificity and positive productive values using full dietetic assessment as the gold standard. The sensitivity, specificity and positive predictive value were reported as 72%, 90% and 55% respectively for the STAMP tool. These values were 59%, 92% and 47% respectively for the nurse-rated PYMS tool. Discriminant and concurrent validity were also tested in the PYMS study.

Good reproducibility (agreement between users of a given tool) is clearly a desirable characteristic. Reproducibility was tested in the SGNA, STAMP and PYMS tools, showing fair agreement in SGNA (Secker and Jeejeebhoy, 2007) and fair to moderate agreement in

STAMP (McCarthy et al., 2008 and 2012) and PYMS (Gerasimidis et al., 2010 and 2011) tools. Gerasimidis et al. reported that The PYMS rating completed by the two dieticians concurred with the nursing staff for 86% of low and medium-risk patients. This is in agreement with the fact that objective measurements are likely to be associated with better inter-rater agreement than subjective measures (Elia and Stratton, 2011).

Table 1.5: Reproducibility and validity of the screening tools

Tools	Sensitivity	specificity	Gold or reference standards for validation	Type of validity	Reliability (reproducibility)
PNRS	_	_	Risk of losing weight during hospitalisation	Predictive	_
SGNA	_	_	Objective nutritional assessment	Criterion	Third assessor; kappa, 0.28
			Complication frequency	Predictive	
STAMP	70%	91%	Full dietetic assessment	Criterion	Full dietetic assessment vs STAMP; kappa, 0.54
PYMS	59%	92%	Full dietetic assessment	Criterion	Dieticians vs nursing staff; kappa, 0.53
			Other screening tools	Concurrent	
			Lean and fat index	Discriminant	
STRONG kids	_	_	Length of hospital stay	Predictive	_

PNRS: Paediatric Nutrition Risk Score; SGNA: Subjective Global Nutritional Assessment; STAMP: Screening Tool for the Assessment of Malnutrition in Paediatrics; PYMS: Paediatric Yorkhill Malnutrition Score; STRONGkids: Screening Tool for Risk of Impaired Nutritional Status and Growth.

1.3.3.3.4 Limitation and applicability

A valid and reliable tool may be of little value if in practice it is not acceptable for users, administered in different ways, and related to poor compliance (Elia and Stratton, 2011).

However, there is a paucity of data on the application of the different paediatric screening tools in clinical practice, and important aspects of their applicability are described below.

Ease and speed of administration

A nutritional screening tool should be completed quickly by different types of healthcare professionals that have apparent attraction. The type and number of items in the tool can obviously influence the time taken for administration. Taking a long time to complete renders the tool wholly impractical for use, particularly on the busy admissions ward. In the original description of PRNS, it was mentioned that it took 48 hours to complete all components of the tool. Although referred to as a screening tool, SGNA is better referred to as a structured nutritional assessment, and one of its limitations for use in clinical practice may be the time required to complete it. However, the time taken to complete the SGNA or the necessary level of training and expertise of the assessors has not yet been reported, both of which are important considerations that need clarification.

The other three paediatric screening tools consider ease and speed of use in their criteria. A cross-sectional study (Ling et al., 2011) found that STAMP and STRONGkids took 15 and 5 minutes to apply. It has been reported that the longer time the STAMP tool takes may due to the element of anthropometric measurement in this tool (Joosten and Hulst, 2014). Gerasimidis et al. (2012) published a paper that complements their work on the validity and clinical performance of PYMS (Gerasimidis et al. 2010, 2011). They examined the feedback of hospital nursing staff on aspects of PYMS use in clinical practice by using a self-administered questionnaire and included questions on nurses' work area, qualifications and specifically on the use of PYMS. Considerations of the PYMS included ease of use, time taken to complete, ease of integration into clinical practice, any increase in nursing workload, impact on patient care, and any issues with the PYMS use and its components. Prior to launching PYMS, nursing staff attended a one-hour awareness session and received training on the use of anthropometric techniques. It was reported that eighty nurses (about half of all nursing staff) completed the survey. The majority of nurses found PYMS easy and quick to use in routine clinical practice. 85% of nurses reported the PYMS took less than five minutes to complete, and registered nurses who attended a training session needed less time to complete the tool. This suggests that in contrast to Ling's et al. study (2011), anthropometric measurement is unlikely to influence the time necessary for the completion of the PYMS tool.

Regarding the findings of Ling's et al. study, STAMP may have taken longer to use partly due to the plotting of growth and BMI centile charts.

Feasibility (compliance)

Although in Gerasimidis's et al. study (2012), the BMI step was perceived to be the most challenging, nursing staff did not find the calculation of BMI difficult using a wheel. Rather, the measurement of height was reported the most difficult aspect of the BMI step, particularly on specialist wards where some patients are unable to be measured for height. In this case, it has been recommended that the BMI step can be replaced with measurement of body weight. It is noted that PYMS can be practical and feasible for routine clinical nursing use, although training is fundamental for its efficient use. However, the majority of nursing staff (83%) reported that completing PYMS increased their workload. Thus, one of the limitations of the PYMS is that it would need essential resources if it is to be introduced in routine clinical practice (Gerasimidis et al., 2012).

It was reported in the original manuscript of the STRONGkids tool (Hulst et al., 2010) that while in this study nearly all the children (98%) could be investigated by applying STRONGkids tool, data collected in the McCarthy et al study lacked essential information (weight and/or height) for about 17% of children needed to calculate STAMP risk score (McCarthy et al., 2008).

1.3.4 Approaches to design and evaluation of screening tools

1.3.4.1 What has been done so far?

To date five paediatric nutritional screening tools have been developed and evaluated for children admitted to the hospital. While SGNA, PYMS and STRONGkids were developed using the ESPN guidelines, PRNS and STAMP were developed based on the factors that had been already found as the significant predictors of nutritional risk in previous studies. Identifying children at risk of malnutrition and need for intervention was the main aim of the above mentioned tools, but STAMP, PYMS and SGNA also assessed nutritional status on admission. PYMS, SGNA and STRONGkids were also described as being useful to predict of clinical outcome but there is a controversial debate that the effect of nutritional intervention on clinical outcome should be determined by screening tools.

These tools have been also validated using different gold standards - PNRS and SGNA were validated for predictive outcome, and STAMP for full dietetic assessment. However, their practicality in clinical use is questionable. PYMS and STRONGkids were also validated by full dietetic assessment and predictive outcomes respectively, and their practicality have been reported to be fairly good. STRONGkids can be used to identify only the patients who are at risk of becoming malnourished during hospitalisation, whereas PYMS can be applied for the identification of both patients who are currently malnourished and those who are at risk of becoming malnourished.

1.3.4.2 What has been assessed and what is still unknown

Many screening tools have been developed and validated for paediatrics, but there is no universally accepted tool to use in paediatrics inpatients. Considering that various gold standards have been used to validate the nutritional screening tools, there is a need for agreement on the definition of malnutrition and the gold standard used in validation studies. Moreover, there is a scarcity of data on the application of paediatric nutrition screening tools in routine clinical practice. Although the applicability of the STRONGkids and PYMS tool has been assessed in some aspects, there is a need to determine the practicality and applicability of the paediatric screening tools. Furthermore, none of the currently developed screening tools were designed to predict the clinical effects of nutritional interventions in order to provide evidence of the true nutritional outcome and the effectiveness of the tool. Thus, interventional trial studies are needed to evaluate the effectiveness of the nutrition screening tools. Finally, as none of current screening tools developed for children are suitable for nutritional screening of infants, it is important that a nutritional screening tool is designed and validated specifically for infants.

1.4 Contextual overview of the settings in which the study was done

This thesis was designed to be conducted in two different hospital settings; The Royal Hospital for Sick Children, UK, and Tabriz Children's Hospital, Middle East, Iran.

Tabriz, Iran

Geographically, Iran is located in West Asia, encompassing an area of 1,648,000 square kilometres and ranking eighteenth in terms of size of world countries.

Iran's population increased dramatically during the latter half of the 20th century, reaching approximately 75 million by 2011. According to the World Bank statistics population growth in Iran from 1990 to 2008 was 17.6 million, and 32%. In recent years, however, Iran's birth rate has dropped significantly. Studies project that Iran's rate of population growth will continue to slow until it stabilizes above 100 million by 2050. More than half of Iran's population is under 35 years old (2012).

Tabriz is the most populated city in the northwest of Iran. It is one of the historical capitals of Iran, and the present capital of East Azerbaijan Province. Tabriz has a population of 1,545,491.

Tabriz Children's Hospital

Tabriz Children's Hospital is a tertiary, central and University hospital in Tabriz city. Its wards include internal B ward (gastrointestinology, cardiovascular, allergy, asthma, nephrology), internal A ward (neurology), haematology-oncology and haemodialysis as separate wards, NICU-PICU, neonatal and paediatric surgery, ENT, emergency, and infectious diseases wards. There are also out-patient services that encompass specialty and subspecialty clinics. This is a 200-bed-hospital, and has one child per bed policy. The spaces between beds are quite close and some wards, such as the infectious diseases ward, are very crowded. Although the health care system can be rather good, in terms of the dietetic department, there is only one, unregistered, dietitian in this hospital, whereas the Royal Hospital for Sick Children employs 20 registered dietitians.

This central tertiary hospital covers all referrals from the different cities of the East Azerbaijan Province, and also some more critical and complicated patients referred from the three other states (West Azerbaijan, Kurdistan and Ardebil). It should be noted that this hospital is not the only children's hospital in Tabriz, and there are three more general hospitals for children in this city. Patients admitted to the hospital are either sent by other doctors, or with families who come to the out-patients clinic in the hospital. There is no comprehensive referral system in

Iran. However, recently a referral system has been established in one of the big cities (Shiraz) as a pilot system and government plans to expand it in the other cities.

In terms of primary health care system in Iran, It should be noted that health centers in the urban and health houses in the rural areas mainly provide the free publicly funded primary health care by Ministry of Health and Medical Education for people particularly for young children. These are accessible for everyone apart from people who are living in the areas with very limited facilities. Health houses and centers are where malnutrition should be detected. Children from the health house or health center are referred to the hospital by general physicians, rather than Paediatricians although the referral system still is not enough managed everywhere.

Breast-feeding is supported in Tabriz Children's hospital, and mothers come in and can stay with their child in NICU unit. Mothers are supported to express breast milk and avoid formula supplementation. Furthermore, there is a breast-milk bank in the hospital. There is no maternity unit in this hospital, but it is located in another hospital which also has a prenatal-care unit and a very good unit for high risk neonates that is linked with the Tabriz Children's Hospital.

***Royal Hospital for Sick Children, Glasgow*, UK**

Royal Hospital for Sick Children is the only tertiary and University Teaching Hospital in Glasgow, specialising in paediatric healthcare. Care system is based on the NHS Scotland. This hospital provides care for newborn babies up to children around 13 years of age. The Hospital has 266 inpatient beds and handles approximately 90,000 out-patients, 15,000 in-patients every year**.**

Tabriz children's hospital compared to the Royal Hospital for Sick Children, Glasgow

Unlike Iran, there is a good referral system in the UK whereby patients are allowed to come to the hospital if they are referred by their general practitioner (GP). It should be noted that there is a very efficient referral system in the Royal Hospital, UK, and is representative of UK system in general. There is a neonate unit in the Royal Hospital.

Considering the above, it can be concluded that the Iranian health care system is quite different to that of the UK, but that Tabriz children's hospital and Yorkhill Hospital are more

similar in structure, apart from in Tabriz Children's Hospital, families can just turn up in the absence of a referral.

Trends in child's under-nutrition in Iran

For the first time in 1991, the national prevalence of underweight (measurement of weight-for-age) children was determined using the percentile in both urban and rural areas. In 1995, another study presented further information on the national anthropometric indices of children in urban and rural areas using the z-score. Subsequently, a national study in 1998 looked at the same anthropometric criteria in children under six year olds but at a provincial level, and with greater variety including the awareness and performance of the mothers in the area of growth monitoring. This study used cluster sampling, with twelve children under the age of six in each cluster selecting 50 urban and 50 rural areas in each province (UNICEF, Evaluation Report., 1999). This study reported that 5% of children suffered from moderate to severe wasting. The prevalence of wasting was higher in southern compared to northern provinces. Wasting was observed with a greater frequency in the urban areas of provinces which displayed a high population density. At the national level, the prevalence of wasting was similar in boys and girls, but differences were observed at the provincial level. 15% of children suffered from moderate to severe stunting. The prevalence of stunting was reported to highest in eastern provinces, and was significantly higher (two times) in rural areas than in urban ones. The weight of nearly 11% of children was reportedly lower than expected for their age. Underweight children were significantly more prevalent in rural than in urban regions at 13.7% vs 9.6% respectively. Comparison of the findings of this study to previous studies shows that the nutritional status of children has generally improved over a seven-year period. However, a significant difference persists between the prevalence of underweight children in urban and rural areas, and the extent of malnutrition still constitutes a major problem. Furthermore, the proportion of children whose weight is regularly measured and/or registered on growth charts was shown to be low (UNICEF, Evaluation Report., 1999).

WHO categorises the prevalence of underweight in countries using four categories (<10%, 10-19%, 20-29%, and ≥30%) referred to as relatively low, medium, high and very high underweight prevalence (De Onis et al., 1993). The prevalence of underweight in Iran (11% in

1999) can thus be considered as being in medium underweight status and of some public health importance. This rate is similar to the rate of underweight (11.3%) reported for the modelled regional data for Western Asia in 2000 (Onis (De et al., 2004). However, the prevalence of stunting (15%) in Iran in 1999 compared to WHO categories (<20% referred to as low) is lower (De Onis et al., 1993) and less than reported for the modelled regional data for Western Asia (18.7) in 2000 (Onis (De et al., 2004). These suggest that Iran in terms of stunting compared to the both the international and the regional data can be in a better status than of the underweight.

According to the UNICEF's report in 2011, the rate of underweight children in Iran experienced a 50 percent reduction between 1991 and 2007, yet the prevalence of wasting increased by 30 percent from 1998 to 2007. Further, the levels of stunting run as high as 20 percent in some provinces. Also the rate of exclusive breastfeeding for the first six months of a child's life has declined from 50 percent in 2005, to 23 percent in 2010- a trend that can seriously threaten the nutritional status of children from infancy (UNICEF: Report on Regular Resources, 2011).

1.5 Overall conclusion and purpose of the study

The high prevalence of malnutrition in paediatric inpatients worldwide emphasises the importance of the identification and appropriate nutritional management of children who are admitted to hospital. However, malnutrition is often unrecognized and untreated in paediatric hospitals. This is partly due to the fact that there is no gold standard method for undertaking a comprehensive nutritional assessment of children. Although anthropometry can give a basic assessment of nutritional status, body composition assessment can provide more precise details of the nutritional status of a child. However, it may not be possible for paediatricians or dietitians to complete full assessments on all patients. Moreover, nutritional assessment identifies just those patients who have already become malnourished. To prevent nutritional deterioration and improve the early identification of children at risk of malnutrition, nutritional screening is required. The five currently developed paediatric nutritional screening tools (PNRS, SGNA, STAMP, PYMS, and STRONGkids) have been designed with different purposes and processes. There is a controversial debate about the usefulness of the screening tools, which can be determined based on the aspects of validity, reproducibility (reliability),

and practicality of the tool. Currently, because of the lack of universally accepted definition for malnutrition, it is impossible to validate a screening tool with a gold standard. Moreover, none of those tools are suitable for use in infants as they have not been designed specifically for children under 1 year.

The specific aims of this study therefore were:

- To evaluate the effect of a paediatric nursing malnutrition screening tool on collection of weight and height/length
- To evaluate a novel malnutrition screening scheme for infants - the infant Paediatric Yorkhill Malnutrition Score (iPYMS) to find out how well it distinguishes infants who are well-nourished from those undernourished, or at risk of being undernourished (discriminant validity)
- To compare the utility of iPYMS in different hospital settings, in the UK and in the Middle East, Iran
- To compare the usefulness of various anthropometric measures to predict malnutrition in infants
- To determine the factors that correlate with malnutrition in these hospitalised infants
- To measure body composition of hospitalised infants and explore the validity and practicality of the simplified method of analysing bio-electrical impedance to estimate body composition (fat and fat free mass) in infants.

CHAPTER TWO

BACKGROUND TO PYMS PROJECT AND INITIAL AUDIT

2.1. PYMS project

As iPYMS is based on the PYMS principles, the PYMS project is described briefly as a background to the current investigation. The PYMS was developed in Glasgow for use in children (≥ 1 year) admitted to hospital with the aim of identifying those at nutritional risk. There are currently three papers published concerning the PYMS project (Gerasimidis et al., 2010; 2011; 2012). The first two papers describe the process of the development and validation of the PYMS, and also discuss its performance in clinical practice. The third paper reports the impact of the introduction of PYMS on nursing practice.

2.1.1. Development of the paediatric Yorkhill Malnutrition Score (PYMS)

The PYMS was developed by a multidisciplinary health professional team for routine clinical use. It was based on nutritional screening guidelines of the European Society of Clinical Nutrition and Metabolism (ESPEN). The tool needed to be sensitive, quick and easy to use by nursing staff, and easy to do as part of routine hospital practise. The scoring system was designed to "reflect the clinical significance of factors associated with risk of malnutrition, and aim to raise awareness of this risk". The PYMS utilized four elements that were reported as recognised predictors of nutritional risk. These were specified as

"*BMI below the 2nd centile (-2 SD), history of recent weight loss, change in nutritional intake for at least the past week, and the likely effect of the current medical condition on nutritional status of patients for at least the next week"* (Gerasimidis et al., 2010).

Each step scored up to 2 points. Patients scoring 2 or more were referred to a dietician.

2.1.2. Introduction of the PYMS in clinical practice

To evaluate PYMS's validation and performance, it was conducted for the first time in 5 paediatric wards of a Tertiary Paediatric Hospital and the general paediatric ward of a District General Hospital in the UK. Screening was done on eligible patients (1-16 years) within 24 hours of admission. Nursing staff was given a training session managed by research dietician.

2.1.3. Validation of PYMS as paediatric screening tool

The validity of the PYMS was assessed by comparing the nursing screening outcomes with a full dietetic assessment, anthropometric and body composition measurements, since there is no universally definition or method to determine the nutritional status. This validation study aimed to test how the PYMS would perform in actual clinical practice, used by a large number of non-nutrition specialist nursing staff. Ward nursing staff were used as raters, and dieticians were asked to assess their accuracy. The PYMS screening tool demonstrated good diagnostic accuracy compared to full dietetic assessment and identified over half the children at risk of malnutrition. PYMS has showed moderate agreement with the full assessment (k=0.46) and inter-rater reliability (k=0.53) with the research dieticians' results.

Children who have been screened as high risk for malnutrition had significantly lower BMI and lean mass, but there is no evidence to indicate lower fat stores. A low BMI (≤ 2nd centile) has been used in the PYMS to screen for malnutrition risk, but when high risk children identified based on low BMI were excluded, the remainder still had significantly lower BMI and relatively low lean mass. A low BMI was also as a criterion strongly associated with high malnutrition risk on full assessment. This suggests that the children judged as high risk using either method were, on average, not actually malnourished. These children might be more likely to have a long-term nutritional risk and represented the majority of patients who scored high risk in the PYMS study.

In conclusion, the PYMS is an effective and acceptable screening tool for identifying children at risk of malnutrition on admission to hospital, without producing unmanageable numbers of false-positive cases. However, its utility in more specialist paediatric areas and new centres need further research (Gerasimidis et al., 2010).

2.1.4. Performance of PYMS in clinical practice

PYMS performance had to be evaluated prior to its introduction for routine clinical use by assessing compliance; numbers screen positive and service impact as well as seeking dietetic feedback.

They found that the introduction of PYMS in a TPH and a general paediatric ward of a DGH over a 4 month pilot study (between 23rd June and 28th October 2008) demonstrated high completion rates (72.3%). Although the proportion of referrals from the acute receiving wards increased, no major issue about a noticeable increase in workload has been reported in the wards where PYMS had been used. PYMS's compliance has been reported to be more than 75% and the feedback of dieticians regarding the introduction of PYMS was positive. This suggested that it would be possible apply it in routine clinical practice using current resources and not requiring extra staff. More patients at risk of malnutrition were identified without generating unmanageable false positive. They concluded that paediatric inpatients could be screened effectively by nurses using PYMS within available resources and that this would help to identify children with malnutrition (Gerasimidis et al., 2011).

2.1.5. Challenges and impact of introduction of PYMS on nursing practice

The impact of the introduction of the PYMS on nursing practice and feedback has been evaluated in eighty nurses (about 50% of all nursing staff). It was reported that the majority of nurses (96%) found the PYMS quick and easy to use in routine clinical practice during patient admission, with 85% reporting that the completion of PYMS took less than five minutes. This may be due to the fact that PYMS uses information and measurements routinely collected by nursing staff on admission.

Training has been reported to be an important aspect of PYMS implementation, highlighted by the decrease in the time taken to complete the tool by registered nurses and staff who attended the provided training sessions. Furthermore, a higher proportion of those who attended these training sessions reported PYMS as having a practical application for patients.

The step involving BMI measurement was perceived as the most challenging, although rather than the calculation of BMI which was not reported to be problematic, the measurement of height was considered the most complicated aspect of this step. In particular, nurses on specialist wards struggled with obtaining such measurements, as some patients were unable to be measured for height. Time restraints also posed a problem for height measurements in such wards. It is recommended that in such situations, BMI assessment should be replaced with measurement of body weight.

In conclusion, it has been reported that PYMS is practical and feasible for routine clinical nursing use but it may increase self-perceived workload, mainly for trained staff, which may have implications for staffing levels. Training and resources are essential for the effective and efficient use of PYMS to be introduced into routine clinical practice (Gerasimidis et al., 2012).

2.2. Initial audit

An initial audit was carried out at the beginning of the PhD course and aimed to assess the impact of implementation of PYMS on acquisition and utilization of anthropometric measurements. This was published as a research paper in the Journal of Human Nutrition and Dietetics (2013), entitled 'Acquisition and utilisation of anthropometric measurements on admission in a paediatric hospital before and after the introduction of a malnutrition screening tool' (Milani et al., 2013) (see appendix 8).

The audit underlined the importance of applicability and practicality of the nutritional screening tool, and how this affected the effectiveness of the PYNS in routine clinical practice. The findings of this audit were considered by the research team in the development and evaluation of iPYMS, highlighting the need to test the practicality of iPYMS in order for it to be used in routine clinical practice.

It is noted that the practicality of a screening tool is one of the important characteristics for it to be considered as useful in routine clinical practice. Anthropometric measurements such as height and weight are considered in most screening tools. However, one of the factors contributing to the omission of assessment of child nutritional status remains the failure to measure routinely both height and weight in all children admitted to hospital (Sullivan, 2010), and several studies have shown that the rate of anthropometric measurements, particularly height, that require anthropometric measurements on admission to paediatric hospital is low. Thus, the advantage of using screening tools that require anthropometric measurement in routine clinical practice is questionable. An audit conducted in the Children's Hospital in West-mead, the main tertiary paediatric hospital in Sydney, aimed to examine anthropometric assessment of nutritional status, identifying any hurdles and to subsequently make recommendations for service improvement (Connor et al., 2004). In this audit, dieticians

measured height and weight of a representative sample of 245 inpatients, and checked whether these measurements had been recorded on bed charts. They reported that 73% of height, and 12% of both height and weight measurements were missing on patient bed charts. None of 28 undernourished patients were reported in medical notes, and only five of 28 undernourished patients were referred to dietetic services. This audit suggested that barriers to nutritional assessment can lead to failure to diagnose and treat under-nutrition, affecting quality of patient care. Another audit determined the frequency of documentation of growth parameters (height/length, weight, BMI or weight-for-height, and presence of growth charts) in the medical records of a tertiary care paediatric hospital in 491 charts of Canadian children (Cummings et al., 2005). This audit reported that, apart from weight measurements, rates of documentation of growth parameters in the medical record were unacceptably low, with height/length being recorded in only 42% of ward charts whilst BMI/WFH were almost never recorded. Growth charts were present in only 23% of ward charts. A study in the Children's Hospital in Munich, Germany, noted that combined weight and height data were absent in around 25% of admitted children (Pawelleck et al., 2009). It is therefore suggested that there is a need not only for adequate training and education of health professionals undertaking this process, but also to encourage more regular measurements of height.

Thus, the improvement of anthropometric measurements, particularly height, on admission to paediatric hospital settings, is essential for the improvement of the effectiveness of screening tools, and the lack of these measurements render the application of these tools useless. This emphasises the need to test the applicability and practicality of nutrition screening tools in order for them to be applied in routine clinical practice.

BACKGROUND TO THE AUDIT

Acquisition of anthropometric measurements remains poor in hospitalized children (Bunting and Weaver 1997; Lek and Hughes 2009; Ramsden and Day, 2012) despite increasing awareness about nutrition as an integral part of patients' care (Agostoni et al. 2005) and worldwide initiatives to develop references for childhood growth (Wright et al. 2010). Thus health professionals miss the opportunity to identify children who have reduced growth and those patients at risk of undernutrition delaying timely intervention.

Routine use of nutritional screening tools on hospital admission is recommended to identify patients at risk of malnutrition and offer them appropriate care (Agostoni et al. 2005). Since there is no universally applicable definition of malnutrition, these screening tools identify children who might benefit from receiving dietetic intervention. These tools combine a list of questions on predictors of malnutrition risk and anthropometric measurements. Thus introduction of such tools in clinical practice might offer the opportunity to improve acquisition of anthropometric measurements, which might also improve other aspects of patients' care.

This audit aimed to evaluate the effect of the implementation of a novel nursing paediatric malnutrition screening tool (Gerasimidis et al 2010, Gerasimidis et al 2011), on the acquisition of anthropometric measurements and completion of growth charts in a paediatric hospital.

MATERIALS & METHODS

A new malnutrition screening tool, the Paediatric Yorkhill Malnutrition Score (PYMS) was developed locally (Gerasimidis et al 2010, Gerasimidis et al 2011). The tool was piloted over a four month period in four wards (one surgical, one acute medical, two medical specialized) and was subsequently introduced for routine use at the Royal Hospital for Sick Children, Glasgow. PYMS is a 4 step tool completed by the nursing staff on admission. Three steps involve assessing history of recent weight loss, changes in nutritional intake, and the predicted effect of the current medical condition on the nutritional status of the patient. In addition the height/length and weight are measured to calculate BMI and compare this against the 2^{nd}centile of a chart. Each step bears a score and the total sum reflects the patients' degree of nutrition risk (Gerasimidis et al 2010; Gerasimidis et al 2011).

Consecutive patients admitted to the aforementioned wards over a period of 14-28 days were identified from the hospital database until the required number (approximately 150 patients) was achieved. Four different time periods were used: a) one year prior to PYMS implementation (Period A), b) during the pilot introduction of PYMS (Period B), c) 10 days after pilot withdrawal (Period C) and d) one year after its implementation for routine use (Period D) was retrieved from the hospital electronic network. Medical and nursing notes were

reviewed for documentation of weight and height/length measurements performed by the nursing staff during hospital stays and plotting of these measurements on growth charts by medical staff. This audit was registered with the local clinical effectiveness office.

RESULTS

Participants' characteristics

The case notes of a total of 579 inpatients were included in the study. There were no statistical differences in patients' age between the four periods or in the percentage of patients who were reviewed by each ward between the four periods, although one of the medical specialist wards was not open in Period D (Table 1). There were significantly more infants (<1 y) in period D (Table 1).

Acquisition of weight measurements

Weight measurements were recorded in more than 97% of the inpatients during their hospital stay with no statistical difference between the four periods or wards (Table 1).

Acquisition of height/length measurements

Six (4%) inpatients had their height/length obtained in Period A compared to 65% during PYMS pilot introduction ($p<0.0001$). Within ten days of PYMS pilot withdrawal, documentation of height/length decreased dramatically to 15% ($p<0.0001$). During the official introduction of PYMS in routine practice, documentation of height/length measurements increased to levels similar to those during the pilot introduction of PYMS (Table 1). The pattern of change was similar in all wards although the proportional increase in documented height/length measurements during the Periods B (pilot use) was lower in the ward with patients from neurology and immunology specialties (Table 1). Patients who did not have their height/length measurement recorded during the two periods of PYMS implementation were significantly younger (Period B: 2.7±3.8 y; Period D: 3.3±3.7 y) compared with those who did (Period B: 6.4±3.8 y; Period D: 5.6± 3.7; both p-values<0.001). Likewise 18.8% of the children aged less than one year in Period B and 7.1% in Period D had their height/length documented as compared to 67.9% and 77.8% of the children older than one year respectively (Table 1).

Growth chart completion

Only 10 to 15% of the patients' medical notes reviewed had recent admission measurements of height/length and weight plotted on growth charts (Table 1) with no statistical difference between the four periods (Table 1). For each period proportionally more patients from a combined gastroenterology/long term respiratory ward and less from a surgical ward had their growth chart updated with recent height/length measurements (Table 1).

DISCUSSION

Assessment of linear growth should be an integral part of the standard care that the sick child receives in the hospital as it complements health professionals' judgment to identify the malnourished child. This study showed that measurements of weight are very common but those of height/length are not. Our results are similar to those by Lek and Hughes in Cambridge (Lek and Hughes, 2009) and by Bunting and Weaver in the same hospital as this current study, 15 year ago (Bunting and Weaver, 1997). However in our population documentation of weight measurements was better than in the majority of the inpatients reviewed. In the study by Lek and Hughes height/length and weight were measured in 12.5% and 51.5% of the children, and there was only one child under 2 years with height/length measurement (Lek and Hughes, 2009) whereas in the study by Bunting and Weaver there was documentation of height/length measurement for less than 12% of the children (Lek and Hughes, 2009). Despite methodological differences in these two studies, which do not allow a direct comparison of the findings, our study suggest that 15 year after the recognition of poor documentation of growth measurements and despite the development and implementation of local policy and procedures for measuring infants' growth acquisition of anthropometric measurements and particularly those of height/length remained unchanged.

A possible explanation for the high acquisition of weight measurements in our study might be the clinical need to calculate optimum/safe administered drug dosage. This is also supported by the fact that plotting on growth charts of any of the measurements was almost negligible. Likewise poor documentation of height/length prior to the introduction of the malnutrition screening tool can be attributed to the lack of height/length equipment, time required in obtaining measurements in very young and very sick children and a perception by nursing

staff that growth assessment should receive less priority compared to other aspects of patients' care.

Implementation of PYMS which incorporates measurements of height/length and weight significantly improved the documentation of height/length measurements. This change was not temporary, it remained one year after the routine implementation of PYMS in clinical practice. In infants (<1y) where completion of the PYMS by the nursing staff was not valid and hence not indicated, acquisition of height/length measurements remained remarkably poor despite our expectations for a collateral increase due to increased awareness. Nevertheless, use of these data in other aspects of patients' care, namely plotting on growth charts by medical staff, remained poor and was no different between the four different periods. This may indicate either lack of communication between nursing and medical staff who share patients' care or that other aspects of patients' care take precedence.

Despite a substantial improvement in the acquisition of anthropometric measurements, one in three patients did not have a measurement of height/length. This may have been because the PYMS was not performed by the nursing staff, or they were not able to perform height/length measurements in children unable to bear weight or in young children, where measurements of length are more laborious.

Introduction of a screening tool which encompasses measurements of weight and height/length improved the acquisition of anthropometric measurements. However this did not improve completion of growth charts and thus the potential to identify poor growth. Whether such screening tools are otherwise beneficial for patient's care still requires further investigation. This study highlights the need for continuous education to raise nutritional awareness, continuous professional development and improved communication among health professionals. Such initiatives should be endorsed by health services but also supported by senior clinical and management staff.

Table 1: Acquisition of growth measurements and completion of charts before, during and after the pilot and routine implementation of the PYMS, by speciality

Measurement	**Period A:** One year before PYMS pilot (n=146)	**Period B:** During PYMS pilot (n=154)	**Period C:** 10 days after PYMS pilot (n=151)	**Period D:** One year after routine clinical use (n=128)
Age (y): mean (SD)	5.2 (4.3)	5.1 (4.2)	4.4 (4.3)	(4.7 (3.8)
Infants (< 1y): n (%)*	23 (16)	28 (18)	46 (30)	16 (13)
Weight n(%)Total	141 (97)	149 (97)	151 (100)	128 (100)
Surgical	59 (100)	55 (100)	53 (100)	49 (100)
Acute Medical	57 (98)	60 (95)	61 (100)	61 (100)
Gastroenterology/Respiratory	7 (70)	10 (91)	12 (100)	18 (100)
Neurology/Immunology	18 (95)	24 (96)	25 (100)	N/A
Height/Length n(%)Total*	6 (4)	100 (65)	23 (15)	79 (62)
Surgical	0 (0)	35 (64)	11 (21)	30 (61)
Acute Medical	4 (7)	47 (75)	8 (13)	36 (59)
Gastroenterology/Respiratory	1 (10)	7 (64)	3 (25)	13 (72)
Neurology/Immunology	1 (5)	11 (44)	1 (4)	N/A
Growth Chart Completion				
n (%) Total	16 (11)	16 (10)	22 (15)	15 (12)
Surgical	0 (0)	4 (7)	7 (13)	1 (2)
Acute Medical	11 (19)	6 (10)	7 (11)	8 (13)
Gastroenterology/Respiratory	2 (20)	2 (18)	4 (33)	6 (33)
Neurology/Immunology	3 (16)	4 (16)	4 (16)	N/A

N/A: Ward was not operable during period D; * $p<0.0001$ for difference between Periods

CHAPTER THREE

GENERAL METHODS

Although this chapter generally describes the methods and procedures used for both the UK and the Iranian cohorts of this study, detailed methods used for the validation of iPYMS, the identification of predictors and correlates of malnutrition, and the measurement and generation of the body composition values are described elsewhere in this thesis (see chapter 4, 5 and 6 respectively).

3.1. Patient population

This study was conducted on infants admitted to the Royal Hospital for Sick Children in the UK and to the Tabriz Children's Hospital in Iran.

Participants in the UK were eligible infants (0-12 months) admitted to medical and general surgical wards at the Royal Hospital for Sick Children and in Iran, participants were eligible infants (1-12 months) admitted to medical and surgical wards at Tabriz Children's Hospital, the largest children's Medical Centre in the Northwest of Iran, providing tertiary referral care. Patients in the high dependency unit, oncology unit, NICU and PICU were excluded from the study, and those who were transferred from neonatal units, NICU and PICU.

3.2. Study design

3.2.1. Recruitment at Royal Hospital for Sick Children, UK

The researchers identified eligible patients (0-12 months) for screening by visiting the wards during the study period (interval periods between November 2011 and September 2012) and obtaining details of new admissions from the nursing staff. They then issued an information leaflet (appendix 6) for the patient's carer to read, and answered any immediate questions. After at least one hour they returned to the ward and if the carer agreed to participate, the researchers asked him/her to complete a consent form (appendix 7). A copy of the consent form was given to the carer and another was placed in the child's medical notes.

The material was written in accordance for those literate in English. Infants were excluded if neither carer were able to read English. As part of the practice of short admissions, the majority of children admitted to UK hospitals are discharged during the first day of their stay. However, children who stayed in hospital for less than a day were ineligible to participate in

the study. In order to include as many children as possible, researchers aimed to complete assessment on the day following admission. Four student researchers were involved in the collection of data from this cohort.

3.2.2. Recruitment at Tabriz Children's Hospital, Iran

Every day during the study period (between September 2011 and March 2012), the researcher visited the selected wards to review the list of patients who had been admitted to the ward during the preceding 24 hours. The patients identified as eligible (1-12 months of age) for the screening were enrolled on the study. The researcher explained the aim and content of the study to the patients' caregiver, and issued them an information leaflet to read. If the carer agreed to participate in the study, they were required to complete the consent form. A nurse ward was responsible for reading the material to illiterate carers.

The interview was undertaken with the parent or caregiver who spent the majority of time with the patient. If it was impossible to complete the process of recruitment (interview and measurements) on the first opportunity, the researcher revisited the patient/carer a maximum of three times in an attempt to complete recruitment.

In Iran the study was piloted with 6 patients and feedback was received regarding the study design. It was evident that the procedure used in the UK regarding the carers' completion of the SGNA questionnaire-infants/toddlers (appendix 1) and Eating Behaviour Scale (appendix 2) would be impossible to replicate in Iran, as it was assumed that some of the patients' mothers may be illiterate or have only primary school education. Therefore, it was decided that, for the Iran cohort, this questionnaires should be completed by the researcher whilst explaining it through to the patient's carer. Following the pilot phase (September 2011 -March 2012), recruitment for the main study was carried out in the 4 paediatric wards (3 medical, one surgical).

Convenience sampling was used in this study. Originally, all admitted infants were recruited; however this resulted in oversampling of healthy infants who were at low risk of malnutrition. We wished to assess risk groups with an equal number of participants; infants who were more

likely to be malnourished based on their clinical condition or on visual inspection were therefore recruited.

Some difficulties and limitations of data collection were encountered in Iran. As eligible infants were often crying and restless, carers were often occupied with tending to the child. This may have influenced the quality and quantity of recruitment in terms of the accuracy of measurements and questionnaires completed. In such instances, researchers would often visit each patient on several occasions, attempting to approach them when they were most relaxed in order to optimize both convenience for patients and carers, and accuracy of measurements particularly regarding the skinfold measurement and BIA. The wards, particularly the infectious diseases wards where patient turnover is high, were especially busy in the mornings, limiting time available for recruitment of suitable infants.

3.3. Development of the infant Paediatric Yorkhill Malnutrition Score (iPYMS)

A project team consisting of senior nursing, dietetic, research academic and medical staff developed a preliminary tool - iPYMS (appendix 4) based on the principles of the Paediatric Yorkhill Malnutrition Score (PYMS) (see Chapter Two) that is both simple and quick to use. The infant nutritional screening tool consists of four steps that differ from those used for older children (Gerasimidis et al., 2010); (1) Weight centile (using admission weight as opposed to BMI. iPYMS did not include height measurement, as infant's height almost achieves the optimum potential of linear growth by the end of first year. Moreover, the intra and inter reliability of height measurement in infants might be slightly high); (2) Recent poor weight gain (via parental report regarding concerns about weight loss/gain as reported by their attending health visitor (HV), or general practitioner (GP) as opposed to weight loss reported by their carer only; (3) Reduced intake in the previous 5 rather than 7 days and; (4) Effect of current illness on nutritional state. Each step is a predictor of the past, present or future malnutrition, scoring up to 2. A score of 0 or 1 classifies a patient at a low and medium risk of undernutrition whilst a score of 2 or more reflects a high risk of undernutrition. As this tool is based on internationally recognized predictors and symptoms of undernutrition (weight gain, reduced dietary intake), it has face validity to identify children with different levels of malnutrition

During the study period, the iPYMS scoring sheet (appendix 4) and iPYMS Screening Notification (appendix 3) were completed by researchers following patient admission. Inter/intra operator variability of iPYMS score was not tested in this study due to time and staffing restrictions.

3.4. Validation of iPYMS (criterion and discriminant validity)

The iPYMS diagnostic accuracy was tested against the Paediatric Subjective Global Nutrition Assessment (SGNA) (Secker and Jeejeebhoy, 2007) as criterion measure of this study. The diagnostic accuracy of iPYMS, of how well the tool performs in detecting infants who really are at nutritional risk and correctly identifying those who are not (sensitivity and specificity) were calculated. Essentially four terms describe the validity of a screening test: sensitivity, specificity, and predictive value of positive and negative results. Sensitivity and specificity tend to be inversely related. Sensitivity refers to the proportion of patients that is the test positive, whilst specificity is the proportion of patients that has got a negative test. Specificity is a measure of false positive – how many well children are misidentified and sensitivity is how many of ill children are identified. A gold standard or a reference would be needed to assess the sensitivity and specificity of the screening test.

The discriminant validity was assessed using body composition and anthropometric measurements. The hypothesis was that infants at high risk of malnutrition have lower fat stores and possibly lean mass compared with infants at a low risk.

3.5. Comparison of iPYMS with other tools (Concurrent validity)

To test the concurrent validity, the results from the infant screening tool were compared with the results from another reputable nutritional measurement tool, STRONGkids (Screening Tool Risk on Nutritional Status and Growth) (appendix 5) (Hulst et al., 2010).

Equivalent items from the SGNA (about the child's food intake, diarrhea, vomiting, weight loss, or poor weight gain, or no weight gain, during the few days before admission) were extracted which also featured in the STRONGkids scale. An observational assessment of patients was also carried out in terms of diminished subcutaneous fat, muscle mass and hollow

face (subjective clinical assessment - the same as SGNA). In addition, the information recorded in the medical notes of the patient was used to assess patients' underlying illness at risk of malnutrition (e.g. Coeliac disease, Cystic fibrosis, cardiac disease, and trauma).

3.6. Outcome measurements

3.6.1 Global Nutritional Assessment for infants (SGNA)

SGNA is a global nutritional assessment procedure validated in paediatric patients as a measure of current and future malnutrition (Secker & Jeejeebhoy, 2007), developed based on clinical history and examination. Patient history has five components: 1) changes in child's recent height and weight; 2) change in dietary intake compared with normal intake (considering both the duration of the decreased intake and the type of diet consumed); 3) gastrointestinal symptoms (frequency and duration of vomiting, diarrhoea, and anorexia); 4) functional capacity and; 5) disease in relation to requirements i.e. the impact of primary diagnosis and metabolic demand (stress) (Secker & Jeejeebhoy, 2007). Clinical examination includes an assessment of the loss of subcutaneous fat and presence of wasting, edema, and as cites. The patients are categorized into well nourished, moderately nourished, and severely malnourished.

The SGNA questionnaire was completed by the researchers along with carers of the participants in the UK study. For the Iranian cohort of the study, this was translated into Persian and checked for accuracy via translation back into English, and completed by the researcher interviewing the primary carers of patients. A visual assessment of the child's physical signs of loss of subcutaneous fat or muscle wasting (as graded normal, moderate, and severe) was carried out by researchers in both countries.

3.6.2 Anthropometric measurements

Measurement of the thickness of the skin of the arm (triceps) and shoulder blade (subscapular) were carried out to assess fat stores. The carer took off their child's top clothing and the investigator measured the skinfold thickness in triplicate to 0.1 mm on the left side of the child using a Harpender skinfold caliper. Weight and length were measured using

electronic scales and a rigid infantometer (SECA 336 and 416 respectively) in the UK and with a Beurer scales and a flexible Rollameter 100 in Iran. Circumference of their mid upper arm was measured using a simple flexible measuring tape.

3.6.3. Bioelectrical Impedance Analyzer (BIA)

Bioelectrical impedance was measured from hand to-foot using the Bodystat 1500. Self-adhesive electrodes were attached to the right hand palm and foot sole while the child was lying on the bed. Three readings were taken whilst the electrodes were attached and mean value was calculated.

Patients, who became upset, uncooperative, unable to be measured or complete the research process, were excluded from the study.

3.6.4. Additional elements

Length of hospital stay (LOS) was also collected from admissions statistics or via review of the medical notes.

Patients' birth weight was collected from the maternal report in order to calculate weight trajectory since birth. Conditional weight gain, which compares an infant's current weight SD score with the predicted weight using their previous weight SD score, was derived using the LMS Growth software (Pan and Cole, 2012; Cole, 1995). This method calculates weight gain regarding the change in weight distance SD score based on the UK 1990 reference (Freeman et al, 1995), adjusted for regression to the mean, giving the result as an SD score for weight gain.

3.7. Statistical analysis

Data analysis was carried out using SPSS, version 18. Anthropometric measurements of skinfolds, weight, height, BMI and mid upper arm circumference were converted to z- scores according to the UK-WHO reference data for the UK cohort and WHO-2006 reference data for Iran using the LMSgrowth, Microsoft Excel Add-in. Different references were employed

for the two cohorts as, whilst the UK has adopted the growth standards published by WHO in 2006 and incorporated these standards in growth charts used for children under 4 years old (UK-WHO growth reference) (Wright et al., 2010), Iran neither has a national growth reference nor has adopted growth charts. Thus in Iran, the WHO-2006 growth reference was used as reference data. The new WHO charts for children 0 to 4 years old are asserted to reflect the optimal growth in children of all ethnic groups due to the striking similarities in results obtained from the six countries that contributed data (USA, Norway, Oman, Brazil, India, and Ghana). The charts were based on anthropometric measurements obtained from children who were breast-fed for approximately 6 months by relatively affluent, non-smoking mothers who had experienced a healthy pregnancy. The charts have been widely adopted in different countries (Wright et al., 2010).

Differences in anthropometric and body composition characteristics between iPYMS malnutrition risk categories were assessed using one-way ANOVA followed by Bonferonni post-hoc analysis. Differences in the characteristics of patients between groups (e.g. between the two cohorts) were assessed using T-test and Chi-squared test. Fisher's Exact test was used to explore how the proportion of infants with low z-score for skinfolds varied using each tool.

3.8. Ethical considerations

The study was approved by the West Glasgow of Scotland Research Ethics Committee and the Ethical Committee of the Paediatric Health Research Center - Tabriz University of Medical Sciences for the UK and Iran study respectively. Parents/carers received written information on the study and their written consent was obtained.

CHAPTER FOUR

VALIDATION OF INFANT PAEDIATRIC YORKHILL MALNUTRITION SCORE (iPYMS)

Aims

- To evaluate the infant Paediatric Yorkhill Malnutrition Score (iPYMS) to find out how well it distinguishes infants who are well-nourished from those undernourished, or at risk of being undernourished
- To compare the utility of iPYMS in different hospital settings, in the UK and in the Middle East, Iran

Objectives

- To measure iPYMS in two cohorts, in the UK and Iran and compare these to
    a. SGNA rating of malnutrition risk as a comprehensive nutritional assessment method
    b. Low skinfolds (triceps and subscapular) as a marker of low fat stores and acute malnutrition
- To assess the extent of variation of anthropometric measurements (weight, length, BMI, and skinfolds) between the iPYMS scoring risk groups
- To assess the extent to which each components of iPYMS predicts malnutrition risk
- To compare these findings between UK and Iran

Hypothesis

- iPYMS will score more Iranian infants at high risk of malnutrition than the UK infants.
- The majority of infants who are identified by SGNA as being at high risk of malnutrition or those who are at low/ moderate risk will be identified by iPYMS at the same risk. This will be more so in Iranian cohort than the UK.
- Infants scored by iPYMS as being at high risk of malnutrition have lower fat stores compared to those scored as low/ moderate risk. It was expected that in the UK cohort the prevalence of actual malnutrition will be low, but that UK and Iran infants at iPYMS high risk will have low fat stores.
- Infants who are identified by iPYMS as being at high risk of malnutrition will have lower mean anthropometric z-scores compared to those at low risk.
- The majority of infants will be scored by iPYMS as being at high risk of malnutrition due to the first step of iPYMS (weight below < 2nd or 9th centile). This will be more so in Iranian cohort than the UK.

4.1. Introduction

Hospitalized children are at risk of malnutrition in developed, as well as developing countries. Recent studies have reported a high prevalence of malnutrition risk in children on admission to hospital in the Netherlands (Joosten et al., 2010), UK (Gerasimidis et al., 2010), Australia (Aurangzeb et al., 2012), and Belgium (Huysentruyt et al, 2013b), using various methodology and criteria (see Chapter 1, Table 1.2). Malnutrition risk is particularly high in infants (Hecht et al., 2014; Cao et al., 2014). Prolonged undernutrition can be detrimental to children's health due to its potential impact on growth and development (Pawellek et al., 2008). In several recent studies, malnutrition has been associated with concerning clinical outcomes such as increased LOS (Hulst et al., 2010; Aurangzeb et al., 2012), complication rates (Secker and Jeejeebhoy, 2007; Hecht et al., 2014), and consequently increased costs of health care (Campanozzi et al., 2009; Rocha et al., 2006). Specifically, the LOS of children with a low risk score was significantly shorter compared to children with a moderate or high risk score (Hulst et al., 2010). However with regards to these studies, is not possible to rule out reverse causality and is difficult to tease out the effect of disease severity in the association between poor nutrition and clinical outcomes. Furthermore, the adverse effect of hospitalization on nutritional status has been previously reported (Ozturk et al., 2003).

Therefore to provide hospitalized patients with best health and treatment, identifying children at risk of malnutrition is important. There are UK and European guidelines that state all patients should be screened on admission for risk of malnutrition, as well as during their hospital stay using a validated screening tool (NHS QIS 2003; Kondrup et al., 2003; Agostoni et al., 2005), in order to prevent and correct hospital-acquired malnutrition. Although efforts have been made regarding methods of screening and assessing of nutritional state, no complete agreement exists on the optimal way to perform nutritional risk screening or to assess nutritional status (Soeters et al., 2008; Joosten et al., 2010). Several studies have attempted to develop appropriate nutritional screening tools for children on admission (Sermet-Gaudelus et al. 2000; Secker and Jeejeebhoy, 2007; McCarthy et al., 2012; Hulst et al. 2010; Gerasimidis et al. 2010). However, these tools are not viable for infants as they have either not been validated in this age range or if so, they have been are poorly validated for use in infants.

4.1.1 Paediatric nutritional risk screening and assessment tools

An effective nutritional screening tool is considered to be valid, reliable, reproducible (either by the same or different researcher), accepted by the patients and users, quick and easy to use (Cochrane and Holland, 1971), and designed for specific age groups and purposes (Elia et al., 2012). It is important that the screening tool can be applied by any member of health care professionals with no need for specialist nutrition training or knowledge (Baer & Harris, 1997). There are few paediatric screening tools which have been developed and evaluated in the identification of hospitalized children at risk of undernutrition.

The tool, Simple Paediatric Nutritional Risk Score, developed by Sermet-Gaudelus et al. (2000) requiring 48 hours to be completed, is complex and time-consuming. An alternative tool, the Screening tool for the Assessment of Malnutrition in Paediatrics (STAMP) was developed in Manchester (McCarthy et al., 2008, 2012). This involves measuring weight and height along with two questions about disease risk and food intake from child carer. This tool was deemed reliable when compared to a nutritional assessment conducted by a registered paediatric dietician and has been tested previously by nursing staff at the Children's Hospital, Oxford, UK (Ling et al., 2011). Moreover, it has been shown that STAMP is valid and reliable in the identification of undernutrition risk in paediatric patients with spinal cord injuries admitted to the tertiary Spinal Injuries Centre in the UK (Wong et al., 2012, 2013). However, this tool was also found to be time-consuming and complex to use as it requires plotted growth and BMI centile charts, and health care staff are often reluctant to implement time-consuming tools, as was found in the clinical audit described in this thesis (Chapter 2).

Secker and Jeejeebhoy (2007) developed the Subjective Global Nutritional Assessment (SGNA) for children and tested its validity to identify children at high risk of nutrition-related complications and prolonged hospital stay. This procedure consisted of collecting data on the child's recent and current height and weight, parental heights, dietary intake, frequency and duration of gastrointestinal symptoms, functional capacity, and nutrition-associated physical examination. The combination of these items led to a global assessment of the patient's nutritional status, successfully dividing children into one of three groups (well-nourished, moderately malnourished, and severely malnourished). Although SGNA is able to identify children at risk of malnutrition during hospitalization, it is rather complex as further details

relating to the history of the child have to be obtained, which is time-consuming and requires specialist training. Consequently its use has been limited, particularly in daily clinical practice and it is considered more as a comprehensive nutritional assessment method rather than a screening tool.

The Paediatric Yorkhill Malnutrition Score (PYMS) was developed locally to help nursing staff identify undernutrition in children on admission to hospital (Gerasimidis et al., 2010) (see Chapter 2). However, as it has not been designed for infants, this tool is not suitable for the nutritional screening of this age group.

A simple tool for assessing nutritional risk, named STRONGkids (Screening Tool Risk on Nutritional Status and Growth), was also developed and tested in a nationwide study on children aged 31d-17.7 years in the Netherlands (Hulst et al., 2010) . STRONGkids involves the combination of four items; high risk of disease; nutritional intake and losses; weight loss or poor weight gain and; subjective clinical assessment. The assessment of these four items generates a score which corresponds to the child's risk of malnutrition. The four questions in this tool can be completed shortly following admission, allowing nutritional risk to be assessed fairly quickly. When applied to children in Dutch hospitals, a high risk score was associated with a negative SD score in weight for height and a longer hospital stay. However, there was a lack of measuring inter-rater variability and validation against dietetic assessment.

All nutritional tools described above have been developed to screen nutritional risk in hospitalized children. Athough the STRONGkids is a unique nutrition screening tool that has been developed for infants as well as children, its relevance to infants may be restricted as the study may have included a limited number of children less than 1 year (total participants: 424 children, age range: 31 days – 17.7 years).

The current study therefore aimed to evaluate a novel malnutrition screening scheme for infants – the Infant Paediatric Yorkhill Malnutrition Score (iPYMS) to discover how well it distinguishes infants who are well-nourished from those undernourished or at risk of being undernourished, and also to compare the utility of iPYMS in two diverse hospital settings (in the UK and in Iran).

It was of interest to conduct this study in two different countries as, not only do the factors influencing nutritional status differ markedly between the UK and Iran, the presentation and prevalence of malnutrition also varies between the general populations of these countries. In developed countries, undernutrition primarily occurs in association with chronic disease, however in the developing world, malnutrition is a result of socioeconomic and environmental factors in a large majority of children (Grover et al., 2009). These differences may influence studies exploring the relationship between nutritional screening tools and outcomes, and consequently the utilization of the tool. This study therefore aimed to assess the diagnostic accuracy and validity of iPYMS in both cohorts, UK and Iran, by comparing the iPYMS nutritional risk with SGNA as a comprehensive nutritional assessment method, and triceps (TSF) and subscapular skinfold thickness as a marker of low fat stores and acute malnutrition. Additionally, the extent of variation of anthropometric measurements (weight, length, BMI, and skinfolds) was assessed between iPYMS scoring risk groups (discriminant validity).

4.2. Results

4.2.1. Characteristics of patients

Participants in Tabriz Children's Hospital, Iran: There were 310 eligible infants (62% males; 38% females, mean age (SD): 5.4(3.1), 6.1(3.16) months respectively for males and females) admitted to Tabriz Children's Hospital between September 2011 and March 2012. Of these, 187 infants (61% male, 39% females) were interviewed and completed both the screening and assessment tools. 185 (98.9%) of these were measured for anthropometry and 178 (95.2%) for body composition. Of 310 infants those who were not measured and participated in the validation study considered as non-respondents data. Nearly two thirds of the participants (60.4%) partaking in this validation study %) were patients from the infectious diseases ward; an area of high patient turnover. 17.1% were from the surgical ward whilst 14.4% were from GI/Renal/Respiratory wards (Table 4.1). Although the majority of the patients' mothers (76.7%) had received only primary education, 9.3% were educated beyond the age of 18 years (Table 4.2). Paternal education was similar to maternal (84.8% had primary education and 10.5% were educated beyond age 18 years), however illiteracy was more common amongst mothers than fathers (14% vs 4.7%) (Table 4.2).

There were no differences in the mean age (p=0.29) between those screened and those who participated in the validation study (Table 4.1).

Table 4.1: Characteristics of patients admitted to the selected wards of Tabriz Children's Hospital and screened or participated in the validation of iPYMS

Characteristics	Patients screened		Patients participated in the validation	
	Female (n=118) 38%	Male (n=192) 62%	Female (n=73) 39%	Male (n=114) 61%
Age, mean (SD)	6.1 (3.2)	5.4(3.1)	6.0(3.5)	5.2(3.0)
Ward, n (%)				
Surgical	10 (3)	44 (14)	5 (3)	27 (14)
Infectious	83 (27)	99 (32)	55 (29)	58 (31)
Neurology/Cardiology/ Metabolic	13 (4)	17 (5.5)	6 (3)	9 (5)
Gastrology/Nephrology /Respiratory	12 (4)	32 (10)	7 (4)	20 (11)

Table 4.2: Education characteristics of patients' parents who participated in the validation of iPYMS

	n (%)
Mother's education (n=172)	
Illiterate	24 (14)
Primary education	132 (76.7)
Educated beyond age 18 years	16 (9.3)
Father's education (n=171)	
Illiterate	8 (4.7)
Primary education	145 (84.8)
Educated beyond age 18 years	18 (10.5

Participants in Royal Hospital for Sick Children, UK: 210 eligible infants aged 0-12 months admitted to the medical/surgical wards of the Royal Hospital for Sick Children between September 2011 and 2012 participated in the study. Participants were consecutive admissions, representative of the population admitted to the hospital; however recruitment was preferably focused on high risk infants, with the aim of recruiting equal number of participants in all 3 nutritional risk groups (low, medium and high).

There were no significant differences between the two cohorts in terms of participants' gender with boys predominating in both cohorts, and disease condition classification (nearly two-thirds of participants in each cohort suffered an acute condition) (Table 4.3). However, participants in UK cohort were significantly younger than those in Iran (p=0.021). In addition, the proportion of surgical admissions in the UK was significantly higher (p=0.029, chi-square test) compared to the Iranian cohort, although a greater proportion of the participants were medical admissions in both cohorts.

Patients in the Iranian cohort had significantly longer hospital stays- over double that of those in the UK cohort (median LOS: 7 vs. 3 days; IQR: 4-10 days vs. 2-4 days respectively; p<0.0001). There was only a small difference regarding the length of stay between respondents and non-respondents data (p=0.069), which suggests that the Iran cohort was a reasonable representation of the population admitted to the hospital (Table 4.4).

20% of Iranian infants were exclusively breast fed, whilst 28% were fed non-milk drinks alongside breast milk. These figures differed in the UK cohort where only 10% of the UK iPYMS infants were exclusively breast fed, and 0.5% of infants were both breast fed and supplemented with non-milk drinks.. Thus, approximately half of infants in the Iranian cohort were breast fed, whilst only one tenth of infants in the UK cohort were breast fed (Table 4.5). Although nearly two-thirds of UK infants transitioned on to solid foods between 4-6 months, only 37% of Iranian infants had done so by this time (Table 4.6).

The anthropometric characteristics of participants were significantly different between the two cohorts (p<0.0001) (Table 4.7). Participants' mean z-scores of weight, length, MUAC, skinfolds, BMI, birth weights and conditional weights gain were markedly lower in Iranian infants (p<0001).

Table 4.3: Characteristics of patients who were screened and participated in the validation of iPYMS at Royal Hospital for Sick Children, UK and Tabriz Children's Hospital, Iran

	Iran cohort (n=187)	UK cohort (n=210)	p-value*
Gender; n (%)			
Male	114 (61)	125 (59.5)	0.77
Female	73 (39)	85 (40.5)	
Age (years); mean (SD)	0.45 (0.25)	0.39 (0.28)	0.02
Ward (medical/surgical); n (%)			
Medical	155 (83)	155 (74)	0.03
Surgical	32 (17)	55 (26)	
Disease (chronic/acute); n (%)			
Chronic	51 (27)	65 (31)	0.42
Acute	136 (73)	145 (69)	
Length of hospital stay; mean (SD)	8.7 (7.7)	3.65 (2.4)	<0.001

*p-value for difference between two cohorts, derived from T-Test or chi-squared test as appropriate

Table 4.4: Length of hospital stay (LOS) recorded in the UK cohort versus the Iranian cohort (Independent-Samples Mann-Whitney U test)

	N	Median	IQR	Minimum	Maximum
UK	208	3	2-4	1	15
Iran (respondents data)	185	7	4-10	1	50
Iran (respondents and non-respondents data combined)	307	6	4-10	1	50

P value for the difference between median of LOS for two cohorts was <0.0001
Difference between median of LOS for Iran's respondents and non-respondents data was P= 0.069

Table 4.5: Characteristics of infants' feeding in the Iranian and UK cohort

	Iran		UK	
	N	%	N	%
Exclusively breast fed	37	20.1	21	10
Formula fed	57	30.0	170	81
Mixed milk fed (breast fed plus formula fed)	39	21.2	18	8.6
Breast fed plus non-milk drinks	51	27.7	1	0.5
Total	184	100	210	100

Table 4.6: Commence of any kind of solids based on infant's age in the Iranian and UK cohort

	Commence of solid (weaning age)		
	<4mo n (%)	4-6mo n (%)	>6mo n (%)
Iran cohort			
Yes	2 (2.7)	14 (36.8)	68 (95.8)
No	73 (97.3)	24 (63.2)	3 (4.2)
UK cohort			
Yes	2 (1.9)	21 (60)	63 (92.6)
No	101 (98.1)	14 (40)	5 (7.4)

Table 4.7: Comparison of anthropometric characteristics of patients in the Iranian and UK cohort

Anthropometric characteristics	**Iran cohort**		**UK cohort**		
	N	**Mean (SD)**	**N**	**Mean (SD)**	**P value***
Weight z-score (kg)	184	-1.51 (1.59)	209	-0.35 (1.29)	<0.001
Length z-score (cm)	184	-0.58 (1.53)	197	-0.06 (1.33)	<0.001
MUAC z-score (SD)	129	-1.48 (1.43)	110	0.06 (1.74)	<0.001
Triceps z score (SD)	131	-2.05 (1.36)	111	0.58 (1.32)	<0.001
Subscapular z score(SD)	126	-1.76 (1.61)	111	-0.33 (1.38)	<0.001
Mean skinfolds z-score(SD)	126	-1.90 (1.38)	111	0.12 (1.24)	<0.001
BMI z-score (SD)	183	-1.65 (1.39)	182	-0.45 (1.23)	<0.001
Birth weight z-score (SD)	161	-0.69 (1.27)	173	0.21 (1.27)	<0.001
Conditional weight velocity z-score (SD)	160	-1.32 (1.54)	190	-0.59 (1.34)	<0.001

*p-value for the difference between two cohorts derived from T-Test

4.2.2. Prevalence of malnutrition by nutrition screening tool

Assessment of the 187 patients in the Iran cohort, and 208 patients in the UK cohort (using SGNA, iPYMS and STRONGkids revealed a range of nutritional risks which differed considerably between the malnutrition assessment and screening tools (Table 4.8). Out of 187 Iranian infants, 111 (59.4%) and 80 (42.8%) were rated as being at a high malnutrition risk by iPYMS using high nutrition risk thresholds of 2 and 3 respectively. In the UK however, using the same high nutrition risk thresholds (2 and 3), 59 (28.5%) and 30 (14.5%) infants were considered to be at a high malnutrition risk, respectively. In both cohorts, the proportion of patients rated at a high risk of malnutrition by SGNA was less than those rated as such by

iPYMS (p<0.0001, Chi-square). In addition, SGNA and STRONGkids rated more patients at a medium risk of malnutrition compared with the iPYMS (p<0.0001, Chi-square). In both cohorts, increasing the high risk threshold to ≥3 when using the iPYMS rated more patients at a medium risk of malnutrition than those rated by SGNA (Table 4.8).

Compared to those in the UK, more Iranian infants were at a high risk of malnutrition, according to the SGNA (Iran 59, 31.6%; UK 14, 6.7%; p<0.0001; Chi-square test); however with regards to rates to medium risk of malnutrition as determined by the SGNA, rates were comparable between countries (Iran 47, 25.1%; UK 63, 30.3%).

Additionally, in the Iranian cohort, the prevalence of medium and high malnutrition risk rated by SGNA for recruitment without over-sampling (during the first two months of the study) was 20% and 22% respectively.

Table 4.8: Prevalence of malnutrition risk according to malnutrition assessment and screening tools; SGNA, iPYMS, STRONGkids in Iranian and UK cohorts

a)Iran	**Malnutrition risk**		
	Low risk n (%)	**Medium risk n (%)**	**High risk n (%)**
SGNA	81 (43.3)	47 (25.1)**	59 (31.6)*
SGNA (data without over sampling - first two months of recruitment**)**	29 (58)	10 (20)	11 (22)
iPYMS			
Threshold =2	52 (27.8)	24 (12.8)**	111 (59.4)*
Threshold =3	52 (27.8)	55 (29.4)	80 (42.8)
STRONGkids	38 (20.3)	121 (64.7)**	28 (15)

b) UK	Malnutrition risk		
	Low risk n (%)	Medium risk n (%)	High risk n (%)
SGNA	131 (63.0)	63 (30.3)**	14 (6.7)*
iPYMS			
Threshold =2	106 (51.2)	42 (20.3)**	59 (28.5)*
Threshold =3	106 (51.2)	71 (34.3)	30 (14.5)
STRONGkids	60 (28.7)	130 (62.2)**	19 (9.1)

SGNA, Paediatric Subjective Global Nutritional Assessment
iPYMS, infant Paediatric Yorkhill Malnutrition Score
STRONGkids, Screening Tool for Risk on Nutrition Status and Growth
*p<0.001 for the difference in the % of patients scored at high risk between SGNA and iPYMS in both cohorts
**p<0.001 for the difference in the % of patients scored at medium risk between SGNA and iPYMS and also STRONGkids and iPYMS in both cohorts

4.2.3. Length of hospital stay (LOS) and malnutrition risk

In order to identify how LOS might be associated with malnutrition risk, the variation of LOS according to SGNA rating risk was investigated using a Kruskal-Wallis Test. The LOS of infants in the Iranian cohort with a low or moderate SGNA risk was significantly shorter than infants of the same cohort with a high SGNA risk, (median 6 vs. 9.5 days respectively (p=0.001)). In the UK cohort however, the length of stay was not significantly altered between infants at different risks of malnutrition, based on the SGNA (p=0.139) (Table 4.9)

Table 4.9: Association between median of LOS (days) and malnutrition risk based on SGNA rating risk (Iran and UK cohort)

	SGNA					
	Low risk	Medium risk	High risk	P	Median	IQR
UK (n=206)	3	3	3	0.139*	3	2-4
Iran (n=184)	6	6	9.5	0.001**	7	4-10

*p-value between risk group for the UK cohort
**p-value between risk group for the Iran cohort

4.2.4. Criterion validity

The criterion validity of iPYMS was assessed by comparing the patient malnutrition risk with the Paediatric Subjective Global Nutritional Assessment (Table 4.10 and 4.11).

In Iran, 133 (71%) and 158 (84.5%) patients were classified at the same nutrition risk using the SGNA and iPYMS, when screening at threshold of ≥2 (Table 4.10a) and ≥3 (Table 4.11) respectively. At a threshold of ≥2, the iPYMS illustrated high sensitivity (98%) and fair specificity (69%), with positive and negative predictive values of 52% and 99%. The agreement between the SGNA and iPYMS at this level was moderate (kappa=0.46) (Table 4.10c). Increasing the high risk threshold to ≥3, slightly decreased the sensitivity (93%), yet increased the specificity (87%), yielding positive and negative predictive values of 69% and 96%. At a high risk threshold of ≥3, iPYMS demonstrated moderate to good agreement (kappa=0.67), with SGNA. (Table 4.11).

With regards to the UK cohort, 158 (76.7%) and 185 (89.8%) patients were classified with the same nutrition risk when using the SGNA and iPYMS screening at threshold of ≥2 (Table 4.10a) and ≥3 (table 4.11) respectively. iPYMS demonstrated high sensitivity (92%) and fair specificity (76%), with positive and negative predictive values of 20% and 99% respectively, at a high risk threshold of ≥2; however at this threshold, iPYMS illustrated poor agreement with SGNA (kappa=0.26) (Table 4.10c). Increasing the high risk threshold, to ≥3, slightly decreased sensitivity (85%) but increased specificity (90%), yielding respective positive and negative predictive values of 37% and 99%. At this higher threshold (≥3), iPYMS demonstrated a moderate agreement (kappa=0.46), with SGNA, (Table 4.11).

In summary, the diagnostic performance of iPYMS in both cohorts was improved by increasing the high risk threshold from ≥2 to ≥3; an effect that was more profound in Iran than in the UK.

Further analysis was conducted using the new category. As illustrated in Table 4.10b, combining high and medium risk groups in the same category the agreement between iPYMS and SGNA was improved for both cohorts (kappa value=0.65 and 0.45 for Iranian and UK cohort respectively). However, the combination of high and medium risk groups in one

category implied that three-quarters of Iranian infants and more than half of UK infants should be referred for a detailed nutritional assessment, suggesting that this method is not appropriate as it is oversensitive in terms of identifying infants that require further evaluation. On the other hand, if the screening test was conducted using the three risk groups (low, medium and high), this study would have to have been powered with a higher number of participants in order to have an acceptable numbers of patients in each category to establish validity with a 3×3 table. Furthermore, it would be impossible to calculate sensitivity and specificity if using three risk groups and importantly, only those infants at high risk would be referred to the hospital dietitian, which has clinical relevance. Additionally, alternative form of analysis was used to validate the iPYMS with ungrouped data. The ability of iPYMS to identify patients at a medium risk of malnutrition, (the discriminant validity), has been presented and described elsewhere (see Table 4.17 on page 120). Thus, the procedure used for categorizing the risk groups in this study and in other similar studies seems to be an appropriate method used in the validation of the screening tool.

Table 4.10: Cross-classification of patient malnutrition risk based on SGNA and iPYMS at high risk threshold of ≥2 in Iran and UK study

a)	Iran			UK	
	SGNA			SGNA	
iPYMS ≥2	**High (n)**	**Medium /Low (n)**	**iPYMS ≥2**	**High (n)**	**Medium /Low (n)**
Positive	58	53	Positive	12	47
Negative	1	75	Negative	1	146

b)	**Iran**			**UK**	
	SGNA			**SGNA**	
iPYMS ≥2	**High /Medium (n)**	**Low (n)**	**iPYMS ≥2**	**High /Medium (n)**	**Low (n)**
Positive	105	30	Positive	60	41
Negative	1	51	Negative	15	90

c)	Iran study		UK study	
iPYMS as predictor of	**SGNA risk**		**SGNA risk**	
	High	**High /medium**	**High**	**High/ Medium**
Sensitivity	98	99	92	80
Specificity	58	63	75	69
PPV	52	78	20	59
NPV	98	98	99	86
K value	0.46	0.65	0.26	0.45

PPV, positive predictive value; NPV, negative predictive value

Table 4.11: Cross-classification of patient malnutrition risk based on SGNA and iPYMS (increasing the high risk threshold to ≥3) in the Iranian and UK study

	Iran study			UK study		
	SGNA			**SGNA**		
iPYMS	**High risk (n)**	**Low risk* (n)**	**Total (n)**	**High risk (n)**	**Low risk* (n)**	**Total (n)**
High risk	55	25	80	11	19	30
Low risk*	4	103	107	2	174	176
Total	59	128	187	13	193	206
Sensitivity (%)	93			85		
Specificity (%)	81			90		
PPV (%)	69			37		
NPV (%)	96			99		
K value	0.67			0.46		

PPV, positive predictive value; NPV, negative predictive value.
*Low and medium-risk categories grouped.

4.2.5. Validation of the iPYMS using skinfolds

The iPYMS validity was also assessed by comparing the patient malnutrition risk with the mean triceps and sub-scapular skinfolds z-scores. The benchmark regarding fat stores in this study was <-2SD (Table 4.12 and 4.13). According to this benchmark, 54 (42.9%) Iranian infants had low skinfolds, whilst only 6 (5.4%) infants had low skinfolds in the UK cohort.

At high risk thresholds of ≥2 and ≥3, the sensitivity of the iPYMS was found to be 91% and 76% in the Iran Cohort, and 17% and 17% in the UK cohort, respectively. The specificity of the iPYMS in Iran was 53% and 78% at thresholds of ≥2 and ≥3 respectively, whilst in the UK, the specificity of this screening tool was 71% at a threshold of ≥2 and 82% at a threshold of ≥3. At these high risk thresholds, iPYMS demonstrated moderate agreement with mean skinfolds in the Iran cohort, (kappa=0.41(≥2) and 0.53(≥3)); however this agreement was not apparent in the UK.

In Iran, 76 % infants with raised iPYMS had mean skinfolds <-2SD, compared to 19% of the remainder (p<0.0001). However, in the UK only 5.3% had low skinfolds and this was unrelated to iPYMS (Fisher's Exact Test, p=0.720).

Table 4.12: Cross-classification of patient malnutrition based on mean skinfolds z-scores <-2SD and the infant Paediatric Yorkhill Malnutrition Score (iPYMS) at a high risk threshold of ≥2 in the Iranian and UK study

	Iran study			**UK study**		
	Mean skinfolds z-scores			**Mean skinfolds z-scores**		
iPYMS	**<-2SD (n)**	**>-2SD (n)**	**Total (n)**	**<-2SD (n)**	**>-2SD (n)**	**Total (n)**
High risk	49	34	83	1	30	31
Low risk*	5	38	43	5	73	78
Total	54	72	126	6	103	109
Sensitivity (%)	91			17		
Specificity (%)	53			71		
PPV (%)	59			3		
NPV (%)	88			93		
K value	0.41			-0.04		

PPV, positive predictive value; NPV, negative predictive value
*Low and medium-risk categories grouped

Table 4.13: Cross-classification of patient malnutrition based on mean skinfolds z-scores <-2SD and the infant Paediatric Yorkhill Malnutrition Score (iPYMS) at a high risk threshold of ≥3 in the Iranian and UK study

	Iran study			UK study		
	Mean skinfolds z-scores			Mean skinfolds z-scores		
iPYMS	**<-2SD (n)**	**>-2SD (n)**	**Total (n)**	**<-2SD (n)**	**>-2SD (n)**	**Total (n)**
High risk	41	16	57	1	18	19
Low risk*	13	56	69	5	85	90
Total	54	72	126	6	103	109
Sensitivity (%)	76			17		
Specificity (%)	78			82		
PPV (%)	72			5		
NPV (%)	81			94		
K value	0.53			-0.004		

PPV, positive predictive value; NPV, negative predictive value
*Low and medium-risk categories grouped.

4.2.6. Concurrent validity

To test the concurrent validity, the iPYMS was compared with the results of STRONGkids - an alternative reputable nutritional screening tool. At a threshold risk of ≥3, 72.1% of patients in Iran and 86.4% in the UK cohort were classified to have the same risk of malnutrition by both the STRONGkids and iPYMS. The agreement between STRONGkids and the iPYMS was poor in both cohorts (kappa=0.38 and 0.34) (Table 4.14). When the medium and high risk groups were combined into the same category, the agreement between the iPYMS and STRONGkids was moderate to good (kappa=0.62) in the Iranian cohort and moderate (kappa=0.46) in the UK cohort. (Table 4.16).

STRONGkids demonstrated a moderate (kappa=0.49) and poor (kappa=0.38) agreement with SGNA in Iran and UK cohort, respectively (Table 4.15).

Table 4.14: Cross-classification of patient malnutrition risk based on the Screening Tool for Risk on Nutrition Status and Growth (STRONGkids), and the infant Paediatric Yorkhill Malnutrition Score (iPYMS) at threshold risk ≥ 3

	Iran study			UK study		
	iPYMS			PYMS		
STRONGkids	**High risk (n)**	**Low risk* (n)**	**Total (n)**	**High risk (n)**	**Low risk* (n)**	**Total (n)**
High risk	28	0	28	10	8	18
Low risk*	52	107	159	20	168	188
Total	80	107	187	30	176	206
Sensitivity (%)	35			33		
Specificity (%)	100			95		
PPV (%)	100			55		
NPV (%)	67			89		
K value	0.38			0.34		

PPV, positive predictive value; NPV, negative predictive value
*Low and medium-risk categories grouped

Table 4.15: Cross-classification of patient malnutrition risk based on the Paediatric Subjective Global Nutritional Assessment (SGNA), and the Screening Tool for Risk of Nutrition Status and Growth (STRONGkids) in the Iranian and UK study

	Iran study			UK study		
	SGNA			SGNA		
STRONGkids	**High risk (n)**	**Low risk* (n)**	**Total (n)**	**High risk (n)**	**Low risk* (n)**	**Total (n)**
High risk	26	2	28	7	12	19
Low risk*	33	126	159	7	181	188
Total	59	128	187	14	193	207
Sensitivity (%)	44			50		
Specificity (%)	98			94		
PPV (%)	92			37		
NPV (%)	79			96		
K value	0.49			0.38		

PPV, positive predictive value; NPV, negative predictive value
*Low and medium-risk categories grouped

Table 4.16: Cross-classification of patient malnutrition risk based on STRONGkids and iPYMS by combining the medium and high risk groups in the same category (Iran and UK cohorts)

	Iran study			UK study		
	STRONGkids			STRONGkids		
iPYMS	**High risk* (n)**	**Low risk (n)**	**Total (n)**	**High risk* (n)**	**Low risk (n)**	**Total (n)**
High risk*	129	6	135	95	5	100
Low risk	20	32	52	51	55	106
Total	149	38	187	146	60	206
Sensitivity (%)	86			65		
Specificity (%)	84			92		
PPV (%)	95			95		
NPV (%)	61			52		
K value	0.62			0.46		

PPV, positive predictive value; NPV, negative predictive value
*High and medium-risk categories grouped

4.2.7. Discriminant validity

Anthropometric measurements were not obtained for all participants as some were uncooperative or unable to be measured and were subsequently excluded from the validation of iPYMS (Table 4.17 and 4.18). In both cohorts, weight, length, BMI and MUAC z-scores varied significantly by iPYMS risk group at a high risk threshold of ≥2 as well as ≥3. However, iPYMS at high risk threshold of ≥2 was not discriminative between low and medium risk, particularly in the Iran cohort. Overall by increasing the high risk threshold to ≥3, differences between the risk groups became greater and more significant (apart from length z-score in the UK cohort). Furthermore, there were marked differences in skinfold z-score (triceps, subscapular and mean skinfolds z-scores, which were available only for infants over 3 months) and sum of skinfolds measurements by iPYMS risk group at high risk threshold of ≥2 as well as ≥3. There was no significant difference between skinfold measurements and iPYMS rating risk in the UK cohort, even when the iPYMS threshold was increased to ≥3.

The difference between recorded weight and BMI between iPYMS risk groups remained significant in both groups despite the exclusion of patients deemed as high risk based on being underweight(weight ≤ -2 z-score), or due to having a low BMI (≤ -2 z score). The exception to this was the difference in weight and BMI z-score recorded between medium and high risk groups, at an iPYMS threshold risk of ≥2 and ≥3 in the UK cohort, which became insignificant when these patients were excluded from the data.

Table 4.17: Anthropometric and body composition characteristics of patients in the Iranian and UK cohorts who scored at low, medium and high malnutrition risk on the infant Paediatric Yorkhill Malnutrition Score (iPYMS) at threshold risk of ≥2

a) Iran		**Low risk**		**Medium risk**			**High risk**		
	Patients (n)	**Mean**	**SD**	**Mean**	**SD**	**P***	**Mean**	**SD**	**P** **P*****
Weight z-score	184	-0.15	0.87	-0.75	1.07	0.05	-2.32	1.42	<0.001 <0.001
Weight z-score*	120	-0.15	0.87	-0.59	1.00	0.03	-1.11	0.66	<0.001 0.02
Length z-score	184	0.33	1.05	-0.35	1.16	0.05	-1.06	1.60	<0.001 0.03
BMI z-score	183	-0.46	0.84	-0.85	1.08	0.15	-2.38	1.17	<0.001 <0.001
BMI z-score*	112	-0.42	0.81	-0.63	1.00	0.29	-1.28	0.50	<0.001 0.002
Triceps skinfold z-score	131	-0.97	1.19	-1.69	1.29	0.06	-2.48	1.21	<0.001 0.02
Triceps skinfold (n=187)*									
Subscapular z-score	126	-0.58	1.10	-0.86	1.03	0.55	-2.33	1.55	<0.001 <0.001
Subscapular (n=179)*									
MUAC z-score	129	-0.10	1.22	-0.75	0.82	0.09	-2.04	1.21	<0.001 <0.001
Mean skinfolds z-score	126	-0.78	1.04	-1.34	0.96	0.15	-2.4	1.28	<0.001 0.003
Sum of skinfolds	179	13.89	2.39	12.86	2.43	0.09	10.35	2.42	<0.001 <0.001

b) UK		Low risk		Medium risk			High risk		
	Patients (n)	Mean	SD	Mean	SD	P*	Mean	SD	P** P***
Weight z-score	207	0.16	1.12	-0.44	1.03	0.005	-1.22	1.32	<0.001 0.001
Weight z-score*	183	0.22	1.04	-0.31	0.82	0.003	-0.42	0.74	<0.001 0.58
Length z-score	195	0.26	1.10	-0.07	1.09	0.17	-.067	1.98	<0.001 0.02
BMI z-score	180	0.02	1.12	-0.59	1.11	0.005	-1.20	1.15	<0.001 0.01
BMI z-score*	156	0.11	1.02	-0.40	0.86	0.008	-0.52	0.69	0.001 0.59
Triceps skinfold z-score	109	0.64	1.19	0.22	1.57	0.19	0.66	1.31	0.95 0.22
Triceps skinfold (n=187)*									
Subscapular z-score	109	-0.11	1.32	-0.80	1.58	0.04	-0.47	1.28	0.23 0.38
Subscapular (n=179)*									
MUAC z-score	108	0.71	1.37	-0.25	1.38	0.02	-0.85	2.11	<0.001 0.18
Mean skinfolds z-score	109	0.27	1.13	-0.29	1.49	0.07	0.11	1.17	0.53 0.25
Sum of skinfolds	192	16.48	3.41	15.82	3.64	0.33	15.49	3.74	0.10 0.66

MUAC, mid-upper arm circumference; TSF, triceps skinfold; SUB, subscapular skinfold

*Excluding infants who were assessed as high risk due to a low BMI (BMI z-score≤-2SD) or were underweight (weight z-score≤-2SD)

*p for mean value differences between the low and medium risk groups

**p for mean value differences between the low and high risk groups

***p for mean value differences between the medium and high risk groups

*Numbers in the brackets show values without converting to SD scores. By converting to SD scores, figures are decreased due to the lack of WHO skinfolds reference for infants <3 months

Table 4.18: Anthropometric and body composition characteristics of patients in the Iranian and UK cohorts, who scored at low, medium and high malnutrition risk on the infant Paediatric Yorkhill Malnutrition Score (iPYMS) at threshold risk of ≥3

a) Iran		**Low risk**		**Medium risk**			**High risk**		
	Patient (n)	**Mean**	**SD**	**Mean**	**SD**	**P***	**Mean**	**SD**	**P** **P***
Weight z-score	184	-0.15	0.87	-1.05	1.07	<0.001	-2.71	1.36	<0.001 <0.001
Weight z-core*	120	-0.15	0.87	-0.72	0.85	0.001	-1.35	0.54	<0.001 0.002
Length z-score	184	0.33	1.05	-0.33	1.28	0.01	-1.35	1.59	<0.001 <0.001
BMI z-score	183	-0.46	0.84	-1.25	0.95	<0.001	-2.69	1.16	<0.001 <0.001
BMI z-score*	112	-0.42	0.81	-0.89	0.82	0.004	-1.39	0.49	<0.001 0.02
Triceps skinfold z-score	131	-0.97	1.19	-1.81	1.23	0.004	-2.74	1.13	<0.001 <0.001
Triceps skinfold (n=187)*									
Subscapular z-score	126	-0.58	1.10	-1.18	1.38	0.07	-2.78	1.35	<0.001 <0.001
Subscapular (n=179)*									
MUAC z-score	129	-0.10	1.22	-1.07	0.87	0.001	-2.38	1.19	<0.001 <0.001
Mean skinfolds z-score	126	-0.78	1.04	-1.52	1.16	0.008	-2.75	1.13	<0.001 <0.001
Sum of skinfolds	179	13.89	2.39	12.37	2.34	0.001	9.66	2.89	<0.001 <0.001

b) UK		Low risk		Medium risk			High risk		
	Patient (n)	**Mean**	**SD**	**Mean**	**SD**	**P***	**Mean**	**SD**	**P** **P*****
Weight z-score	207	0.16	1.12	-0.46	1.1	<0.001	-1.94	1.27	<0.001 <0.001
Weight z-score*	183	0.22	1.04	-0.28	0.74	0.001	-0.78	0.84	<0.001 0.08
Length z-score	195	0.26	1.10	0.01	1.27	0.20	-1.37	1.49	<0.001 <0.001
BMI z-score	180	0.02	1.12	-0.66	1.06	<0.001	-1.51	1.17	<0.001 0.001
BMI z-score*	156	0.11	1.02	-0.39	0.78	0.001	-0.59	0.79	0.008 0.55
Triceps skinfold z-score	109	0.64	1.19	0.47	1.51	0.54	0.48	1.30	0.65 0.97
Triceps skinfold (n=187)*									
Subscapular z-score	109	-0.10	1.32	-0.50	1.54	0.18	-0.80	1.17	0.06 0.44
Subscapular (n=179)*									
MUAC z-score	108	0.71	1.37	-0.41	2.07	0.002	-0.94	1.31	<0.001 0.25
Mean skinfolds z-score	109	0.27	1.13	-0.02	1.44	0.28	-0.16	1.08	0.19 0.68
Sum of skinfolds	192	16.48	3.41	15.80	3.82	0.23	15.22	3.35	0.11 0.48

MUAC, mid-upper arm circumference; TSF, triceps skinfold; SUB, subscapular skinfold

*Excluding infants who were assessed as high risk due to a low BMI (BMI z-score≤-2SD) or were underweight (weight z-score≤-2SD)

*p for mean value differences between the low and medium risk groups

**p for mean value differences between the low and high risk groups

***p for mean value differences between the medium and high risk groups

*Numbers in the brackets show values without converting to SD scores. By converting to SD scores, figures are decreased due to the lack of WHO skinfolds reference for infants <3 months

4.2.8. Characteristics of infants who were misclassified by iPYMS at high risk compared to the SGNA and skinfold measurements

When using the SGNA as a reference method, 47 infants in UK and 53 in the Iranian cohort were misclassified as high risk when screened with the iPYMS. These infants had a longer hospital stay compared to those who were classified as low risk by both SGNA and iPYMS, (mean (SD); 4.45d (2.48) vs 3.26 d (2.18), p=0.002 and 8.92 d (7.8) vs 6.32 d (4.33), p=0.019 for UK and Iran respectively). Of the 53 misclassified infants in the Iranian cohort, 45 (84.9%) infants were affected by an acute conditions and in the UK cohort, 33 (67.3%) of the 47 misclassified infants suffered from an acute condition. In both cohorts, the majority of the misclassified infants were identified as high risk due to the steps of the iPYMS that consider the impact of the current clinical condition on nutritional status and decreased dietary intake (83% and 70% for the UK; 73 6% and 71.7% for Iran cohort respectively).

On comparison to skinfold z-scores ≥-2SD, 30 infants in the UK and 34 in the Iranian cohort were misclassified as high risk by iPYMS. The mean value of skinfolds z-scores for these misclassified patients were -1.15 (0.71) and 0.17 (1.10) for Iran and UK cohort respectively. Current clinical condition influenced decreased intake in 22 (73.3%) UK and 26 (76.5%) Iranian infants included in the study, whilst nutritional status was impacted by clinical condition in 27 (90%) patients in the UK cohort and 26 (76.5%) in the Iranian cohort. Furthermore, misclassified infants identified as high risk in the UK cohort had longer hospital stays (mean (SD) 5.27(2.93) vs. 3.01(1.76) d, p<0.001) compared to those classified as low risk and had a mean skinfold >-2SD. Nearly two-thirds (21 (61.8%)) of misclassified infants in Iran and one-third (9 (30%)) in the UK cohort were scored as being below the 9th or 2nd centile (Table 4.19).

Table 4.19: Characteristics of misclassified infants at high risk by iPYMS compared to the mean skinfolds z-scores > -2SD in both cohorts

	UK cohort (n=30)	Iran cohort (n=34)
Skinfolds z-scores, mean (SD)	0.17 (I.10)	-1.15 (0.71)
iPYMS steps, n (%)		
Decreased intake	22 (73.3)	26 (76.5)
Nutritional status affected by current conditions	27 (90)	26 (76.5)
Weight centile <9th or 2nd	9 (30)	21 (61.8)

4.2.9. Components of each step of iPYMS

The four individual steps of iPYMS (weight centile, poor weight gain, reduced intake and effect of current clinical condition) were identified as high in 96 (51.3%), 72 (38.5%), 90 (48.1%) and 84 (45.2%) of infants in the Iranian cohort, respectively, and 32 (15.2%), 31 (14.7%), 60 (28.4%) and 57 (27.3%) in the UK cohort, respectively (Table 4.20).

As shown in Table 4.21 infants in the Iranian cohort at a high iPYMS risk (threshold of ≥ 2), 79.3% were classified below the 9th or 2nd centile and 65.1% were identified having poor weight gain. These figures were lower in the UK cohort, 42.4% of infants scored below the 9th or 2nd centile and 39% had poor weight gain. The majority of the high risk infants in the UK cohort were scored as being high risk due to the steps regarding reduced intake (67.8%) and the effect of current disease on nutritional status (78%).

Table 4.20: Components of each step of iPYMS that patients scored at any score in both cohorts

iPYMS steps (components)	Iran cohort (n=187)	UK cohort (n=210)
Weight centile, n (%)		
No	91 (48.7)	176 (84.6)
Below 9th (below <- 1.33SD)	36 (19.3)	14 (6.7)
Below 2nd (below <- 2SD)	60 (32.1)	18 (8.7
Poor weight gain, n (%)		
No	112 (60.9)	177 (85.1)
Yes	72 (39.1)	31 (14.9)
Reduced intake, n (%)		
No (usual intake)	97 (51.9)	149 (71.3)
Yes (decreased intake)	84 (44.9)	50 (23.9)
Yes (no intake)	6 (3.2)	10 (4.8)
Effect of current disease,		
No	102 (54.8)	152 (72.7)
Yes (decreased intake)	83 (44.6)	57 (27.3)
Yes (no intake)	1 (0.5)	-

Table 4.21: Components of each step of iPYMS that patients scored in both cohorts (only for those screened at high risk; threshold of ≥ 2 and ≥ 3)

	Infants at high risk threshold of ≥ 2		Infants at high risk threshold of ≥ 3	
iPYMS steps (components)	**Iran cohort (n=111)**	**UK cohort (n=59)**	**Iran cohort (n=80)**	**UK cohort (n=30)**
Weight centile, n (%)				
No	23 (20.7)	34 (57.6)	7 (8.8)	9 (30.0)
Below 9th (below <- 1.33SD)	28 (25.2)	7 (11.9)	17 (21.3)	6 (20.0)
Below 2nd (below <- 2SD)	60 (54.1)	18 (30.5)	56 (70.0)	15 (50.0)
Poor weight gain, n (%)				
No	38 (34.9)	36 (61.0)	12 (15.0)	15 (50.0)
Yes	71 (65.1)	23 (39.0)	68 (85.0)	15 (50.0)
Reduced intake, n (%)				
No (usual intake)	29 (26.1)	19 (32.2)	20 (25)	9 (30.0)
Yes (decreased intake)	76 (68.5)	30 (50.8)	54 (67.5)	12 (40.0)
Yes (no intake)	6 (5.4)	10 (16.9)	6 (7.5)	9 (30.0)
Effect of current disease, n (%)				
No	33 (30.0	13 (22.0)	20 (25.3)	7 (23.3)
Yes (decreased intake)	76 (69.1)	46 (78.0)	58 (73.4)	23 (76.7)
Yes (no intake)	1 (0.9)	-	1 (1.3	-

4.2.9.1 Components of each step of iPYMS related to malnutrition and undernutrition risk (Iran cohort)

In order to identify the component of the iPYMS that is the strongest predictor of malnutrition, the association between the components of each step and the outcomes of undernutrition was assessed. The component of step one (weight centile), step two (poor weight gain) and step three of iPYMS with the current threshold score illustrated significant association with mean skinfold (using T-Test, $p<0.001$), but the association between step four (effect of current disease) and mean skinfold was found to be weak ($p=0.06$) (Table 4.22). There was a significant relationship between patients' malnutrition risk based on SGNA and the components of all four steps of iPYMS ($p<0.001$, chi-square) (Table 4.23).

Multivariate logistic regression analysis highlighted that the relationship between malnutrition risk (based on SGNA) with weight status (<-2nd and 9th centile ($p<0.001$)), reduced intake ($p<0.004$) and weight gain ($p<0.001$) were significant, but when using mean skinfold (z-score <-2) as the primary outcome, only weight centile and weight gain remained significant. Thus, step one (weight centile) and step two (weight gain) were the best predictors for identification of malnutrition risk using either SGNA or skinfolds as our benchmark measurements.

Table 4.22: Mean skinfolds z-score of patients related to the components of each step of iPYMS (Iran cohort)

iPYMS steps	Mean skin folds z-scores		
	Mean	**SD**	**P value**
Weight centile			
No	-1.0	1.05	<0.0001
Below 9th, 2nd or (below <- 1.33SD, <- 2SD)	-2.65	1.16	
Poor weight gain			
No	-1.39	1.23	<0.0001
Yes	-2.65	1.27	
Reduced intake			
Usual intake	-1.48	1.41	0.02
Decrease and no intake	-2.25	1.26	
Effect of current intake			
No	-1.56	1.35	0.06
Yes	-2.21	1.3	

Table 4.23: Patients' malnutrition risk based on SGNA risk group related to the components of each step of iPYMS (Iran cohort)

iPYMS steps	SGNA			
	Low risk	**Medium risk**	**High risk**	**P value**
Weight centile				
No	71 (78)	19 (20.9)	1 (1.1)	<0.0001
Below 9th, 2nd or (below <-1.33SD, <-2SD)	10 (10.4)	28 (29.2)	58 (60.4)	
Poor weight gain				
No	78 (69.6)	24 (21.4)	10 (16.9)	<0.0001
Yes	1 (1.4)	22 (30.6)	49 (68.1)	
Reduced intake				
Usual intake	62 (63.9)	20 (20.6)	15 (15.5)	<0.0001
Decrease and no intake	19 (21.1)	27 (30)	44 (48.9)	
Effect of current intake				
No	67 (65.7)	15 (14.7)	20 (19.6)	<0.0001
Yes	14 (16.7)	32 (38.1)	38 (45.2)	

4.3. Discussion

Sick children are at high risk of poor feeding and undernutrition. Based on the national and international guidelines (NHS QIS 2003; Kondrup et al., 2003; Agostoni et al., 2005), the risk of malnutrition should be identified at admission to the hospital using a validated screening tool to minimise hospital-acquired malnutrition. Many nutrition screening tools were developed as diagnostic tools for the purpose of detecting malnutrition, whereas others were developed as prognostic tools for the purpose of predicting clinical outcomes (Elia and Stratton, 2011). Although, recent studies have attempted to develop nutrition screening tools for use in children, they have been mostly considered children aged above 2 years and are not suitable specifically for children under 1 year, as the criteria required to detect malnutrition in younger children may differ from those for older children. Moreover, the clinical utility of current paediatric nutrition screening tools remains to be evaluated, because they incorporate different criteria to detect malnutrition that results in discrepancies between the tools (Elia et al., 2012). The Infant Paediatric Yorkhill Malnutrition Score (iPYMS) was developed and evaluated its performance as the first study and novel (unique) nutrition screening tool for hospitalized infants in two different hospital settings, UK and Iran. The score encompasses 4 steps: weight $<2^{nd}$ and 9^{th} centile and 3 elements concerning the history of nutritional issues (poor weight gain: health professional's concerns of weight gain, reduced intake and predicted effect of current disease on nutritional status: whether current disease is likely to cause undernutrition). A total score of ≥ 2 or ≥ 3 indicates high risk of undernutrition. It is performed on admission to the hospital for early identification of infants who are at high risk of being malnutrition. In this study the diagnostic accuracy and validity of iPYMS in both cohorts, UK and Iran, was assessed by comparing the iPYMS nutritional risk with the SGNA that determine malnutrition risk and mean of triceps and subscapular skinfolds z-scores below <-2SD as the benchmark of our study for low fat stores and acute malnutrition

The utilization and suitability of iPYMS in both cohorts:

iPYMS compared to SGNA:

We hypothesized that the majority of infants who are identified by SGNA as being at high risk of malnutrition or those who are at low/ moderate risk will be identified by iPYMS at the same risk and this will be more so in Iranian cohort than the UK. This was true; in the current study, iPYMS presented high sensitivity and fair specificity in both cohorts compared to the patient

malnutrition risk with the Paediatric Global Nutritional Assessment (SGNA) as the main risk outcome of our study. Increasing the high risk threshold from ≥ 2 to ≥ 3, decreased slightly the sensitivity, but increased the specificity. iPYMS in UK illustrated a sensitivity of 85% and a positive predictive value (PPV) of 37%, but in Iran these were 93% and 69%. Overall, we found the diagnostic performance of iPYMS improved with the cut-off ≥ 3 in both cohorts, but more profound in Iran than the UK. iPYMS demonstrated moderate to good agreement with SGNA in Iran, and moderate agreement in the UK cohort. The higher sensitivity and positive predictive values of iPYMS in Iran cohort reflect a greater probability that a child who is identified as being at malnutrition risk using the tool will be truly so. Huysentruyt et al., (2013b) reported a similar sensitivity (94.6%) for STRONGkids used by nurses against nutritional intervention although with very low PPV of 18% and low Specificity of 49% and 52% compared with WFH and nutritional intervention respectively. These differences can be described due to the fact that iPYMS and STRONGkids tools have been designed for different purposes and validated with different references in the lack of a gold standard to assess the sensitivity and specificity of the test. In fact low specificity obtained in Huysentruyt et al. study suggests that STRONGkids tool may create an extra burden on dietitians with unnecessary referrals, although detecting nearly all the children with a nutritional intervention as being at high risk (Ling et al., 2011). However, it is known that sensitivity and specificity tend to be inversely related and in the screening unlike assessment, specificity is more important, because too many false positive leads to workload.

iPYMS against skinfolds:

In our study, we used skinfolds thickness as an objective measurement of established undernutrition to assess the performance of iPYMS, and expected that in the UK cohort the prevalence of actual malnutrition will be low, but that UK and Iran infants at iPYMS high risk will have low fat stores. However this was not true in terms of the UK cohort. We discovered that in Iran 76% infants with raised iPYMS had mean skinfolds <-2SD, compared to 18% of the rest, but in the UK only 5% had low skinfolds and this was unrelated to iPYMS. This can be explained that using the criterion of skinfold for validation of iPYMS in Iran cohort, where the background prevalence of under nutrition was high, can be very appropriate, but in the UK cohort considering the low prevalence of undernutrition in the community, we might need different criteria in order to be able to establish the validation of iPYMS for identification of malnutrition risk in sick infants. Various benchmarks have been used in validation studies, but

there is no standardized approach to nutritional screening for paediatric inpatient (Hartman et al., 2012). Therefore, the criteria and cut-offs used for the screening and diagnosis of malnutrition (acute and chronic) might be the main issues that should be taken into account (Joosten and Hulst, 2011). In contrast to our study, Hulst et al. did not include any objective assessment for validation of the STRONGkids tool.

There are some more advantages using skinfold to assess malnutrition in clinical settings. It is indicated of fat stores and wasting (acute undernutrition). It can be measured quickly and easily in young children and infants with proper precision by well-trained medical staff. There are available reference data to covert skinfold data to the SD scores value and use it as z scores. The limitation of skinfold is that it might have low precision and accuracy to assess overnutrition (obese children). However, this cannot be the case in the studies that are looking at the assessment and identification of undernutrition. Furthermore, measuring the change and alteration in body composition (fat mass and fat free mass), can be an appropriate method to assess malnutrition in children in the clinical settings, as various diseases have different effect on the size of fat and fat free mass. For this purpose, measure of skinfold thickness can be suggested as a bedside method and more robust criterion compared to other anthropometric measures (BMI and Weight) to assess malnutrition-associated disease in young children in routine clinical practice. BMI is a simple baseline measurement of relative weight, but is not able to differentiate between fat and fat free mass, which is very important in the clinical settings. Patients may have low BMI, but it can be because of low lean mass and disease and at the same time normal fat mass. BMI may mislead in hospital patients, where children apparently malnourished in terms of BMI in fact have an increase in relative body fat and a decrease in lean mass. This may be important for their nutritional management, as the low BMI may lead to unsuitable overfeeding. These all suggest that skinfolds thickness can be an appropriate measurement to assess undernutrition in young children as well as an objective measurement to assess the diagnostic performance of iPYMS.

iPYMS is considered as a unique nutrition screening tool developed for infants and there has been no nutrition screening tool mainly developed to use for identification of infants at risk of undernutrition on admission to hospital at time; Hulst developed STRONGkids for children, aged from 1 month to 17 years. However, it was not designed as a validation study as noted in the published paper (Hulst et al., 2010) and there was nothing reported about the sensitivity or

specificity of the STRONG kids tool, but recently the use of STRONG kids by nurses has been validated against WFH, LOS and nutritional intervention as parameters of prospective validity in a Belgian population of hospitalized children (Huysentruyt et al., 2013b). Athough the STRONGkids has been developed for children as well as infants; it involves only a small number of children less than 1 year.

Discriminant validity and LOS:

In both cohorts, we demonstrated that infants in the moderate and high risk groups based on iPYMS rating risk, had significantly lower mean SD-score for anthropometric - weight, height and BMI on admission. This was in agreement with the hypothesis that Infants who are identified by iPYMS as being at high risk of malnutrition will have lower mean anthropometric z-scores compared to those at low risk. We also showed that in Iran, but not UK cohort, infants who were classified as being at high risk of malnutrition on admission had longer hospital stay. Similar to our finding, in Secker and Jeejeebhoy (Canada) and Hulst et al. (Netherlands) studies, using both SGNA and STRONGkids tools, three risk groups were defined and related to anthropometric (weight–for-height) and recorded that a higher risk score was related to low SD score and prolonged hospital stay. Moreover, in the present study, by excluding patients who scored at high risk based on low BMI ($\leq$ -2 z-score) or were underweight (weight $\leq$ -2 z-score), overall the differences in weight and BMI remained significant in both cohorts. This shows that iPYMS was able to identify infants, who may not have had apparent (severe) evidence of malnutrition, which could be reflected on anthropometric signs or who were on the early stage (mild or moderate) of being undernourished.

iPYMS steps or elements:

We did not include a question about the presence of underlying disease, in our tool as STRONG kids and STAMP considered the clinical condition as an important element of their tool based on the notion that there is strong evidence indicating important nutritional consequences of certain diseases in children, such as cystic fibrosis, cerebral palsy and Crohn's disease (Sentongo et al., 2000; Sermet-Gaudelus et al., 2000; Sullivan et al., 2002; Weidemann et al., 2007). However, the development phase of McCarthy's et al., study (2012) demonstrated that clinical condition was unrelated to nutritional risk. We thought that the effect of the clinical condition on nutritional risk can be more complicated regarding the

different diseases. We therefore did not include clinical condition in our tool but instead we decided to use the impact of any acute condition on factors which determine the nutritional status of the patients.

Compared tools:

In current study, iPYMS demonstrated better sensitivity than STRONGkids compared to SGNA in both cohorts, and STRONGkids demonstrated moderate and poor agreement with SGNA respectively in Iran and UK cohort. Unlike our study findings, a recent publication (Moeeni et al., 2012; 2013) comparing the utility of different nutrition screening tools in New Zealand and Iran reported that STRONGkids was reliable tool in New Zealand, but it had variable utility in Iran. This study (Moeeni et al., 2013) also recorded that 93% of patients who were referred to dieticians by ward physicians were recognized by STRONGkids and STAMP to be at medium and high risk and only 63% of the children were classified at risk groups by PYMS and also three undernourished children was misclassified by PYMS as being at low risk. However, it can be noted that the first element of the PYMS tool assesses children using the criterion of BMI below the 2nd centile (-2SD) and it means that PYMS should be able to screen all the undernourished patients where the objective criterion of Moeeni's study was weight for height or BMI. We therefore believe that there might have been a mistake in the result analysis of that for the calculation of the misclassified children by PYMS (Gerasimidis et al., 2014a).

Comparison of iPYMS and STRONGkids:

In our study, the agreement between STRONGkids and iPYMS was poor in both cohorts. This can be described that iPYMS as a tool that was developed and evaluated for the nutritional risk screening of infants, whereas STRONGkids was mainly developed for identification of nutritional risk in children of all ages. This finding of our study is in agreement with the results observed by Wiskin et al study that reported poor agreement between PYMS and STRONGkids in children with inflammatory bowel disease (Wiskin et al., 2012). On the other hand, a recent review has also suggested that the comparison between tools might not be useful as a concordance comparison, because each is designed for different purpose (Elia et al., 2011; 2012). Although, iPYMS and STRONGkids, both attempt to classify infants and children into three nutrition risk categories; low, medium or high, in fact each of those contains different components and therefore may not be freely interchangeable.

Similarly, a modest agreement (kappa=0.3) between PYMS and STRONGkids was reported (Wiskin et al., 2012).

Malnutrition and risk of undernutrition

The results obtained of this study illustrated that more infants in Iran were rated as high risk for undernutrition (high SGNA risk was found in 32% Iranian infants compared to only 7% in the UK (P=0.0001)) and had acute undernutrition than UK.

Previous studies have also demonstrated a high prevalence of malnutrition risk in paediatric inpatients in developed as well as developing countries in economic transition ((Joosten et al., 2010; Aurangzeb et al., 2012; Huysentruyt et al, 2013a and 2013c). However, few studies exist on the nutritional status and risk on Iranian children particularly infants requiring admission to hospital (Mahdavi et al., 2009; Moeeni et al., 2012). In Moeeni's et al. study, over a quarter of the hospitalized children were reported as having moderate or severe under-nutrition (17.6% moderate malnutrition, 4.2% severe wasted and 4.2% severe stunted). This was slightly higher in the Iranian cohort of the current study - 28.6% of infants had BMI z-score <-2SD and 20.4% had weight z-score <-2SD). However in contrast Moeeni's et al. study, half of those malnourished infants were severe. In fact, the rate of severe malnutrition in Iranian infants was twice of those children in the Moeeni's et al. study. Similar to this finding, in other studies a higher prevalence of malnutrition in hospitalized infants has been reported (Hecht et al., 2014; Cao et al., 2014). Furthermore, the discrepancies observed in current study and Moeeni's et al. study in terms of the rate of malnutrition risk identified by nutritional screening tools can be expected because the tools incorporate different components, purposes, scoring system and age groups.

Misclassified infants by iPYMS (false positive) in both cohort and similarities and differences between steps scored

In our study, 47 infants in the UK and 53 in Iran cohort were misclassified as false positive with iPYMS compared to SGNA. These misclassified infants had longer length of stay in both cohorts, which suggests that those infants might be still at risk of malnutrition as identified by iPYMS. Moreover, most of the misclassified infants compared to SGNA as well as skinfolds, in both cohorts scored high at the steps of iPYMS regarding the changes in intake and effect of clinical condition. We cannot ascertain whether nutritional risk in these infants was overidentified or our benchmarks were not appropriate for use. It can be that those

misclassified infants were still at risk of nutritional status deterioration as the result of an acute illness despite no apparent evidence of changes in weight or skinfolds.
It seems that two steps of iPYMS, including changes in intake and effect of clinical condition, might be good predictors of the risk.

About two thirds of misclassified infants (at high risk by iPYMS compared with the skinfolds z-scores ≥-2SD) in the Iranian and one third in the UK cohort had weight <9th or 2nd centile. This means that if these infants had low weight centile then probably iPYMS scored them correctly but skinfolds were not good here to pick up these underweight infants.

Components of iPYMS steps in Iran and UK cohort

In the Iranian cohort, 91% of high risk infants at high risk threshold of ≥3 were scored below weight <9th or 2nd centile. This suggests that weight alone without applying other elements of iPYMS might be able to identify the majority of infants at risk of malnutrition, but in the UK cohort, we might require weight centile as well as the history of intake to screen the at risk infants. Similar to our findings in Iran cohort, McCarthy et al., (2012) in the development phase of their study reported that the objective information relating to weight and height was the strongest predictor of nutrition risk. Although, anthropometric measurements are commonly used as the only defining criteria for under-nutrition and over-nutrition, those measurements alone do not give a complete picture of nutrition risk in a clinical setting, and additional (although somewhat subjective) information, such as dietary intake and management, is also required.

Furthermore, in the Iranian cohort infants at high iPYMS risk(threshold of ≥ 2), 79.3% and 65.1% were scored as being below <9th or 2nd centile and having poor weight gain respectively, but these were only 42.4% and 39% in the UK cohort. In fact, most of the high risk infants in the UK cohort were scored as being high risk due to the steps of reduced intake (67.8%) and the effect of current disease on nutritional status (78%). These findings suggest that UK infants might be at early stage of malnutrition risk (risk of development) or illness that can be affected by reduced dietary intake. Thus, the last two steps of iPYMS might be more predictive of malnutrition risk for the UK cohort. In contrast, Iranian infants might be mostly at risk of severe malnutrition, which leads to deterioration of nutritional status and

suboptimal body composition. Thus, it is not surprising that the first step of iPYMS (weight centile) is the strongest predictor of malnutrition risk in Iran cohort.

In both cohorts, by increasing the high risk threshold to ≥ 3, the proportion of infants who scored being at high risk due to the weight below <9th or 2nd centile and poor weight gain increased respectively to 91.2% and 85% in Iran and 70% and 50% in the UK cohort**.** This suggests that the first step of iPYMS (weight centile) at this level can be a strong predictor of malnutrition risk in both cohorts, but in Iran this is much stronger than in the UK. This was in agreement with the hypothesis that the majority of infants will be scored by iPYMS as being at high risk of malnutrition due to the first step of iPYMS (weight below < 2nd or 9th centile) and This will be more so in Iranian cohort than the UK.

Strengths and limitations of the study

The strengths of this study are: 1) this is the first and unique nutrition screening tool – infant Yorkhill Malnutrition Score (iPYMS) developed and validated for sick infants. 2) The utility of tool was assessed in two completely different hospital setting, UK and Middle East.

A weakness of this study is the fact that there is no gold standard for assessment of nutritional status and risk in infants, but in this study we used SGNA rating risk as a comprehensive globally assessment tool for identification of under-nutrition risk in paediatric inpatients and skinfolds thickness < -2SD as a criterion of fat stores and acute malnutrition.

In this study, the intra/inter operator variability was not assessed. In Iran cohort all assessments were conducted by one investigator and that was not compared to anyone else assessments, so it is not known how repeatable it would be. In fact, the investigator carried out a model that a nurse would do. In other words, nurses just collect this information and it is not checked for the repeatability, so it can be a realistic and pragmatic assessment, but it is a good point to know that whether actually two nurses would come up with the same answer on the same child. It is not known how consistently people would use iPYMS. The fact that this would be possible if there were more than one person calculating iPYMS score or the investigator calculated it more than once. If only one investigator is rating iPYMS then the inter-rater variability cannot to be tested. Because one person couldn't back and rate the child

at the second time - that would be very difficult because she remember the child and what she has done before. Further work needs to be done on that in the future studies.

As outlined earlier, although inter- rater reliability was not possible to be assessed in current study, this comparison was made for older children (Gerasimidis et al., 2010). PYMS form was completed by the research dietitian to assess its inter-rater reliability with the nursing staff. It was reported that the PYMS completed by the two dietitians compared with the nursing staff showed moderate inter-rater agreement ($k = 0.53$) and concurred for 86% of patients.

The screening tool for the UK cohort was performed by different researchers; this might influence the results of the study, because using SGNA to identify children at risk of undernutrition is considered to be a subjective judgment and may be unreliable when it is applied by researchers with different professional levels and skills. However all researchers were trained by the same senior researcher. Additionally, anthropometric measurements, particularly skinfolds, are reported to be subject of error (imprecise), but trained researchers can minimise the measurement error. On the other hand, the ideal tool however is the one that can be usable by different health professionals. In this study 2 nutrition and 1 medical student and 1 dietician contributed in the recruitment of patients for UK cohort. Therefore, contribution of different researchers in the screening of patients in the UK cohort should not be considered as a weakness.

As the use of any screening tool to identify infants with or at risk of malnutrition can only be considered effective if it results in early intervention and improved clinical outcomes. We therefore recommend determining the effectiveness of iPYMS in such aspects in future intervention studies.

Conclusion

Results of the present study demonstrated that iPYMS scored more Iranian infants at high risk of malnutrition than the UK infants. iPYMS might perform well in Iran as a country with a high background prevalence of undernutrition and could be used by health professional to identify infants with malnutrition. In contrast, in the UK, iPYMS would mainly identify infants at risk of malnutrition because of the low prevalence of undernutrition. Moreover, we

found that the fist component of iPYMS (weight below < 2^{nd} or 9^{th} centile) is a strong predictor of malnutrition risk. Therefore iPYMS may not add any advantage over the simple objective measurement of weight alone to identify infants at risk of malnutrition.

CHAPTER FIVE

PREDICTORS AND CORRELATES OF MALNUTRITION

This chapter describes the predictors and correlates of malnutrition in the Iranian cohort of this study. The UK cohort was excluded from the correlates study, as the prevalence of undernutrition was low in UK infants.

Aims

- To compare the usefulness of various anthropometric measures to predict malnutrition in infants
- To determine the factors that correlate with malnutrition in these hospitalised infants

Objectives

- To explore the predictors (anthropometric measures) showing the occurrence of malnutrition in sick infants defined as SGNA high risk and sum skinfolds z-scores <- 2SD.
- To compare the predictive value of iPYMS total score with the anthropometry to identify the risk of malnutrition in sick infants
- To assess the relationship between SES and infant feeding practice and malnutrition

Hypothesis

- The majority of infants who are identified as being at high risk of malnutrition will have low weight and low weight velocity (z-scores<-2SD). ROC analysis will show that infants' weight velocity will be a better predictor than admission weight of malnutrition risk using either sum skinfolds z-scores <- 2SD or SGNA high risk as the main outcomes.
- Infants' weight velocity and iPYMS total score will be better than admission weight, as predictors of malnutrition risk when using either SGNA or sum skinfolds z-scores as the main outcomes.
- Infants who are in less affluent SES will identified by SGNA as being at higher risk of malnutrition and will have lower sum skinfolds z-scores compared to those in more affluent SES.
- Formula-fed infants will be rated by SGNA as being at higher risk of malnutrition and will have low fat compared to those who are exclusively breast-fed.

5.1. Introduction

Hospitalised infants are considered to be at high risk of undernutrition (Hecht et al., 2014; Cao et al., 2014), but little is known about the risk factors for malnutrition in paediatric inpatients. Furthermore, several different criteria have been used to define malnutrition, and it is not known whether children identified to be malnourished by the various criteria can be identified by a set of risk factors. A cross-sectional study conducted in a tertiary paediatric hospital reported that children younger than 2 years who were on the period of normally rapid growth and those with chronic medical conditions had a higher prevalence of acute and chronic malnutrition based on the Waterlow criteria (Hendricks et al., 1995). Another study as a multi-center European study illustrated that children with BMI <-2SD were associated of lower quality of life, and more frequent occurrence of diarrhea and vomiting and had longer hospital stay (Hecht et al., 2014).

There have been few studies on risk factors of malnutrition affecting hospitalised children, particularly in developing countries. Most of the existing studies have been carried out in community-based settings (Sheikholeslam et al., 2004), where various factors have been known to affect the development of malnutrition including inappropriate child feeding, illiteracy, poor nutritional knowledge of mothers, low household income, food scarcity and poor sanitation practices that place children in a vicious cycle of infection and malnutrition (Sheikholeslam et al., 2004). A national survey in Iran in 1998 reported that in rural areas, 12.8% of under 5-year olds suffered from mild to severe nutritional stunting, 13.7% were underweight and 4.8% wasted. This survey highlighted that the prevalence of underweight amongst children under 6 months old was similar to a developed community (3%), and this prevalence increases after this age, peaking at 13.8% in 2-year-olds (Sheikholeslam et al., 2004). A community-based intervention study to reduce malnutrition amongst children aged 6-35 months in Iran used a range of interventions including nutrition, health and literacy education for mothers, improved growth monitoring and fostering rural cooperatives and income generation schemes. This intervention was conducted between 1996 to 1999 in rural areas of 3 provinces with high prevalence of malnutrition in children under 5 years old. Before this intervention, the prevalence of underweight, stunting and wasting based on the different areas, was reported to be 12-28%, 25-41% and 5-9% respectively. After the intervention, the

prevalence of underweight and stunting was significantly lower, at 10-14% and 12-19% for underweight and stunting respectively (Sheikholeslam et al., 2004).

In this part of the study, we aimed to compare the usefulness of various anthropometric measures to identify malnutrition in infants and to explore the factors that correlated with malnutrition.

5.1.1 Anthropometric predictors of malnutrition

5.1.1.1. Weight-for-age (WFA), Height-for-age (HFA), Weight-for-height (WFH), Body Mass Index (BMI), and mid-upper arm circumference (MUAC)

Anthropometry is widely used in assessment of nutritional status in infants, but it is not clear what measures are most informative.

WFA

Body weight is a dimension of size rather than composition. It is the easiest index to assess nutritional status. However, it does not distinguish between present and long-term malnutrition. Underweight (low WFA) is, therefore, a combined measure of stunting (low HFA) and wasting (low WFH) (Carlson and Wardlaw, 1990). It is particularly useful in infants under one year of age in whom length measurement is difficult to take accurately and fluctuates more. However, it is not a reliable indicator in the presence of fluid retention which can occur in conditions such as chronic cardiac failure (Taylor and Dhawan, 2005). Furthermore, it fails to distinguish tall, thin children from those who are short with adequate weight (Gorstein et al., 1994).

HFA

HFA values indicate long-term nutritional status as compared to weight; this parameter responds slowly to changes in negative nutritional status, although with recovery, some permanent impairment in height may remain (Mascarenhas et al., 1998). Children are susceptible to stunting (low HFA) with any prolonged or severe illness or impaired nutrition during the period of rapid growth, especially during the first two years of life. HFA fails to

differentiate between deficits in height due to past events, or due to a chronic and ongoing event, which is an important consideration in the management of children (Ojo et al., 2000). Height/length for age < -2 SD is indicative of stunting and used as a marker of chronic malnutrition in developing countries and in children with chronic illness (WHO Tech Rep Ser, 1995).

WFH,

WFH describes acute malnutrition that is suggested as providing valid criteria for the identification and treatment of severe acute malnutrition in children (Isanaka et al., 2009). Although it can be used for the screening of acute malnutrition, its diagnostic value is limited when attempting to identify children at early stages of undernutrition, or in patients at risk of deterioration in nutritional status as the result of a medical condition.

WFH is more useful than WFA alone (Mascarenhas et al., 1998). This measure indicates whether wasting, stunting, or both have occurred (Mascarenhas et al., 1998). It is useful in developing countries where the age of the child may not be known due to poor documentation of birth records (Gorstein et al., 1994).

Wasting is low WFH and is characteristic of acute undernutrition. It indicates a deficit in tissue and fat mass compared with the amount expected in children of the same height or length. It may result from failure to gain weight or weight loss. Wasting is a useful index for short-term actions such as screening in emergency surveys and assessing effects of short-term interventions.

In developed countries, WFH standards are less available than age specific BMI standards (Olsen et al., 2007; Ling et al., 2011). WHO has recommended the cut-off BMI < -2 SD to describe malnutrition in terms of thinness in children (WHO Multicentre Growth Reference Study Group, 2006a; Cole et al., 2007). A cross-validation study in Brazil showed that performance of BMI and WFH in predicting underweight in children aged 2-19 years was similar (Mei et al., 2002).

BMI

BMI should be interpreted with age and gender specific reference values (Cole et al., 2000) or standard deviation scores in children. It is easily measured and is less subject to errors when

compared to other anthropometric parameters such as SFT (Poustie et al., 2005). As an absolute measure of fatness in individuals, BMI has poor accuracy (Ellis et al., 1999, Wells, 2000). BMI is limited by its failure to distinguish between FM and LBM (Maynard et al., 2001). Low BMI has been proposed as a measurement of body composition. Moreover, it is not always a reliable indicator of FFM, and only when BMI is very low is it likely that FFM will be low. Thus BMI as an indicator of malnutrition may be meaningful only at the lowest extreme (Meijers et al. 2010).

MUAC

MUAC is a compound measure of muscle, fat, and bone. It has been used as an alternative index of malnutrition in rapid nutritional surveys where weight and height measurements are not feasible to obtain (WHO Technical Report, 1995). MUAC is sensitive to current nutritional status (Frisancho, 1981). Advantages of MUAC are its simplicity, particularly for screening children in emergency situations of field epidemiological surveys.

5.1.1.2. Weight velocity

Poor weight gain in infancy is considered a condition associated with undernutrition and growth disorders, but assessing weight gain requires data to be collected prospectively within the first year of life. Assessment of growth velocity using current weight charts assumes that a normally growing infant stays close to his initial weight centile. However, theoretically this is inappropriate. Growth charts are derived from cross-sectional data, and only allow single weights to be expressed as a centile relative to the reference population, adjusted for age and sex. These charts only identify infants whose weight centile are low and cannot reliably quantify changes in weight, as over a period of time, infant weight tends to regress towards the median. There is a tendency for difference in infant weight to become less extreme with passing time. Thus, an infant on the 2nd weight centile is likely to show catch-up growth, whereas 98th centile infants tend on average to 'catch down'. As a solution to this, Wright et al. (1994) suggested the 'thrive index', as a measure of conditional change in weight SD score between 6 weeks and 12 months.

Conditional weight gain is calculated from the linear regression of current weight SD score (SDS2) on previous weight SD score (SDS1). The predicted value of SDS2 can be derived by

r×SDS1, where r is the correlation coefficient between SDS1, and SDS2 (Wright et al., 1994). Thus;

$$\text{Conditional weight gain} = SDS2 - r \times SDS1$$

Cole further described how an SD score for conditional weight gain can be derived from the following equation (Cole, 1995);

$$SDSgain = SDS2 - r.SDS1/\sqrt{1-r^2}$$

The correlation coefficient- r between SDS1 and SDS2 varies according to the two ages of measurement. Weight gain should be calculated over the longest available time interval, as this reduces measurement error.

In this study, conditional reference for infant weight gain (Cole, 1995) was considered, which allows for the average tendency of light infants tend to catch up, and heavier infants 'catch-down'. This assesses weight gain of infants over a time period of four or more weeks, through the first two years of their life, by converting any pair of ages between 4 weeks and 2 years. In other words, the reference of conditional weight gain compares an infant's current weight SD score with the value predicted from their previous weight SD score. This method calculates weight gain using the change in weight SD scores, derived using the UK 1990 reference (Freeman et al, 1995) and adjusted for regression to the mean, giving the result as a SD score for weight gain. Cole's conditional weight gain reference has been validated using a second dataset, and thus can be applied to other populations (Cole, 1995).

5.1. 2. Socioeconomic status (SES) as a predictor of malnutrition

Socioeconomic classification is an established predictor of malnutrition and poor growth in developing countries (Vollmer et al., 2014; Tzioumis and Adair, 2014; Silveira et al., 2015). However, this association has not been explored thoroughly in societies experiencing the economic transition, such as Iran, particularly with regards to disease -associated malnutrition.

In contrast to the UK where there are established socioeconomic classification systems, such as Carstairs and the Scottish Index of Multiple Deprivation, this is not replicated in Iran. There is a range of different classifications of SES in Iran. One socioeconomic classification has been described in the assessment of the association of dietary patterns with socioeconomic

factors in Tehran (Rezazadeh et al., 2010). It assessed individual SES factors, comprising the variables of university education degree, employment status, housing, total monthly family income. Each of these variables was related individually to dietary patterns.

Another hospital-based prospective study assessed the association of SES and low-birth weight in the north-western area of Iran (Jafari et al., 2010) using individual SES variables such as: mother and father's education (university degree, high school, secondary and primary), and mother (employed, housewife), and father's occupation (private non-governmental, farmer, worker, governmental). Each of these variables was individually correlated to low-birth weight.

Another study assessed some related factors (SES, nutritional status, etc) to exclusive breast-feeding amongst 2520 children aged 6-60 months in Northern Iran (Veghari et al., 2011). In this study, economic status was categorised based on possession of 10 consumer items necessary for life. The economic status then was classified considering those items as low (<3), moderate (4-6), and good (7-19). These studies highlight that there is no standard procedure for classification of the SES in Iran.

There is currently little evidence that has explored SES as a predictor of disease-associated malnutrition in sick children of communities undergoing an economic transition. This is an important area of study as it may be an additional determinant of poor nutrition and growth to consider in children with poor health. There have been some evidence from individual studies that show that the intervention programmes providing cash or transferring food to poor people have some effects on younger children (Ruel et al., 2013). It can be therefore suggested that an established welfare payment system may be beneficial for families who have low socio-economic status or who have young children. Furthermore, in the communities such as those in Iran, where families may not have access to appropriate weaning foods (as discussed with Prof Rafeey, gastroenterologist at Tabriz Children's Hospital), the administration of suitable weaning food supplements may also prove to be an effective intervention.

5.1.3. Feeding as a determinant of malnutrition

Breastfeeding has always been the gold standard for infant feeding. The new WHO guidelines recommend exclusive breastfeeding for 6 month, and the introduction of complementary feeding after this age. Exclusive breastfeeding is defined as providing breast milk and no other liquids or solids except for those containing vitamins, minerals, or medicines to the baby from birth (Kramer and Kakuma, 2002).

There is strong evidence of many benefits of breastfeeding for children. Breastfed infants do not share the same illness or mortality rates as formula-fed children, even in developed countries (Kremer and Kakuma, 2002, 2004; Rbhan et al 2009). Formula-fed infants have significantly higher rates of acute otitis media, non-specific gastroenteritis, severe lower respiratory tract infections, and asthma (Ip, 2007).

A national retrospective study in Iran (Olang et al., 2009) using the Integrated Monitoring Evaluation System (IMES) collected data demonstrating that 90% of infants were still partially breastfed between 12 and 15 months. However, rates of exclusive breastfeeding were only 57% at 4 months and 28% at 6 months. This survey suggested that SES is not the most important factor in Iran determining whether or not mothers feed their infants with breast milk. However, SES was reported based only on whether areas of residence were known as being with low, middle or high SES class.

Aims

The aim of this study is to explore the predictors of malnutrition, as well as to find out the association between demographics, SES, and infant feeding practices in infants admitted for care in a paediatric hospital of a community in economic transition. In other words, this study aimed to find out the most robust predictors showing the occurrence of malnutrition in these sick infants and to determine the major risk factors that may result in this condition.

5.2. Methods

As predictors of malnutrition we defined;

1. Growth velocity (conditional weight gain)
2. Weight
3. MUAC
4. BMI

As correlates of malnutrition in this study we defined:

5. LBW, gender, infant's order
6. Socioeconomic status
7. Milk feeding history

The outcomes used were SFT, which indicates low lean mass, and SGNA which incorporates other predictors.

5.2.1. SES data

Socioeconomic information was collected using a questionnaire that comprised four questions: housing, parental education, parental occupation, and family income. This information was collected at recruitment by asking the patient's parent to respond to each of the above questions. These variables were selected and categorised based on the advices of my colleagues in Iran (housing, father's education, father's occupation and family income were categorised into 2, 4, 4 and 3 categories respectively) as shown in Table 5.1. Professor Saeed Dastgiri in Iran, and a consultant in social sciences and statistics were consulted, as were some previous studies carried out in Iran, in order to make an informed decision regarding the selection of the SE variables, and then to score them (Dastgiri et al., 2006; Jafari et al., 2010; Vegari et al., 2011). Maternal education was not included in the socioeconomic classification of this study, as the SES score was modeled based on the existing score that had been instructed and used previously (by the consultant in social sciences and statistics). Each of the SES measures was then divided into two categories as low and high, by considering scores of zero to low as more affluent, and score of one to high as less affluent for each variable (Table5.1). The individual was allocated a score, which lay somewhere between 0 and 4 and was termed the deprivation score, which was calculated by combining the scores of each SES. The average value was then computed for each scored variable considering any missing data. For example, there was more missing data for the variable of family income in which case, the average was computed dividing by three instead of four (Table 5.2). The advantage of

calculating the average value for only the scored variables was that missing data did not have to be imputed. The average values of the SES scores were subsequently categorized into two categories based on the median, in order to derive the socioeconomic class as low (n=78 (49.1%)) or medium (n=81 (50.9%)).

Cut-off for family income data

Regarding the variable of family income, the parents of patients' were just asked for the amount of their monthly income, and this information was then categorised first into one of three categories based on the cut-offs developed after discussion with the statistics consultant and the consideration of the cut-offs used in other Iranian studies (Rezazadeh et al., 2010). These were then re-categorised into two categories, as nearly two-thirds of individuals were considered to be below the lowest cut-off.

Table 5.1: Measurements used and categories of measures scored for classification of patients' SES

Measures scored	Frequency, n (%)
Housing (0-1)	**n=160**
Rental=0	41 (25.6)
Owner=1	119 (74.4)
Father's education (0-5)	**n=171**
Illiterate=0	8 (4.7)
Primary school=1	48 (28.1)
Secondary school=2	50 (29.2)
High school=3	47 (27.5)
BSc=4	16 (9.4)
MSc and above=5	2 (1.2)
Father's education (Two categories) (0-1)	**n=171**
Illiterate and primary school=1	56(32.7
Secondary school, High school, BSc and MSc=0	115(67.3)
Father's occupation (0-4)	**n=171**
Jobless=0	3 (1.8)
Low skilled manually occupation (for example, workers,	88 (51.5)
Markers, taxi drivers, etc=2	56 (32.7)
Clerks, teachers, etc (state or private)=3	23 (13.5)
Managers (state or private)=4	1 (0.6)
Father's occupation (two categories) (0-1)	**n=171**
Jobless and low skilled manually occupation=1	91(53.2)
Markers, clerks, teachers, managers(state or private)=0	80(46.8)
Family income (1-3)	**n=100**
Below 500000 tomans=1	60(60)
500000-100000 tomans=2	32(32)
1-3 million tomans=3	8(8)
Family income (two categories) (0-1)	**n=100**
Below 500000 tomans=1	60(60)
500000-100000 tomans and more=0	40(40)

Table 5.2: Average of each SES scored variables, as a deprivation score for the study population

	Distribution	
Deprivation score	**Number**	**Percent**
0.00	39	22.8
0.25	26	15.2
0.33	22	12.9
0.50	24	14
0.66	27	15.8
0.75	23	13.5
1.00	10	5.8
Total	171	100

5.2.2. Infants feeding data

Infant feeding information was retrieved from the SGNA questionnaire. The data was then summarised into five variables, each categorized into two categories (yes and no) comprising of: currently receiving breast milk, currently receiving formula milk, currently receiving other non-milk drinks, currently receiving any kind of solids, and ever breast fed in which an extra category was introduced (no, yes still feeding, yes but stopped).

5.2.3. Weight velocity data

In order to calculate conditional weight gain, birth weight the first weight measurement was collected from the maternal report. The second weight measurement, used to calculate velocity, recorded on admission to the hospital.

Conditional weight gain was derived using the LMS Growth software (Pan and Cole, 2012; Cole, 1995) and converted into weight gain SDS. These variables were then categorised into two z-scores groups (z-scores≤-2 and z-scores>-2). Unconditional weight gain was also derived simply by subtracting the birth weight z-scores from the admission weight z-scores. Receiver Operating Curves (ROC) analysis was also conducted for conditional weight gain,

anthropometric, and body composition data using SGNA high risk group and sum skinfolds z-scores ≤-2 as the main outcomes of undernutrition risk and acute malnutrition.

ROC analysis is a graphical plot which illustrates the performance of a binary classifier, as its discrimination threshold is varied. A curve is created by plotting the true positive rate against the false positive rate at various threshold settings. The former is known as sensitivity and the latter as specificity. The ideal test is one in which specificity remains constant despite an increase in sensitivity. Threshold can be changed, with sensitivity and specificity calculated for each threshold. In this study, we set out to investigate whether growth velocity is in fact better than a single admission weight as suggested by Wright et al. (1994) and Cole (1995) in predicting malnutrition risk, as growth velocity and admission weight were incorporated as components of iPYMS tool and considered as indications of past and present malnutrition.

5.3. RESULTS

187 hospitalised infants aged 1-12 months (Iranian cohort) were assessed for the identification of possible correlates of malnutrition on hospital admission. The UK cohort was excluded from the correlates study, as the prevalence of undernutrition was very low and it is unlikely that SES is a significant predictor of malnutrition in developed communities.

5.3.1. ANTHROPOMETRIC PREDICTORS OF MALNUTRITION

5.3.1.1. Weight Velocity

Patient weight velocity using either conditional or unconditional weight gain method varied strongly by SGNA rating risk based (Table 5.3). Using bivariate analysis, growth velocity demonstrated a moderate negative correlation with SGNA rating risk (Pearson's r= -0.78). There was also a moderate correlation between growth velocity and sum of skinfolds and fat residual ($p<0.0001$, Pearson's r=0.59 and 0.73 respectively). Thus, infants who had low weight gain were at high risk of malnutrition and had lower fat residues.

Table 5.3: Patients' growth velocity according to SGNA rated malnutrition risk groups

		Low risk		Medium		High risk		
	Patient(n)	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**P**
Growth Velocity z-score (conditional)	160	-0.14	0.95	-1.31	0.64	-2.96	1.20	<0.0001
Growth velocity z-score (unconditional)	160	0.11	1.03	-0.68	0.95	-2.12	1.17	<0.0001

5.3.1.2. Weight, MUAC, BMI

In order to compare how growth velocity and admission weight acted as predictors in the identification of risk of malnutrition, these variables were categorised into two groups (z-score ≤-2 and z-score >-2), after which their association with the SGNA risk scored groups was assessed (Table 5.4). Both the growth velocity and admission weight significantly predicted malnutrition risk ($p<0.0001$, Chi-square), however the growth velocity might be more strongly predictive of malnutrition risk (Cramer's v = 0.8, 0.72 for growth velocity and weight respectively).

Using ROC analysis alongside SGNA as the main outcome of the risk of malnutrition, it was demonstrated that growth velocity was only a slightly stronger predictor than admission weight (Figure 5.1). Weight and BMI have nearly the same predictive value for risk of malnutrition, and both are stronger than MUAC (Figure 5.2). Skinfolds sum and fat residual data recorded almost the same results for risk of malnutrition (Figure 5.3). Weight was a slightly stronger predictor than the skinfolds sum z-scores (Figure 5.4). Using sum skinfolds z-score as the main outcome instead of SGNA demonstrated that admission weight and growth velocity had almost the same predictive value (Figure 5.5). BMI and MUAC achieved nearly the same results, and weight was a slightly stronger predictor of risk of malnutrition. (Figure 5.6). Weight velocity, admission weight, and iPYMS total score were very similar in terms of prediction of malnutrition when using either SGNA or sum skinfolds z-scores as the main outcomes (Figure 5.7 and 5.8).

Table 5.4: Growth velocity and admission weight as predictors of malnutrition risk based on SGNA rated risk groups

	Low risk n (%)	Medium risk n (%)	High risk n (%)	P value
Admission Weight z-score ≤-2	4 (5)	11 (23.9)	49 (84.5)	<0.0001
z-score >-2	76 (95)	35 (76.1)	9 (15.5)	
Growth velocity z-score ≤-2	0 (0)	4 (9.8)	40 (80)	<0.0001
z-score >-2	69 (100)	37 (90.2)	10 (20)	

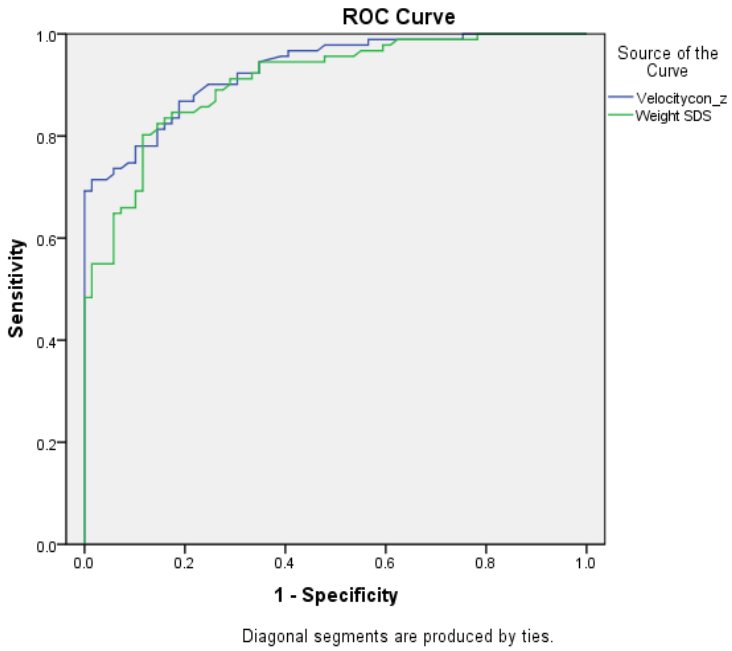

Figure 5.1. ROC curves of growth velocity and weight (using SGNA as the main outcome)

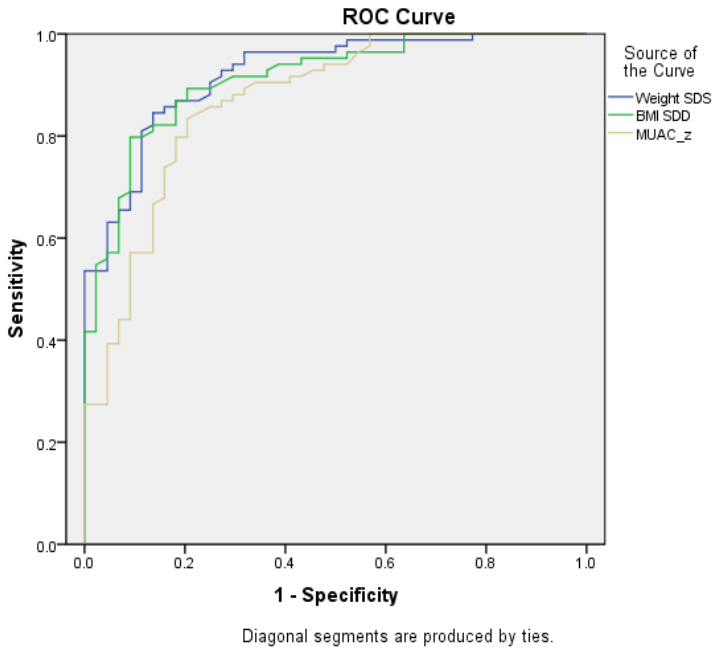

Figure 5.2. ROC curves of Weight, BMI and MUAC (using SGNA as the main outcome)

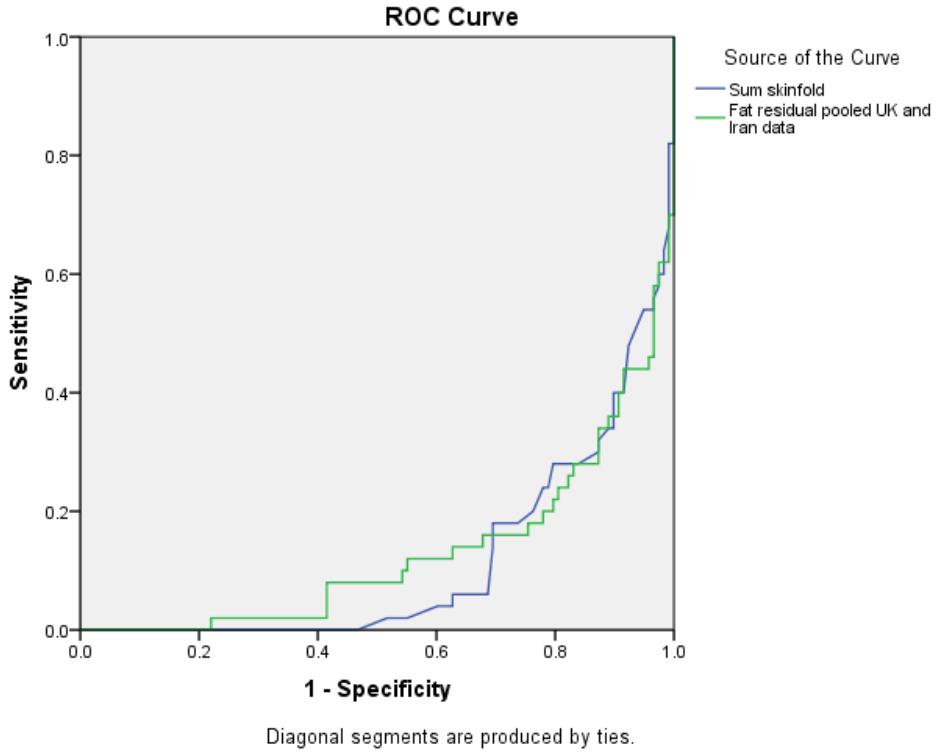

Figure 5.3. ROC curves of skinfolds sum and fat residual (using SGNA as the main outcome)

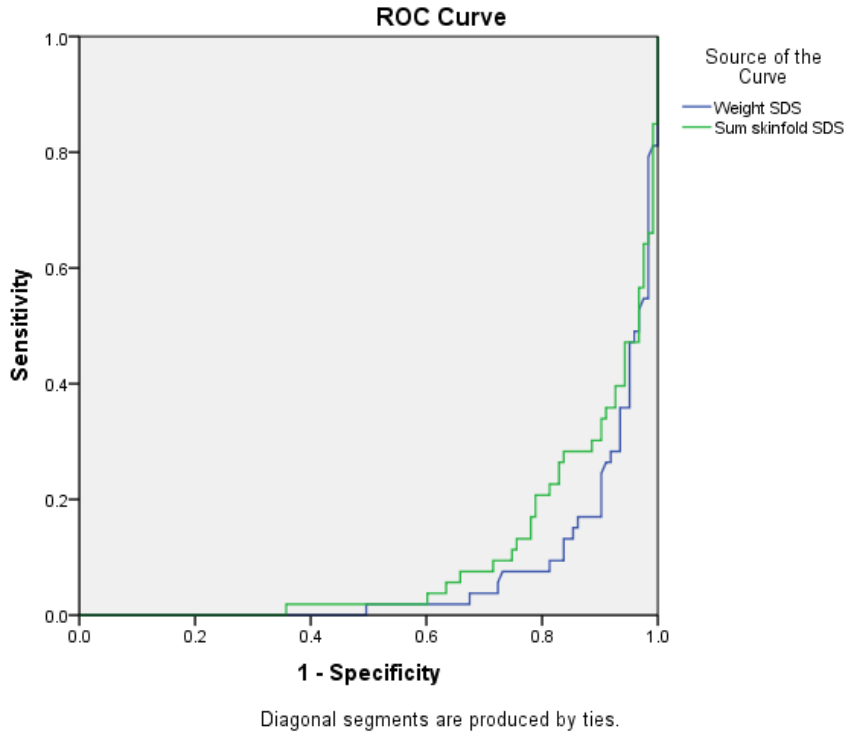

Figure 5.4. ROC curves of weight and sum skinfolds z-scores (using SGNA as the main outcome)

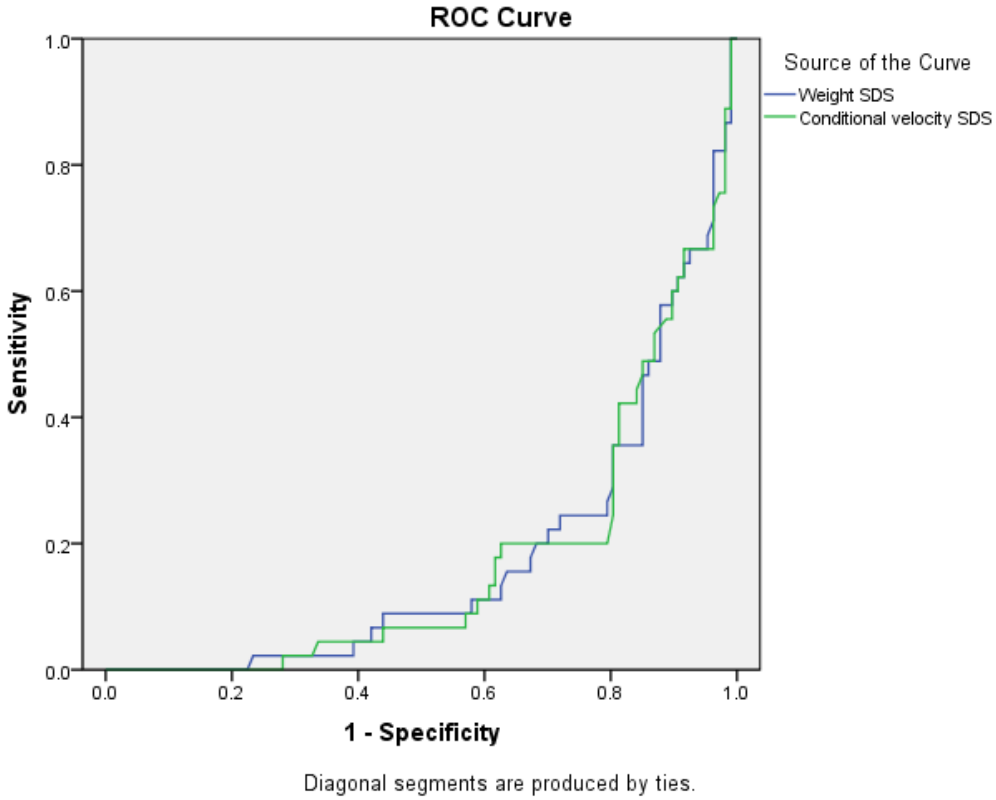

Figure 5.5. ROC curves of weight and growth velocity (using sum skinfolds z-scores)

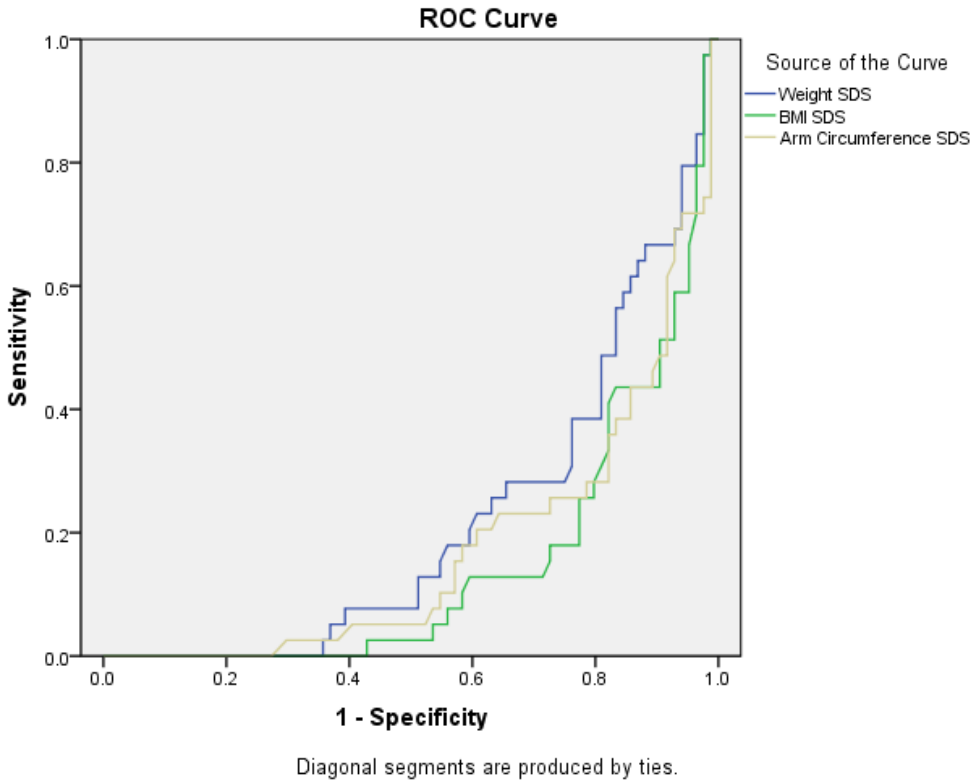

Figure 5.6. ROC curves of BMI, MUAC and weight (using sum skinfolds z-scores as the main outcome)

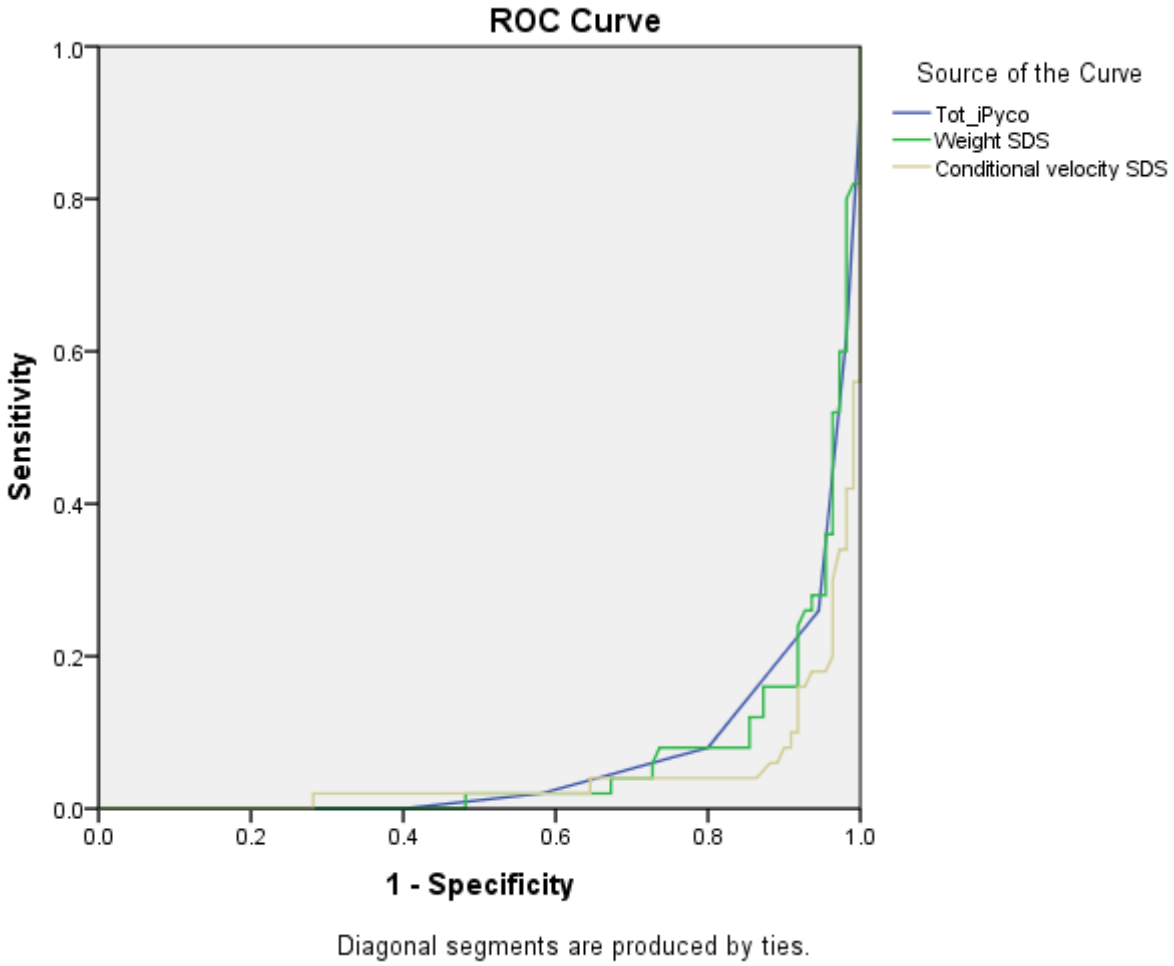

Figure 5.7 : ROC curves of growth velocity, weight and total iPYMS score (using SGNA as the main outcome)

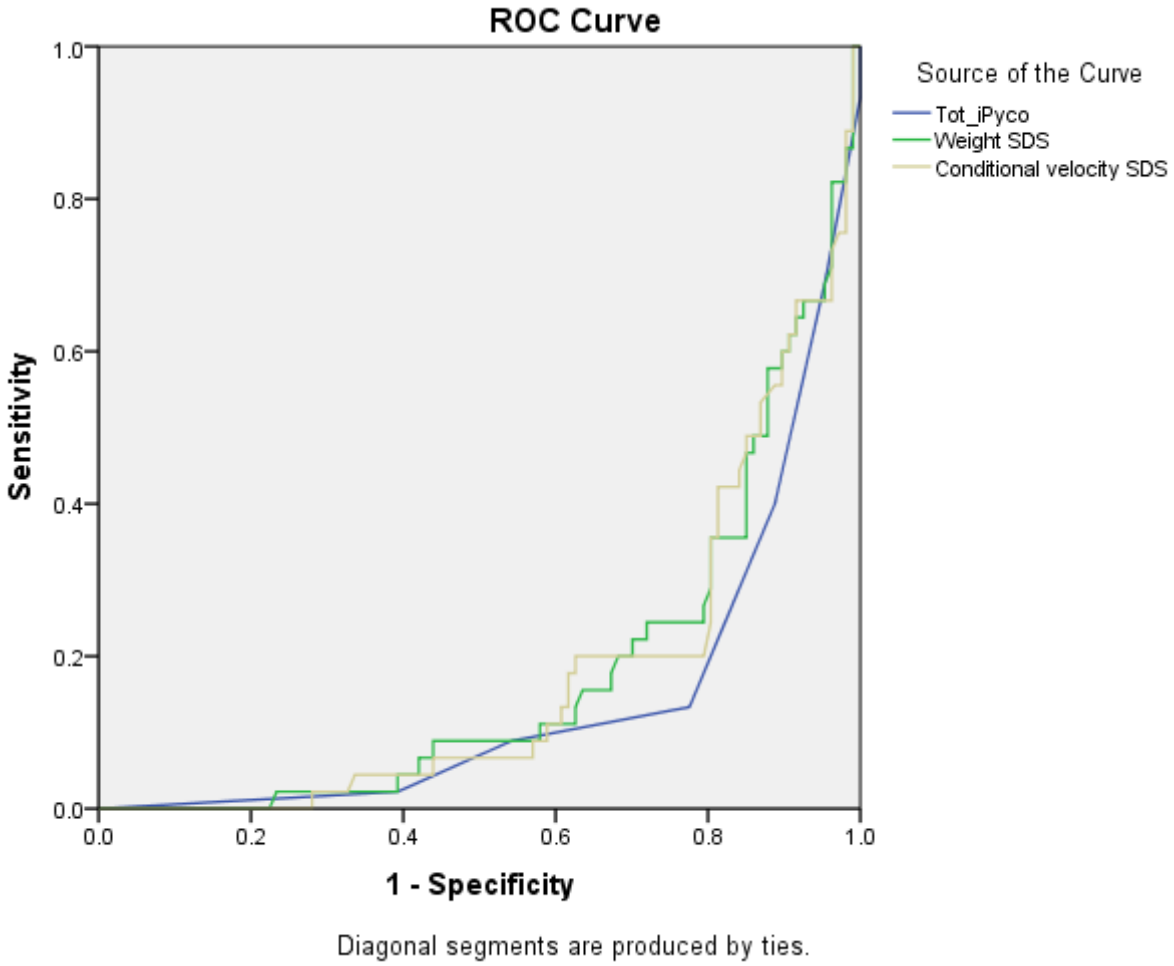

Figure 5.8 : ROC curves of growth velocity, weight and total iPYMS score (using sum skinfolds z-scores as the main outcome)

Summary of results for anthropometric predictors of malnutrition

Growth velocity demonstrated a moderate negative correlation with SGNA rating risk (Pearson's r= -0.78). A moderate correlation was found between growth velocity and sum of skinfolds and fat residual ($p<0.0001$, Pearson's R=0.59 and 0.72, respectively)

Both the growth velocity and admission weight significantly predicted malnutrition risk ($p<0.0001$, Chi-square). ROC analysis implied that growth velocity and latest weight measurement do not differ greatly as predictors of malnutrition risk. ROC analysis, using SGNA as the main outcome, illustrated that weight and BMI were very similar predictors of malnutrition risk, and stronger predictors than MUAC. Using sum skinfolds z-score as the main outcome demonstrated that BMI and MUAC had high similarity as predictors of

malnutrition risk, and both were slightly stronger predictors than weight. Weight velocity, admission weight and iPYMS total score were very similar predictors of malnutrition.

5.3.2. CORRELATES OF MALNUTRITION

5.3.2.1. Birth prematurity, Low Birth Weight (LBW), infant's gender and birth order

Using chi-square, SGNA rated risk groups showed no variation with birth prematurity (p=0.77) or patient gender (p=0.39), and there was a weak, yet non-significant association with LBW (p=0.11) (Table 5.5).). Birth order, which was organised into two categories (category 1 was assigned to first babies, whilst category 2 represented second baby or above), was also unrelated to SGNA risk group (p=0.67) (Table 5.5). A relationship nearing significance was found between sum skinfolds z-scores, fat residual and LBW (p=0.018 and 0.037 respectively) (Table 5.6).

Table 5.5: Patient birth prematurity, LBW, gender and birth order by SGNA risk group as low, medium and high

	SGNA			
	Low risk n (%)	**Medium risk n (%)**	**High risk n (%)**	**P value**
Prematurity (n=187)				
No	71 (43.6)	42 (25.8)	50 (30.7)	0.77
Yes	10 (41.7)	5 (20.8)	9 (37.5)	
LBW (n=161)				
No	62 (46.6)	32 (24.1)	39 (29.3)	0.11
Yes	7 (25)	10 (35.7)	11 (39.3)	
Gender (n=187)				
Male	50 (43.9)	25 (21.9)	39 (34.2)	0.39
Female	31 (42.5)	22 (30.1)	20 (27.4)	
Birth order (n=184)				
First child	42 (38.5)	35 (32.1)	32 (29.4)	0.67
≥second child	37 (49.3)	12 (16)	26 (34.7)	

Table 5.6: Patient prematurity, LBW, gender and birth order related to the sum skinfolds z-score and fat residual

	Sum skinfolds z-score			Fat residual		
	Mean	SD	P value	Mean	SD	P value
Prematurity						
No	-1.47	0.97	0.38	0.01	0.16	0.02
Yes	-1.67	1.24		-0.07	0.19	
LBW						
No	-1.40	0.95	0.02	0.02	0.16	0.04
Yes	-1.88	0.96		-0.05	0.13	
Gender						
Male	-1.49	1.02	0.88	-0.01	0.17	0.53
Female	-1.51	1.98		0.01	0.16	
Birth order						
First child	-1.54	0.92	0.43	-0.01	0.15	0.59
≥second child	-1.42	1.14		0.01	0.18	

5.3.2.2. Socioeconomic status (SES)

A weak trend of an association was noted between patient SES and risk of malnutrition using SGNA (Table 5.7). There was no relationship between SES and sum skinfolds z-scores (Table 5.7). There was some missing data with SES variables, particularly in those regarding family income, of which nearly half of this data was missing as illustrated in Table 5.1. However, missing values were not imputed in the analysis, and instead the average value for each scored variable was computed by dividing by three instead of four.

Table 5.7: Patient SES related to SGNA rating risk and sum of skinfolds z-scores

SES class	SGNA rating risk				Sum skinfolds z-score		
	Low N (%)	Medium n (%)	High n (%)	P value	Mean	SD	P value
Low	30 (41.1)	22 (50.0)	32 (59.3)	0.04	-1.54	0.98	0.47
Medium	43 (58.9)	22 (50.0)	22 (40.7)		-1.43	1.04	

Each of the socioeconomic scored variables were individually related to the sum of skinfolds z-scores (Table 5.8), and also to SGNA rating risk (Table 5.9). No associations were reported between the majority of the socioeconomic variables individually (housing, father's education, family income), and sum skinfolds z-score and SGNA rating risk, apart from father's occupation, which illustrated a weak association with skinfolds sum (T-Test, p=0.075) and a significant relationship with SGNA based rating risk (chi-square test, p=0.019). Thus, patients whose father had a particularly low skilled occupation may be more likely to be at high risk of malnutrition and have low fat compared to patients whose father had a more highly skilled occupation in either state or private employment.

Table 5.8: Association between each of the socioeconomic variables individually and sum skinfolds z-score as nutritional outcome

Socioeconomic variable	Sum skinfolds z-score		
	Mean	SD	P value
Housing (0-1)			
Rental=1	-1.16	0.94	0.25
Owner=0	-1.41	0.99	
Father's education (0-1)			
Illiterate and Primary school =1	-1.43	1.03	0.62
Secondary school, High school, BSc and MSc=0	-1.51	1.00	
Father's occupation (0-1)			
Jobless and low skilled manually occupation (e.g. workers, farmers, etc)=1	-1.62	0.99	0.07
Markers, Clerks, teachers, Managers (state or private)=0	-1.34	1.02	
Family income (0-1)			
Below 500,000 tomans=1	-1.52	0.96	0.25
500,000-1,000,000 tomans and more=0	-1.27	1.13	

Table 5.9: Association between each of socioeconomic variables individually and SGNA as nutritional outcome

Socioeconomic variable	SGNA rating risk			
	Low n (%)	Medium n (%)	High n (%)	P value
Housing (0-1)				
Rental=1	15 (36.6)	9 (22)	17 (41.5)	0.13
Owner=0	54 (45.4)	33 (27.7)	32 (26.9)	
Father's education (0-1)				
Illiterate and Primary school =1	23 (41.1)	15 (26.8)	18 (32.1)	0.82
Secondary school, High school, BSc and MSc=0	50 (43.5)	29 (25.2)	36 (31.3)	
Father's occupation (0-1)				
Jobless and low skilled manually occupation (for example, workers, farmers, etc.)=1	33 (36.3)	22 (24.2)	36 (39.6)	0.02
Markers, Clerks, teachers, Managers (state or private)=0	40 (50)	22 (27.5)	18 (22.5)	
Family income (0-1)				
Below 500,000 tomans=1	25 (41.7)	14 (23.3)	21 (35)	0.23
500,000-1,000,000 tomans and more=0	20 (50)	11 (27.5)	9 (22.5)	

5.3.2.3. Mother's education related to malnutrition and SES

Mother's education demonstrated a weak association with sum of skinfolds z-scores (chi-square test, p=0.066), with infants who had less educated mothers having less fat stores compared to those with more educated mothers. As would be expected, mother's education showed a significant association with socioeconomic class (Table 5.10).

5.3.2.4. Area of residence related to malnutrition

Nearly two-thirds of admitted patients (111, 61%) were from the countryside or other nearer cities to the hospital, whilst the remainder of patients (72, 39%) were from Tabriz city. There was no relationship between the area of patient residence and SGNA rating risk, sum skinfolds z-scores and socioeconomic class (Table 5.10).

Table 5.10: Mother's education and the area of patient residence related to the SGNA rating risk, skinfold z-scores and SES class

	SGNA rating risk			Sum skinfold z-scores		Socioeconomic class	
	Low n (%)	**Medium n (%)**	**high n (%)**	**≥-2SD n (%)**	**<-2SD n (%)**	**Medium n (%)**	**Low n (%)**
Mother's education							
Illiterate, primary and Secondary school =1	47 (42.7)	26 (23.6)	37 (33.6)	70 (66)	36 (34)	46 (42.2)	63 (57.8)
High school and BSc=0	27 (43.5)	18 (29)	17 (27.4)	47 (79.7)	12 (20.3)	41 (66.1)	21 (33.9)
			P= 0.60		P=0.07		P=0.003
Area of residence							
Tabriz city	30 (41.7)	20 (27.8)	22 (30.6)	48 (70.6)	20 (29.4)	33 (50)	33 (50)
Countryside or other cities	48 (43.2)	27 (24.3)	36 (62.1)	76 (61.3)	31 (29)	53 (51)	51 (49)
			P=0.98		P=0.95		P=0.90

5.3.2.5. Infant's feeding

Overall, 20% and 28% of infants were exclusively breast-fed or breast-fed alongside non-milk drinks. In other words, about half of infants in the Iranian cohort were breast-fed (Table 5.11). 37% of Iranian infants commenced solids between 4-6 months (Table 5.12).

Table 5.11: Characteristics of infant feeding in the Iranian cohort

	Feeding characteristics	
	N	%
Exclusively breast fed	37	20.1
Formula fed	57	30.0
Mixed milk fed (breast fed plus formula fed)	39	21.2
Breast fed plus non-milk drinks	51	27.7
Total	184	100

Table 5.12: Commence of any kind of solids based on infant's age in the Iranian cohort

	Commence of solid (weaning age)		
	<4mo n (%)	4-6mo n (%)	>6mo n (%)
Iran cohort			
Yes	2 (2.7)	14 (36.8)	68 (95.8)
No	73 (97.3)	24 (63.2)	3 (4.2)

As illustrated in Table 5.13, the proportion of formula-fed infants who were scored as high risk of malnutrition using SGNA rating risk was significantly (p=0.006) higher than those who were breastfed (61% versus 39%). Infants who had stopped breast-feeding were also at a significantly higher risk of SGNA compared to those who were still breastfed (p=0.004). Thus, formula-fed infants may be more likely to be at risk of being malnourished compared to breast-fed infants (Table 5.13).

Table 5.13: Infant feeding based on SGNA rating risk as low, medium and high (Iran cohort)

	SGNA rating risk			
	Low n (%)	Medium n (%)	High n (%)	P
Receiving breast milk				
Yes	59 (75.6)	32 (68.1)	36 (39.0)	0.07
No	19 (24.4)	15 (31.9)	23 (61.0)	
Receiving formula milk				
Yes	30 (38.5)	30 (63.8)	36 (61.0)	0.006
No	48 (61.5)	17 (36.2)	23 (39.0)	
Receiving another non-milk drink				
Yes	28 (35.9)	10 (21.3)	13 (22.0)	0.06
No	50 (64.1)	37 (78.7)	46 (78.0)	
Baby ever breast fed				
Yes, still feeding	59 (86.8)	32 (71.1)	34 (64.2)	0.004
Yes, but stopped	9 (13.2)	13 (28.9)	19 (35.8)	
Baby eating any kind of solids				
Yes	32 (41.0)	25 (53.2)	27 (45.8)	0.53
No	46 (59.0)	22 (46.8)	32 (54.2)	

Significant relationships were noted between the type of infants' feeding and sum skinfolds z-score and fat residual as outcome measures of malnutrition (Table 5.14). Skinfolds and fat residual in breastfed infants were significantly higher compared to those who were Formula-fed or had stopped breastfeeding. Thus, formula feeding is likely to be a considerable risk factor for infant malnutrition.

In order to illustrate how socioeconomic class might influence the type of infant's feeding, we looked at the association of each of feeding variables and SES (Table 5.15), and found that there was no relationship between SES and infants feeding. Table 5.16 shows that malnutrition risk did not vary by infant age category based on the SGNA rating risk or sum of skinfolds z-scores.

Table 5.14: Infant feeding related to mean skinfolds z-score and fat residual

	Sum skinfolds z-score				Fat residual			
	N	Mean	SD	P	N	Mean	SD	P
Receiving breast milk								
Yes	121	-1.36	0.98	0.002	117	0.001	1.68	0.004
No	54	-1.86	0.99		55	-0.78	1.57	
Receiving formula milk								
Yes	91	-1.72	0.95	0.005	90	-0.60	1.59	0.004
No	84	-1.29	1.02		82	0.14	1.70	
Receiving another non-milk drink								
Yes	49	-1.36	1.02	0.191	50	0.49	1.57	<0.001
No	126	-1.58	0.99		122	-0.55	1.63	
Baby ever breast fed								
Yes, still feeding	119	-1.36	0.98	0.016	115	0.02	1.68	0.011
Yes, but stopped	39	-1.81	1.10		40	-0.77	1.68	
Baby eating any kind of solids								
Yes	82	-1.58	0.89	0.398	80	0.21	1.49	0.001
No	93	-1.45	1.09		92	-0.64	1.74	

Table 5.15: Association between type of infant feeding and SES (Iran cohort)

	Socioeconomic class		
	low class	medium class	P
Receiving breast milk			
Yes	62 (73.8)	59 (48.6)	0.45
No	22 (26.2)	27 (31.4)	
Receiving formula milk			
Yes	39 (46.4)	48 (55.2)	0.22
No	45 (53.6)	38 (44.2)	
Receiving another non-milk drink			
Yes	30 (35.7)	21 (24.4)	0.11
No	54 (64.3)	65 (75.6)	
Baby ever breast fed			
Yes, still feeding	62 (78.5)	57 (70.0)	0.51
Yes, but stopped	17 (21.5)	20 (26.0)	
Baby eating any kind of solids			
Yes	43 (51.2)	37 (43.0)	0.29
No	41 (48.8)	49 (57.0)	

Table 5.16: Risk of malnutrition related to population age, based on SGNA rating risk, mean skinfolds z-score and sumskin folds z-scores (Iran cohort)

	Age categories		
	<6mo	>6mo	P
SGNA risk: n (%)			
Low	49 (42.6)	32 (44.4)	0.66
Medium	28 (24.3)	19 (26.4)	
High	38 (33.0)	21 (29.2)	
Sum skinfolds z-scores			
≤-2SD	30 (27.8)	22 (31.4)	0.60
>-2SD	78 (72.2)	48 (68.6)	

5.3.2.6. Multivariate analysis

Multivariate analysis of logistic regression was carried out by feeding variables and age into the same model, using SGNA or sum of skinfolds z-scores as outcomes, afterwhich it was revealed that none of these variables remained significant predictors. Feeding variables and SES by SGNA or the sum of skinfolds z-scores also showed that none of those variables remained significant predictors (apart from SES by SGNA, which demonstrated a very weak association, P=0.068). Feeding variables and fathers' occupation by SGNA demonstrated that only fathers' occupation remained a significant predictor (p=0.021), but this did not remain significant by sum of skinfolds z-scores. Feeding variables and maternal education by sum of skinfolds z-scores revealed that only mothers' education remained a significant predictor (p=0.012). These variables by SGNA showed that only mothers' education remained a weak predictor (p=0.079).

By modeling the variables in one by one analysis with sum skinfolds z-scores, we discovered that breast feeding was an independent predictor of malnutrition. Other variables were also tested and checked, and although there were observable trends, none were significant.

5.4. Discussion

The most effective measure to predict malnutrition in hospitalised infants

In this study, we aimed to compare the usefulness of various anthropometric measures to identify malnutrition in hospitalised infants. It was found that both growth velocity and admission weight were significantly associated to malnutrition risk. Furthermore, it was illustrated that growth velocity and latest weight perform as similar predictors of malnutrition risk, although it was expected that infants' weight velocity will be a better predictor than admission weight of malnutrition risk. This suggests that admission weight can be used as a robust and easy measure of malnutrition prediction in hospitalised infants. However, weight measurements are limited as they represent a dimension of size rather than body composition and do not distinguish between present and long-term malnutrition. Although assessment of WFA fails to distinguish tall, thin children from those who are short with adequate weight for their height (Gorstein et al., 1994), this assessment is appropriate for use in infants under one year of age as length measurements are difficult to accurately measure in this group. Although length/height measurements may be underestimated due to difficulties associated with keeping children fully stretched out, the WHO Multicentre Growth Reference Study indicated that infants and older children are measured with equal reliability (WHO, 2006b).

We hypothesised that infants' weight velocity and iPYMS total score will be better than admission weight as predictors of malnutrition risk, but the ROC analysis demonstrated that weight velocity, admission weight, and iPYMS total score were very similar in prediction of malnutrition risk using either SGNA or sum skinfolds z-scores as the main outcomes. This suggests that iPYMS may not add any more over weight alone to identify malnutrition risk in infants.

In this study, Iranian infants showed a high prevalence of malnutrition. The proportion of infants with acute and severe malnutrition (sum skinfolds z-score <-2SD) differed significantly by SGNA rating risk groups, as 72% of infants with high SGNA risk had low skinfolds, compared to 3% of those with low risk. Therefore, skinfold measurements reveal that in an area of high prevalence of malnutrition in the community, infants at high SGNA risk

are already malnourished. These findings suggest that skinfold measurements can be used in clinics to effectively predict malnutrition in hospitalised infants in areas where a high prevalence of malnutrition risk exists.

Skinfold measurements are a good predictor of total body fat stores and acute/chronic malnutrition. Moreover, new reference data is available (WHO reference and national references) and hence these measurements may be the most suitable parameter of malnutrition prediction in the clinical setting, particularly in hospitalised infants in Iran, who exhibit low fat stores. However, trained health professionals are necessary to conduct these measurements.

BMI and MUAC were also found to be predictors of malnutrition. ROC Analysis, using SGNA as the main outcome, illustrated that weight and BMI were similar in their effectiveness in the prediction of malnutrition risk, and both were stronger predictors than MUAC. Using sum skinfolds z-score as the main outcome demonstrated that BMI and MUAC were almost equivalent predictors, and both were marginally superior predictors than weight.

BMI/WFH is mostly used with nutritional screening tools to identify past malnutrition risk in hospitalised children. BMI should be interpreted with age and gender-specific reference values (Cole et al., 2000) or standard deviation scores in children. As an absolute measure of fatness in individuals, BMI has poor accuracy (Ellis et al., 1999, Wells, 2000). In developed countries, WFH standards are less available than age-specific BMI standards (Olsen et al., 2007; Ling. et al., 2011). A cross-validation study in Brazil showed that performance of BMI and WFH in the prediction of children aged 2-19 years being underweight was similar (Mei et al., 2002). It is noted that using BMI to determine nutritional status in sick children is not considered an appropriate clinical tool for identifying individual underweight children (Fusch et al., 2013). However, WHO and UNICEF (2009) recommend the use of WFH below -2 and -3 SD to identify infants and children as having moderate and severe acute malnutrition.

MUAC is a measure of muscle, fat and bone at a site that is sensitive to current nutritional status (Frisancho, 1981). The primary advantage of MUAC is its simplicity, particularly in the screening of children in emergency situations. WHO has recommended MUAC < 115 mm as an indication of severe acute malnutrition.

Predictors of malnutrition in Iran

Although, it was expected that infants who are in less affluent SES will be identified by SGNA as being at higher risk of malnutrition and will have lower sum skinfolds z-scores compared to those in more affluent SES, very little evidence was found for an association between patient SES and malnutrition (defined by SGNA rating risk and sum skinfolds z-scores < - 2SD). In other words, socioeconomic factors did not predict malnutrition in this study population. This may be slightly biased, as there were an abundance of missing data concerning SES, particularly regarding the family income variable, for which nearly half of the data was absent. Missing values were not imputed in the analysis. Alternatively the average value for each scored variable was calculated by dividing by three instead of four. However, it can be inferred that disease-associated factors may be more important predictors of malnutrition in these sick infants than SES. Essentially, malnutrition is either caused by a nutrient-imbalance due to disease or is non-disease-associated (starvation associated), whereby environmental/behavioural factors negatively influence nutrient intake. There can be also an overlap between these two types of malnutrition. (Mehta et al., 2013). In non-disease-associated malnutrition, or starvation associated malnutrition, environmental factors that cause malnutrition often involve socioeconomic conditions associated with inadequate food availability, or complicating behavioural disorders such as anorexia and food aversion. These factors may be behavioural/social, or may be disease-related (Mehta et al., 2013). In contrast, the most important etiological factor in disease-related malnutrition is reduced dietary intake in response to a reduction in appetite caused by changes in cytokines, glucocorticoids, insulin and insulin-like growth factors (Jackson, 2003), often with the interrelationship of more than one mechanism such as reduced nutrient intake, changed nutrient utilization or increased losses. Thus, in this study, considering the weak association between SES and malnutrition, disease-associated factors may be the leading cause.

Furthermore, confounding factors such as infant's age and feeding may have influenced the results concerning the association between infant SES and malnutrition. In order to make a true SES effect, these confounding factors were considered by using multivariate analysis and then modeling the variables one by one. In this study, breastfeeding was found to be a strong independent predictor of malnutrition. It was assumed that breastfed infants might be from low SES class, protecting them from becoming malnourished. However, there was no association

between of each of the feeding variables and SES. Malnutrition did not vary by infant age category, however a weak association was shown between maternal education and sum of skinfolds z-scores. As expected, maternal education also showed a significant association with socioeconomic class.

Although some confounding effects were ruled out, revealing the true SES effect, SES factors remained as weak predictors of malnutrition in this study population.

Infant feeding and SES class

In the current study, no association was found between infant feeding practice and socioeconomic class. There are various reports in the literature regarding the relationship between these variables, with two recent studies implying similar results to ours. A retrospective study in 30 urban and rural provinces in Iran reported that SES is not the most important factor for determing whether or not mothers breastfed (Olang et al., 2009). Another study in Northern Iran reported that the father's occupation and economic status did not have any correlation with either exclusive breast-feeding duration or total breast-feeding duration (Veghari et al., 2011). In contrast to these findings, results obtained from previous studies in Iran have demonstrated that fathers with well-paid occupations and mothers with a high educational level were factors that had a negative influence on the duration of breastfeeding (Marandi et al., 1993). Although there is still a high rate of breast-feeding in developing countries, it is falling among the poorer residents. Studies in developed countries indicate that there has been an increase in the rate of breast-feeding amongst educated mothers in the middle and higher socioeconomic classes. In developing countries however, the higher rates and longer duration of breast-feeding are observed in rural and poor urban areas (Marandi et al., 1993). It can be concluded that Iran might be in a state of transition in terms of infant feeding and socioeconomic class.

Maternal education and exclusive breast-feeding

Results from studies across the world concerning the relationship between educational levels and breast-feeding have not been consistent. A study in southeast Iran (Rakhshani and Mohammadi, 2009) reported that the education level was a risk factor for the continuation of breast-feeding. Another study in Northern Iran reported that higher maternal education was associated with an increased exclusive breast-feeding duration, in which 95% of college

mothers fed their children for at least the initial five months of life (Veghari et al., 2011). This suggest that educated mothers may have an enhanced awareness of the both the short and long term benefits of exclusive breastfeeding in human health and nutrition, and this knowledge has encouraged them to feed their child longer. Maternal education can thus have a crucial role in nutrition interventional programmes. It was found that in the Iranian cohort, breast-feeding was an independent predictor of malnutrition risk. There is evidence implying that parental schooling is strongly associated with child nutrition (Reuel et al., 2013). On the other hand, a large study of child growth patterns in 36 low-income and middle-income of developing countries reported that economic growth is at best associated very small and in some cases show no declines in levels of early childhood undernutrition (Vollmer et al., 2014). This suggests that interventions that directly impact health and nutrition are needed to tackle child undernutrition.

Malnutrition and infant age

This study found a high prevalence of malnutrition in infants which did not differ by infant's age category. In contrast to the findings of this study, previous and recent population based studies in Iran have reported that the rate of malnutrition increased with child age, and the prevalence of malnutrition amongst infants is less than in other age groups (Sheikholeslam et al., 2004; Payandeh et al., 2013). It is noted that this is due to the high rate of breast feeding of Iranian infants (Saki et al., 2010; Saki et al., 2013; Payandeh et al., 2013). These studies imply that intervention programs are mostly aimed at children aged from 6 to 60 months (Sheikholeslam et al., 2004), and infants aged under 6 months are often sidelined. However, a study in 21 developing countries (Kerac et al., 2011) reported that a large numbers of infants under 6 months are wasted (defined as weight-for-height z-score < -2 using either) and it is important for health and nutrition programmers to plan, monitor and evaluate treatment services for infants under 6 months (Kerac et al., 2011). The different result reported in this study may be explained by the fact that the other studies explored malnutrition in community settings rather than in a hospital, and it is likely that disease factors overrule the impact of sociodemographic factors on the onset and perpetuation of malnutrition.

The strongest correlates with malnutrition

In our study, nearly half of infants were breast fed (20% exclusively breast fed and 28% breast fed plus non-milk drinks). This is similar to the results reported from a retrospective study

based on 6307 infants less than 24 months of age in all the 30 urban and rural provinces of Iran, in which the exclusive breastfeeding rates were reported to be 57% at 4 months and 28% at 6 months (Olang et al., 2009).

Current breastfeeding was found to be the strongest predictor of malnutrition in our cohort. It was shown that body fat in breastfed infants was markedly higher compared to that of infants who were formula fed or had stopped breastfeeding. Using SGNA rating risk, formula fed infants were more likely of being at risk of malnutrition compared to breast fed infants. This is in agreement with the hypothesis that formula-fed infants will be rated by SGNA as being at higher risk of malnutrition and will have low fat compared to those who are exclusively breast-fed.

However, it is possible that some hospitalised infants are not exclusively breastfed due to their illness and this may have confounded the results of this study. There is a lack of information in this area within our study, but there are some reports which consider it in current literature. A retrospective study in 30 provinces of Iran reported that the most common reasons for discontinued breastfeeding cited by mothers of infants up to 24 months of age, were physicians' recommendation and insufficient breast milk (self-perceived or true). Only 6% of infants stopped breastfeeding because of infant illness (Olang et al., 2012). Another study reported that the most frequent reason given by the mothers for discontinuing to breast-feed their children under 2 years of age was milk insufficiency (39% of cases). Only 3.8% stopped feeding due to child's illness (Marandi et al., 1993). Our study did not ask for reasons for discontinued breastfeeding, however based on the findings of previous studies, the proportion of mothers who stopped due to their child’s illness was probably.

Conclusion

Admission weight was a strong predictor of malnutrition risk in infants and it can be considered as a useful and easy measure of malnutrition risk in clinical settings. Moreover, SFT may also offer an effective method of malnutrition prediction in the clinical environment. In Iran, breast-feeding was an independent predictor of malnutrition risk. On reflection of the findings of this study, it is recommended that more attention should be given to formula-fed infants, and this group may benefit from nutritional intervention programmes.

CHAPTER SIX

MEASURING BODY COMPOSITION IN INFANCY

Aim

- To measure body composition of hospitalised infants and explore the validity and practicality of the simplified method of analysing bio-electrical impedance to estimate body composition (fat and fat free mass) in infants.

Objectives

- To measure body composition of infants using two measurements: 1) measurement of fat and fat free mass via BIA using the simplified approach of Wells et al (2007); 2) triceps and subscapular skinfolds thicknesses
- To explore the variation of two measures of body composition related to SGNA scoring risk:
  a. Triceps and subscapular of skinfolds thicknesses converted to z-scores using our own reference data (iPYMS skinfolds reference)
  b. Fat and fat free mass using BIA using the simplified approach of Wells et al (2007) to discover whether this method of analysing bio-electrical impedance data is practical and effective in this young age range population
- To compare the values of body composition derived from UK and Iranian infants

Hypothesis

- Measurement of body composition of sick infants will be practical using simplified method of BIA and triceps and subscapular skinfolds thicknesses.
- Infants in UK and Iran who are identified by SGNA as being at high risk of malnutrition will have lower fat stores compared to those at low risk.
- Infants who are identified by SGNA as being at high risk of malnutrition will have lower fat and lean mass compared to those at low risk.
- UK infants overall will have higher lean and fat compared with the Iranian infants.

6.1. Introduction

This chapter was not amongst the original purposes of this thesis. However, although the assessment of body composition in children is an important measurement when evaluating nutritional status in health and disease (Norgan, 2005; Ellis,2007; Wells and Fewtrell, 2008), to date there has been a constant challenge to find an acceptable method to measure body compartments accurately and precisely (Wells and Fewtrell, 2006a), particularly in infancy. Thus, this study collected and analysed data regarding body composition to determine the practicality of using bio-electrical impedance (Wells et al., 2007) to assess body composition of hospitalised infants.

In epidemiological and field studies, predictions of body fatness are often made from anthropometric measurements such as body mass index (BMI). However, BMI does not precisely characterize body fat or muscle mass (Burnham et al., 2005), and there is a variation across age, sex, and ethnic groups (Wang et al., 2000; Womersley, 1977; Wells, 2006b; Deurenberg et al., 1999, 2003; Lukaski, 2009; Rennie et al., 2005; Stone et al., 2008). Wright et al. (2008a) illustrated that BMI does not directly measure fat in children, and the relationship between BMI, body fatness, and the risk of subsequent related disease is not known. Thus, BMI is considered a poor proxy for body fatness (Piers et al., 2000) and is a non-specific indicator of body composition (Wellens et al., 1996; Prentice, 2001).

Considering the limitations of BMI as an indicator of nutritional status and risk, assessments of body composition have been recommended as an alternative approach. The measurement of body composition could be important in the identification, and appropriate management, of malnutrition in young children, particularly in clinical settings.

Various methods have been established aimed at assessing body composition, including dual-energy x-ray absorptiometry (DXA), doubly labeled water, densitometry and magnetic resonance imaging (MRI) (Wells and Fewtrell, 2006a). However, these methods are

expensive, not easily portable, time-consuming, and require highly-trained operators, rendering them unsuitable for most field and clinical settings.

Thus, practical, cheap, safe and validated methods of body composition assessment need to be developed. Currently, the most commonly used field techniques are skinfold thickness (SFT) and bio-impedance analysis (BIA) (Norgan, 2005). However as there is a lack of validated methods suitable for the assessment of body composition in infancy, this study aimed to address this issue using two measurements of body composition; 1) measurement of fat and fat free mass via BIA using the simplified approach of Wells et al (2007) and; 2) triceps and subscapular skinfolds thicknesses, converted to z-scores using our own reference data.

The primary aim of this study was to assess the application of BIA in infancy, an additional aim was to identify the variation of lean and fat mass in relation to SGNA risk scoring, comparing the values derived from UK and Iranian infants.

6.2. Method

6.2.1. Skinfolds

Data was collected as described in the general methods (Chapter Three).
For infants aged over 3 months, the skinfolds were converted into the z-scores using the LMS growth, Microsoft Excel Add-in and the WHO reference values, and the mean score was calculated from triceps and subscapular skinfolds z-scores**.**

As the WHO standard only starts at 3 months, skinfolds z-scores for infants up to 3 months were excluded. However, as it is more reliable than the sole measurement at one site, the sum of the two skinfolds measurements (triceps and subscapular) was calculated for all ages, allowing more infants to be considered in the analysis, but this varied with different ages during infancy (see Figure 6.1).

A new skinfold reference was generated for the research team using the iPYMS dataset for the UK cohort by Professor Tim Cole (Institute of Child Health, UCL), a senior statistician from

London. This reference will hencefore be referred to as iPYMS skinfolds reference. It was generated using the LMS modelling method to allow the calculation of z scores adjusted for age and gender. This supplied z-scores for triceps, subscapular and sum of skinfold thicknesses in populations with low rates of malnutrition risk, and skinfold thicknesses known to be largely within the WHO range for infants over the age of 3 months. The new iPYMS skinfold reference allowed us to convert our skinfold measures for infants less than 3 months old into the z-scores and included in the analysis. This was impossible to carry out using the WHO reference, because of the lack of WHO skinfold reference for this age.

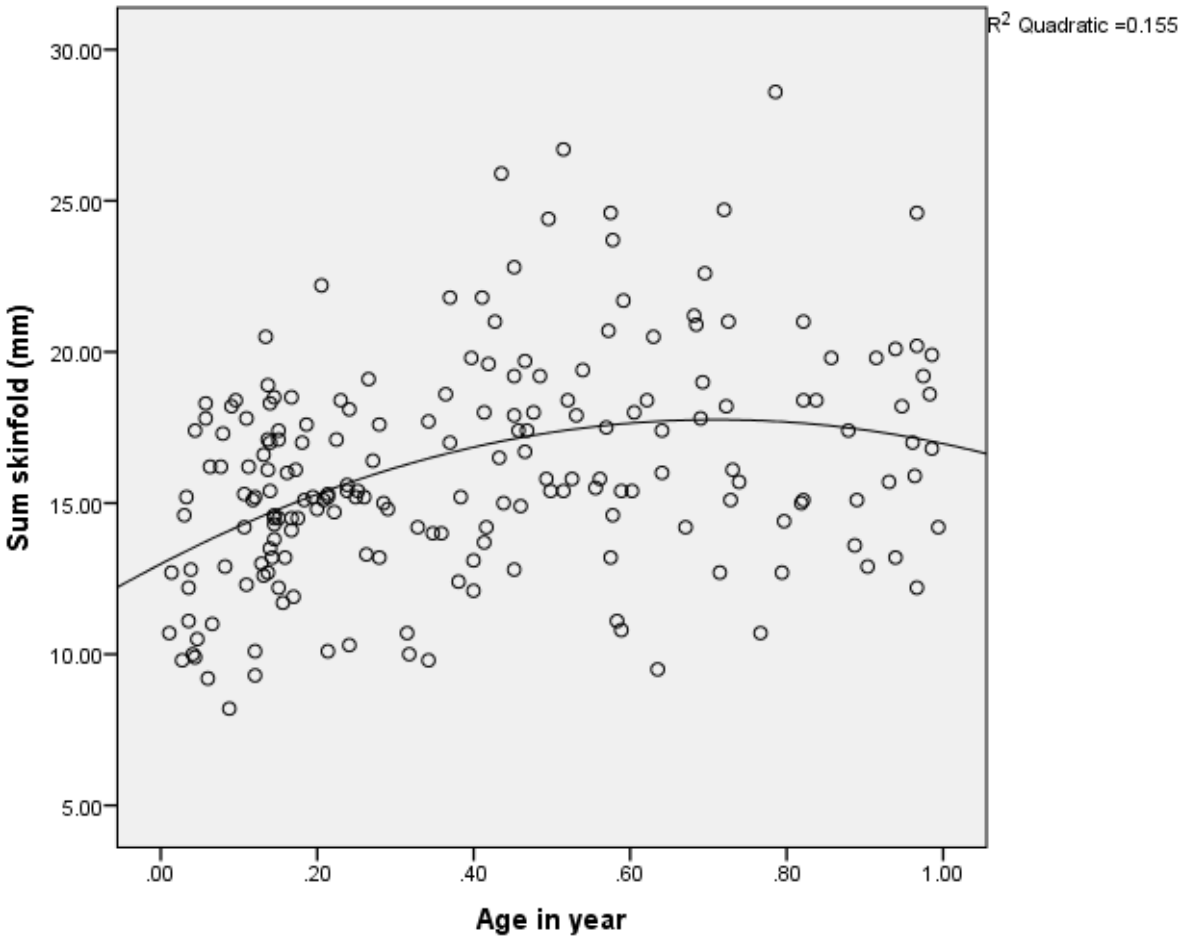

Figure 6.1. Scatterplot of the sum of skinfolds against infants' age for the UK cohort (n=195)

To identify how the fat mass of the study population varied during infancy, participants were categorized into four age categories (1-3, 3-6, 6-9, and 9-12 months). Statistical analysis using

an ANOVA test revealed that in Iranian infants, the sum of the triceps and subscapular skinfold thickness generally increased (mean (SD)) 11.31 (3.15) to 12.74 (2.77) between 1-9 months, before gradually declining. Thus the fat mass of Iranian infants peaked between the ages of 6-9 months, according to the sum of the skinfold measurements (Table 6.1). A similar trend was evident amongst the UK infants; however, unlike the Iranian cohort, the sum of the skinfolds remained steady between 6-12 months (Table 6.1).

Table 6.1: Sum skinfolds and infants' age for both cohorts Iran and UK

Age categories	Sum skinfolds					
	Iran cohort			UK cohort		
	Mean	**SD**	**P****	**Mean**	**SD**	**P***
1-3	11.31	3.16	0.061	14.7	2.89	<0.001
3-6	11.33	2.51	0.22	16.55	3.56	<0.001
6-9	12.74	2.77	0.052	17.7	3.96	0.086
9-12	11.45	3.18		17.2	3.86	

*p-value between age categories for the UK cohort
**p-value between age categories for the Iran cohort

Comparing the new iPYMS skinfolds reference with the WHO-2006 reference (figure 6.2) demonstrated that by the end of the first year of age, triceps subcutaneous fat was greater when using iPYMS reference infants than the WHO reference (mean values -50th percentile). However, mean subscupular skinfold thickness was similar between both references. Therefore, the iPYMS reference overlapped with the WHO reference in terms of subscapular skinfold on the 5th centile.

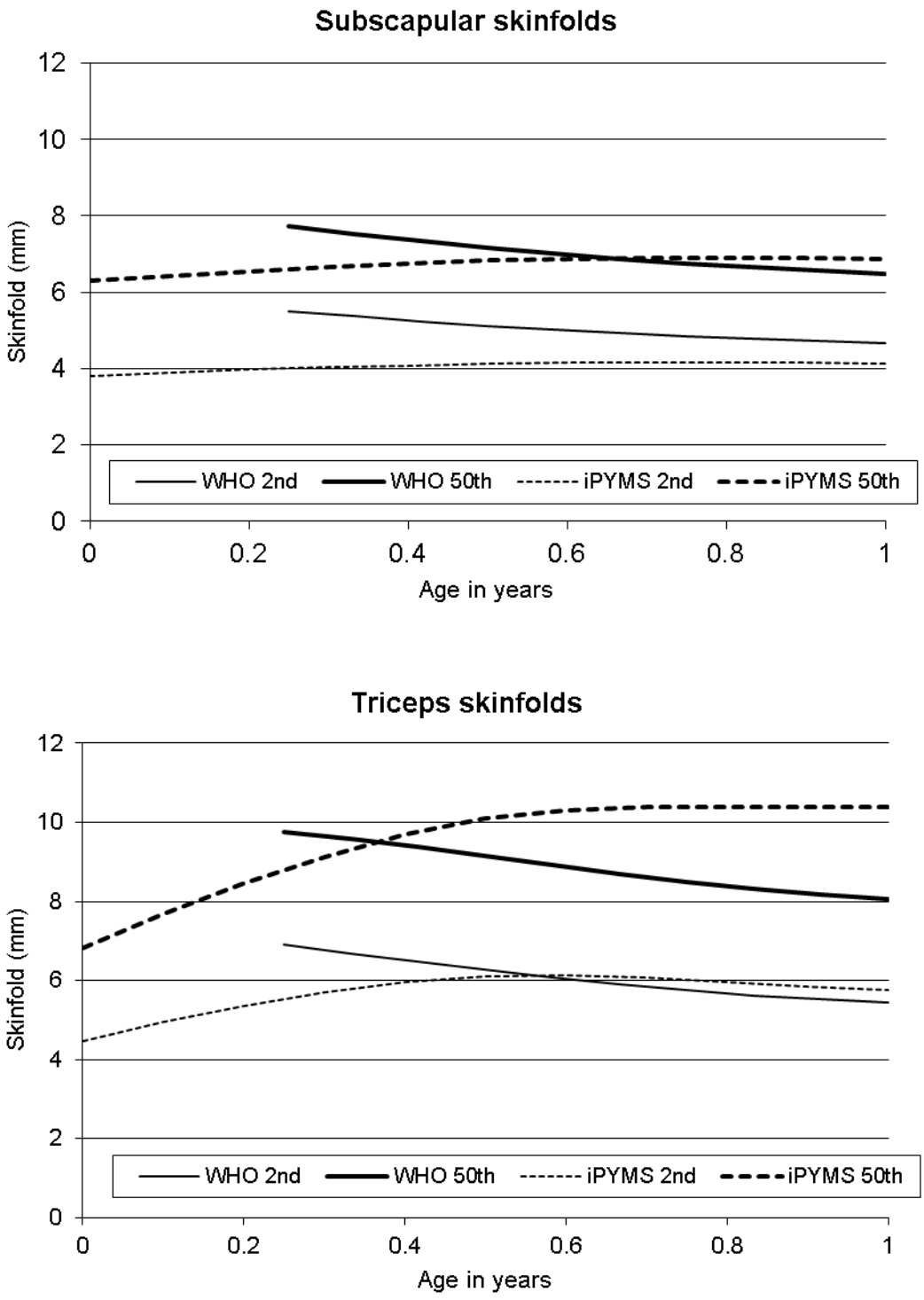

Figure6.2. Comparison of the 50th and 2nd centiles for the iPYMS skinfolds reference (which uses pooled gender) and the WHO 2006 reference using the mean of the male and female values

6.2.2. Bioelectrical Impedance Analyzer data (BIA)

As described in the methods chapter, bioelectrical impedance was measured using hand-foot Bodystat 1500. As discussed in the literature review (Chapter 1) we first generated the Lean residual (1/Impedance), which is proportionate to Lean adjusted for size. We then used linear regression of Lean residual against BMI for the whole cohort to derive a fat residual (the residual variation in BMI not explained by lean residual) as follows:

Fat residual= BMI- (1/z × B+C)

B and C being the regression constant and intercept respectively

Data that was measured below 500 ohms by the BIA were excluded from the analysis of the UK data cohort (approximately 20 cases), as on review of the entire data for both cohorts, it was evident that the BIA generated some extremely low values in some UK cases. These extreme values indicate a high lean mass that is deemed physiologically impossible, highlighting an issue with one of the machines used to collect BIA in the UK cohort. Furthermore, the lowest value measured by BIA in the Iranian cohort was 500; a value that is again, physiologically unrealistic. Thus, these values were excluded from further analysis.

6.3. Results

6.3.1. Relationship between Body Composition and SGNA

Fat residual and skinfolds variables varied significantly with SGNA risk group in both cohorts ($p<0.001$, ANOVA) when using either WHO or iPYMS reference. However, BIA lean differed significantly only for the Iranian cohort (Table 6.2). The proportion of patients with mean skinfolds <-2SD and sum skinfold z-scores <-2SD differed significantly by SGNA for the Iranian cohort ($p<0.001$, Chi-square), but not in the UK cohort (Fisher-exact) (Table 6.2).

Table 6.2: Body composition characteristics of Iranian and UK infants who were assessed to have a low, medium and high malnutrition risk using the Paediatric Subjective Global Nutritional Assessment (SGNA)

a) Iran				Low risk		Medium risk		High risk		
WHO	**Mean**	**SD**	**N**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**P***
Mean SF z-score	-1.90	1.38	126	-0.85	1.00	-1.97	1.14	-3.00	1.05	<0.001
Sum SF			179	13.58	2.39	11.42	2.10	9.11	1.99	<0.001
Sum SF z score (iPYMS)	-1.50	1.01	178	-0.78	0.75	-1.61	0.65	-2.45	0.71	<0.001
BIA fat residual	-0.25	1.66	175	0.77	1.44	-0.39	0.86	-1.84	1.33	<0.001
BIA lean residual	0.11	0.02	178	0.12	0.16	0.11	0.15	0.11	0.19	<0.001
	N	**%**		**N**	**%**	**N**	**%**	**N**	**%**	**P****
Mean SF <-2SD	54	42.9	54	3	6.7	18	45	33	80.5	<0.001
Sum SF z score <-2SD(iPYMS)	52	29.2	52	2	2.6	12	25.5	38	71.7	<0.001

b) UK				Low risk		Medium risk		High risk		
WHO	**Mean**	**SD**	**N**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**P***
Mean SF z-score	0.12	1.23	110	0.33	1.09	-0.26	1.42	-0.95	1.00	0.008
Sum SF			194	16.74	3.42	15.15	3.59	13.51	2.59	<0.001
Sum SF z score (iPYMS)	0.06	0.98	191	0.22	0.92	-0.13	1.01	-0.76	0.75	<0.001
BIA fat residual	0.27	1.93	176	0.87	1.99	-0.49	1.52	-1.03	1.25	<0.001
BIA lean residual	0.13	0.21	184	0.15	0.05	0.14	0.04	0.12	0.02	0.18
	N	**%**		**N**	**%**	**N**	**%**	**N**	**%**	**P****
Mean SF<-2SD	6	5.4	6	2	2.7	3	10.3	1	16.7	0.05 0.14
Sum SF z score <-2SD	5	2.6	5	2	1.6	2	3.6	1	7.1	0.19

*p value for difference between risk groups using ANOVA test

**p value for difference between risk groups using Chi-square test

6.3.2. Bioelectrical impedance data

There were 178 and 184 participants in the body composition data in the Iranian and UK cohort respectively. The large majority of both cohorts were boys. On average, boys had significantly (p=0.002, Independent- sample t-test) higher lean residual compared with girls in the Iranian cohort, yet no significant difference for fat residual was found between genders in both cohorts.

A mean difference of 0.01 and 0.02 was recorded for the lean and fat residual respectively; however this was not found to be statistically significant (Table 6.3). UK infants had significantly higher fat and lean residual compared to Iranian infants (p<0.001 and p= 0.008, respectively) (Table 6.4).

Table 6.3: Lean and fat residual, and infants by gender

a) Iran	Lean residual (1/z *100)				Fat residual			
	N	Mean	SD	P value*	N	Mean	SD	P value**
Male	109	0.12	0.02	0.002	107	-0.30	1.69	0.61
Female	69	0.11	0.02		68	-0.17	1.64	

b) UK	Lean residual (1/z *100)				Fat residual			
	N	Mean	SD	P value*	N	Mean	SD	P value**
Male	114	0.14	0.02	0.10	109	0.19	1.67	0.52
Female	70	0.13	0.02		67	0.41	2.28	

*p value for difference of lean residual between boys and girls
**p value for difference of fat residual between boys and girls

Table 6.4: Lean and fat residual by country

Cohort	Lean residual (1/z *100)				Fat residual			
	N	Mean	SD	P value*	N	Mean	SD	P value**
Iran	178	0.11	0.02	<0.001	175	-0.25	1.67	0.008
UK	167	0.13	0.02		159	0.28	1.93	

*p value for difference of lean residual between two cohorts, UK and Iran
**p value for difference of fat residual between two cohorts, UK and Iran

6.4. Discussion

Use of skinfolds to assess nutritional status

Skinfold and infant's age

This study aimed to investigate two measures of body composition and their variation related to SGNA scoring risk: 1) Triceps and subscapular of skinfolds thicknesses converted to z-scores using our own reference data (iPYMS skinfolds reference); 2) fat and fat free mass using BIA using the simplified approach of Wells et al (2007) to discover whether this method of analysing bio-electrical impedance data is practical and effective to assess fat mass in this young age range population.

It was hypothesised that infants in UK and Iran who are identified by SGNA as being at high risk of malnutrition will have lower fat stores compared to those at low risk. We found that this was true in the Iranian cohort, as 72% of high SGNA risk infants had low skinfolds, compared to 3% of infants in the low risk category. However, in the UK infants there was no such association (7% high risk, 2% low risk). Therefore this hypothesis was not proved in the UK cohort. Furthermore, although fat residual measured by BIA varied significantly with SGNA rating risk group in both cohorts, lean residual differed between risk groups only for the Iranian cohort. As expected Iranian infants had much lower mean lean and fat residual than the UK infants.

In the current study, the sum of triceps and subscapular skinfold measurements in UK infants varied with age. This value was increased from birth to 6 months old, where it remained stable for a maximum of 2 months (i.e. until 8 months old), after which it slightly decreased until 12 months of age. A non-linear relationship is evident between the sum of skinfolds and patients' age. The prevalence of malnutrition was much lower in the UK cohort, suggesting this is a true representation of fat acquisition in infancy.

Development of the new infancy skinfold references (iPYMS skinfold refrence)

The assessment of an individual’s nutritional depletion requires appropriate references (standards) and cut-offs (thresholds). Thus, although the sum of skinfold measurements may be useful for determining group means, unless this value is converted to z-scores, it is not an informative assessment of malnutrition risk. As the WHO standard (2007) data for skinfolds is

applicable only after 3 months of age, a new reference curve relating to the sum of skinfolds was developed for use in this study using data from the UK infants, in order to include infants under 3 months in the analysis. This decreased the potential for age bias, which may have occurred if our sample size had been reduced due to the exclusion of children in the first 3 months of life.

iPYMS skinfold reference compared to the WHO reference

iPYMS skinfold references illustrated reasonable correspondence with the WHO standard, although with a different trajectory. Data demonstrated that by the end of the first year, triceps subcutaneous fat is greater in iPYMS reference infants than in the WHO standard at the mean values - 50^{th} percentile. This may be explained by enhanced feeding of formula milk in UK infants. However, the mean subscapular skinfold thickness of UK infants recorded by the iPYMS reference was similar to that of the WHO standard. In other words, iPYMS reference overlaps with the WHO references in terms of subscapular skinfold on the 50^{th} centile and the triceps skinfold on the 2^{nd} centile. Thus, the relatively small differences noted between these two references may not pose a major problem for the current study, as the purpose of this study was to assess undernutrition rather than overnutrition. Therefore the iPYMS skinfold reference, considering that it was generated using a population with low rates of risk of malnutrition (iPYMS dataset for the UK cohort) who had skinfold levels mainly within the WHO range beyond age 3 months, can be a valid reference for use in this study, but might not be suitable for assessing overweight infants or for use in areas with predominantly breastfed infants.

Utility of skinfolds z-scores

The major novel finding of this study is the results derived from the comparison of skinfolds between at risk infants in two contrasting countries. In the current study skinfolds z-scores compared to SGNA risk groups varied in both cohorts, but a larger variation was evident in the Iranian cohort in comparison to the UK cohort. As aforementioned, data from the Iranian cohort indicated a relationship between high malnutrition risk and low skinfold measurements, however this association was not apparent in the UK. The proportion of patients with acute and severe malnutrition (sum skinfolds z-score < -2SD) therefore differed by SGNA risk groups only in the Iranian cohort, yet was unrelated for the UK cohort. Thus, skinfolds measures in infants indicate that in an area where malnutrition has a high prevalence, infants at

high SGNA risk are already malnourished, whilst this is not the case where malnutrition prevalence is lower. These findings suggest that skinfold measurements might be useful at the individual level in clinical settings, where a high prevalence of risk of malnutrition exists, but it might be considered as an inappropriate criterion measure of risk in areas where the prevalence of undernutrition risk is low.

Previous studies have reported poor validity and utility of skinfold thickness methods in estimating body composition (body fat equations) in children (Reilly et al., 1995; Wells et al., 1999; Parker et al., 2003; Eisenmann et al., 2004). However, recent studies have shown its usefulness for estimating total fat mass in children (Midorikawa et al., 2011; Ramirez et al., 2012; Bammann et al., 2013). Midorikawa et al. (2011) reported strong correlations between total fat mass by DXA measurement and the prediction equation of fat mass from skinfolds (sum skinfold thickness obtained from triceps and scapular sites × height) in healthy Japanese children as a large scale research method. Very recently, Bammann et al (2013) reported that combining skinfold (measured at two-six sites) and circumference measurements compared to body fat mass derived by a three component (3C) model as a reference value, accounted for 91% of the observed fat mass variance in children aged 4-10 years, from four different European countries. The findings of our study are in agreement with the results of other studies which have used untransformed skinfold measurements. Midorikawa's et al study (2011) particularly, though of a different design, may corroborate the utility of skinfold tests in infants or younger age groups of children.

BIA for assessing nutritional status in infants

How did BIA compare with skin folds?

In this study, fat and lean residual estimated by BIA vary with gender for both cohorts as expected. This is similar to Butte's et al findings (2000).

The mean values of fat and lean residual measured by BIA shows important differences between the two cohorts – Iranian infants had much lower fat and lean than the UK infants. In fact, this concurs with the results obtained using the criterion of skinfolds, which showed that the Iranian infants were at increased high risk of undernutrition and had more severe acute malnutrition. Also, fat derived from BIA correlated linearly to skinfold thickness for both cohorts, it was stronger in the Iranian than the UK cohort. Inter-correlate fat values

(correlation matrix) also illustrated higher correlation in the Iranian than the UK cohort. It can be recommended that applying BIA in this way can be capable of differentiating the variability of fat in groups of infants and it might be useful to detect trends in relation to other variables (for instance skinfolds in the current study) or to test for significant differences between groups, whilst skinfolds expressed as z-scores can rank individuals as well as groups. Hence, estimating of body fat in this way (using the methods developed by Wells et al., 2007 and Wright et al., 2008) might make a robust and strong predictor of risk of malnutrition in infants, particularly where a high prevalence of undernutrition exists.

How did BIA fat and fat free mass vary with SGNA?

In this study, it was not possible to compare body composition as assessed by BIA with gold standard methods (four compartment methods). However, it was possible to establish how the fat and lean indices derived from BIA vary by the SGNA risk groups.

Fat residual varied by SGNA rating risk group in both cohorts, however, lean residual differed between risk groups only in the Iranian cohort. Malnutrition was much more prevalent in the Iranian infants compared to the UK infants, particularly in the form of severe malnutrition, which may lead to the depletion of muscle mass as well as fat stores. It is likely that malnourished infants in the UK cohort were in the initial stages of malnutrition, or had mild/moderate malnutrition, which impacts only fat stores and not muscle mass.

Differences in study design, methods, and age ranges employed may limit the comparison of data generated in this study with results derived from other studies. The majority of other studies have been conducted by comparing body composition derived from BIA (using different equation and machines) with the reference method of DXA, reporting various findings in children (Reilly et al, 2010; Ramirez et al., 2012; Khan et al., 2012; Gerasimidis et al, 2014b) and infants (Butte et al., 2000). Butte et al. (2000) reported important differences amongst the methods of estimating fat mass in infants and children, and noted that the magnitude of the results obtained via different methods varied with age.

What are the limitations of using BIA as opposed to skinfolds?

There are a number of limitations of using BIA as opposed to skinfolds that need to be addressed. The primary issue for using BIA in infants and young children in a clinical setting

is the lack of an appropriate reference data for body composition (standard deviation scores for different measurements i.e. fat and free mass) for this age range. The estimation of body composition via BIA requires population specific validation equations before application. Furthermore, in this study, Bodystat machines were used for measurement of body composition (fat and lean mass index) which, although is suitable for use in infants, it is essential to consider that different BIA machines require new estimates of constants (Wells et al., 1999; Parker et al., 2003). However, using the simplified approach developed by Wells et al. (2007) avoids the need for this validation**.**

Finally, in the current study, data was collected in two contrasting hospital settings, in the UK and in the Middle East. Infants partaking in the UK cohort were recruited by four researchers, whilst in Iran only one recruiter was involved. This may have increased the inter-observer error in the body composition data in the UK cohort. To minimise the potential for error, the researchers were trained before performing the measurements. Nevertheless, BIA measurements below 500 were deemed unrealistic and thus excluded from the analysis.

How and where might BIA be useful in future?

Although many studies have attempted to demonstrate the validity and usefulness of BIA for estimating the body composition of paediatric populations, the practicality of using BIA in routine clinical settings with young children is questionable. However, the findings of the simplified method of BIA used in this study is in agreement with results derived from other studies suggesting that this method of BIA measurement is a valid and useful method to estimate body composition in groups of individuals. However, due to the lack of reference data available for younger children, the application of this method is restricted to clinical settings for individual children. Therefore, it is important that normative data regarding body composition of infants and younger children is created to make the use of BIA available to individuals in routine clinical settings in the future.

Conclusion

The identification of the optimal large scale method for accurately estimating body composition in younger age groups is challenging. It is not currently clear what measures are informative with regards to the assessment of nutritional status of hospitalized infants. The simplified method of BIA used in this study highlights important variations in the nutritional

status of infants in clinical settings, particularly in areas where the prevalence of malnutrition is high. This method differentiates variability of fat and lean mass in groups, but in order for BIA to be an acceptable method for measurement of body fat and lean mass in younger children, access to reference data is necessary. Although some studies have provided reference data on a national level for body composition, large-scale multicentre studies are required in order to create an internationally valid reference data for body composition in childhood populations. Validation of BIA assessment of body composition against the 4-compartments model or staple isotope dilution in future studies will further inform its diagnostic validity.

Skinfold measurements might be a useful and effective method to identify undernutrition in infants in clinical settings, where the prevalence of malnutrition is high, but it might be considered as a less effective criterion measure of risk in areas where the prevalence of undernutrition risk is low. However, measuring skinfolds might be more reliable than conventional screening to identify truly malnourished infants in countries with a low background prevalence of undernutrition.

CHAPTER SEVEN

GENERAL DISCUSSION

7.1 General discussion and conclusions

Although malnutrition-associated disease is reported to be a common problem in paediatric inpatients in developed and developing countries, it remains under-recognized and untreated (Pawellek et al., 2008; Huysentruy, 2013a). This is most likely due to the lack of gold standard methods and criteria to assess and screen nutritional status of children particularly infants in the hospital settings or limited nutritional awareness among health professionals to screen for it. The primary aim of this PhD was therefore to evaluate the performance of a novel nutrition screening tool for infants – the Infant Paediatric Yorkhill Malnutrition Score (iPYMS) and to determine its usefulness in two different hospital settings, the UK and Middle East, Iran.

In summary the aims of this study were:

- To evaluate the infant Paediatric Yorkhill Malnutrition Score (iPYMS) to find out how well it distinguishes infants who are well-nourished from those undernourished, or at risk of being undernourished
- To compare the utility of iPYMS in different hospital settings, in the UK and in the Middle East, Iran
- To compare the usefulness of various anthropometric measures to predict malnutrition in infants
- To determine the factors that correlate with malnutrition in these hospitalised infants
- To measure body composition of hospitalised infants and explore the validity and practicality of the simplified method of analysing bio-electrical impedance to estimate body composition (fat and fat free mass) in infants

The relative diagnostic accuracy and validity of iPYMS in both cohorts

iPYMS nutritional risk compared to SGNA rating risk

In this study, more infants in the Iranian cohort were rated as high risk for under-nutrition than the UK. The diagnostic performance of iPYMS was improved with the cut-off ≥ 3 in both cohorts, but more so in Iran than the UK. iPYMS in the UK illustrated a sensitivity of 85% and a positive predictive value (PPV) of 37% to predict malnutrition risk, but these values were 93% and 69% in Iran. These discrepancies in both cohorts can be explained due to the

high prevalence of actual malnutrition in Iranian infants as compared with the UK. Essentially, the prevalence of disease in a population affects the yield of a screening test; in low prevalence settings, even very good tests may have poor positive predictive value (Altman, 1991). On the other hand, in the absence of a universally agreed definition of malnutrition and the lack of any proved gold standard (Meijers et al., 2010; Joosten and Hulst, 2014), the sensitivity and specificity analysis of screening tools have resulted in the use of many different reference standards and consequently very different results. In the present study the validity of iPYMS for identification of malnutrition risk was assessed compared to the SGNA (Secker and Jeejeebhoy, 2007) as this is a comprehensive paediatric nutritional assessment tool. There is evidence that SGNA is a valid surrogate for a detailed nutritional assessment of paediatric patients. For instance, a study (Carniel et al., 2015) validated the SGNA tool with 242 patients, aged 30 days to 13 years, in a tertiary hospital in Brazil and showed that SGNA was a valid and reliable instrument with high sensitivity and good inter-observer reliability for the assessment of the nutritional status of pediatric patients compared with anthropometry and the main predictive outcome which was the need for admission/readmission within 30 days after hospital discharge. Another study (Vermilyea et al., 2013) on 150 children, aged 31 days to 5 years admitted to the PICU reported that SGNA ratings demonstrated moderate to strong correlation with anthropometric measurements and moderate inter-rater agreement. Recently, similar to the current study, White et al. (2014) have developed a new tool in Australia named paediatric nutrition screening tool (PNST) and also validated it with the paediatric SGNA and anthropometry. The sensitivity and specificity of PNST compared with the paediatric SGNA were reported to be 78% and 82% respectively. These suggest that SGNA can be considered as a valid reference for use in the validation studies of paediatric nutritional screening tools.

iPYMS nutritional risk compared to mean skinfolds z-scores below < -2SD

It was found that a high proportion of Iranian infants had low skinfolds, while this was low for the UK cohort.The criterion of skinfold for validation of iPYMS in the Iranian cohort, where the background prevalence of under-nutrition was high, was very suitable, but in the UK cohort considering the low prevalence of undernutrition in the community, we might need different criteria in order to be able to establish the validation of iPYMS for identification of future malnutrition risk in sick infants. Thus, the performance of any screening tool should always been evaluated in the context of its benchmark measurement. For example SGNA aims

to identify children at different stages of established malnutrition whereas the screening tools aim to identify also those at risk. This difference between the UK and Iranian cohort may explain the different performance of iPYMS in the two countries. Otherwise, it can be noted that the UK infants may not be actual malnourished. They may be ill and at risk of malnutrition and in need of more support to prevent of becoming malnourished. This is particularly important as in UK the main scope of screening tools is to identify children in need of further review by the dietician and in order to avoid future onset of malnutrition whereas in Iran, where the prevalence of malnutrition in the community is high and dietetic resources are limited priority may be given to those children who already have overt symptoms of malnutrition. Therefore, infants who are identified being malnourished at admission can receive timely treatment to prevent of worsening and its long term adverse effects.

It is expected the prevalence of under-nutrition in the community in Iran and UK would not be comparable. Wright et al (2008b) reported that 0.6-3.6% of the UK children less than five years old were undernourished using the WHO-UK growth reference and the criterion of weight below second centile. In contrast, a national survey in Iran in 1998 using WHO/NCHS standards and the cut-offs of <-2SD reported that in rural areas 12.8% of under 5-year old suffered from nutritional stunting, 13.7% were underweight and 4.8% wasted. The prevalence of underweight among children under 6 months was similar to a developed community (3%), but the prevalence of underweight increases after this age, peaking at 13.8% in 2-year-olds (Sheikholeslam et al., 2004). Moeeni et al. (2012) assessed the nutritional status of hospitalized and healthy children from the same community in Iran. They reported that according to WHO criteria 17.6% of children were moderately undernourished (-3< WFH z-score <-2), 4.2% were severe stunted (HFA z-score <-3) and the same rate, 4.2% were wasted (HFW z-score <-3), but interestingly only 3% (1% moderate stunting, the same rate, 1% moderate wasting and another 1% severe wasting) of children from the same community were malnourished. According to WHO report (WHO Global Database on Child Growth and Malnutrition, 2012) from a national study in Iran in 2004, the prevalence of underweight, stunting and wasting were 4.6%, 7.1% and 4.8% respectively.

On the other hand, considering various benchmarks which have been used in validation studies; there is no standardized approach to nutritional screening for the paediatric inpatient

and it is impossible to validate a tool with gold standard. Validation of any clinical tool should depend on the intended purposes and available resources in clinical practice. For example, we may recommend that iPYMS can be validated with a full dietetic assessment for the UK hospital as considered a gold standard for validation of PYMS (Gerasimidis et al., 2010) and STAMP (McCarthy et al., 2012) tools. However, it might be questionable; especially in the countries that there is no dietetic team in the hospital and their role thus may vary depending on the country (Joosten and Hulst, 2014). Therefore deciding the criteria that should be used in the validation of nutritional screening tools in different settings is an important issue that should be taken into account.

iPYMS components (steps) and malnutrition risk

In both cohorts, the first step of iPYMS (weight below <9th or 2nd centile - weight z scores < -1.33 SD or < -2 SD) was illustrated to be a strong predictor of malnutrition risk, more so in Iran; in the Iranian cohort, 91% (21% <9th; 70% <2nd) and in the UK 70% (20% <9th; 50% <2nd) of infants above the high risk threshold of ≥ 3 were scored as being high risk due to the weight below <9th or 2nd centile. This suggests that weight alone without considering the other elements of iPYMS would be able to identify the majority of infants who are at risk of malnutrition considering SGNA as the benchmark of malnutrition risk. Similarly, McCarthy et al., (2012) in the development phase of STAMP tool reported that the objective information relating to weight and height was the strongest predictor of nutrition risk. In fact, these findings emphasize the importance of using simple anthropometric measures for identification of patients who are at risk of malnutrition particularly where the resources are limited**.**

Usefulness of anthropometric measures in identification of malnutrition

In this study, we compared the usefulness of various anthropometric measures to identify malnutrition defined as sum skinfolds z-score <-2 SD and high SGNA rating risk in hospitalised infants. We found that both growth velocity and admission weight significantly predicted malnutrition risk almost equally. The admission weight thus can be considered as a useful and easier measure of malnutrition risk in clinical settings without however undermining the importance of serial assessment of growth. ROC Analysis with SGNA as the main outcome illustrated that weight and BMI were nearly the same predictors of malnutrition risk, but stronger than MUAC. Using sum skinfolds z-score as the main outcome demonstrated that BMI and MUAC were nearly the same predictors, but slightly stronger than

weight. These findings although interesting, may be expected to some extent as growth faltering is part of the SGNA, and we may have introduced a circular argument in our analysis. However, it was shown that using sum skinfolds z-score as the main outcome instead of SGNA the admission weight and growth velocity had almost the same predictive value. This suggests that weight velocity is no improvement on weight alone as a predictor of malnutrition. Additionally, weight velocity, admission weight and iPYMS total score were found to be nearly the same predictors of malnutrition. This also suggests that iPYMS may not add any more than objective measure of anthropometry to identify malnutrition risk.

Predictors and correlates of malnutrition in Iranian cohort

In the current study, we found a much higher rate of malnutrition in Tabriz Children's Hospital than seen in the community. This can be explained by the fact that Tabriz Children's Hospital is a tertiary, central and paediatric teaching hospital in Tabriz, which covers all patients referred from the different cities of the East Azerbaijan Province and also some more critical and complicated patients referred from three other states (west Azerbaijan, Kurdistan and Ardebil). This suggests that the Iranian infants may have been sicker than UK infants, and thus more likely to be undernourished.

We discovered that current breast feeding was independent predictor of malnutrition in Iran. It is noted that breastfed infants are less likely to become malnourished and be admitted to a hospital for infections. Breastfeeding can protect infants against infections (Paricio et al., 2006; Quigley et al., 2007; Fisk et al., 2010); a large population- based survey – the UK Millennium Cohort Study (Quigley et al., 2007) reported the protective effect of breastfeeding, particularly six months of exclusive breastfeeding, on hospitalization for diarrhoea and lower respiratory tract infections in the first 8 months after birth. This study estimated that above half (53%) of diarrhoea hospitalizations and nearly one third (27%) of lower respiratory tract infection hospitalizations could have been prevented each month by exclusive breastfeeding. Similarly, another prospective birth cohort study (Fisk et al., 2010) reported an inverse association between the duration of breastfeeding and the prevalence of lower respiratory tract infections and gastrointestinal morbidity in infants during the first year of life that was robust to adjustment for a wide range of maternal and infant factors. Furthermore, data from Infant Feeding Survey in the UK showed that infants who were breastfed for at least 6 months were significantly less likely than other babies to experience sickness, diarrhoea and chest

infections (Bolling et al., 2007). The findings of these studies suggest that promotion of breastfeeding and increase duration can have substantial effects in reducing morbidity in infancy. In addition to this, there has been reported some short term and long term health benefits of breastfeeding for the infant and mother (Hortsa et al., 2007; Hoddinott et al., 2008).

It also needs to be considered that there may be some reverse causation: infants who are unhealthy are more likely to be supplemented or unable to breastfeed. So, we don't know what causes what – breastfeeding prevent malnutrition, but for sick children we may have to stop breastfeeding. However, unwell infants are most in need of the benefits of breast milk, for instance breastfed infants with cardiac conditions benefit from better oxygen saturations, faster weight gain and shorter hospital stay (Combs and Marino, 1993). Robust evidence correlates exclusive breastfeeding with a reduced incidence of different diseases (Huston et al., 2014; Stuebe, 2009; Wilson et al., 1998). This is important, but has particular relevance when considering breastfeeding as a protective factor for the challenges of infants undergoing surgery for congenital heart conditions or hospitalized for other serious illness (Mylod, 2015). In children's hospitals, breast feeding is challenged by infant's illness, prematurity, fasting or maternal/infant separation, unless mothers express their milk for their infants to consume either though alternative routes immediately or freezing it for a later date. Once clinically stable, these mothers and infants need to be afforded the opportunity to safely and effectively transition from expressed breast milk to direct breast feeding (Harris, 2014).

We thus recommend that more attention should be given to the infants who are formula-fed as these groups of children may be a risk group in need of nutritional intervention programs.

Socioeconomic factors were found to be weak predictors of malnutrition in this population. We ruled out the confounding effects of other factors (such as infant's age and feeding), but SE factors still remained as weak predictors. The reasons for this can be explained by the fact that Iran is a country in economic transition state and there are relative prosperity. Moreover, there are cash benefits for the families, who are in low socio-economic status in a welfare system, but this is not a consistent program. Regarding the food security however, a study in northwest of Iran (Dastgiri et al., 2011) reported that total prevalence of food insecurity was 59 % and there was a significant association between household food insecurity with some variables mainly economic factors. On the other hand, a large study (Vollmer et al., 2014) of

child growth patterns in 36 low-income and middle-income of developing countries has reported that economic growth is at best associated very small and in some cases show no declines in levels of early childhood undernutrition. This suggests that interventions that directly impact health and nutrition are needed to deal with child undernutrition.

There is no standard classification of socio-economic status in Iran. Various classifications have been used in the studies. We thus recommend that there is a need to establish a standard classification of SES in Iran.

Measuring body composition in infancy using skinfolds and BIA

The WHO standard (2007) for skinfolds only starts at 3 months, so this excluded nearly one third of infants in the Iranian cohort and more than half in the UK cohort**.** An iPYMS skinfold reference was thus generated using the iPYMS dataset for the UK cohort, as this was a population with low rates of malnutrition risk who had skinfold level mainly within the WHO range beyond age 3 months. It can be thus valid for using in this study, but might not be suitable reference for assessing in an area with predominantly breastfed infants, as we found that the rate of breast feeding was very low (10%) in the UK sample. This is about three times lower than the rate expected in the community, since 74% of mothers breastfed at birth in the UK, falling to 47% by 6-8 weeks of age (Department of Health, 2014) and data from Southampton Women's Survey also showed that 25% were breastfed up to 6 months (Fisk et al., 2011). Furthermore, iPYMS skinfold reference was generated from the cohort who were sick infants and this may influence its suitability as a reference data, which obviously should be created from a healthy population. However it is expected that a very small proportion of acutely sick children will suffer from chronic malnutrition

In Iran cohort most of the high SGNA risk infants had low skinfolds compared to the UK reference. Thus skinfold thickness can be a useful measurement for identification of fat stores and undernutrition in infants in clinical settings, particularly in areas with high rate of malnutrition, but it requires trained health professionals. In the UK cohort considering, a low proportion of infants had low skinfolds and this was unrelated to SGNA high risk, it can be noted that measure of skinfolds can ensure that undernutrition is absent in the infants of this sort of clinical settings.

In this study, no comparison was made with gold standard method (four compartment methods) and this needs to be explored in the future. We found that fat measured by BIA varied by SGNA rating risk group with both cohorts in the expected pattern, but lean mass differed between risk groups only for the Iranian cohort. Using the simplified method of analysing bio-electrical impedance data, Iranian infants had much lower mean lean and fat mass than the UK infants. We thus recommend that this simplified method of using BIA should be explored further in future validation studies.

On the other hand, the main issue for using BIA in clinical setting in young children is the lack of an appropriate reference data for body composition (standard deviation scores for different measures – fat and free mass) of this age range (Wells, 2014), which limits its application in the clinical setting in individual level. Although an approach has been developed to overcome this problem in adults (Wells, 2014) this needs to be studied more in children where changes in body fat and lean stores are complicated by biological changes with age. Future studies should undertake the development of a universal reference for body composition of young infants.

Limitations of paediatric nutritional screening tools such as iPYMS

The applicability/practicality of the current paediatric nutritional screening tools is the most important element that limits the usefulness of the tools. There is a lack of data on the application of current paediatric screening tools in routine clinical practice (Elia and Stratton, 2011). It is noted that the screening tools that involve the objective measures of anthropometry might not be more applicable in routine clinical practice, as they are considered to be time-consuming and also necessitates interpretation of the growth charts (Ling et al., 2011; McCarthy et al., 2008). However, the ideal screening instrument will be one that can quickly and reliably triage the nutritional status of children, so as to identify the high-risk groups who need more detailed assessment and intervention (Sullivan, 2010). For example, in a cross-sectional study the applicability of the STAMP tool versus the STRONGkids by two trained investigators was reported that STAMP took approximately ten minutes longer than STRONGkids (15 vs 5 min) (Ling et al., 2011). It has been reported that the reason for this is due to the addition of anthropometric measurements in the STAMP tool. In contrast to Ling's et al. study, Gerasimidis et al., (2012) noted that anthropometric measurement is unlikely to

influence the time taking to complete the PYMS tool. However, in the Ling et al. study, taking longer time to complete STAMP tool might relate partially to the plotting of growth and BMI centile charts. Considering iPYMS has been designed based on the PYMS, it can be expected to have almost the same applicability for iPYMS. Furthermore, it was shown that anthropometry in screening for nutritional status and growth in sick children was substantial and clinical visual inspection cannot be a substitute for that. Visual inspection was inadequate for screening the growth and nutritional status of hospitalized children, although important (McKechnie and Gerasimidis, 2015).

Another important limitation of the tools is that none of the current paediatrric nutritional screening tools have been evaluated for the impact and the effectiveness of intervention and treatment on improvement of the clinical outcomes. The use of any screening tool to identify infants with or at risk of malnutrition can only be considered effective if it results in early intervention and improved clinical outcomes

Implications for using iPYMS in routine clinical practice

The performance of a validated tool in routine clinical practice is an important aspect of using any malnutrition screening tool and one which has not been addressed thoroughly (Gerasimidis et al., 2011).

Implications in the UK

We found a low prevalence of actual malnutrition in UK hospitalized infants. iPYMS in UK identifies only infants at risk of malnutrition. Thus using the nutritional screening tool may have a risk of over-diagnosis of malnutrition. However**,** the scope of screening tools is also to identify children who are in need of dietary support, and not only those children who are truly malnourished. Therefore the screening tool might be useful to prevent malnutrition and future problems and in the long term to improve the clinical outcome. Moreover, implementation of a screening tool might improve other aspects of patients' care, as we have shown in our clinical audit, and increase the nutritional awareness in the health care professionals. Therefore, the implication of using screening tools in nursing practice might not be simply to find children with malnutrition. It may be to increase awareness in the health and medical team of the importance of screening for a sick child and this may improve children's outcomes (Gerasimidis et al., 2012).

In conclusion, screening of young children at risk of under-nutrition and referring them to dieticians for timely intervention might improve the quality of care delivered to paediatric patients and allow for a more effective use of available resource. Therefore we recommend that the effectiveness and clinical performance of using nutrition screening tool in clinical settings should be explored in the future studies.

Implications in Iran

We discovered a high prevalence of background malnutrition in Iranian hospitalized infants. iPYMS can thus identify infants who are truly malnourished. This is a useful approach to use in Iranian sick infants**,** but what is needed is to establish how the screening would happen and how would these infants be treated once identified? This depends on the resources available. There is no dietetic department in the Tabriz Children's hospital where the Iran cohort of this study was undertaken. There was only one professional with a BSc degree in nutrition to undertake the management of all patients in the hospital. This means that although children at risk of malnutrition are identified, clinical management pathways of dietetic resources are not in place to intervene. Thus there is a crucial need to establish and organize a formal and effective treatment program for those infants who are identified as being malnourished in Iran hospital. On the other hand we found that the first step of iPYMS (weight below 2nd and 9th centile) independently is able to identify the majority of infants at risk of malnutrition. Furthermore, ROC analysis showed that admission weight and iPYMS were nearly the same predictors of malnutrition. These all suggest that iPYMS may not add any more advantages over simple objective measurement alone to identify infants at risk of malnutrition.

While iPYMS may be useful to identify malnutrition there is still the question of how best to intervene? Considering, the high prevalence of malnutrition in Iranian hospitalized infants, the question is that what would be done with infants screened in this hospital? Obviously, the priority should be given to the treatment of the malnourished infants particularly in the lack of resources (dietetic team or department) those infants could be identified using admission weight alone that was shown to be as a robust predictor of malnutrition and nearly the same predictor as iPYMS. Weight and height are routinely measured at admission to the hospital and there is no need to apply for extra resources. It can be suggested that in the lack of dietetic

team, clinicians or nurses may play their role and may prescribe feeds or oral nutritional supplements.

It can be suggested that using the WHO program for management of severe acute malnutrition (WHO, UNICEF, 2009; WHO, 2013) might be a useful approach. There are treatment programs for severe acute malnourished children (SAM) proposed by WHO (2013) and WHO, UNISEF (2009). The question is that how many infants per week would be expected to be severe malnourished? Findings obtain from the present study illustrated that about one third of infants were at risk of malnutrition using the criterion of SGNA scoring risk. As these participants had been recruited with over-sampling, another analysis was then run for only the first two months of recruitment that had been carried out without over-sampling, to look at the actual proportion of risk and malnutrition. It was found in this period that 22% of infants were at risk of malnutrition using SGNA rating risk and 20.4% were malnourished using weight z scores <-2SD). Half of those malnourished infants (10%) were severe (weight z score <-3SD). Approximately 950 children were admitted to the certain wards of the hospital over the six months period of the study recruitment in Tabriz Children's Hospital and about one third of those admissions were infants. Thus, it can be expected that about 1-2 infants (1.4 infants) per week should be receiving the nutritional treatment based on the WHO proposed program for treatment of severe acute malnutrition.

The procedure that malnourished infants are currently identified and treated in Tabriz Children's Hospital

Identification and treatment of malnourished infants in Tabriz Children's Hospital are essentially done by paediatricians. As seen above there is no nutrition team or department in this hospital. Infants at admission to the hospital are assessed for growth and developmental disorders using WHO growth charts and ASQ (Ages & Stages Questionnaires). On admission, infants' weight and length are measured and plotted on the growth chart, if a child's weight or length was below the third centile or had some neuro-developmental disorders, then he/she is referred to the gastroenterology or endocrinology and metabolism wards for consultation and more detailed assessment. These all are carried out by residents (final year paediatric students) who are responsible to visit patients at the time of admission to the hospital. However, this process may not be completed for all admissions and not documented in children's cases notes.

Growth charts are not documented in the patients' hospital cases notes, but those are placed with the child's case note in the gastroenterology and endocrinology clinic (specialist outpatient clinic) that is located in the hospital. However, it is recommended that patient's growth chart should be documented in her/his case note in the ward.

Infants, who are diagnosed as being malnourished, are fed using various commercial ready food supplements. Children, who are in low socioeconomic class, are given food supplements free. However few of these meet WHO criteria for re-feeding in SAM and they are costly and may not be accessible in the location where they are living.

Parenteral Nutrition is applied whenever it is required, but the solutions do not contain some of elements (e.g. Copper, Zinc) that may be needed for some patients and this treatment modality is high risk and particularly dangerous in SAM. Enteral Nutrition is rarely applied in this hospital, as there is a very limited access to the products used for this purpose. In few cases, the one as only nutritionist working in the hospital makes some mixtures to use in this case.

In general, paediatricians are responsible for the treatment of malnourished infants and if it is necessary they ask for nutritional specialist consultation. Patients after discharging are followed up by the specialised (gastrology/endocrinology) clinic in the hospital. Based on this information we assume that very small number of malnourished infants may be recognized using this procedure.

WHO protocol for treatment of severe acute malnutrition (SAM) in infants and children

According to WHO, UNICEF recommendations (WHO, UNICEF, 2009) and WHO recently updated guideline (2013) on management of severe acute malnutrition, infants and children 6–60 months of age who are below -3 SD of the WHO standards are most likely to benefit from therapeutic feeding. Currently children with severe acute malnutrition (weight-for height of below -3 SD) are treated with special therapeutic foods, most commonly Ready-to-Use-Therapeutic Foods or F75 and F100 milk-based diets. It is noted that the current treatment protocols for managing severe acute malnutrition have no known risk, and minimize negative social consequences. There are different discharge criteria; it is recommended that the discharge criterion be based on percentage weight gain of children 6–60 months of age (WHO,

UNICEF, 2009). For children admitted at -3 SD weight-for-height defined by the WHO standards, a discharge at -2 SD and at -1 SD corresponds on average to a weight gain of 9% and 19% respectively. For simplicity, it is possible to use 15 % weight gain as discharge criterion for all infants and children admitted to therapeutic feeding programmes. However, WHO updated guideline (2013) recommends different discharge criteria for infants and children 6-60 months and infant 0-6 months of age. It is noted that infants and children with severe acute malnutrition who are discharged from treatment program should be periodically monitored to avoid a relapse.

Proposed solutions for Tabriz

As seen above malnutrition is a major problem in Iranian cohort, we thus recommend that establishing WHO treatment protocol on severe acute malnutrition (SAM) can be a benefit for infants who are identified as being severe malnourished at admission to the Tabriz Children Hospital. Although the WHO guidelines on malnutrition assume that children just have malnutrition and may not really give help about how to manage the sick child who is malnourished, its impact on patients' recovery can be determined in this hospital in future work. It is important also to look at the practically of the impact of implementation of the screening program on improving the service and patients care in future studies.

According to the UNICEF's report in 2011, by integrating nutrition into routine health programmes, the nutritional status of malnourished children could improve dramatically in response to proper care; the rate of underweight children in Iran experienced a 50 percent reduction between 1991 and 2007, yet the prevalence of wasting increased by 30 percent from 1998 to 2007. Over the last several years UNICEF supported the piloting of a community based model for the management of malnutrition through nutrition counselling centres and affiliated health posts in the three provinces in Iran. This pilot model has been subsequently adapted by the Ministry of Health and expanded to 140 locations countrywide. It was shown that regular resources are of particular importance for Iran, where they have been used to benefit programmes related to nutrition, immunization, and the promotion of breastfeeding (UNICEF, Report on Regular Resources, IRAN, 2011).

Thus, it is to be hoped that an organized and systematic program for identification and management of the malnutrition in children in the hospital settings in Iran as part of regular

resources could lead to timely treatment and prevention of the adverse effects of malnutrition-associated disease in sick infants and children will improve outcomes for sick children.

Conclusion and recommendations for future research

Malnutrition was common in this tertiary children's hospital in Iran. iPYMS might perform well in Iran as a country with a higher background prevalence of under- nutrition than the UK and could be used by health professional to identify infants with malnutrition. In contrast, in the UK, iPYMS would mainly identify infants at risk of malnutrition, because of the low prevalence of under-nutrition there.

On the other hand, we found that weight alone (the first component of iPYMS) is a robust predictor of malnutrition risk and can be used to identify infants who are at risk of malnutrition. Therefore, iPYMS may not add any more advantages over the simple objective measurement alone to identify infants at risk of malnutrition. This is particularly essential where there are limited resources for implementation of a nutritional screening program and established timely intervention. Thus, this approach can be recommended in other Iranian Children's Hospitals.

Moreover, skinfolds measurements may offer a useful and effective method to identify undernutrition in infants in clinical settings, where the prevalence of malnutrition is high, but also it might be more reliable than conventional screening to identify truly malnourished infants in countries with a low background prevalence of undernutrition.

We recommend that studies should be continued to explore a suitable and appropriate gold standard to test the validity of the tools, particularly in low prevalence settings. This would need future interventional studies to achieve the true outcome of malnutrition risk and its effectiveness in paediatric population.

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APPENDICES

Appendix 1: SGNA questionnaire – infants/toddlers

SGNA QUESTIONNAIRE – INFANTS/TODDLERS

1. a) How much did your baby/toddler weigh at birth? _____
   b) How long (or tall) was your baby/toddler at birth? _____
   c) When was the last time your baby/toddler was measured by a health professional?_____
   d) How much did your baby/toddler weigh then? _____
   e) How long (or tall) was your baby/toddler then?_____
   f) How tall is your/your child's: mother?: _____ father?: _____
2. a) What type of milk do you give your baby/toddler? (please check all that apply)
   - □ breastmilk
   - □ formula
   - □ cow's (or goat's) milk → □ homo, whole fat, 3.25% fat □ 2% □ 1% □ skim
   - □ other kind of milk (explain) _____

   b) How do you feed milk to your baby/toddler?: (please check all that apply)
   - □ breastfeed
   - □ bottle feed
   - □ cup
   - □ feeding tube

3. <u>Breastfeeding</u>
   a) Is this your first time breastfeeding? □ No □ Yes
   b) Do you alternate the breast that you start each feed with? □ No □ Yes
   a) How many times in a 24 hour period do you breastfeed your baby/toddler? _____
   c) How long does it usually take to breastfeed your baby/toddler? _____ (in minutes)
   d) How do you recognize that your baby/toddler is hungry? _____Full? _____
   e) Do you have any concerns related to breast-feeding? □ No □ Yes (explain)_____

Bottle-feeding or Tube-feeding

   b) What is the name of your baby's feeding or formula? _____
   c) How do you make the feeding or formula? (what are the amounts of expressed breastmilk or formula, water, other things you add?) _____
   d) How many times in a 24 hour period do you feed your baby/toddler? _____
   e) What is the average amount that your baby/toddler takes at each feeding?_____(in ounces or mL)
   f) How long does it usually take to feed your baby/toddler?_____(in minutes)
   f) Do you have any concerns related to bottle or tube-feeding? □ No □ Yes (explain)_____

Cow's Milk or Other Kinds of Milk

   a) What is the average amount of milk that your baby/toddler drinks in a day?_____(in ounces or mL)

5. Do you give your baby/toddler other things to drink?
   □ No □ Yes → please fill out the chart below:

I give my baby/toddler:	How much of these things does your baby/toddler drink each day? (in ounces or mL)
□ water	
□ fruit juice or fruit drinks	
□ herbal drinks	
□ pop	

□ other (explain)_____	

5. a) What kinds of food does your baby/toddler eat each day?: (please check all that apply)

	Size of the portion eaten
□ cereals and grains (like baby cereal, breakfast cereal, bread, rice, pasta)	
□ vegetables and fruit	
□ meat, fish, chicken, or alternatives (like eggs, tofu, lentils, legumes)	
□ milk products (like cheese, yogurt, pudding, ice cream)	

b) What is the texture of the foods your baby/toddler eats?
□ jarred baby food or homemade foods put in a blender (this is called "pureed")
□ chopped into tiny pieces the size of ground meat (this is called "minced", like hamburger meat)
□ cut into small pieces or cubes (this is called "diced")

6. a) Please pick the word that best describes your baby's/toddler's appetite?
□ excellent □ good □ fair □ poor

b) Compared to your infant's/toddler's usual intake, has your infant's/toddler's intake changed recently?
□ No

□ Yes → Has it: □ increased? □ decreased?

How long has it been since it changed? _____ (in days, weeks, or months)

8. Do any of the following feeding or eating problems affect your infant/toddler's intake? (Please check all that apply)

	No	Yes
Problems with sucking, swallowing, chewing, or biting		
Crying, choking, coughing, gagging, or retching during a meal or at the sight of food or a bottle		
Refusing to eat by hiding the chin in the shoulder, arching the back, biting on the spoon, etc.		
Refusing to swallow food		
Refusing to eat food if it has little pieces or chunks in it (a fear or dislike of food with textures)		
Food allergies, intolerances, special diets: (specify)_____		
Other: (specify)_____		

9. Is anyone else in your family on a special diet?
□ No

□ Yes → (explain) _____

Is your baby/toddler also on this diet? □ No □ Yes

10. Does your baby/toddler currently have any gastrointestinal problems *that restrict his/her drinking or eating*?: (please check for each problem)

Problem	**Never or Almost Never**	**Every 2-3 days**	**Daily**	**How long has your baby/toddler had this problem?**	
				< 2 weeks	≥ 2 weeks
Lack or loss of appetite (anorexia)					
Throwing up (vomiting/reflux)					
Diarrhea					
Constipation					

11. a) Please pick the word that best describes your baby's/toddler's amount of energy or activity?
□ high □ average □ low

b) Compared to your baby's/toddler's usual amount of energy or activity, has it changed recently?
□ No

□ Yes → Has it: □ increased? □ decreased?

How long has it been since it increased or decreased? _____(in days, weeks or months)

PHYSICAL EXAMINATION – INFANTS/TODDLERS

The physical exam supports and adds to findings obtained by the history. Observe areas where adipose tissue and muscle mass are normally present to determine if significant losses have occurred.

1. WASTING

A lack of adipose tissue indicates severe energy deficit. Are the facial cheeks full and the face round or is the buccal fat reduced and the face flat and narrow? Are the arms full and round and is it difficult to lift folds of skin from the elbow or triceps area, or is the skin loose and easily grasped and pulled away from the elbow or triceps? Is the chest full and round with the ribs not evident, or is there progressive prominence of the ribs with obvious loss of intercostal tissue? Are the gluteal fat pads of the buttocks full and round or is there almost no evident gluteal fat of the buttocks and the skin is deeply wrinkled? Are the legs full and round or are they thin with the skin loose at the thigh and calf?

Site	**No Wasting**	**Moderate Wasting**	**Severe Wasting**
temple			
facial cheeks			
arms			
chest			
buttocks			
legs			

2. EDEMA (nutrition-related)

The presence of pitting edema at the ankles or over the sacrum may indicate hypoproteinemia; however, coexisting disease (i.e. renal, congestive heart failure) modifies the implication of the findings. The presence of edema should also be considered when evaluating weight change.

Site	**Absent**	**Moderate**	**Severe**
sacral area (infants or toddlers that are constantly lying down)			
foot; ankles (mobile infant and toddlers)			

3. Other physical signs that were observed that are suggestive of malnutrition:

_____

Appendix 2: Eating Behaviour Scale

Eating Behaviour Scale

To be completed by the parent or carer who most commonly feeds the child. Please answer all questions, if you cannot answer a question put a line through it.

Child's name _____ Child's sex *Male/ Female*

What relation are you to the child? *Mother -- Father -- Other*: _____

1. Was your baby ever breast fed?

a. *No --- Yes, still feeding --- Yes, but stopped when baby aged:*

b. *Less than one week --- 1 to 6 weeks --- 6 weeks to 4 months --- 4 to 6 months --- over 6 months*

2. How much milk does your child currently take?

a. Number of breast feeds per 24 hours _____

b. Number of other milk feeds per 24 hours _____ c. Size of feed _____ ounces

d. Type of milk: *formula---cow's milk---other*: _____

3. What sorts of food is your child eating now and when approximately did they first start them?

a. Soft, smooth spoonable foods (e.g. baby rice, purees) Age _____ months --Not taking

b. Lumpy, firm spoonable foods (e.g. mince, macaroni cheese) Age _____ months --Not taking

c. Melt in the mouth finger foods (e.g. rusk, crisps) Age _____ months --Not taking

d. Soft finger foods (e.g. potato, pasta, banana) Age _____ months --Not taking

e. Hard or chewy finger foods (e.g. roast meat, pizza) Age _____ months --Not taking

4. Circle the answer that best describes <u>how your child is</u> most of the time.

a. My child's appetite is *Poor ----All right----Good----Very Good----Exceptionally Good*

b. My child is hungry A*lways--Usually--Frequently--Sometimes--Rarely*

c. My child is easy to feed A*lways--Usually--Frequently--Sometimes--Rarely*

d. When eating, my child is easily satisfied A*lways--Usually--Frequently--Sometimes--Rarely*

e. My child eats solids slowly A*lways--Usually--Frequently--Sometimes--Rarely*

f. My child prefers self feeding to being fed A*lways--Usually--Frequently--Sometimes--Rarely*

g. My child cries or screams during meals A*lways--Usually--Frequently--Sometimes--Rarely*

h. My child holds food in his/her mouth A*lways--Usually--Frequently--Sometimes--Rarely*

i. My child takes milk slowly A*lways--Usually--Frequently--Sometimes--Rarely*

j. My child prefers milk to food A*lways--Usually--Frequently--Sometimes--Rare***Circle the answer that best describes <u>what you do</u> most of the time.**

5. When you are giving your child solids to eat, what do you do?

a. Sit with your child A*lways--Usually--Frequently--Sometimes--Rarely*

b. Spoon (or hand) feed your child *Entirely----Mostly -----Partly-----Not at all*

6. If your child does not finish part of a meal, what do you do?

a. Encourage him/her to eat A*lways--Usually--Frequently--Sometimes--Rarely*

b. Offer something else A*lways--Usually--Frequently--Sometimes--Rarely*

c. Offer something else later A*lways--Usually--Frequently--Sometimes--Rarely*

d. Make him/her eat the food A*lways--Usually--Frequently--Sometimes--Rarely--Never*

7. How do you feel about your child's eating?

a. I find feeding my child stressful A*lways--Usually--Frequently--Sometimes--Rarely*

b. I worry that my child isn't eating enough A*lways--Usually--Frequently--Sometimes--Rarely*

8a. Does anyone else regularly feed your child? *No / Yes*

b. *If 'Yes'* : who is this?_____

9a. Has your baby had any major health problems since birth? *Yes / No*

b. *If 'Yes'*: can you describe them?

10. Have you ever consulted anyone because of worries about your child's eating/feeding or growth?

Midwife---Health Visitor---GP---Paediatrician ---Dietician---Other, please specify:

11. Can you write in here the **<u>weight at birth</u>** you have for your child

a. Birth weight _____ pounds _____ ounces <u>or</u> _____ Kg

b. Was your child born at full term (37 weeks or after)? *Yes / No*

c. *If 'No'*: how early? _____ weeks

THANK YOU FOR YOUR HELP!

Appendix 3: iPYMS Screening Notification

iPYMS Screening Notification

To be filed in Hospital notes

Child's name _____ _____

Date of assessement ___ / ___ / ___

This child has been assessed as part of the Infant PYMS evaluation project.

The result of her Subjective Global Nutrition Assessment rating suggest that s/he is

	At low risk – no action advised unless other nutritional concerns
	Medium risk - no action unless worsening or other nutritional concerns
	High risk of malnutrition – consider dietetic referral

The other main results of her nutrition screening were as follows:

	Measured	Centile	SD score	Comment
Weight				
Length				
Body mass index				Normal / thin / very thin
Triceps skinfold				Fat stores normal / low / very low
Subscapular skinfolds				Fat stores normal / low / very low
Weight gain since birth		NA		Normal / slow / very slow

Appendix 4: iPYMS form

iPYMS

Name:		**Hospital No:**		
DoB:		**Date of Recruit:**	**Weight**	
Ward:		**Sex: F / M**	**Length/Height**	
Step 1	**Is the weight of the child below the 2nd or 9th centile?**	NO	**0**	
		YES below **9nd**	**1**	
		YES below **2nd**	**2**	
Step 2	**Is your GP/HV/HP concerned about your child's weight gain?**	NO	**0**	
		YES	**1**	
Step 3	**Has your child had a reduced intake (including feeds) for at least the past 5 days?**	NO Usual intake	**0**	
		YES Decrease of usual intake for at least the past 5 days	**1**	
		YES No intake (or a few sips of feed only) for at least the past 5 days	**2**	
Step 4	**Will the child's nutrition be affected by the recent admission/condition for the 5 days?**	NO	**0**	
		YES For at least the next 5 days • Decreased intake and/or • Increased requirements and/or • Increased losses	**1**	

		YES No intake (or a few sips of feed only) for at least the next 5 days	**2**	
Step 5	**Calculate total score** (total of steps 1-4)	**Total PYMS Score**		

Weight Scoring Guide

Age (months)	**Birth**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**18**	**20**	**22**	**24**
Boys 2nd	2.47	4.28	5.52	6.31	6.87	7.31	7.69	8.04	8.38	8.7	9.01	9.31	9.61
Boys 9th	2.83	4.70	6.00	6.84	7.43	7.91	8.32	8.70	9.07	9.42	9.76	10.09	10.42
Girls 2nd	2.38	3.91	4.98	5.69	6.21	6.63	6.99	7.34	7.68	8.01	8.33	8.65	8.98
Girls 9th	2.72	4.30	5.44	6.20	6.76	7.21	7.61	7.98	8.34	8.70	9.05	9.40	9.75

Appendix 5: STRONG$_{kids}$ form

STRONG$_{kids}$

(Screening Tool for Risk on Nutritional Status and Growth)

Name:	Date:
Surname:	Ward:
DOB:	Consultant:
Age:	Hospital No.:
Sex: F/M	CHI:

THE COMPONENTS of STRONG$_{kids}$

NO.	ITEM	DESCRIPTIONS	SCORE	
1	Subjective Clinical Assessment	Is the patient in a poor nutritional status judged by subjective clinical assessment (diminished subcutaneous fat and/or muscle mass and/or hollow face)?	1	
2	High Risk Disease	Is there an underlying illness with a risk of malnutrition or expected major surgery? See Table 2	2	
3	Nutritional Intake and Losses	Is one of the following items present? • Excessive diarrhoea (≥ 5 per day) and/or vomiting (>3 times/ day) the last few days? • Reduced food intake during the last few days before admission (not including fasting for an elective procedure or surgery)? • Pre-existing dietetically advised nutritional intervention? • Inability to consume adequate intake because of pain?	1	
4	Weight Loss or Poor Weight Gain	Is there weight loss or no weight gain (infants <1 year) during the last few weeks/months?	1	
Total Score				

Hulst JM, Zwart H, Hop WC and Joosten KFM (2010) Dutch national survey to test the STRONGkids nutritional risk screening tool in hospitalized children. Clin Nutr 29(1), 106-11.

Appendix 6: Carer Information Sheet

Carer Information Sheet

Development and Evaluation of a New Infant Nutrition Screening Tool (iPYMS Score)

Your child and you are being invited to take part in a study. Before you decide it is important for you to understand why the research is being done and what it will involve. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

Nutrition is very important for children's health. Poor diet affects growth, brain development, admission and length of stay in the hospital. National Health Service standards now require that all children are checked for their nutrition status on admission. However no quick, simple and accurate method to do that exists at the moment. Health professionals and researchers in NHS Greater Glasgow and Clyde have recently developed a new nutrition screening method for children on admission at the hospital. The purpose of this study is to test the accuracy of this method to assess the nutrition of younger infants.

Why has my child been chosen?

Your child was chosen for this study because he/she has had been admitted to Yorkhill hospital and is aged under two years.

Do we have to take part?

No. It is up to you to decide whether to take part. If you decide to take part you will be asked to sign a form that says that you have been informed about the study and you are happy to participate. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care that your infant receives.

What do we have to do?

If you decide to participate in the study, you will be asked to complete a questionnaire about your child's eating and diet and weight gain before admission.

After that the researcher will measure:

1. Your child's **length** and **weight** and his/her **upper arm width**
2. The **thickness of the skin and fat** on his/her arm and shoulder blade with a special instrument. Your infant has to take off his/her top for that.
3. Your child's **body resistance** in order to measure their amount of muscle and fat. This involves taking off his/her shoes and socks and attaching two sticky electrodes to their right hand and hand right foot. These then pass a tiny electric current through the body – but your child won't be able to feel this!

These measurements should take about 20 minutes to complete

Are there any risks or disadvantages of taking part?

We do not anticipate any major risk of disadvantages of taking part in this study. If your child is very upset or uncooperative with any of them we will not continue with that measurement.

Are there any possible benefits of taking part?

If the measurements or your answers suggest that your child is at risk of becoming undernourished we will let your clinical team know so they can refer him/her for further assessment or treatment. The information we get from this study will help us to improve patients' health treatment.

Will my infant's participation in this study be kept confidential?

Yes. Any information about your child, which leaves the hospital, will have his/her name and address removed so that he/she cannot be recognised from it. However we will let the clinical team looking after you in hospital know all the measurement results, as these may help their clinical assessment.

What will happen to the results of the research study?

The results of this study will be presented to managers of the hospital and other staff in NHS Greater Glasgow and Clyde. The results of the study are likely to be reported to scientific meetings or published in scientific journals, but without identifying your name or other data able to identify you. The data of this study may be accessed by the research and development office at Yorkhill Hospital for audit and monitoring purposes. This will not affect confidentiality.

Who is organising the study?

The study is organized by the PEACH Unit which is part of Glasgow University, with advice and support from the Nutritional Care Group at Yorkhill. The study has been reviewed by the local Research Ethics Committee and Research and Development office.

Can I complain about the study?

If you have any complaints about the study you can contact the Patients Liaison Officer Mrs K Colquhoun at 0141 201 0000.

For further information you can get in contact with:

Ms Shamsi Milani, PhD researcher: 0141 201 0230;

Professor Charlotte Wright: Professor in Community Child Health: 0141 201 6927

Dr Konstantinos Gerasimidis: Researcher in Paediatric Nutrition: 0141 201 0486

Dr Diana Flynn: Consultant in Paediatric Gastroenterology and Nutrition: 0141 201 0503

Appendix 7: Consent form for main carer

CONSENT FORM FOR MAIN CARER

Study title: Development and Evaluation of a New Infant Nutrition Screening Tool (Infant Yorkhill Malnutrition Score)

1. I confirm that I have read and understand the information sheet dated 1/10/2010 for the above study and have had the opportunity to ask questions. ☐

2. I understand that the participation is voluntary and that we are free to withdraw or not complete parts of the study at any time, without giving any reason, without medical care or legal rights being affected. ☐

3. I understand that sections of any of my infant's medical notes (not parent's notes) relevant to this study may be looked at by the researchers involved in this study and from the Research & Development Department in Yorkhill hospital. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

_____	_____	_____
Name of Guardian	Date	Signature
_____	_____	_____
Researcher	Date	Signature

1 for patient; 1 for researcher; 1 to be kept with hospital notes

Appendix 8: Acquisition and utilisation of anthropometric measurements on admission in a paediatric hospital before and after the introduction of a malnutrition screening tool.

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CLINICAL NUTRITION

Acquisition and utilisation of anthropometric measurements on admission in a paediatric hospital before and after the introduction of a malnutrition screening tool

S. Milani,* C. Wright,* O. Purcell,† I. Macleod,‡ & K. Gerasimidis*

*School of Medicine, College of Medicine, Veterinary and Life Sciences, University of Glasgow, Royal Hospital for Sick Children, Glasgow, UK
†Department of Dietetics, Royal Hospital for Sick Children, National Health Service Greater Glasgow and Clyde, Glasgow, UK
‡Department of Paediatric Gastroenterology, Hepatology and Nutrition, Royal Hospital for Sick Children, National Health Service Greater Glasgow and Clyde, Glasgow, UK

Keywords
growth chart, height, malnutrition screening tool, weight.

Correspondence
K. Gerasimidis, School of Medicine, College of Medicine, Veterinary and Life Sciences, University of Glasgow, Royal Hospital for Sick Children Glasgow G3 8SJ, UK.
Tel.: +44 (0)141 201 6969
Fax: +44 (0)141 201 9275
E-mail: konstantinos.gerasimidis@glasgow.ac.uk

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Abstract

Background: Acquisition of anthropometric measurements and assessment of growth in paediatric inpatients remains poor. The introduction of malnutrition screening tools that incorporate weight and height/length measurements might improve their acquisition and utilisation in other aspects of patient care.
Methods: Documentation of weight and/length measurements and their plotting on growth charts was evaluated using a case notes review in paediatric inpatients who were admitted before (n = 146), during (n = 154) and after the pilot (n = 151) and official (n = 128) clinical use of a screening tool.
Results: Documentation of weight was high in all periods (> 97% of patients). Height/length measurement documentation was negligible (4% of patients) but improved after the introduction of the screening tool (> 62%; $P < 0.0001$), except in infants, who were not part of the screening programme.
Conclusions: Introduction of a screening tool improved the acquisition of anthropometric measurements by nursing staff, although its utilisation by medical staff remained poor.

Introduction

Acquisition of anthropometric measurements remains poor in hospitalised children (Bunting & Weaver, 1997; Lek & Hughes, 2009; Ramsden & Day, 2012) despite increasing awareness about nutrition as an integral part of patient care (Agostoni *et al.*, 2005) and worldwide initiatives to develop references for childhood growth (Wright *et al.*, 2010). Thus, health professionals miss the opportunity to identify children who are faltering growth and those patients at risk of undernutrition delaying timely intervention.

Routine use of nutritional screening tools on hospital admission is recommended for identifying patients at risk of malnutrition and offering them appropriate care (Agostoni *et al.*, 2005). Because there is no universally applicable definition of malnutrition, these screening tools identify children who might benefit from receiving dietetic intervention. These tools combine a list of questions on predictors of malnutrition risk and anthropometric measurements. Thus, the introduction of such tools in clinical practice might offer the opportunity to improve acquisition of anthropometric measurements, which might also improve other aspects of patient care.

The present study aimed to evaluate the effect of the implementation of a novel nursing paediatric malnutrition screening tool, which incorporates measurements of weight and height/length (Gerasimidis *et al.*, 2010, 2011), on the acquisition of anthropometric measurements and the completion of growth charts in a paediatric hospital.

Materials and methods

A new malnutrition screening tool, the Paediatric Yorkhill Malnutrition Score (PYMS), was developed locally (Gerasimidis *et al.*, 2010, 2011). The tool was piloted over a 4-month period in four wards (one surgical, one acute medical, two medical specialised) and was subsequently introduced for routine use at the Royal Hospital for Sick Children, Glasgow. PYMS is a four-step tool completed by the nursing staff on admission. Three steps involve assessing history of recent weight loss, changes in nutritional intake, and the predicted effect of the current medical condition on the nutritional status of the patient. In addition, the height/length and weight are measured to calculate body mass index and compare this against the second centile of a chart. Each step bears a score and the total sum reflects the patients' degree of nutrition risk (Gerasimidis *et al.*, 2010, 2011).

Consecutive patients admitted to the aforementioned wards over a period of 14–28 days were identified from the hospital database until the required number (approximately 150 patients) was achieved. Four different time periods were used: (i) 1 year prior to PYMS implementation (Period A); (ii) during the pilot introduction of PYMS (Period B); (iii) 10 days after pilot withdrawal (Period C); and (iv) 1 year after its implementation for routine use (Period D) was retrieved from the hospital electronic network. Medical and nursing notes were reviewed for documentation of weight and height/length measurements performed by the nursing staff during hospital stay and plotting of these measurements on growth charts by medical staff. This audit was registered with the local clinical effectiveness office.

Results

Participants' characteristics

The case notes of a total of 579 inpatients were included in the present study. There were no statistical differences with respect to patient age between the four periods or in the percentage of patients who were reviewed by each ward between the four periods, although one of the medical specialist wards was not open in Period D (Table 1). There were significantly more infants (< 1 year) in period D (Table 1).

Acquisition of weight measurements

Weight measurements were recorded in more than 97% of the inpatients during their hospital stay, with no statistical difference between the four periods or wards (Table 1).

Table 1 Acquisition of growth measurements and completion of charts before, during and after the pilot and routine implementation of the Paediatric Yorkhill Malnutrition Score (PYMS) by speciality

Measurement	Period A: 1 year before PYMS pilot (n = 146)	Period B: during PYMS pilot (n = 154)	Period C: 10 days after PYMS pilot (n = 151)	Period D: 1 year after routine clinical use (n = 128)
Age (years), mean (SD)	5.2 (4.3)	5.1 (4.2)	4.4 (4.3)	4.7 (3.8)
Infants (< 1 year), *n* (%)*	23 (16)	28 (18)	46 (30)	16 (13)
Weight, *n* (%)				
Total	141 (97)	149 (97)	151 (100)	128 (100)
Surgical	59 (100)	55 (100)	53 (100)	49 (100)
Acute medical	57 (98)	60 (95)	61 (100)	61 (100)
Gastroenterology/respiratory	7 (70)	10 (91)	12 (100)	18 (100)
Neurology/immunology	18 (95)	24 (96)	25 (100)	NA
Height/length, *n* (%)				
Total*	6 (4)	100 (65)	23 (15)	79 (62)
Surgical	0 (0)	35 (64)	11 (21)	30 (61)
Acute medical	4 (7)	47 (75)	8 (13)	36 (59)
Gastroenterology/respiratory	1 (10)	7 (64)	3 (25)	13 (72)
Neurology/immunology	1 (5)	11 (44)	1 (4)	NA
Growth chart completion, *n* (%)				
Total	16 (11)	16 (10)	22 (15)	15 (12)
Surgical	0 (0)	4 (7)	7 (13)	1 (2)
Acute medical	11 (19)	6 (10)	7 (11)	8 (13)
Gastroenterology/respiratory	2 (20)	2 (18)	4 (33)	6 (33)
Neurology/immunology	3 (16)	4 (16)	4 (16)	NA

*$P < 0.0001$ for difference between Periods.

NA, not available; ward was not operable during period D.

Acquisition of height/length measurements

Six (4%) inpatients had their height/length obtained in Period A compared to 65% during the PYMS pilot introduction ($P < 0.0001$). Within 10 days of PYMS pilot withdrawal, documentation of height/length decreased dramatically to 15% ($P < 0.0001$). During the official introduction of PYMS in routine practice, documentation of height/length measurements increased to levels similar to those during the pilot introduction of PYMS (Table 1). The pattern of change was similar in all wards, although the proportional increase in documented height/length measurements during the Periods B (pilot use) was lower in the ward with patients from neurology and immunology specialties (Table 1). Patients who did not have their height/length measurement recorded during the two periods of PYMS implementation were significantly younger [Period B: 2.7 (3.8) years; Period D: 3.3 (3.7) years] compared with those who did (Period B: 6.4 (3.8) years; Period D: 5.6 (3.7) years; both $P < 0.001$]. Similarly, 18.8% of the children aged < 1 year in Period B and 7.1% in Period D had their height/length documented compared to 67.9% and 77.8% of the children older than 1 year, respectively (Table 1).

Growth chart completion

Only 10–15% of the patients' medical notes reviewed had recent admission measurements of height/length and weight plotted on growth charts (Table 1), with no statistical difference between the four periods (Table 1). For each period, proportionally more patients from a combined gastroenterology/long-term respiratory ward and less from a surgical ward had their growth chart updated with recent height/length measurements (Table 1).

Discussion

Assessment of linear growth should be an integral part of the standard care that the sick child receives in the hospital and it complements the health professional's judgment for identifying the malnourished child. The present study shows that measurements of weight are very common, although those of height/length are not. Our results are similar to those by reported previously (Lek & Hughes, 2009), as well as those reported in the same hospital as the present study some 15 years ago (Bunting & Weaver, 1997). However, in our population, the documentation of weight measurements was better in the majority of the inpatients reviewed. In the study by Lek & Hughes (2009), height/length and weight were measured in 12.5% and 51.5% of the children, and there was only one child aged <2 years with a height/length measurement (Lek & Hughes, 2009), whereas, in the study by Bunting & Weaver (1997), there was documentation of height/length measurement for < 12% of the children Lek & Hughes, 2009). Despite methodological differences in these two studies, which do not allow a direct comparison of the findings, the findings of the present study suggest that, 15 years after the recognition of poor documentation of growth measurements and despite the development and implementation of local policy and procedures for measuring infants' growth (Maclean, 2007), the acquisition of anthropometric measurements and mainly those of height/length remained unchanged.

A possible explanation for the high acquisition of weight measurements in the present study might be the clinical need to calculate optimum/safe administered drug dosage. This is also supported by the fact that plotting on growth charts of any of the measurements was almost negligible. Similarly, poor documentation of height/length prior to the introduction of the malnutrition screening tool can be attributed to the lack of height/length equipment, the time required in obtaining measurements in very young and very sick children, and a perception by nursing staff that growth assessment should receive less priority compared to other aspects of patient care.

Implementation of PYMS that incorporates measurements of height/length and weight significantly improved the documentation of height/length measurements. This change was not temporary because it remained 1 year after the routine implementation of PYMS in clinical practice. In infants (< 1 year) where the completion of the PYMS by the nursing staff was not valid and hence not indicated, acquisition of height/length measurements remained remarkably poor despite our expectations for a collateral increase as a result of increased awareness. Nevertheless, the use of these data in other aspects of patient care, namely plotting on growth charts by medical staff, remained poor and was no different between the four different periods. This may indicate either a lack of communication between nursing and medical staff who share patient care or that other aspects of patient care take precedence.

Despite a substantial improvement in the acquisition of anthropometric measurements, one in three patients did not have a measurement of height/length. This may have been because the PYMS was not performed by the nursing staff, or they were unable to perform height/length measurements in children who were unable to bear weight or in young children where measurements of length are more laborious.

The introduction of a screening tool which encompasses measurements of weight and height/length improved the acquisition of anthropometric measurements. However, this did not improve completion of

growth charts and thus the potential to identify poor growth. Whether such screening tools are otherwise beneficial for patient care still requires further investigation. The findings of the present study highlight the need for continuous education to raise nutrition awareness, continuous professional development and improved communication among health professionals. Such initiatives should not only be endorsed by health services, but also be supported by senior clinical and management staff.

Conflicts of interest, sources of funding and authorship

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KG and CW designed the study. SM, OP, IM and KG collected the data. KG, SM and CW analysed and interpreted the data. SM and KG drafted the manuscript. All authors reviewed and approved the final version for publication submitted for publication.

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