MALNUTRITION SCREENING AND BODY COMPOSITION MEASUREMENTS IN PAEDIATRIC PATIENTS WITH COMPLEX DIAGNOSIS

Translating research into clinical practice

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I, Nara Elizabeth Lara Pompa confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

Background. Paediatric patients have a high risk for malnutrition, and there is an increasing consensus worldwide on the need to find better tools to identify the risk, diagnose, and manage this condition to avoid the long-term consequences in child health and development.

Objective. Evaluate the practical aspects of measuring body composition (BC) in paediatric patients with complex conditions, and their possible advantages over measurements of weight/height to predict clinical outcomes and as possible malnutrition diagnostic parameters; while also validating three paediatric malnutrition screening tools (MSTs).

Design. This prospective study recruited and measured 152 children 5-18yr with different anthropometric and BC techniques within 48hr of admission and at discharge to a tertiary level hospital. MSTs (PYMS, STAMP, STRONGkids) were completed on admission and data collected on clinical outcomes: length of stay, complications, and worsening nutritional status.

Results. BC measurements by different techniques are practical and acceptable overall in paediatric patients. Malnutrition was prevalent in 13-20% of patients, measured by different anthropometric/BC parameters. Patients were on average short and underweight compared to healthy children, and had abnormal BC (low lean mass, variable fat mass). The parameters were significantly associated with clinical outcomes, and there seemed to be an advantage for BC to predict increased LOS and complications.

Similarly, malnutrition risk on admission varied depending on the MST used. STAMP and STRONGkids were significantly associated with baseline weight, height, lean and fat mass; while PYMS had better associations to clinical outcomes (increased LOS).

Conclusion Malnutrition is relatively common, and BC measurements seem to have a place in the diagnosis and possibly the nutritional management of paediatric patients. Future work with specific patient groups and outcomes should help clarify what parameters/tools are the most helpful to ultimately decrease the prevalence of hospital malnutrition.

Keywords: body composition, malnutrition, screening, paediatric patients, clinical outcomes

Preface

Sick children have a high risk of malnutrition both on admission and during their hospital stay, and the prevalence in both developing and developed countries has remained largely unchanged despite scientific medical advances. Identifying and treating this condition is important considering its associations with increased morbidity, mortality and healthcare costs; in addition to the long-term consequences for child growth and development.

A possible cause for the continued high prevalence could be the lack of effective diagnostic parameters to identify malnutrition in routine clinical practice, especially in children diagnosed with complex and chronic conditions. Anthropometric measurements, weight and height, have traditionally been used to diagnose malnutrition. However, these measurements, together with Body Mass Index, have limitations that might become even more relevant in the presence of chronic disease. One of the main limitations of these measurements is they are not able to distinguish between different body tissue components, which may be markedly affected by the underlying disease. Additionally, the amounts of fat mass and lean mass could influence the response to treatment, the metabolism of medical substances, and affect patient recovery. Consequently, body composition measurements of fat and lean mass have been proposed to better identify children with malnutrition and guide nutritional management more effectively than weight and height alone in hospitalised children.

The use of body composition measurements in the clinical setting, however, has been limited due to the lack of appropriate reference data in healthy children and evidence that these measurements can indeed improve the identification, management of malnutrition and ultimately improve the clinical outcomes of these children. With recently published UK reference data on body composition, it is now possible to measure body composition in children by a range of techniques and calculate a standardised score based on the comparison with reference values from healthy children of the same age and sex.

At the same time, to address the high prevalence of hospital malnutrition, it is important not only to be able to diagnose the condition, but also to identify the children that are at risk of developing it during their stay. Malnutrition screening tools have been developed to carry out this task and refer high risk patients for a more comprehensive nutritional assessment and management. However, available tools for paediatric patients, contrarily to the case in adult patients, are scarce; and evidence is still needed to determine if their use can indeed impact on the clinical outcomes of sick children with or at risk of malnutrition.

Considering these factors and limitations, this thesis will investigate the use of different anthropometric and body composition parameters in clinical practice, as well as three available paediatric malnutrition screening tools, to predict the clinical outcomes in children with complex conditions admitted to a tertiary level paediatric hospital. This is regarded as a much-needed first step to inform future research into intervention trials for improving the nutritional screening and management of these children, thereby seeking to alter the rate of hospital malnutrition and its negative consequences for health and development.

Chapter 1 contains a background literature review on paediatric malnutrition, malnutrition screening and the use of body composition measurements in clinical practice; highlighting gaps in the evidence so far and justifying the need for the present research. This will be followed by the aims of the thesis outlined in **Chapter 2. Chapter 3** will then describe the general methods used to investigate these aims.

Chapters 4 to 6 will deal with the methodological and pragmatic aspects of measuring body composition in a clinical setting. Chapter 4 will detail the acceptability, practicality and validity of different techniques for measuring body composition that have been previously suggested to be suitable methods for clinical practice. Chapter 5 will consider the adaptation and adjustment of results from 2 techniques used to measure lean mass: standing BIA Tanita and supine multi-frequency BIA QuadScan, given that the reference data for body composition makes use of standing BIA Tanita but many children in clinical practice are unable to stand to undertake the measurement. Finally, Chapter 6 will focus on the problem of estimating height in those patients who are unable to stand, and will test ulna and tibia length measurements as alternatives to assess growth and calculate some derived nutritional parameters in these children.

Chapters 7 to 9 will focus on the clinical aims of the thesis, testing different parameters and tools for identifying and screening for malnutrition in paediatric patients. Chapter 7 will describe the nutritional status, assessed by several different parameters, of children from various specialties on admission and during hospitalisation, to determine the extent of malnutrition in the population. Chapter 8 will then compare the use of body composition measurements of fat and lean mass with the simpler parameters of weight and height, in their ability to identify children who are likely to develop worse clinical outcomes; thus, suggesting the best parameter(s) to diagnose malnutrition in this population. Chapters 9 will compare the tools available for malnutrition screening in paediatric patients, especially with regards to their ability to predict clinical outcomes, and against the anthropometric and body composition parameters analysed in Chapter 8.

Chapter 10 will describe a feasibility study designed to explore the views and opinions from paediatric dietitians at several expert centres in the UK and USA regarding the use of body composition measurements in clinical practice. This will detail current practice in nutritional assessment, understanding on body composition techniques, and the barriers and opportunities perceived for implementing these measurements in the future for the routine nutritional management of these children.

Finally, **Chapters 11 and 12** will discuss and draw conclusions from the presented results with regards to the thesis aims, will identify the strengths and limitations of the present research, and propose future research directions.

Abbreviations & units

abSDS	Abnormal standard deviation score
BC	Body composition
BIA	Bioelectrical impedance
BMI	Body Mass Index
BMT	Bone marrow transplantation
CF	Cystic fibrosis
CI	Confidence interval
CP	Cerebral Palsy
CR	Coefficient of repeatability
DXA	Dual energy x-ray absorptiometry
EN	Enteral nutrition
FM	Fat mass
FMI	Fat mass index
GI	Gastrointestinal
GOSH	Great Ormond Street Hospital NHS Foundation Trust
GS	Grip strength
HC	Head circumference
HT	Height
ICC	Intraclass correlation coefficient
κ	Cohen's kappa
kg	kilogram
LM	Lean mass
LMI	Lean mass index
LOA	Limits of agreement
LLOA	Lower limit of agreement
LOS	Length of stay

m	Meter
mm	Millimetre
cm	Centimetre
MB	Mean bias
MST	Malnutrition screening tool
MUAC	Mid upper arm circumference
n	Sample size
N	Newton
NS	Nutritional status
Ω	ohms
p	p-value
P	Power – gradient of regression
PN	Parenteral nutrition
r	Pearson's correlation coefficient
SD	Standard deviation
SDS	Standard deviation scores
SE	Standard error
SFT	Skinfold thickness
TBW	Total body water
UK	United Kingdom
ULOA	Upper limit of agreement
USA	United States of America
WT	Weight
Z	Whole body impedance
yr	Years

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1 Introduction

1.1. Malnutrition in paediatric patients

1.1.1. Definition

It has long been recognized that hospitalized children have a high risk of malnutrition. The term ‘malnutrition’ refers to a state of disturbed nutritional status in which “a deficiency or excess of energy, protein and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcomes” (Lochs et al. 2006). Similarly, the American Society of Enteral and Parenteral Nutrition (ASPEN) proposed a new definition specific for paediatric malnutrition as “an imbalance between nutrient requirements and intake that results in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development and other relevant outcomes” (Mehta et al. 2013).

Taking into consideration the aetiology of the condition, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the British Association of Parenteral and Enteral Nutrition furthermore proposed a definition of malnutrition as a state resulting from decreased nutrient uptake/intake that leads to a decreased body cell mass and function, and in which inflammatory activity is a contributing factor in most individuals (Stratton et al. 2003; Lochs et al. 2006; Soeters & Schols 2009), thus exemplifying the recognition of inflammation as an important factor in the development of clinical malnutrition.

Despite these similar conceptual definitions of malnutrition, the pathophysiology and diagnostic parameters, and in fact the term itself, are currently still the focus of debate. A recent consensus statement by ESPEN (Cederholm et al. 2015) highlighted the inconsistencies in the use of the terms ‘undernutrition’ and ‘malnutrition’ in clinical settings and scientific literature. They comment that the term ‘malnutrition’ is slightly more commonly used, but having the same meaning as ‘undernutrition’. This is furthermore complicated by the existence of other related terms such as ‘wasting’, ‘cachexia’, ‘failure to thrive’, and ‘protein-energy malnutrition’.

Although ‘malnutrition’ traditionally used to refer only to a state of undernutrition, it might also encompass a state of overnutrition and obesity by some more-recent definitions (Soeters & Schols 2009; Aurangzeb et al. 2012). Considering the rates of paediatric overweight and obesity have increased worldwide, this has also been reflected in the observed prevalence in hospitalised children (Jones Nielsen et al. 2013; Co-reyes et al. 2013).

1.1.2. Causes

Malnutrition (undernutrition) in the general population of developed countries, such as the UK, is relatively low compared to that in lower income countries; where hospital child malnutrition broadly corresponds to the incidence of malnutrition in the general population (Campanozzi et al. 2009). Yet, developed countries also report an incidence of hospital malnutrition similar to that of lower income countries, and longer hospital stays correlate with increased malnutrition risk, suggesting hospitalization in itself is associated with a substantial multifactorial risk for this condition (Aurangzeb et al. 2012; Pawellek et al. 2008).

Illness leads to increased metabolic and nutritional demands for recovery, and children have lower nutrient stores and greater demands for growth than adult patients, placing them both at a higher risk of nutritional deficiencies and long-term consequences in terms of growth and development (Agarwal & Hemamalini 2012; Garcia & Rodriguez 2013). Additionally, although developments in technology have helped improved child survival, they have also resulted in a greater proportion of premature children surviving and being born at lower gestational ages. These children have higher nutrient demands, and lower nutrient stores and metabolic capacity predisposing them to a higher risk for malnutrition (Embleton et al. 2001). Several disease states might also compromise nutritional intake, nutrient absorption, metabolism, and/or increase losses; all of which further compromises the nutritional status of the patient (Aurangzeb et al. 2012) (Figure 1.1). Most studies have reported that younger patients (<2 years of age) are at increased risk for malnutrition, as are those with pre-existing chronic conditions or admitted to certain specialty areas (surgical, renal, intestinal failure), and those with longer hospital stays (Agarwal & Hemamalini, 2012; Burgos et al., 2012; Campanozzi et al., 2009; de Souza Menezes et al., 2012). This suggests, as supported by observations of prevalence, that lower gestational age, younger age on admission and disease severity all place hospitalized children at a higher risk of disease-related malnutrition.

Finally, several hospital practices regarding nutrition and food provision have been reported to influence the prevalence of malnutrition in clinical settings. Medical staff can often fail to recognize the signs of malnutrition and the importance of preventing and treating it (McWhirter & Pennington 1994; Baxter 1999). Likewise, food intake is often compromised due to medical procedures, lack of protected meal times, inappropriate food selection and quality, and an inadequate environment/support to encourage eating (Agarwal & Hemamalini 2012; Beck et al. 2003). All this translates to increased risk of malnutrition, not only at the time of admission, but throughout the hospital stay (de Souza Menezes et al., 2012).

1.1.3. Consequences

Malnutrition, with its various practical definitions, can lead to multiple adverse effects both in terms of clinical and financial outcomes (Correia, 2003). A poor nutritional status has been correlated to increased lengths of stay and complications (Hecht et al. 2014; Aurangzeb et al. 2012; Huysentruyt, P Alliet, et al. 2013), such as higher rates of infection, poor wound healing and immune dysfunction (de Souza Menezes et al. 2012). Increased mortality rates have also been reported in children with severe malnutrition in low income countries (Rice et al. 2000), although not consistently in developed countries (de Souza Menezes et al. 2012).

In addition to the effects on morbidity and mortality, children also have significantly larger requirements for growth and development that might be compromised by malnutrition and result in long-term consequences even beyond this critical period (Skillman & Wischmeyer 2008). Figure 1.1 summarizes the described components in the pathogenesis of child hospital malnutrition, from the risk factors to the consequences and outcomes of this condition; while section 1.3.1. further analyses the evidence from these studies regarding the association of malnutrition parameters with clinical outcomes.

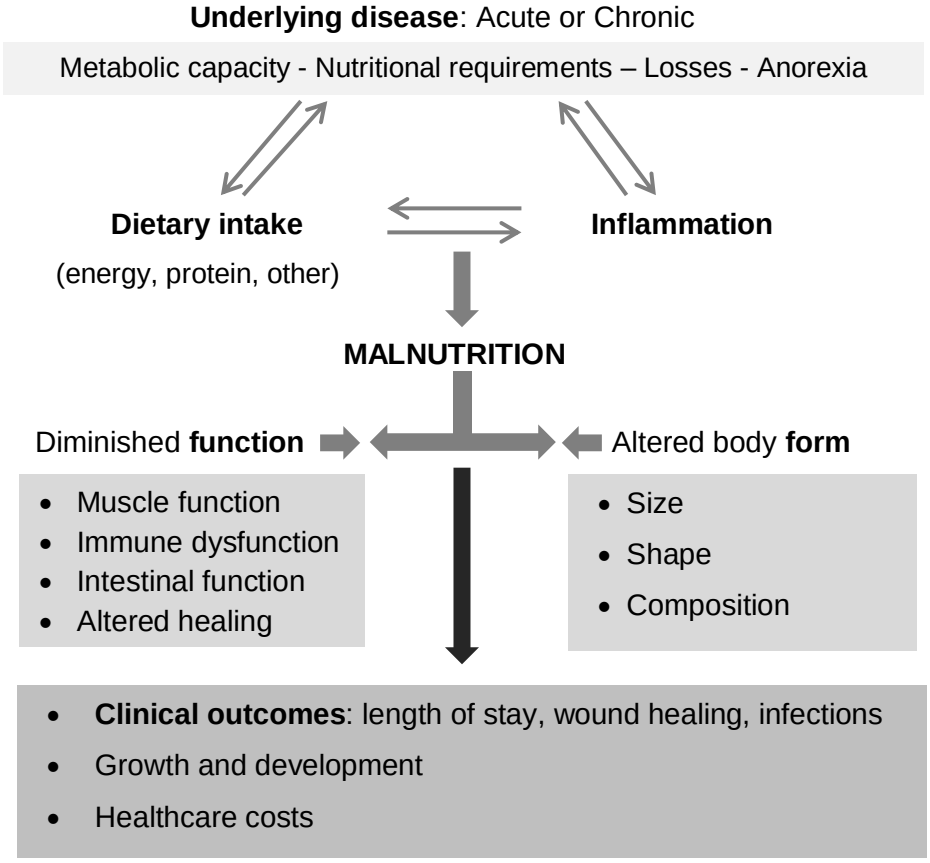


Figure 1.1. Pathogenesis of hospital paediatric malnutrition

Adapted from Mehta et al. (2013) and Beer et al. (2015).

Some studies have estimated the financial burden that malnutrition places on national healthcare costs. It is unsurprising that due to increased length of stay and complications, malnutrition imposes a substantial financial burden (Amaral et al. 2007; Burgos et al. 2012). A study in the UK concluded that identifying and treating malnutrition in hospitalized adults could result in £266 million per year of savings (Lennard 1992). Thus, efficiently targeting malnutrition diagnosis and treatment could potentially translate into significant savings that could then be invested in other aspects of patient care.

1.2. Classification and indicators of paediatric malnutrition

Although the effects of malnutrition on child recovery and growth have been emphasized for several years, 40 years after some of these reports its prevalence in hospitalized children continues largely unchanged despite advances in other fields of medical technology and treatment (Cao et al. 2014; Corkins 2016). Though the general concept of malnutrition can be regarded as well-accepted overall, the definition of the condition nonetheless lacks clear and accepted diagnostic criteria. This lack of criteria not only impacts the recognition and management of malnutrition in clinical practice, but also impacts the advancement of research in this area by complicating the evaluation of nutritional interventions and comparison between studies (Cederholm et al. 2016; Becker et al. 2014).

The timely recognition of malnutrition in children is especially important, considering detection and intervention at this early age is more likely to prevent long-term adverse effects (Becker et al. 2014). This requires standardised methods for diagnosis, as the subjective identification of malnutrition by medical and nursing staff can often be inaccurate and lead to a poor diagnosis and referral for nutritional management (Joosten & Hulst, 2011). Furthermore, this is often an unrecognised or underestimated problem in paediatric wards (Huysentruyt et al. 2013). A study showed clinical staff estimated a prevalence of approximately 17% while the measured prevalence was about 35% (Restier et al. 2015).

Malnutrition could be objectively identified by measuring body function and/or body form in agreement with the conceptual definition of malnutrition (Figure 1.1.). The most common way of assessing this is Anthropometry, or the ‘measurement of body form’; and this is one of the main components of current nutritional assessment practices. Anthropometric measurements assess different aspects of body shape, and require the use of calibrated and sometimes specialised equipment, various degrees of training, and an understanding of the strengths and limitations of each technique (Goulet 1998). The following sections will describe the different classifications and diagnostic criteria that have been proposed to characterise this condition both in the community and clinical settings.

1.2.1. Early classifications and indicators

In 1971, a joint FAO/WHO Expert Committee in Nutrition had already identified the need for an accepted and standardised classification and definition for malnutrition (undernutrition) that allowed the quantification of prevalence worldwide and comparisons between countries and studies (Waterlow 1972). Considering growth is one of the best ways to assess nutritional status in children, the use of growth curves was and still is the easiest way to perform this in the community and clinical settings. Weight and height measurements are the basis of growth assessment, and unsurprisingly have been the first and most widely-used criteria to assess nutritional status and define malnutrition (Joosten & Hulst 2011).

One of the first classifications for malnutrition in children was developed by Gomez et al. (1955), and later by Waterlow (1972). These classifications used weight and height measurements compared with standards to determine if acute malnutrition was present, and the degree: 'mild', 'moderate', or 'severe'. Table 1.1. summarises the criteria from both classifications. The Gomez classification was developed to detect undernutrition specifically (indeed the authors advocate the term 'desnutricion' in Spanish – meaning undernutrition) in developing countries in Latin America and Africa where the rates of malnutrition in children in the community were still high and linked to socioeconomic factors. The Waterlow classification proposed weight-for-height (WFH) instead of the weight-for-age (WFA) criteria used in the Gomez classification, with the purpose of providing a measurement of nutritional status that was independent of age and improving on the assessments made using non-population specific standards for the comparisons. Some years later, the WHO developed standard references for growth assessment of children based on an international-collected sample of healthy breastfed infants and young children <5yr, and later for children 5-19yr, and determined the cut-offs for WFH based on standard deviation scores (SDS) to classify the degree of malnutrition using these standards (WHO 1999).

Classification	Indicator	Acute malnutrition severity		
		mild	*moderate*	*severe*
Gomez (1955)	WFA	75-90%	60-74%	<60%
Waterloo (1972)	WFH	80-90%	70-80%	<70%
WHO (1999)	WFH		-2 to -3 SDS	<-3 SDS

Table 1.1. Classifications of acute malnutrition

Adapted from Waterlow (1972); Gomez et al. (1955); and WHO (1999).

These early classifications on the severity of malnutrition reported associations with mortality. Gomez et al. (1955) showed a correlation between the severity and death; while a report by the WHO/UNICEF indicated children with a WFH SDS <-3 had 9 times the risk of death than those children with a WFH SDS of -1 (Mehta et al. 2013; Becker et al. 2014).

Another factor to consider in the classification of malnutrition aside from the severity, is duration. Malnutrition/undernutrition is most commonly classified as acute or chronic (disease lasting more than 3 months) (Becker et al. 2014). The described parameters are applied to detect acute cases of malnutrition ('wasting'), while the parameter of height-for-age (HFA) is used to describe chronic undernutrition ('stunting'), defined by the WHO standards as having a HFA <-2SDS (WHO 1999; Becker et al. 2014).

So far, it is clear that even with these first classifications and diagnostic indicators all based on weight and height, the assessment of malnutrition was still influenced by factors such as the scale for comparison (centiles, percentiles, SDS) and indicators used (weight-for-age, weight-for-height, height-for-age). Furthermore, the publication of the WHO growth standards and subsequent studies of implementation on different countries (both low and high-income) have highlighted differences and thus the importance of the choice of reference data for the diagnosis of malnutrition and referral (Wright et al. 2008; de Onis et al. 2007; LaCourse et al. 2015; Nichols et al. 2012; Duggan 2010; Mehta et al. 2013).

1.2.2. Other classifications, related terms and indicators

As previously mentioned, malnutrition is often also associated to other terms, such as 'protein-energy malnutrition' and 'cachexia', that usually make reference to the aetiology and clinical picture of the condition. Recently, a consensus statement by ESPEN looked to homogenise some of these terms (Cederholm et al. 2016). They describe a classification of clinical malnutrition that considers the presence of inflammation and/or disease, and this is summarised in Figure 1.2.

Although not the norm, studies have also looked at using additional indicators for the diagnosis of malnutrition in the clinical setting, especially considering the additional factors of inflammation and underlying disease. These include other anthropometric measurements such as skinfold thicknesses and circumferences (mid-arm), biochemical assessments such as serum Albumin, Transferrin and Retinol-binding protein; and other functional assessments such as grip strength (Baxter 1999). The use of biochemical parameters is beyond the scope of this review and thesis, but the use of other anthropometric and functional measurements will be discussed further in the following sections.

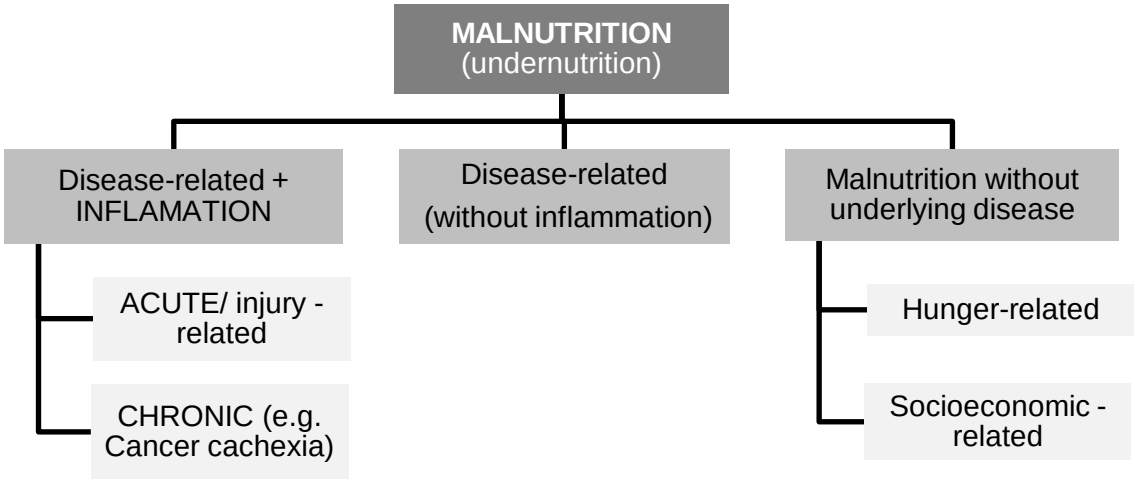


Figure 1.2. Aetiology-based classification of malnutrition (undernutrition)
Adapted from Cederholm et al. (2016)

1.2.3. Prevalence of malnutrition in clinical settings

This prevailing ambiguity in the diagnostic parameters for malnutrition makes it difficult to describe the extent of this condition in hospitalised children (Soeters & Schols 2009; Mehta et al. 2013). Data has been reported in both high and low-income countries worldwide with values ranging between 6-60% on admission and during hospitalization (Aurangzeb et al., 2011; Edington et al., 2000; Hendricks et al., 1995; O'Connor et al., 2004; Pawellek et al., 2008). For example, a recent study by Hubert et al. (2016) showed malnutrition to be present in 23.8% of children on admission, and an in 26% of children during their hospital stay.

The major challenges in quantifying the prevalence of malnutrition is not only the wide range of criteria used to diagnose it, but also the variability in the study characteristics, as can be seen from Table 1.2. This sample of studies presented all use the described measurements of weight (WT) and height (HT), in addition to the derived Body Mass Index (BMI), but make use of different reference data, cut-off points and classifications (Ferreira & Franca 2002). This is also complicated by the nature of the studies themselves (prospective, retrospective) and the patient inclusion criteria in terms of age range, as well as the hospital setting for the study (general, academic, private) (Joosten & Hulst, 2008). Furthermore, studies have shown that the underlying disease is the strongest predictor for malnutrition at the time of admission (Joosten et al. 2010; Mehta et al. 2013). Thus, differences in prevalence can be expected depending on the diagnosis of the population described. To exemplify this, a study by Pawellek et al. (2008) reported a range of prevalence values according to diagnosis: 40% in neurological diseases, 33.3% in Cystic Fibrosis, 27.3% in Oncology patients, and 23.6% in gastrointestinal diseases.

Study	Population	Malnutrition *(%)*	Malnutrition parameter	Type of malnutrition
Joosten (2008)	All ages	11	WFH < -2 SDS	Acute
Pawellek (2008)	All ages	6	<70-80% moderate	
Marino (2006)	All ages	34	WFH <-2 SDS	
Rocha (2006)	<5 y	7	WFH <-2 SDS	
Marteletti (2005)	2 m-16 y	11	WFH <-2 SDS	
Dogan (2005)	1 m-23 y	28	WFH <-2 SDS	
Ozturk (2003)	2-6 y	9	% ideal WFH <80%	
Sermet (2000)	> 1 m	19	% ideal WT <80%	
Hankard (2001)	> 6 m	21	BMI < -2 SDS	
Hendrikse (1997)	7 m-16 y	8	WT/HT < 80%	
Hendricks (1995)	0-18 y	7	WFH < 80%	
Moy (1990)	3 m–18 y	14	WFH < -2 SDS	
Hendricks (1995)	0-18 y	13	HFA < 90%	Chronic
Hendrikse (1997)	7 m-16 y	8	HFA < -2SDS	
Rocha (2006)	<5 y	18	HFA < -2SDS	
Joosten (2008)	All ages	9	HFA < -2SDS	
Sylvestre (2007)	Renal disease	64	HFA < -2SDS	
Perreira (2000)		63	HFA < -2SDS	

Table 1.2. Malnutrition (undernutrition) prevalence in paediatric hospitals

Adapted from Joosten & Hulst (2008). Weight-for-height (WFH), Height-for age (HFA).

Despite the challenges, the overall consistency with which studies have shown the presence of malnutrition in hospitalized children worldwide, and the consequences that the condition can have for growth and development, strongly suggests this is a problem that needs to be addressed both on admission and throughout the hospital stay (Corkins 2016). Identifying the optimal procedures/tools to detect the risk factors involved in the development of malnutrition and the effects it has on body form and function is likely the key step towards improving the diagnosis and nutritional management of this condition.

1.3. Use of simple anthropometric indicators to identify malnutrition in clinical settings: advantages and limitations

Weight and height are still the most common anthropometric measurements used in clinical practice to assess malnutrition, as can be seen from studies on prevalence described in the previous section. Historically, they have been widely used both in the community and clinic because they are fast and simple measurements that, in the case of WT at least, need no highly specialized equipment or training (Daniels 2009). Furthermore, WT and HT should usually be measured on admission as part of routine assessment of growth, planning of medical interventions, and for calculating drug dosages (Pichler et al. 2014).

BMI is derived from the measurements of WT and HT, and is also commonly used in clinical practice to assess nutritional status, either as an absolute index or compared to a reference (e.g. WHO standards) to obtain SDS normalised for age and sex (Cole et al., 2000). Its interpretation in children, unlike the use of set cut-off points in adults to classify them into thinness categories, needs these standards because the cut-offs are dependent upon age (Joosten & Hulst 2011). BMI is often considered not just an indicator of overall nutritional status, but as an indicator for adiposity, and will be further discussed in subsequent sections.

1.3.1. Associations with clinical outcomes

Studies have shown associations between several simple anthropometric parameters with longer lengths of stay, mortality, and complications in children admitted to hospital (Aurangzeb et al. 2012; Becker et al. 2014). A recent multi-centre study in Europe (Hecht et al. 2014) showed associations between a BMI <-2SDS and increased stay, lower quality of life, more frequent vomiting and diarrhoea in hospitalised children. Table 1.3. summarises other reported effect sizes in paediatric patients. In addition, some studies have reported associations between obesity and adverse clinical outcomes (Ursula G. Kyle et al. 2005; McClendon et al. 2014), although few of these have been in children (Bechard et al. 2016).

Most of these studies have been observational prospective or retrospective, meaning a causal relationship with clinical outcomes is difficult to confirm. The inconsistencies in the way the parameters are measured and assessed, as with studies of prevalence (Table 1.2.), also makes it difficult to compare and determine the cause for any inconsistencies between results. For example, documented associations of BMI to clinical outcomes is not always consistent, and is less clear in children/adolescents than in adults (Wells & Fewtrell 2006; Siervogel et al. 2000; Vogtle 2015).

Study	Design	Population	Outcome	Result
Akinbami et al. 2010	Prospective	*n* =164 Africa	Hospital mortality	BMI<-2SDS predicted mortality
Bejon et al. 2008	Prospective	*n* =13307 Africa	Hospital mortality	BMI<-3SDS predicted mortality
Nangalu et al. 2016	Prospective	*n* =400 India ICU	Hospital mortality	Severe malnutrition (WFA <60%) correlated with mortality
Öztürk et al. 2003	Prospective	*n* =170 Turkey	Hospital weight loss	Low BMI predicted weight loss during hospitalisation
Campanozzi et al. 2009	Prospective	*n* =496 Europe	Hospital weight loss	BMI<-2SDS predicted hospital weight loss
Bhattacharya et al. 1993*	Prospective	*n* =608 USA GI surgery	Pneumonia and sepsis	Increased risk in WFH<80% (*RR*: 10 and 6 respectively)
Stey et al. 2014*	Retrospective	*n* =90,392 USA Surgical	Urinary tract infection and pneumonia	Increased risk for WFA <5th centile (*RR*: 1.8 and 2.7 respectively)
Anderson et al. 2011*	Retrospective	*n* =55 USA Surgery	Infection-related complications	WFA<-2SDS increased risk of infection (*RR*=3.6)
Bechard et al. 2016	Prospective	*n* = 1,622 Multi-country PICU	Infections, hospital discharge, mortality, respirator-free days	BMI<-2SDS correlated with infection (*OR*=1.9), mortality (*OR*=1.5), less likely to get discharged (hazard ratio=0.7) and 1.3 less ventilator-free days.
Abdelhadi et al. 2016	Retrospective	*n* = 6,280,710 USA (national database)	LOS, hospital costs, and requiring post-discharge care	'Malnutrition' associated with increased stay (*RR*=2.5), hospital costs (>3 times higher), and 3.5 times more likely to need post-discharge care.

Table 1.3. Summary of associations between anthropometric indicators of malnutrition and clinical outcomes in paediatric patients

RR= Risk ratio, OR=Odds ratio, LOS=length of stay, n=sample size, (*) adapted from Hill et al. (2016).

1.3.1. Practical limitations in clinical conditions

Measurements of weight and height are often difficult to obtain in clinical practice, particularly in patients with complex diagnoses, despite their apparently established common use. This is especially true for HT, as evidenced by a clinical audit in a tertiary paediatric hospital in the UK that indicated WT was the only consistently collected measurement on admission. HT was frequently omitted, with 65% of children having a measurement documented in their patient notes, and only 41% of them having this measurement performed on admission (Pichler et al., 2014). Similar findings have been observed consistently in other paediatric studies (Williams et al. 2015; Larsen et al. 2014; Sarni et al. 2009)

It has been suggested that obtaining these measurements is generally a low priority on admission (Bouma 2017), and indeed, the measurement and documentation of WT and HT on admission has been shown to be overestimated by healthcare professionals. A study on the paediatric wards of a university hospital showed that clinical staff estimated that about 81% of patients had their WT and HT taken on admission, when only 43% of them had the measurements performed. Surprisingly, this was most often true for staff directly involved in performing the measurements (Restier et al. 2015).

Situations related to the patient's condition could make WT and HT measurements challenging to perform. Critically ill children might be considered too sick to move, or might be placed in isolation rooms. The availability of alternative equipment (portable stadiometers, sitting and bed-scales) can sometimes help in obtaining serial measurements in these children (Mehta et al. 2013). The use of portable equipment, mostly in field studies, has been reported to be accurate and reliable (Voss & Bailey 1994), although this equipment might not be available in all wards and clinical settings.

Some conditions could furthermore make the obtained measurements inaccurate. Acute illness is also often accompanied by fluid shifts and oedema, and the presence of dressings and implants can all make WT measurements unreliable (Mehta et al. 2013). HT can be particularly difficult to obtain because several conditions that might prevent the patient from standing upright to take the measurement, for example in patients with contractures or lower limb deformities (Vogtle 2015). A study showed that the use of alternative height measurements such as recumbent length, estimations based on arm span or knee height, or even parent-reported height, can lead to different assessments of both height and BMI, and should be used with caution (Froehlich-Grobe et al. 2011).

1.3.2. Limitations for identifying different body tissue compartments

Despite their associations with outcomes, the described anthropometric parameters have an additional limitation that might be particularly important in the context of disease: they do not distinguish between different body tissue components, mainly fat (FM) and lean (or non-fat) mass (LM) (Daniels, 2009; Demerath et al., 2006; Phan et al., 2012; Wells et al., 2002). Consequently, WT and BMI alone could be unable to identify children who have abnormal patterns of fat and lean mass (Daniels 2009; Freedman et al. 2005; Wells et al. 2002), as has been reported in studies with children diagnosed with cerebral palsy (Sullivan et al. 2006), children undergoing treatment for cancer (haematological and solid tumours) (Murphy et al. 2010), on long-term parenteral nutrition for intestinal failure (Pichler, Chomtho, et al. 2014), and those with chronic renal failure and post-renal transplantation (Rashid et al. 2006; Mastrangelo et al. 2013).

The use of weight and BMI alone could furthermore lead to under-diagnosis of malnutrition (undernutrition) in some diseases or clinical conditions that make weight measurements unreliable. For example, a study with paediatric patients with solid tumours showed that BMI missed many of the children classified as malnourished by other methods, such as MUAC (Shah et al. 2015). Similarly, the administration of high-volume infusions and fluid shifts, as is often the case for renal patients undergoing dialysis (Edefonti et al. 2001; Schmidt & Dumler 1993) or in critically ill children (Mehta & Compher 2009), all cause an increase in WT without reflecting actual muscle or fat mass increases.

With regards to BMI, although this measurement has been considered a parameter to assess adiposity, especially in adults, its use in children had been increasingly questioned considering associations seem to vary depending on age, sex, ethnicity, maturity and disease state (Siervogel et al. 2000; Demerath et al. 2006; Wells, Coward, et al. 2002). BMI is not a direct measurement of body fat, and although changes in BMI during childhood have been described, these changes could be underpinned by different changes in body tissue compartments. A study by Wells (2000) suggested past associations between BMI and fatness in childhood might not have been analysed in the best way, and calculated Hattori body composition charts for infants and children in this study showed that for a given BMI, a wide range of fatness was observed for both male and female.

In agreement with these observations, some studies in adults have reported that BMI seems to underestimate the prevalence of low and high fat mass, and that high fat mass seems to reduce the sensitivity of BMI to detect nutritional depletion in both healthy and hospitalised adults (Ursula G. Kyle et al. 2005). A recent meta-analysis (Javed et al. 2015) showed that BMI has a high specificity but a low sensitivity to detect excess adiposity in

paediatric patients, misdiagnosing more than a quarter of children with high fat mass. This has been reported in several individual studies in both healthy children and patients, with suggestions that assessment of adiposity in individual children should be performed using more accurate methods and that BMI should be considered a measurement of mass rather than adiposity (Fusch et al. 2013; Forsum et al. 2013; Kim et al. 2006).

1.3.3. Alternative anthropometric measurements

Considering the challenges to WT and HT in some settings, alternative measurements have been proposed to assess nutritional status of paediatric patients. Mid-upper arm circumference (MUAC) has been proposed as a proxy for WT, and head circumference (HC) as a proxy for HT (Mehta et al. 2013). HC is an index used to assess nutritional status and, particularly, brain development in the first 2 years of life. Studies have reported the associations between nutritional status, head size and brain development/function (Mehta et al. 2013). Chronic malnutrition in early year, as with stunting, can lead to decreased brain development, and this parameter has been shown to have a close relationship to length patterns in infants (Caino et al. 2010).

MUAC is an anthropometric parameter that, although less commonly assessed compared to WT, can be used to assess nutritional status. It is quick, easy and requires no specialised equipment (Becker et al. 2014). It has the added advantage that it can be performed bed-side. It is mostly commonly used in community settings, particularly in developing countries and emergency situations, as a simple cut-off indicator for malnutrition because it shows a strong association with mortality and adverse outcomes (Fernández et al. 2010; Briend et al. 2012; Goossens et al. 2012; Myatt et al. 2006). However, there are also standards available by the WHO (De Onis et al. 1997) and others (Frisancho 1981), meaning MUAC measurements in children and adolescents can be assessed as MUAC-for-age, similarly to weight/height parameters in clinical practice (Becker et al. 2014).

The use of MUAC to assess nutritional status is based on the premise that depletion of whole-body stores from poor nutrition will also be reflected in decreased stores, and therefore circumference, on the site of the measurement. Strong associations between MUAC and BMI have been confirmed in healthy and acutely-ill children and adults (Becker et al. 2014). Although MUAC can be used as an indicator for poor nutritional status, particularly when WT measurements might be unfeasible as with the presence of oedema (Mehta et al. 2013), it could become affected only with more advanced or severe cases of body stores depletion and might not identify more subtile and early changes in the patient's nutritional status, especially when used as a simple cut-off indicator (Ali et al. 2013; Himes & Zemel 2016). This

measurement can also be used to estimate the amounts of fat and lean mass, and like BMI, will be further discussed in subsequent sections.

Similar to the case for WT and BMI, associations between MUAC and body tissues have not always been convincingly described; and only a couple of studies have analysed the associations between MUAC and clinical outcomes, mostly in developing countries (Mastrangelo et al. 2013; Akinbami et al. 2010; Bejon et al. 2008).

There have been some reports of poor reliability of MUAC measurements, both in terms on intra and inter-operator, in clinical settings (Mastrangelo et al. 2013; WHO 2006). Even with measurements of WT and HT, which as usually reported to have good reliability and accuracy, serial monitoring by the same observer and adequate training has been advocated (Voss & Bailey 1994; Mehta et al. 2013; West et al. 2011; Leppik, A; Jurimae, T; Jurimae et al. 2004; Becker et al. 2014). Furthermore, there have been reported differences (though small) between anthropometric measurements preformed on the right and left sides of the body, suggesting it is necessary to standardise the measurement technique for the assessment of anthropometric parameters (Moreno et al. 2002).

Thus, the validity of the different anthropometric parameters for the assessment of nutritional status is likely to vary depending on the population of children being assessed, and a combination of measurements, adequate training and serial measurement might help improve their use for assessment of individual patients (Mehta et al. 2013).

1.4. Body composition in the context of disease and clinical settings

As the previous sections described, there is a possibility that anthropometric parameters might not always reflect differences and changes in fat and lean mass that are present at least in some clinical conditions (Murphy et al. 2016). This section will look at the evidence for the possible advantages of assessing different body tissue components for the clinical management of paediatric patients.

1.4.1. Importance of different body tissues

FM and LM might be important in terms of clinical management, since they could differentially influence body function, nutritional requirements, response to treatment, and recovery (Halpern-Silveira et al. 2010; King et al. 2010; Wells & Fewtrell 2008; Müller et al. 2002; McCarthy et al. 2014).

Low muscle mass, strength and low fitness have all been related to metabolic risk and insulin sensitivity on children and adolescents (Benson et al. 2006; McCarthy et al. 2014). Loss of body cell mass (or LM) could impact recovery after trauma or disease, since muscle mass serves as a fuel substrate and precursor for acute phase proteins (Soeters et al. 2008), and muscle weakness in the ICU has been associated with failure to wean off ventilation (Berger et al. 2016). Additionally, because muscle mass is a major site for glucose metabolism and disposal, loss of this tissue could influence whole-body glucose homeostasis and mediate insulin resistance states (DeFronzo et al. 1985). The amount of fat mass is also a relevant factor in the context of disease and malnutrition, since it will likely influence the duration of successful starvation, serving as fuel substrate, sparing loss of lean mass, and thus influencing survival (Soeters et al. 2008).

Although historically lean mass, and particularly muscle mass, has been regarded as the most functional and dynamic weight component, it is now also increasingly recognised that fat mass also has an important metabolic and regulatory function in the body (Ahima et al. 2000). Also considering that some disease states, including the increasingly prevalent obesity, involve specifically alterations in the amount and/or distributions of body fat; there has been an increasing interest in assessing both LM and FM in paediatric patients (Wells et al. 2012; Wells & Fewtrell 2008).

1.4.2. Monitoring and changes with dietary treatment

As with the current practice for nutritional assessment, nutritional interventions are often monitored using WT and BMI serial measurements. However, the goal of nutritional interventions in undernourished patients is generally agreed to be promotion of lean/muscle mass deposition alongside FM, meaning it might be useful to monitor changes in both tissues to ensure increases in WT are not due to FM alone (Phang & Aeberhardt 1996; Wells, Mok, et al. 2002), especially in those populations where body composition has already been shown to be abnormal (e.g. cerebral palsy, oncology, intestinal failure patients) (Murphy et al. 2016). There is some evidence of conditions were BMI or simple WT measurements might be too crude to discern relevant changes in both LM and FM (Wells & Fewtrell 2008). Studies in adult obesity report BMI exhibits a U-shape association to mortality, while both high FM and low LM are independently associated with adverse outcomes, suggesting a closer assessment of these individual tissue compartments might provide additional information for monitoring the treatment of patients with obesity (Wells & Fewtrell 2008). Similarly, children diagnosed with eating disorders show a loss of both fat and lean mass that is thought to impact bone health among other outcomes, meaning BC measurements might provide an advantage over simple BMI or WT assessment (Nicholls et al. 2002).

Low BMI or WT that is due to low LM and high/normal FM could also potentially lead to overfeeding of patients, further increasing the adverse consequences of excess fat mass (Wells & Fewtrell 2006; Wells, Mok, et al. 2002). A study with gastrostomy feed children with cerebral palsy confirmed these children have a low energy expenditure and high FM, suggesting a risk of overfeeding with current protocols (Sullivan et al. 2006). A follow-up study then showed that linear growth promotion while avoiding a disproportionate increase in FM was possible by prescribing a low-energy and micronutrient-complete feed to these children (Vernon-Roberts et al. 2010).

A similar finding was reported in a study with paediatric patients in the ICU, were children were found to have lower energy expenditures and weight gain patterns similar to healthy children, but with lower LM deposition and disproportionate higher FM increases (Wells et al. 2002). The authors suggest the potential role of using body composition measurements (especially LM) to calculate resting energy requirements, although these disease-specific prediction equations are yet to be developed and tested.

Consequently, the routine measurement of the patient's body composition in addition to simple anthropometry in certain patient groups may be a promising approach to better identify malnutrition and guide nutritional support in hospitalized children. The following section will describe the different techniques and models available.

1.5. Measuring body composition in clinical practice: models and techniques

Though the use of body composition (BC) measurements in research has been growing in recent years, its use as part of routine clinical practice has been so far limited in paediatric patients (Wells & Fewtrell 2008). Given that the gold standard for the analysis of BC comes from cadaver analysis, *in vivo* assessment of BC is performed by a series of techniques that instead predict it based on measurements of different body properties. This means that, additionally to the possibility of methodological errors in collecting the raw data, these techniques also have a second error from the assumptions each use to convert the raw values into the final values of BC (Wells & Fewtrell 2006). The different techniques have different advantages and limitations, as well as varied levels of complexity. Consequently, it is unlikely a single technique will be suitable for all subjects at all times.

1.5.1. Simple BC methods and predictive techniques

There are several simple techniques to measure and/or predict certain body components, each with their own assumptions, advantages and limitations, as summarized in Table 1.4.

Skinfold (SFT) measurements have regularly been used to assess the size of certain subcutaneous fat depots and to rank individuals against healthy subjects of the same age and sex. Measurements are usually obtained from 3-4 sites in the upper body (triceps, biceps, subscapular and suprailiac), thus ignoring measurements of lower body fatness (such as leg and calf), constituting a limitation in some cases (Tanner & Whitehouse 1975; Wells & Fewtrell 2006). Raw individual SFT values can serve as indices of regional fatness, and can also be converted to SDS using reference data specific for the population studied. In the UK, the reference data traditionally used is that of Tanner and Whitehouse (1975), and SDS calculated using the LMS method (Davies et al. 1993). SFTs are relatively simple and inexpensive, though there might be some intra and inter-observer error that it is suggested to be less than between-subject variability except in the case of obese children; and it usually requires training and practice to standardize the measurements (Wells & Fewtrell 2006; Cederholm et al. 2015).

Waist circumference can also be used as a simple proxy of abdominal fat, with some published evidence on the association of this measurement with adverse outcomes and risk in children, similarly to the case in adults (Savva et al. 2000). UK reference data for this measurement is available for the calculation of SDS (McCarthy et al. 2001).

Technique	Body component	Assumptions	Reference data	Advantages	Disadvantages
SFT – raw data	Regional fat	Constant skin protein content	✓	Simple measurement of regional fat	No measurement of lean mass
Waist circumference	Abdominal fat	Waist predicting central fat	✓	Simple, quick measurement of abdominal fat	Less accurate for measuring visceral fat

Table 1.4. Simple BC methods

Adapted from Wells & Fewtrell (2006).

1.5.2. The 2-compartment model of BC

The 2-compartment model divides the body into FM and LM compartments. These models use assumptions about the composition of lean and fat tissues, and use techniques to measure and/or predict FM and LM by measuring a certain aspect of the body (Table 1.5). Prediction equations are then used to estimate the amount of FM and LM from these measurements, meaning the accuracy of the assessment is dependent on the use of population-appropriate data and equations that can be limited or out-of-date (Wells et al. 1999). Additionally, techniques might vary in the number of assumptions and predictions; since some measure only one tissue (or a tissue property) and predict the other by subtracting it to weight (e.g. BIA), while others measure both tissues (e.g. DXA).

Technique	Estimates	Measures	Assumptions	Advantages	Disadvantages
SFTs – predictive equations	Total body fat	Regional subcutaneous fat	Subcutaneous fat predicting total body fat	Simple, quick	Population specific, poor accuracy in individuals and groups
MUAC + SFT – predictive equations	Regional body fat and lean mass	Regional subcutaneous fat and arm circumference	Arm body fat and muscle (estimated) predicting total body fat and lean	Simple, quick	No better than skinfolds alone
Deuterium	Total body lean mass	Body water	Constant water content in lean mass	Accuracy of body water measurement Relatively simple and non-invasive	Expensive and more complicated analysis
BIA	Total body lean mass	Body water (estimated from electric current flow)	As above + conductivity predicting body water (equations)	Simple, quick	Population specific, poor accuracy in individuals and groups
DXA	Body fat and lean mass	Body fat, bone and non-bone tissues	Tissue hydration	Accuracy	More complex technique and specialised equipment

Table 1.5. Predictive methods for 2-compartment BC
Adapted from Wells & Fewtrell (2006).

Methods assessing regional fat mass

Raw data from SFT can also be used to predict body components using regression equations. However, this introduces further assumptions and possibility of error (predictive error). Equations using 2 or more SFT measurements can be used to estimate body density and subsequent equations then convert this value to percentage body fat (Janz et al. 1993; Rodríguez et al. 2005). However, most equations have been derived for healthy white populations and may be unsuitable for other ethnic groups given the reported differences in fat patterns, and there also seems to be poor agreement for individual follow-up and according to the degree of fatness (Reilly et al. 1995; Slaughter et al. 1988). Because of these limitations, SFTs are best used to assess regional fat deposits from raw measurements (as described in the previous section) rather than to predict total body fat or other components not measured directly by this technique (e.g. lean mass) (Wells & Fewtrell 2006).

SFT measurement can also be accompanied by measurement of MUAC. This measurement, taken together with triceps SFT to predict FM in this region, estimates the amount of LM by calculating mid-upper arm muscle area and fat area with a series of equations (Fernández et al., 2010; Wells & Fewtrell, 2006). MUAC, together with triceps SFT, is often used as a means to quickly assess malnutrition because it is simple and can be measured in almost all patients and children in the community; although its use in practice is then dependent on population-specific reference data and equations (Fernández et al. 2010). Arm anthropometry has been shown to be good at predicting regional FM but performing poorly for regional LM, with regional values not necessarily representing a good estimate of total values of BC (Chomtho et al. 2006). If a single cut-off is to be used to diagnose malnutrition, it should be considered that the optimal cut-off might be dependent on the population characteristics (Fiorentino et al. 2016).

Methods assessing body water to predict lean mass

Bio-electrical impedance (BIA) and stable isotope dilution methods are used to predict and measure total body water (TBW) respectively. These techniques result in a measure (or prediction on the case of BIA) of TBW, and then predict LM by multiplying it by a hydration factor (age-specific); and FM by subtracting LM from WT. The hydration factors however, might not be appropriate for some disease states that cause fluid shifts, since these techniques assume a constant composition and hydration of the LM for given age and sex (Wells et al. 1999; Cederholm et al. 2015; Buchholz et al. 2004).

The deuterium dilution method involves giving a known dose of deuterium-labelled water, allowing time for equilibration (mixing with the rest of the body water pool) and subsequently

measuring its concentration from saliva, blood or urine samples, taking into account the pre-dose concentration in each subject. Samples are analysed by isotope ratio mass spectrometry. Consequently, stable isotope measurements might not be appropriate or feasible in many clinical settings, especially for individual patients (Wells & Fewtrell 2006; Ramírez et al. 2009; Cederholm et al. 2015).

BIA measures the resistance to the flow of a small electrical current to predict body water, since dissolved electrolytes in aqueous tissues conduct electricity better than fat and bone, which have lower conductance properties. It is thus highly correlated with lean mass and prediction equations can be used to determine LM. It assumes the body is a single cylinder with electrodes placed at either end (wrist and ankle). Adjusting the resulting BIA values for the length of the cylinder (height or length) estimates the volume of the cylinder, or in other words the proxy for TBW. Regression equations are used to predict TBW by dividing the square of the height by the impedance value (Buchholz et al. 2004). These equations are influenced by age and other population-specific characteristics, with most of published equations in paediatric populations developed for specific disease states such as HIV or cystic fibrosis rather than healthy populations (Groeneweg et al. 2002; Palchetti et al. 2013; Pietrobelli et al. 2003). BIA is becoming more common in the clinical setting, especially as mentioned among certain specialties (Pencharz & Azcue 1996; Elliott et al. 2015), and although it requires more specialized equipment, measurements can be obtained with relative ease in most age groups and settings (Pirlich et al. 2000; Kyle et al. 2015).

BIA can be measured by different equipment using different frequencies and electrode placements. The simplest machines use a frequency of 50 KHz conducted from hand-to-foot or foot-to-foot. Foot-to-foot measurements are less accurate since they only assess the lower body conductivity (Bosy-Westphal et al. 2008). BIA utilizing both hand and foot plates can additionally allow segmental measurements of conductivity, although different devices could result in different measurements with variable agreement between them (Bosy-Westphal et al. 2008; Demura et al. 2004; Jartti et al. 2000). Furthermore, equipment using different frequencies can discern between different body water compartments, since low frequencies (5 kHz) cannot penetrate cell membranes and thus correlates with extracellular water, while high frequencies (200kHz) penetrate cell membranes measuring TBW (Buchholz et al. 2004). The difference between both extracellular and total water can then be used to calculate intracellular water, if the equations and their predictions are to be believed. Thus, this last method is good for monitoring hydration in the clinical management of patients with certain conditions, mostly in the case of adults but more recently also explored in the paediatric context. Theoretically, if used with predictive equations, it could provide information on the direction of changes in LM, although not accurately quantifying the magnitude of the change

in LM or suitable to assess FM (Hosking et al., 2006; Pietrobelli et al., 2003; Wells & Fewtrell, 2006). However, this technique is not currently in routine use in paediatric patients.

Methods measuring both fat and lean mass

Dual-energy X-ray absorptiometry (DXA) has become more common in research studies on BC in children, although initially developed to assess bone mineral density with high precision in adults. It distinguishes between bone and soft tissue, and between lean and fat tissue in regions that do not contain bone. A whole-body scan has about 40-45% of the pixels in the image containing bone, so that the proportion of FM and LM is assessed in the remaining pixels and then generalised to the rest of the body. Since the trunk has a larger proportion of pixels obscured by the pelvis, spine and ribs (especially in lean individuals), tissue composition is largely predicted rather than measured, as opposed to limbs where more soft tissue pixels are unobscured by bone (Wells & Fewtrell, 2006). Although it is a relatively simple and easy technique to perform, the equipment might not be available in all clinical settings and the variability in equipment and software complicates the comparison of results, as does the hydration of the lean mass in some disease states, although this has a more moderate effect compared to BIA (Pietrobelli et al. 1998; Shypailo et al. 2008; Tothill, Avenell, & Reid 1994; Tothill et al. 1999). The technique does involve some radiation exposure, although this is considered to be minimal (Njeh et al. 1999) and is dependent on the device used and the patient's age (Cederholm et al. 2015).

Other methods of measuring BC using a 2-compartment model but that require more specialized equipment and are beyond the scope of this review or thesis, include magnetic resonance imaging and total body potassium.

1.5.3. 4-component model

To increase the precision of BC assessment, the 4-component model combines several techniques and divides weight into protein, fat, water and mineral. This minimises the assumptions made when using each of the previously-described individual techniques, such as the constant hydration of LM, and is therefore generally considered the gold-standard to assess BC *in vivo*. This model actually measures key body properties, resulting in accurate measurements of the density, hydration and mineralization of LM (Wells et al. 1999; Wells & Fewtrell 2006). Although more accurate than the other simple methods, it requires specialized equipment and is more time-consuming, meaning it is used in research rather than routine clinical management. Thus, several 2-component models and techniques have been compared to the 4-component model.

1.6. Limitations & new opportunities for BC measurements

Despite the range of techniques available to measure BC, this is not routinely assessed in most paediatric hospitals and clinical specialties. Recent international consensus statements (Cederholm et al. 2015; Cederholm & Jensen 2016; Becker et al. 2014) focusing on diagnostic parameters to be used in defining malnutrition have now begun to consider BC measurements, but still mention the perceived difficulty in implementing this in clinical practice and the prevailing uncertainty over which technique to use for the assessment of BC in individual patients (Elia 2013).

Moreover, there has been a historical lack of appropriate reference data in paediatric populations obtained by different techniques, and there is also limited evidence that routine measurements of BC can actually relate to clinical outcomes and can be used to improve the nutritional management of these children (Wells & Fewtrell 2006; Wells & Fewtrell 2008).

1.6.1. Validity of different techniques to assess BC

Air displacement plethysmography (BodPod), a technique used as part of the 4-compartment model, and TBW using stable isotopes have reported the best agreement to the gold-standard 4-component model. However, once more, routine assessment of BC using this techniques might not be feasible in clinical practice considering the need for specialised equipment and patient compliance (Silva et al. 2013; Zanini et al. 2015).

DXA has shown to have a good agreement for identifying children with abnormal SDS for both FM and LM (Zanini et al. 2015; Atherton et al. 2013; Cederholm et al. 2015; Wells et al. 2010). Thus, although it might still have limitations, it is generally considered the reference method technique for BC in studies, particularly in the clinical setting (Elberg et al. 2004; Cederholm et al. 2015; Eston et al. 2005; Eisenmann et al. 2004).

Although there have been several studies validating one technique to another in adults, children, and different conditions; studies are once more influenced by the choice of equipment, calculated parameters and analysis (e.g. reference used, use of predictive equations, reported as percentage or SDS) making comparisons difficult. In a study by Atherton et al. (2013) recently evaluated different techniques all using a standardised analysis for obtaining SDS from raw measurements of impedance (BIA), SFTs and DXA. In this study, BIA also showed a good agreement for LM assessment and in identifying individuals with abnormal scores compared to a 4-component model. Contrarily, BMI and SFT could reasonably predict abnormal FM scores but not absolute values of FM SDS, thus

suggesting they perform best when used for measuring adiposity in groups rather than individuals (Atherton et al., 2013).

Nevertheless, it should also be considered that the different BC techniques have their own advantages and limitations, and their use might be limited in certain settings or clinical conditions where measurements are not feasible or the assumptions of the technique are not valid (Wells & Fewtrell 2006; Cederholm et al. 2015).

1.6.2. New UK reference data for BC

Inconsistencies in how BC measurements are assessed are some of the main practical limitations to their use, as highlighted in the previous sections (Wells et al. 2012). Flexibility to choose between different BC methods, while still being able to compare between assessments by different methods, is important because hospitalized children have different mobility issues, isolation procedures and alerts, fluid shifts, among other conditions limiting the choice of technique; in addition to the availability of the equipment and trained staff (Atherton et al. 2013).

Reference data for paediatric BC in the UK has recently been published from 565 children aged 4-23yr using the 4-component model, as well as other techniques that might be more suitable in a clinical setting: BIA, SFTs and DXA (Wells et al. 2012). Thus, it is now possible to interpret individual BC measurements obtained by this range of techniques and obtain a SDS adjusted for age and sex, analogous to assessments using WT, HT and BMI. The study by Atherton et al. (2013) made use of this reference to obtain SDS adjusted for age and sex, comparing several of the more-simple techniques against the 4-component model in generally healthy children. They suggested that DXA, BIA and to a lesser degree SFTs and BMI, might be useful measurements in clinical practice, and thus will be investigated further in this thesis in a sample of paediatric patients with complex diagnoses.

1.6.3. Associations of BC to clinical outcomes

There is just limited evidence that BC measurements of fat and lean mass can predict clinical outcomes, and even less showing they can be influenced to improve on these outcomes (Wells & Fewtrell 2008). In adults, a study by Kyle et al. (2005) and Pichard et al. (2004) showed associations between low LM (and high FM) assessed using BIA were associated with increased length of stay. Associations with mortality on older adults have also been reported (Slee et al. 2016), and a study by Barbosa-Silva & Barros (2005) and Schiesser et al. (2009) showed associations to post-operative complications following gastrointestinal surgery. Evidence in children is much more limited. A study by Radman et al. (2014) reported

worse clinical outcomes in paediatric patients after surgery for congenital heart defects depending on total body fat assessed using SFTs. Associations between fat mass assessed with SFTs or DXA have also been associated with pulmonary function in children with Cystic Fibrosis (Chaves et al. 2009; Pedreira et al. 2005).

The few current studies on associations to clinical outcomes have several important limitations, as suggested in a review by Elia (2013). The range of population ages and characteristics, the different disease states, variety of BC measurements, predictive equations used, and calculated parameters all make it difficult to reach a consensus on the limited and sometimes conflicting evidence (Wells & Fewtrell 2008). The present study will take advantage of the available UK BC reference data for different techniques to assess associations between BC parameters and clinical outcomes using a systematic approach in sick children admitted to a tertiary level hospital with a range of diagnoses.

1.7. Screening for malnutrition in hospitalized children

National guidelines in the UK indicate all children should be screened for malnutrition on admission (Brotherton et al. 2010). Screening by the nursing staff should help identify those children who are malnourished on admission or at risk of developing this condition during their hospital stay, so they can be referred for a more comprehensive nutrition assessment and management (Aurangzeb et al. 2011; Joosten & Hulst 2014).

Malnutrition screening tools (MSTs) are composed of a series of scored questions that seek to quantify the risk of malnutrition by identifying the presence of risk factors (Cao et al. 2014). They generally assess 4 main domains (Kondrup et al. 2003; Joosten & Hulst 2014):

- The current condition ➔ nutritional status on admission
- Stability of the condition ➔ recent weight loss
- Condition likely to deteriorate during stay ➔ increased losses, reduced dietary intake
- Disease that might accelerate nutritional deterioration ➔ severity of the disease

MSTs should be simple, fast, cost-efficient, and require no nutritional expertise or comprehensive training. The scores from these individual questions are combined in a final score that classifies the patient into low, medium or high risk categories, with often assigned recommendations for referral or monitoring (Joosten & Hulst 2014; Kondrup et al. 2003).

1.7.1. Screening in paediatric patients: different tools and their characteristics

Although several MSTs have been developed and validated for adult populations, especially in the elderly, there are just a few validated tools for paediatric populations (Aurangzeb et al. 2012), and there is currently no consensus on what the ideal screening tool is for children admitted to hospital (Joosten & Hulst 2014).

Some of the available MSTs for children include the Paediatric Yorkhill Malnutrition Score (PYMS) developed in Glasgow, UK (Gerasimidis et al. 2010); the Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP) from Manchester, UK (McCarthy & McNulty 2008), and the Screening Tool for Risk of Impaired Nutritional Status and Growth (STRONGkids) from the Netherlands (Hulst et al. 2010) as outlined in Table 1.6.

MST	Population	Age	n	Aims		
				Identify nutritional status	*Need for nutritional intervention*	*Predict clinical outcome without intervention*
PYMS	Medical and surgical	1-16yr	247	✓	✓	✓
STAMP		2-17yr	110	✓	✓	
STRONG kids		1month – 18yr	423		✓	✓

Table 1.6. Paediatric MSTs and their characteristics

PYMS population excluded cardiac, renal, orthopaedic and critical care patients. Adapted from Joosten & Hulst (2014).

These three tools were developed for European paediatric populations (medical and surgical patients), are meant to be performed on admission to hospital and weekly for those patients with prolonged stays. Both PYMS and STAMP were developed to be used by nurses (Gerasimidis et al. 2010; McCarthy et al. 2012), while STRONGkids was meant to be completed by parents (2 of the domains) and junior/paediatric physicians, although it is used widely by dietitians and nurses (Joosten & Hulst 2014). They all use a scoring system to assign an overall risk score of ‘low’, ‘moderate’ or ‘high’. However, the allocation of points to each question/domain in the tool, as the maximum score, and cut-offs used to assign a risk category are all different (Hulst et al. 2010; Gerasimidis et al. 2010; McCarthy et al. 2012; Joosten & Hulst 2014). They also all recommend referral to a dietitian or nutrition team for individualised nutritional plan for those patients categorised as ‘high’ risk.

Although these tools consider similar domains for calculating the overall malnutrition risk score, they use different parameters/questions within each domain. Notably, to assess the current nutritional status of the patient, PYMS uses BMI (Gerasimidis et al. 2010), while STAMP uses weight and height measurements (McCarthy & McNulty 2008). STRONGkids uses a subjective evaluation by the clinician, as an anthropometric measurement is considered to constitute more nutritional assessment rather than screening (Hulst et al. 2010). Table 1.7. shows how each MTS compares to the described 4 main domains/principles for screening tools by ESPEN (Kondrup et al. 2003).

MST	Current nutritional status	Weight loss	Reduced intake	Disease severity
PYMS	✓	✓	✓	✓
STAMP	✓		✓	✓
STRONGkids	✓	✓	✓	✓

Table 1.7. Principles assessed by different paediatric MSTs
Adapted from Joosten & Hulst (2014), comparison to ESPEN principles for MSTs (Kondrup et al. 2003)

1.7.2. Applicability of MSTs in a hospital setting

A few studies report findings on the success of completing the MSTs on admission, especially in those studies validating the tools for the first time. STRONGkids had the highest reported success, being completed on 97.1% and 98% of approached patients (Hulst et al. 2010; Huysentruyt et al. 2013), while Gerasimidis et al. (2011) reported the PYMS questionnaire was completed in 72.3% of patients. The main reasons for failed completion were inability to take measurements of weight and, especially, height. This is a common reported problem in various hospital settings (Huysentruyt et al. 2013; Thibault & Pichard 2012) that in the case of PYMS is particularly relevant since it requires an objective assessment of nutritional status from BMI in the scoring system, while STRONGkids uses a subjective evaluation of nutritional status. Consequently, PYMS was also more successfully implemented in acute rather than specialized wards (75% vs 70%), where possibly more complex clinical conditions and procedures could interfere with accurate measurements of height and weight. Similarly, STAMP reported incomplete data from weight and height in 17.6% of assessed patients (McCarthy & McNulty 2008). Despite completion rates seeming high, these studies were conducted by the clinicians involved in their development and who tested the questionnaire in their own settings. Thus, a risk of bias and overestimating the success of implementation is possible.

In addition to the success of implementation, some of the initial studies also reported the views of dietitians and staff involved in the screening process. The study validating PYMS (Gerasimidis et al. 2011) reported all 6 dietitians agreed the tool could identify patients at risk of malnutrition that would have otherwise been missed, and found the action plan detailed by PYMS feasible. There was however, one report of increased dietetic workload and 2 reports of concerns that it might be overestimating the risk in acute patients. Although the authors conclude the tool is feasible overall, there is no sufficient detail on how they obtained these reports and whether the sample might have been biased, for example if the dietitians were somehow involved in the development of the tool or whether the characteristics between the responders and non-responders varied. Similarly, a study validating STAMP did describe the necessary training needed to be delivered to nurses in order to be able to complete the MSTs as "minimal", with reports that the tool was "quick to use and easily interpreted" (McCarthy et al. 2012), but other than this subjective assessment no more detail is provided.

Regarding the speed at which the tools could be completed, a study by Ling et al. (2011) reported STRONGkids was completed in 5 minutes, while STAMP was applied in 10-15 minutes. Once again, they report a likely cause for the additional time in STAMP is due to the need to perform anthropometric measurements (weight and height).

1.7.3. Reliability of MSTs

There are similarly a few reports on the reliability of the MSTs, most assessed in the initial validation studies. In terms of inter-rater reliability, Gerasimidis et al. (2010) compared the agreement between the nursing staff and dietitians for PYMS, showing a moderate agreement (kappa [κ]=0.53). STRONGkids reported a slightly higher inter-rater reliability of κ=0.61 (Huysentruyt et al. 2013) but no detail is given on the observer's previous training and knowledge on the tool. Since STRONGkids uses subjective assessment of nutritional status, there is a potential risk of bias depending on the characteristics of the observers. Similarly to PYMS, STAMP had had a report of κ=0.752 between nursing staff and dietitians (Wong et al. 2013), however this study was done in a very specific group of spinal cord injury patients that might not reflect the variability of a wider and more varied population.

Regarding intra-rater reliability, STRONGkids reports a high intra-rater reliability of κ=0.66 (Huysentruyt et al. 2013), while a study assessing STAMP reported a κ=0.63 (Wong et al. 2013).

1.7.4. Validation of MTS: concurrent, criterion and predictive

MSTs can be assessed in terms of their ability to predict clinical outcomes (predictive validity), the extent to which they agree with other tools (concurrent validity), or how they correlate to a gold standard assessment (criterion/diagnostic validity) (Joosten & Hulst 2014). Initial studies for STAMP, PYMS and STRONGkids assessed the new tools using different criteria (Table 1.8). A full summary of the available validation studies is found in Appendix 11.

	Criterion		Concurrent	Predictive	Other
	Sensitivity [a]	Specificity [a]			
PYMS	59%	92%	vs SGNA and STAMP		LM and FM [b] (discriminant)
STAMP	72%	90%			
STRONG kids	-	-		Length of stay	

Table 1.8. Initial validation of three paediatric MSTs

Adapted from Joosten & Hulst (2014). (a) vs full dietetic assessment, (b) assessed by impedance (foot-to-foot analyser, Tanita TBF-300) in >5yr and by arm anthropometry in <5yr (Gerasimidis et al., 2010).

Some studies have since assessed the concurrent validity between MSTs. Ling et al. (2011) reported a high agreement between STAMP and STRONGkids, with most high-risk patients being identified by both tools, with the difference that STRONGkids identified more patients as medium risk rather than high risk. This could be due to slight differences in the criteria of both tools, mainly the scoring of underlying condition and the subjective vs. objective nutritional assessment trough weight and height. Considering the study reports most differences occur within specific disease groups, however, it is likely this is due to the scoring of nutritional risk from the underlying condition.

Comparing STAMP to PYMS, agreement was reported to be κ=0.314 (Wong et al. 2013). This could be explained by the fact that these tools have more different criteria, mainly PYMS using BMI and including a question on whether the nutritional intake will be affected during their stay. Similar to the previous results, other studies showed a good agreement between STAMP and STRONGkids (κ=0.6), and a poor agreement of both tools to PYMS (κ=0.3) (Moeeni et al. 2012; Wiskin et al. 2012). The variety in patient populations, the consistency in the result patterns and the plausible explanations on the differences based on the scoring criteria seem to suggest these results could be expected in other populations. Nonetheless,

concurrent validity has limited use without the additional evidence on diagnostic and predictive validity, otherwise studies are simply comparing one tool to another without providing us with evidence on which might be a better alternative for certain situations.

There are some studies assessing diagnostic/criterion validity, but they take different approaches. Most use anthropometric measurements as diagnostic criteria of malnutrition, however, even with these measurements (commonly WFH, HFA and/or BMI for age) each study uses different reference data and cut-off criteria to define malnutrition, making comparison of different studies, even within the same MST and population, difficult. Furthermore, some use the calculated SDS while other use cut-offs for the diagnostic testing analysis. Recently, there has also been an increased use of BC, mainly assessed by BIA (Gerasimidis et al. 2011), but this has been scarcely tested. The available studies (Cao et al. 2014; Durakbaşa et al. 2014; Hulst et al. 2010; Huysentruyt et al. 2013; Ling et al. 2011; Mărginean & Pitea 2014; Moeeni et al. 2012; Spagnuolo et al. 2013; Wiskin et al. 2012) report a significant or nearly significant tendency for worst anthropometric indices or higher rates of malnutrition in the high-risk categories compared to low/medium risk. Nonetheless, here we come across another inconsistency between studies in that they group the 3 risk categories differently for the purposes to diagnostic testing and some even alter the scoring criteria of the tool. The large variation of these study variables makes it nearly impossible to clearly summarize and conclude on the ability of the MSTs to detect abnormal nutritional status.

Perhaps one of the most important components to assess the validity of the MSTs is how much they can predict and correlate to relevant clinical outcomes. Some studies have tested the predictive validity of STRONGkids against length of stay (LOS) and weight loss, although this last outcome proved non-significant in most cases (Huysentruyt et al. 2013; Cao et al. 2014; Hulst et al. 2010; Lama More et al. 2012). LOS seems to consistently be longer in those patients with higher risk of malnutrition, however LOS is quite a generic outcome and most studies do not report adjusting for confounding and thus bias in the results, especially important given these are observational studies. Recently, a study using STAMP also showed correlations with some clinical outcomes such as LOS, ventilation and organ dysfunction but this was done in a very specific patient group in the PICU (Cao et al. 2014).

A recent study (Chourdakis et al. 2016) validated these three MSTs in 12 European countries. The rates of completion were 86%; 84%: and 81% for PYMS, STAMP and STRONGkids respectively. The classification of children into the risk categories was different, showing an overall agreement of 41% between tools. With regards to criterion validity, 22% and 8% of high-risk patients by PYMS also had low scores for BMI (<-2SDS) and HFA respectively. For STAMP, this was 19% and 14%; while STRONGkids this was 23% and

19%. For all MSTs, high-risk patients had significantly longer LOS than children classified as low risk, staying on average 1.4 days for PYMS and STAMP, and 1.8 days for STRONGkids, but it was unclear how much of the associations could be explained by the underlying disease or as an effect of malnutrition. Thus, the authors could not conclude if one tool was superior to the other for assessing risk in paediatric patients.

Identifying malnutrition risk using these tools could have further implications in research and clinical practice. A recent study (PEPANIC trial) used STRONGkids to assess malnutrition risk in a sample of critically ill children in the PICU (Fivez et al. 2016). The results from the study showed that children classified as 'high risk' had a greater benefit (higher likelihood of earlier live discharge from the PICU) from delaying parenteral nutrition, than those classified as 'medium' or 'low risk'.

1.8. Summary of current knowledge and gaps

Overall, malnutrition in paediatric patients is a common finding in various countries and clinical settings, leading to poor short and long-term outcomes. Although it has been identified for several decades, its continued prevalence especially in clinical settings and in children with chronic conditions, has led to a renewed interest in finding better ways to identify and manage this condition.

It has been proposed that both nutritional assessment and malnutrition screening should be implemented with the purpose of reducing malnutrition in hospitalised children (Huysentruyt, De Schepper, et al. 2016). While nutritional assessment is aimed at diagnosing patients with malnutrition, screening has the purpose of also identifying children who are likely to develop malnutrition and that might benefit from nutritional intervention. However, there is still inconclusive evidence on the parameters that should be used to diagnose malnutrition, and the tools that would best identify those children at risk.

Diagnostic parameters have generally been informed by studies and practice in adults or community settings. However, hospital malnutrition in children poses unique challenges that might limit the use and validity of these commonly used measurements (weight, height, BMI), and thus measurements of BC have been suggested improve the diagnosis of malnutrition. Available evidence is still limited by differences in study design, where issues of patient population selection and differences in technique, references, cut-offs and analysis all make results between studies hard to assess. Moreover, despite recent consensus statements now considering the use of BC as diagnostic parameters, there is prevailing view that these measurements are difficult to obtain in clinical practice and uncertainty on which

technique(s) would be the best alternative. Similarly, studies of paediatric MSTs are still scarce, and available evidence is still not enough to recommend a particular tool for the assessment of malnutrition risk. In both cases, evidence on how implementing these diagnostic parameters and screening procedures could lead to improved clinical outcomes in hospitalised patients is lacking.

Thus, the present thesis work will look at assessing different standardised anthropometric and BC technique measurements with regards to the practicality, validity for the assessment of fat and lean mass, and their associations to clinical outcomes in paediatric patients with complex diagnoses. At the same time, the three paediatric MSTs will be compared in terms of their concurrent, criterion/diagnostic and predictive validity.

2 Research questions

The work in this thesis will explore the practicalities of measuring BC in paediatric patients, and whether the use of standardised BC measurements can identify children with/at risk of malnutrition and predict clinical outcomes better than simple weight or BMI. It will also contribute to the validation of three malnutrition screening tools in this population. The specific aims will be both methodological and clinical.

2.1. Methodological aims

1. Explore the practical aspects of using different anthropometric and body composition techniques in a tertiary paediatric hospital.
2. Cross-calibrate supine BIA measurements using a multi-frequency QuadScan to standing BIA measurements using Tanita, to allow SDS for LM to be calculated when the child cannot have a standing measurement performed.
3. Investigate the use of segmental bone measurements: ulna and tibia; as a proxy for height in those children in whom a standing height measurement cannot be obtained.

2.2. Clinical aims

4. Describe the body composition and other anthropometric parameters of children admitted to GOSH with a range of clinical conditions on admission and during their hospital stay, to quantify the prevalence of malnutrition and the factors associated.
5. Determine the best diagnostic parameter for malnutrition by examining whether baseline body composition expressed as absolute values or indices of fat and lean mass can predict clinical outcomes: length of stay (LOS), complications, and worsening nutritional status (NS); better than simple weight or BMI measurements.
6. Validate paediatric malnutrition screening tools: STRONGkids, STAMP and PYMS; by assessing how they relate to each other, baseline body composition, and clinical outcomes on discharge; and compare them to the use of body composition and anthropometric parameters in their ability to identify children at risk of malnutrition.
7. Explore the views of paediatric dietitians regarding the use of body composition measurements in routine clinical practice in the UK and USA.

3 General Methodology

Research aims 1-6 were investigated in a prospective study (BodyBasics study) recruiting paediatric patients on admission to a tertiary paediatric hospital. Aim 7 was investigated in a separate study using a mixed-methods approach that included semi-structured interviews and an online nation-wide survey as described in detail in Chapter 10. The following sections in this chapter describe the methods used in the BodyBasics study.

3.1. Subjects

3.1.1. Inclusion and exclusion criteria

Research aims 1-6 were investigated in patients recruited to the BodyBasics study. Children and their families were approached for recruitment after consultation with a member of their clinical team to ensure they fulfilled the following inclusion criteria:

1. New hospital admissions (within 48 hours).
2. Age ≥ 5 years, as this is the lower age limit for the new BC reference data (Wells et al. 2012) used in the study.
3. Likely to remain in hospital for 3 or more days, which was considered the minimum time required to possibly see a change in anthropometric/BC measurements.

Baseline measurements also needed to be obtained before any major procedure (e.g. surgery or administration of large volume intravenous fluids). The inclusion criteria were deliberately broad to cover as wide a spectrum of patients as possible, which was then expected to help identify potential patient groups to focus on for future research.

3.1.2. Setting: hospital wards & specialties

The BodyBasics study was conducted at the Great Ormond Street Hospital for Children NHS Foundation Trust (GOSH), a tertiary referral paediatric hospital in London, UK. All inpatient wards were targeted for recruitment. Considering GOSH is a tertiary-level hospital, all children admitted and approached for recruitment had been diagnosed with complex and/or chronic conditions and were admitted for diverse medical treatments, diagnostic or surgical procedures. Chapter 7 gives a more detailed description of the number of patients recruited from each ward. Towards the end of the study, recruitment was especially targeted for patients admitted for spinal surgery, Bone Marrow Transplantation (BMT), and to the

Cystic Fibrosis (CF) and Gastroenterology wards, as these were identified as the most common groups of patients recruited to the study and who might be especially interesting for subsequent sub-group analysis.

3.1.3. Patient recruitment & consent procedures

In the case of a planned admission (e.g. for elective surgery), study leaflets were sent in advance or the family was met in pre-assessment clinics to give them the opportunity to consider the study and ask questions before the child was admitted. The family was then approached following admission to confirm their resolve to participate. Eligible children in the case of unplanned admissions were identified from medical handover meetings and daily visits to each ward. After confirming with the medical team and ward staff that the patient could be approached, appropriate-age information sheets (Appendix 1) were provided and sufficient time (2 hours minimum) given for the patient and their family to consider the study and ask questions before deciding if they would take part.

Figure 3.1 shows the number of patients identified as meeting the eligibility criteria, those approached, recruited and completing follow-up measurements (at the moment of discharge). For the case of medical specialties/wards, considering recruitment had to be performed ward-by-ward throughout the hospital every morning, there was a chance some patients meeting the eligibility criteria could have been missed (e.g. if admitted last-minute or out-of-hours, if nursing staff did not inform the researchers on these new admissions). There was no documentation of the number of cases when this occurred, however, informal observations in the hospital electronic system of the patients per ward while following on the recruited patients throughout the study did not very often identify children who were not approached and who would have met the eligibility criteria. From those approached to take part in the study, approximately 60% were able to be enrolled in the study, with 58 patients refusing to take part and 47 patients interested in taking part but unable to be recruited on the present admission (usually due to conflicting medical procedures schedule) and the study finished before they were re-admitted and had the chance to be enrolled. A further 35 patients were missed by the time of hospital discharge (unplanned or out-of-hours).

To give consent, parents were asked to sign a consent form and verbal assent was taken from children under 12 years (yr) of age, while children 12-16yr were asked to sign an assent form. Patients 16yr and older could consent for themselves (Appendix 2). Consultants, ward managers and Dieticians were informed of the research in advance and had the opportunity to seek further information before the commencement of the study. Consultants could also

choose for their patients not to be approached for the study, although none expressed any objection.

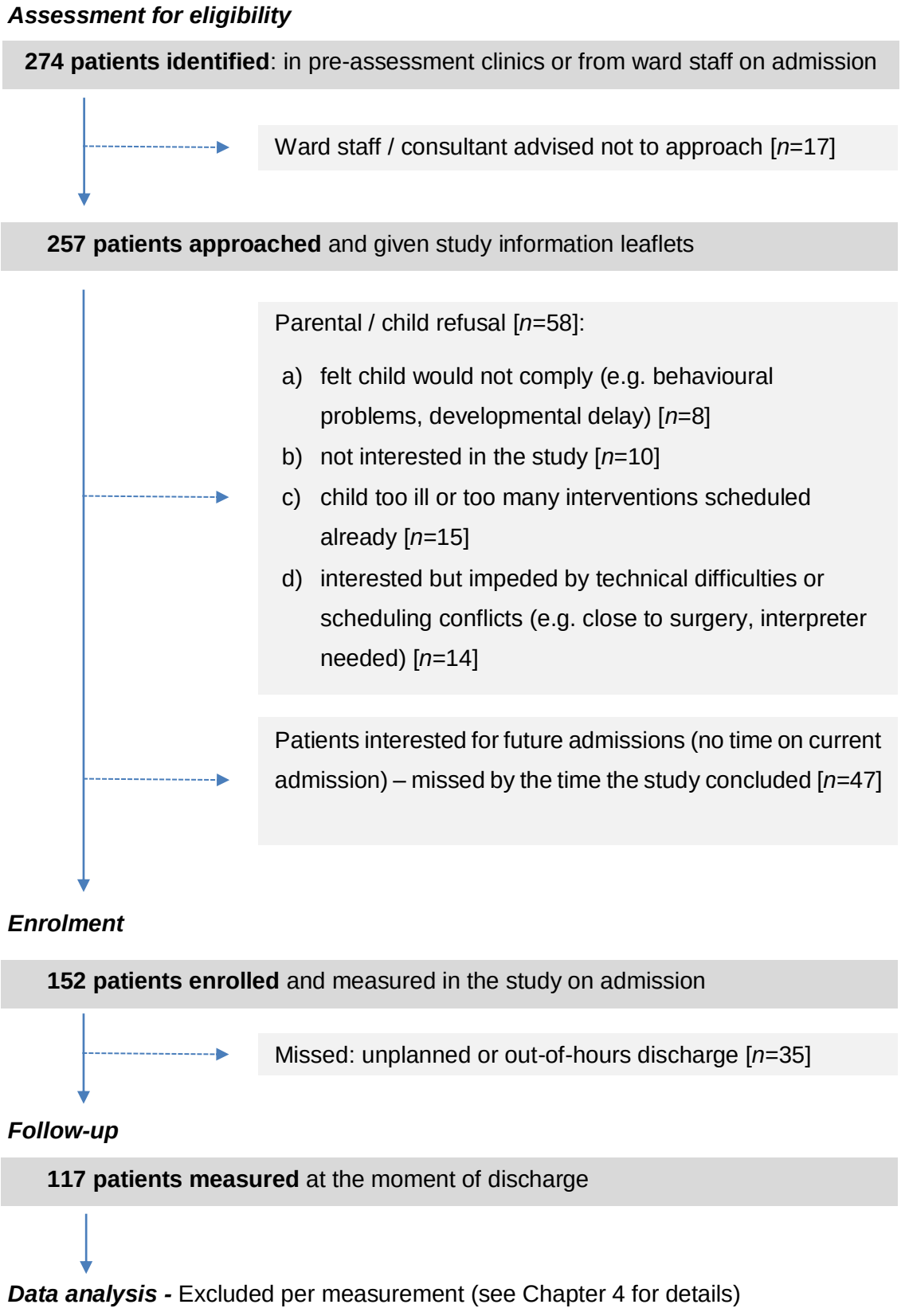


Figure 3.1. Flow diagram of patient recruitment and follow-up.

3.1.4. Sample size considerations

There were no published data on which to base a sample size calculation for the association between baseline BC and clinical outcomes such as LOS, and it was expected that this study would help generate data to inform the design and power calculations for subsequent research.

A Dutch study (Joosten et al. 2010) reported a 45% (±3.7%) increase in the duration of hospital stay for children with acute malnutrition (defined as weight for height <-2 SDS) on admission, compared to children without malnutrition. However, this study included children admitted to a range of different hospitals, both general and academic, and is therefore not strictly comparable to the situation at a tertiary hospital like GOSH. On the other hand, a single study using the PYMS screening tool reported a difference of 0.65 SDS in lean mass assessed by BIA between children classified as 'low' versus 'high' risk for malnutrition on admission to three medical and one surgical ward at a tertiary hospital and a paediatric ward at a local district hospital (Gerasimidis et al. 2010).

Given the lack of data on which to base a sample size estimation, the number of subjects required to detect a difference of 0.5 SDS (difference considered clinically relevant) between high and low risk malnutrition groups was estimated. Calculations were performed using Excel automated spreadsheets from the Epilab Centre for Applied Statistics (University College London, UK). Results (Appendix 9) showed that to detect a 0.5 SDS difference in BC between 'low' and 'high' risk groups using one of the MSTs, with an 80% power, assuming a standard deviation (SD) of 1.2 SDS in BC measurements (Atherton et al. 2013), 102 children needed to be recruited into both 'high' and non-high risk groups. From previous figures from a clinical nutrition audit at GOSH (Pichler, Hill, et al. 2014), it was estimated that approximately 20% of GOSH patients would be in the 'high' risk category. Adjustments for unequal groups resulted in a final sample size of 320 patients (64 'high risk' and 256 'non-high' risk). Based on this audit, it was also estimated that 20 children could be recruited per month. To allow for fluctuations in patient numbers, 18 months were initially allocated for recruitment, with a plan to review the proportion of patients classified as high risk as the study progressed.

Preliminary data analysis of 128 recruited patients who had completed the study by October 2014 indicated a greater proportion of the patient sample was classified as 'high' risk, with an average 30% depending on the MST used: PYMS 28%, STAMP 38% and STRONGkids 21%. Thus, the current sample could already detect the desired difference of 0.5 SDS with a 0.05 precision, also taking into account the observed SD of the measurements (1.0-1.2 SDS), with a power of 64-74%. Considering this new information and the remaining

recruitment time available, it was estimated that 150 patients could be included in the study by the end of the 18 months. Calculations showed that this final sample would have power of approximately 80% (PYMS 78%, STAMP 84% ad STRONGkids 71%).

Recruitment stopped with 152 patients after the 18 months allocated for data collection. The precision of calculated estimates and the power of statistical inferences was analysed retrospectively to detect any possible limitations due to the final sample size. Adjustments for multiple statistical testing were also performed (see Section 3.6).

3.1.5. Other study cohorts used in the analysis

Anonymised data previously collected for other studies undertaken by our research group, were used for part of the analyses in Chapter 5 and 6. Chapter 5 used anonymised data from a cohort of UK healthy children and CF patients at GOSH collected from February 2002 to 2012 (Williams et al. 2010; Wells et al. 2012). This data was used to corroborate the generalisability of the proposed adjustments obtained in the BodyBasics study. The cohort's characteristics and other specifics on the recruitment procedures are detailed in Chapter 5, Section 5.3.1. Chapter 6 also used the anonymised data from the healthy children cohort to obtain prediction equations for height from tibia length measurements. In addition, data from another healthy cohort (Fewtrell et al. 1999) was used to obtain prediction equations using ulna length. Chapter 6, Section 6.3.1 and 6.4 details the cohort's characteristics.

3.2. Study design

An overview of the recruitment and data collection stages for the BodyBasics study can be seen in Figure 3.2. The following data was collected from each patient enrolled in the study within 48 hours of admission (for collection forms see Appendix 3). Further details on each measurement technique and tool are given in a later section of this chapter.

- Basic anthropometry: weight (WT), height (HT), mid-upper arm circumference (MUAC) and head circumference (HC), and Body Mass Index (BMI) calculated from weight and height measurements. (Section 3.3.1)
- BC measurements: Dual Energy X-ray Absorptiometry (DXA), Bioelectric Impedance Analysis (BIA), and skinfold thicknesses (SFT; Biceps, Triceps, Subscapular, Suprailiac). (Section 3.3.2-3.3.4)
- Segmental bone measurements: ulna length, tibia length, and arm span. (Section 3.3.5)
- Measurement of grip strength as a parameter of muscle function (Section 3.5.3).

- Acceptability scales for each measurement technique performed. (Section 3.3.7)
- Malnutrition screening tools (MSTs): PYMS, STRONGkids and STAMP, plus the nutrition screening flow chart for Great Ormond Street Hospital for Children. (Section 3.3.8)
- Baseline data collection: age, sex, diagnoses, admission ward, predicted LOS, steroid prescription, fluid restriction, physical activity, current nutritional management and dietetic input. (Section 3.4)

The MSTs and baseline data was collected on all recruited patients, while the measurements (anthropometric, BC and grip strength) were obtained in as many patients as possible, as the study also aimed to assess the practicality of the different measurements.

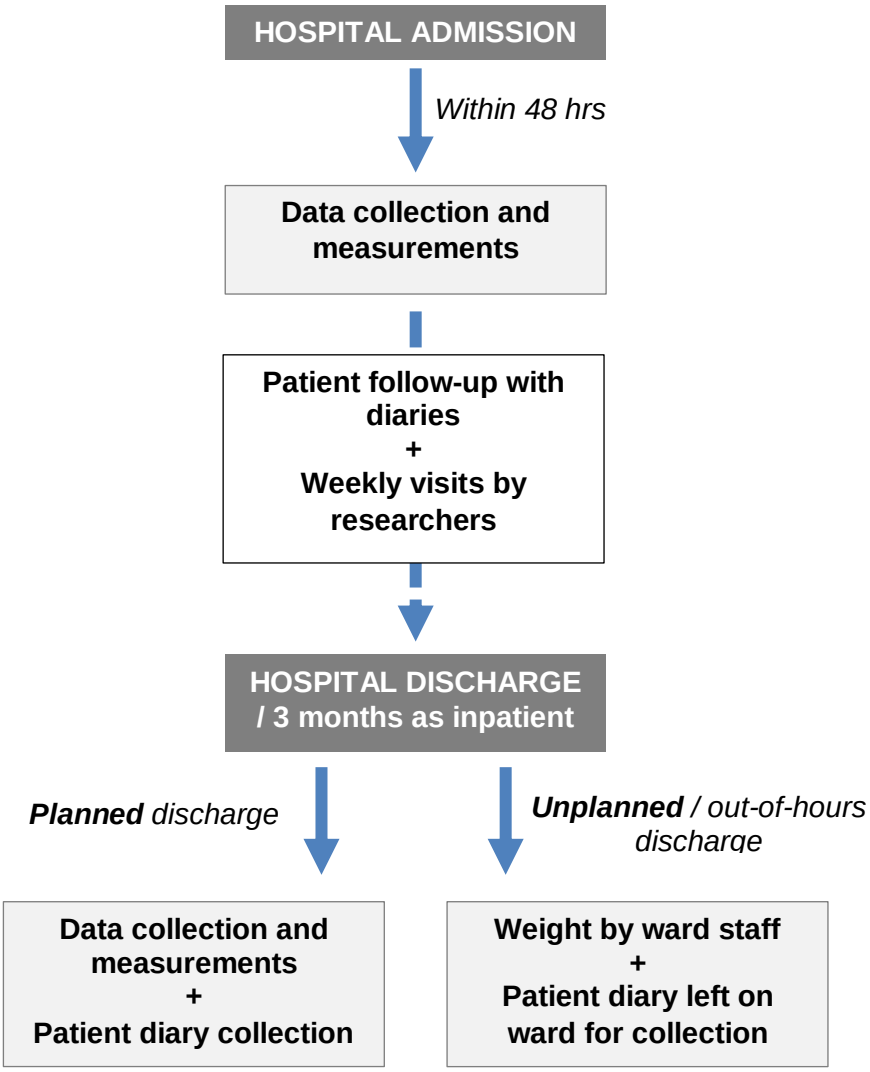


Figure 3.2. Overview of study design

A patient diary was left with the families to follow any changes during hospitalization that could impact the children's nutritional status by discharge. Patients and their families were asked to complete it every day for a week and on 2 days per week thereafter. Families were visited in the wards every week to collect the completed diary, resolve any uncertainties or mistakes, and distribute a new diary for the subsequent week. (Section 3.3.9)

The following data was collected at the moment of discharge or after 3 months if the child was still an inpatient:

- Basic anthropometry: WT, HT, MUAC, HC and BMI.
- BC measurements: BIA and 4-site SFTs; and grip strength.
- Acceptability scales for each of the techniques performed.
- Discharge data collection: duration of hospital stay, medical/surgical intervention(s), complications during stay, changes in steroid prescription, fluid restrictions, nutritional management and dietetic input during stay. (Section 3.4.5)

DXA measurements were only performed on admission. Although the technique involves some radiation exposure, this is almost negligible. The main reason for not repeating the measurement at discharge was that it was considered that any change in BC over such a short period would most likely be within the measurement error of the machine. Generally, measurements are not repeated within 6 months (for assessment of bone mass), unless a huge change is expected in which case the measurement might be repeated at 3 months.

When a patient discharge occurred last-minute or out-of-hours, ward staff were asked to weigh the patient and record the measurement on the cover of the patient diary, which was left in the ward for collection. In those cases, as much of the discharge data as possible (medical/surgical procedure, discharge weight or height, etc.) was obtained from the patient's medical notes.

3.3. Data collection & measurement techniques

Consent procedures and data collection were completed by 3 researchers, all of whom received training on how to perform the anthropometric and BC measurements using the same protocols prior to the start of the study. Additionally, all scales and stadiometers in the wards were audited to ensure they were up to date with maintenance and calibration. The results (Appendix 10) confirmed the equipment was calibrated per the hospital's guidelines, with only a few exceptions which were reported to the ward managers and remedied.

A previous study (Atherton et al. 2013) compared the extent to which different BC measurement techniques are interchangeable in diagnosing children with abnormal BC. This is an essential step in translating these measurements into clinical practice, since it is unlikely that a single technique would be available or suitable for use in all patients on all occasions. Their results demonstrated that DXA, BIA and to a lesser extent SFT measurements may be suitable candidates for monitoring BC in a clinical setting. Thus, these techniques were chosen to be investigated further in this study.

All the techniques used are considered non-invasive and harmless, however it was expected that some children would be unable to be measured by all the techniques due to isolation procedures, scheduled interventions, availability of access to the equipment, or parental/patient preference. Therefore, a record was kept of any measurements that could not be performed and the reasons why. Additionally, considering one of the study aims was to investigate how these measurements perform in everyday clinical practice, these were performed adhering to the protocols as much as possible but in cases where there was something minor impeding an optimal measurement (e.g. patient position, presence of cannulas or other devices obstructing access to measurement site), a record was kept of any changes in time or conditions of the measurements (e.g. right side, after large-volume infusions, etc.). When the data was analysed, statistical tests were re-run excluding these sub-optimal measurements to ensure they did not affect the final conclusions of the study.

3.3.1. Anthropometry: weight, height, MUAC and HC

WT was measured to the nearest 0.01kg using a standing, sitting or hoist electronic scale (Seca, Germany) found in the wards, or in the Radiology department just before performing the whole-body DXA scan. Children were measured in light clothes whenever possible, and asked to remove their shoes before performing 2 consecutive measurements.

HT was measured to the nearest 0.1cm using a wall-mounted digital display stadiometer (Seca, Germany) in the Radiology department, a Harpenden wall-mounted stadiometer (Holtain, UK) in the wards, or a portable mechanical stadiometer (Seca, Germany) which could be taken into the rooms of patients placed on isolation procedures. Again, children were asked to remove their shoes and stand with their backs to the stadiometer, their head placed in the Frankfurt horizontal plane, for 2 consecutive readings. Subsequently, BMI was calculated using the equation:

$$BMI\ (kg/m^2) = WT\ (kg) / HT^2\ (m^2)$$

MUAC and HC were measured in duplicate to the nearest 0.1cm with a non-stretchable fiberglass tape. To measure MUAC, the midpoint between the tip of the elbow (olecranon process) and the shoulder (acromion) was found with the subject's arm bent at the elbow at a 90-degree angle. The measurement around the left arm was then taken with the child's arm hanging loosely at their side. HC measurements were taken with the child's head in the Frankfurt plane, aligning the tape above the ears, mid-way between the hairline and the eyebrows, and on the occipital prominence in the back of the head (Bartram et al., 2005).

The mean of the two consecutive measurements taken for WT, HT, MUAC and HC was calculated and used for the subsequent statistical analyses. SDS for all measurements were obtained using the UK 1990 reference data (Freeman et al. 1995; Cole et al. 1995).

3.3.2. Skinfold thickness measurements

SFTs at four sites: biceps, triceps, subscapular and suprailiac; were obtained in triplicate to the nearest 0.2mm using calibrated skinfold calipers (Holtain, UK) on the left side according to the method described by Lohman et al. (1988). The mean for each set of measurements was calculated, and the SDS for each skinfold site was then obtained using the new UK BC reference data (Wells et al. 2012).

3.3.3. Dual-energy X-ray absorptiometry

Bone mineral content (BMC), FM and lean tissue mass (LTM; non-bone lean mass) were determined using a Lunar Prodigy scanner (GE Medical Systems, USA; using Lunar encore software version 6.7). Patients were asked to wear light indoor clothing with no removable metal objects and to lie in a supine position on the scanner for a single whole-body scan taking approximately 5 minutes, depending on the patient's height. Scans were only performed on those children who could be taken to the Radiology department, could lie down still for the required amount of time and did not have metal implants that could interfere with the measurement of bone mass. The radiation exposure (maximum 2 microSv) for a whole-body scan is calculated to be well below daily background radiation levels in the UK, and the precision of soft tissue analysis for a similar DXA instrument model (Lunar DPX-L) was reported to be 1% for LM and 2% for FM from repeated measurements on 4 successive days in adults (Kiebzak et al. 2000).

The amount of LM was calculated from LTM and BMC reported DXA values as follows:

$$LM\ (kg) = LTM\ (kg) + BMC\ (kg)$$

SDS for FM and LM were then calculated using UK BC reference data (Wells et al. 2012).

A study published by Wells & Cole (2002) highlighted the need to adjust BC measurements for body size in children, especially when making comparisons across different groups and within individuals/groups over time. Traditionally, FM has been reported as a percentage of weight (% FM), however few studies reported adjusted values for LM. The authors furthermore made the argument that %FM is still an unsatisfactory method, since changes in this percentage can be affected by changes in either FM or LM. An alternative approach is to normalise FM and LM using HT. If BMI is an index describing the WT relative to HT, WT can then be divided into components of FM and LM, so that:

$$BMI\ (kg/m^2) = \frac{WT\ (kg)}{HT^2\ (m^2)} = \frac{LM\ (kg) + FM\ (kg)}{HT^2\ (m^2)}$$

The fat mass index (FMI) and lean mass index (LMI) can thus be calculated as follows:

$$FMI\ (kg/m^2) = FM\ (kg) / HT^2\ (m^2)$$

$$LMI\ (kg/m^2) = LM\ (kg) / HT^2\ (m^2)$$

These indices, similar to BMI, are in familiar units and can be easily calculated in a clinical setting. However, the use of HT^2 for normalising BC is based on the relationship that WT has to HT, and might not necessarily reflect the relationships that FM and LM each have to HT. Based on their observations, Wells & Cole (2002) propose 3 approaches for normalising FM and LM values: 1) When groups or individuals of similar HT are being compared, the FMI and LMI using HT^2 can be used without further adjustment. 2) If the difference in HT between individuals or groups is small, LMI using HT^2 is usually suitable, while the expression of FM as FMI using HT^2 can be confirmed by regressing the HT and group variables on FM. 3) If the HT differences are large, LMI could still be accurate, but expressing FM adjusted by HT^2 would be inaccurate. The power by which HT should be raised to calculate the right index can be obtained by performing a log-log regression: $logFM = a + \beta(logHT)$, where β indicates the power by which to rise HT.

In this study, adjustments of BC measurements to size might be particularly important, considering many children admitted to GOSH have chronic conditions likely affecting their linear growth. FMI and LMI were thus calculated using HT^2 because: 1) the UK BC reference data used (Wells et al. 2012) had also been calculated in this manner, 2) these values are easy to calculate and more likely to be implemented in clinical practice. Nevertheless, Chapter 4 describes the results from approaches 2 and 3 as suggested by Wells & Cole (2002), exploring the most appropriate adjustments for the study population.

3.3.4. Bio-electrical impedance

Standing BIA (BIA_{st}) measurements were obtained using a Tanita Body Fat Analyser (model BC-418 MA, USA), using a constant current of 50kHz and electrodes placed on each hand and foot; resulting in a measurement of resistance in each extremity and the whole body. Patient age, sex and HT were entered before the measurements, the patient was asked to stand barefoot on the foot plates on the machine platform and hold two hand-grips for less than one minute; obtaining a single reading for whole-body raw impedance.

Supine BIA measurements are also commonly used in clinical practice, meaning it is important to determine if measurements from both methods are interchangeable or if adjustments are necessary, especially considering the UK BC reference data (Wells et al. 2012) was obtained using the technique/equipment described for BIA_{st}. Therefore, supine BIA measurements (BIA_{sup}) were obtained in the study using a Quad-Scan 4000 instrument (BodyStat Ltd, UK), a multi-frequency analyser utilising currents of 5kHz, 50kHz, 100kHz and 200kHz. Patient age, sex, height and weight were entered in the instrument and sticky electrodes placed on the left hand and foot, while the patient was lying down in bed. Two consecutive measurements were taken, each taking less than a minute to complete. The mean of the repeated measurements was calculated and used for subsequent analyses.

Only the raw values for whole body impedance (*Z*) for 50kHz were used for analysis, since the values reported for LM and FM by the machine are generated using equations that might not be population-specific and make assumptions that might increase the error of the measurement (Wells et al. 2012). The impedance index was calculated using the raw impedance from each BIA technique with the equation:

$$\textit{Impedance index } (HT^2/Z) = HT^2\ (cm^2) / Z\ (\text{ohms}, \Omega)$$

The impedance indices for both BIA_{sup} and BIA_{st} were then compared to the UK reference (Wells et al. 2012) to obtain SDS.

3.3.5. Segmental bone measurements: ulna, tibia and arm span

After the commencement of the study, it was apparent that a significant proportion of patients being targeted for recruitment had conditions interfering with the measurement of standing height. Considering many of the anthropometric and BC parameters being measured in the study made use of HT, different approaches for estimating height based on segmental bone measurements were explored as well (Chapter 6).

Ulna and tibia lengths were measured to the nearest 0.1cm by duplicate on the left side using a non-stretchable fiberglass tape. Ulna length was obtained by measuring the distance between the tip of the elbow (olecranon process) and the midpoint of the prominent bone of the wrist (styloid process) while the left arm was bent across the chest with the fingers pointing to the opposite shoulder (BAPEN 2003; Madden et al. 2012). Tibia length was measured from the knee to the ankle joints in the left leg while seated (Gauld et al. 2003; Yousafzai et al. 2003). The use of tape measurements was chosen as opposed to measurements taken with an anthropometer because most wards were not expected to have any specialized equipment available, and the aim was to find an easy way of assessing HT in everyday practice.

Measurements of half arm span, taken with a non-stretchable fiberglass tape from the tip of the middle finger to the midline of the sternal notch with the arm outstretched at a right angle to the body and palms facing forward (Yousafzai et al. 2003; Nestle Nutrition Institute 2001), were attempted but abandoned after it became apparent that most of the children with neuromuscular disorders who had problems with standing height were also unable to maintain the required position. Indeed, the position was challenging for many other children without neuromuscular conditions.

3.3.6. Cut-offs and dichotomisation of BC scores

Unlike a situation where the outcome is the presence or absence of a disease, there are no studies validating appropriate cut-offs for defining “normal” and “abnormal” BC in clinical practice. Thus, initially, values were treated as continuous variables using the calculated SDS for each anthropometric and BC measurement. In later analysis, however, ‘diagnostic accuracy tests’ were performed to determine the positive and negative predictive value of the measurements. To do this, the continuous variables were dichotomised using the somewhat arbitrary cut-offs of > 2SDS or <-2 SDS, since these are commonly used to indicate normality in clinical practice.

3.3.7. Acceptability scales

The acceptability of each BC technique was assessed either by the patient (if old enough) or by their parent using a continuous Likert scale (1-10cm), allowing for the statistical analysis of the resulting scores as continuous variables. The score was calculated as a percentage (0-100%), with 100% being the best possible score. These scales were completed on admission as part of the patient diary (Appendix 6) and repeated at the moment of discharge.

3.3.8. Malnutrition screening tools

The tools used to screen for malnutrition in the study were (Appendix 5):

- Paediatric Yorkhill Malnutrition Score (PYMS), Glasgow, UK. (Gerasimidis et al. 2010).
- Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP), Manchester, UK. (McCarthy & McNulty 2008).
- Screening Tool for Risk of Impaired Nutritional Status and Growth (STRONGkids), Netherlands. (Hulst et al. 2010).
- Nutrition Screening Flowchart developed for patients at Great Ormond Street Hospital (GOSH, UK).

These tools included questions such as the child's nutritional intake, current weight or BMI, weight loss, subjective appearance of malnutrition, increased losses and/or requirements, and risk associated with the underlying disease. PYMS, STRONGkids and STAMP assign a score to the patient based on these questions, which is then is used to classify them into 'low', 'medium' or 'high' risk categories, and 'high' risk patients are referred for dietetic management.

The GOSH flowchart, unlike the other MSTs, will simply refer the patient for dietetic management if any of the 3 questions included in the tool are positive: increased weight loss, increased losses or decreased food intake. GOSH hospital guidelines indicate this tool should be completed by the nursing staff as part of routine admission procedures for all children.

Data from the MSTs was analysed as categorical variables of 'low', 'medium' and 'high' risk, and subsequently as binary outcomes of 'high' risk and 'non-high' risk (in other words, referred for dietetic assessment or not), in which case the GOSH flowchart could also be included in the analysis.

3.3.9. Patient study diaries

Patients were given a weekly diary which contained 10 questions regarding food intake, intravenous fluids, losses and appetite (Appendix 6). Patients and/or their parents were asked to complete the study diary every day for 1 week, and 2 days a week thereafter. Two versions were designed for younger and older children, but both with the same questions and general layout. The younger children's version included stickers designed for the study with the days of the week to be included for each daily diary entry to encourage compliance.

3.4. Confounding variables

Data was collected on variables that were likely to affect the patient's nutritional status and could potentially confound the relationship of BC and anthropometric measurements to clinical outcomes. The variables and data collected on admission and discharge can be seen on the study data collection sheets found in Appendix 3. This section summarises the variables collected and used for data analysis.

3.4.1. Diagnosis and admission specialty

Information was gathered on admission regarding the patient's underlying diagnoses and the specialty/ward they were admitted to. The families were asked about the diagnoses and these were later confirmed from the patient's medical notes. Up to 5 diagnoses were noted for each patient, with the primary diagnosis later re-classified for summary purposes due to the large heterogeneity in the study sample (details in Chapter 7).

3.4.2. Steroid prescription

Patients were asked if they had received a 'high' or 'low' dose of steroids in the past 6 months. Where possible, additional information was collected on the steroid name, dose and frequency of administration. The collected data allowed for the calculation of 2 variables used in the statistical analyses:

- Steroid prescription: no, low dose/short term, high dose/long-term.
- High Steroid prescription: no, yes.

3.4.3. Dietary intake

To determine whether patients were meeting their nutritional requirements, their dietary intake was assessed in terms of: reliance on artificial nutrition – enteral nutrition (EN) or parenteral nutrition (PN), dietary restrictions, changes in appetite and food intake, and prior dietetic advice. To assess the patient's appetite, admission and discharge Likert appetite scales (Appendix 4) were used. The following variables were derived:

- Feeding mode: oral self; oral with carer's help; oral and EN/PN self; oral self and EN/PN with carer's help, oral and EN/PN with carer's help, EN/PN with carer's help.
- EN or PN feeding regime: none, partial or full feeds.
- EN or PN prescription: no, yes (partial or full).
- Differences in diet (restrictions): same as the family diet, minor differences only (e.g. food consistency), on a restricted diet (e.g. excluding whole food groups), on EN/PN feeds.

- Restricted diet: no, yes.
- Difference in appetite: difference and percentage difference between the appetite score at 1 week versus 6 weeks before admission.
- Loss of appetite before admission: no, yes.
- Restricted food intake: none, short-term nil by mouth (NBM) as preparation for a clinical procedure, long-term restriction due to medical condition.
- Prior dietetic advice (seen by a Dietitian) within the last 6 months: no, yes.

These variables assessed different aspects of the patient's diet (e.g. mode of feeding, amount, what was fed). Initial analysis and description of all these variables (Chapter 7) informed the selection for subsequent analyses (Chapters 8 and 9) as relevant indicators of the patient's dietary intake.

3.4.4. Fluid restriction

Patients were asked about any fluid restrictions prior to admission, as these could potentially affect the anthropometric or BC measurements, as well as impact the NS of the patient. The variables used for the analysis were:

- Fluid restriction: none, short-term NBM for procedure, long-term restriction due to medical condition.
- Restricted in fluid intake: no, yes.

3.4.5. Physical activity

Information about physical activity at the time of admission was collected with questions on whether the child was ambulatory or in a wheelchair, if he/she regularly took part is sports, and a parent's assessment on their child's physical activity compared to a healthy child of the same age. The calculated variables for the data analysis were:

- Activity level assessed by the parent: much less, less, same, more, much more.
- Activity level: wheelchair user with no regular physical activity, wheelchair user taking part in physical activity, ambulatory not taking part in sports, ambulatory taking part in sports.
- Wheelchair user: no, yes.

3.4.6. Variables on discharge

Patients were visited again at the moment of discharge from the hospital and/or study (if still inpatient after 3 months). Information was collected regarding any changes in the following variables during their hospital stay:

- Steroid prescription
- Dietary regime and fluid restriction

Additionally, patients were asked about:

- Treatment or medical intervention performed
- Complications (e.g. infections, delayed wound healing)

Where necessary, the patient's medical notes and/or a member of their clinical care team was consulted to clarify inconsistencies or ambiguity in the data collected.

3.5. Clinical outcome variables

The outcome variables for associations with baseline BC and MSTs scores were LOS, complications, decreased muscle function, and worsening NS. These outcomes were chosen, as opposed to more disease-specific clinical outcomes, because of the large heterogeneity of patients expected in the study, meaning these could be obtained from all patients regardless of their clinical condition. However, they also had the disadvantage of being affected by other clinical factors during hospitalization.

3.5.1. Length of stay

Considering the heterogeneity of patients, the absolute LOS in hospital was also expected to be highly variable, thus complicating its analysis. Hence, the actual number of days spent in hospital noted on discharge was compared to the predicted LOS on admission. Predicted LOS on admission was based on the judgement of the clinical team and standard times for scheduled procedures (e.g. a 'standard' LOS for patients undergoing posterior spinal fusion was 2 weeks). This information was collected from the hospital's medical records on admission (PiMS), which specifies an expected discharge date for all patients admitted to the hospital, and corroborated with a member of the patient's clinical team. This approach allowed the LOS to be analysed as continuous (difference and % difference),

categorical (‘shorter than expected’, ‘expected’, or ‘greater than expected’), and binary (‘greater than’ or ‘equal/less than’ expected) variables.

3.5.2. Complications

Data was collected on patient ward/hospital transfers, artificial nutrition prescription and fever/infection episodes. A patient was considered to have experienced ‘complications’ during their stay if they had any of the following: 1) were transferred to the Intensive Care Unit or to their local hospital rather than discharged home, 2) had an unplanned increased reliance on artificial nutrition (EN and/or PN) to meet their nutritional requirements during their stay, 3) had reported periods of fever or infection treated with antibiotics.

3.5.3. Decreased muscle function: grip strength

Two consecutive repeated measurements of grip strength using a Takei 5401 Digital Dynamometer (Takei Scientific Instruments Co. Ltd., Japan) were taken at the moment of admission and discharge along with all the other anthropometric and BC measurements. Patients were asked to stand and hold the dynamometer with their dominant hand, their arm relaxed by their side, and squeeze it as hard as possible and hold for a couple of seconds. When the patient was unable to use the dominant hand (e.g. due to IV insertions or wounds to the hand/arm), the measurement was taken with the other hand and a note made on the data collection forms regarding the change to the protocol conditions. The mean of both repeated measurements was obtained and compared between admission and discharge to determine the difference (in kilograms-force, kgf; and as a percentage). Subsequently, categorical (‘same’, ‘increased’ or ‘decreased’) and binary (‘decreased’ or ‘not decreased’) variables were calculated.

3.5.4. Worsening nutritional status

Worsening NS during hospitalisation was assessed by the difference in measurements at discharge compared to admission for the following parameters: WT, BMI, and BIA. Variables were treated as continuous numeric (difference and % difference), categorical (‘same’, ‘increased’ or ‘decreased’) and binary (‘decreased’ or ‘not decreased’).

Figure 3.3. below summarises the variables and parameters measured in the study and how they relate with the pathophysiology of malnutrition as discussed in Chapter 1. While information on LOS and complications was recorded for all patients, the anthropometric and BC measurements and grip strength was obtained in a variable number of patients on admission and on discharge.

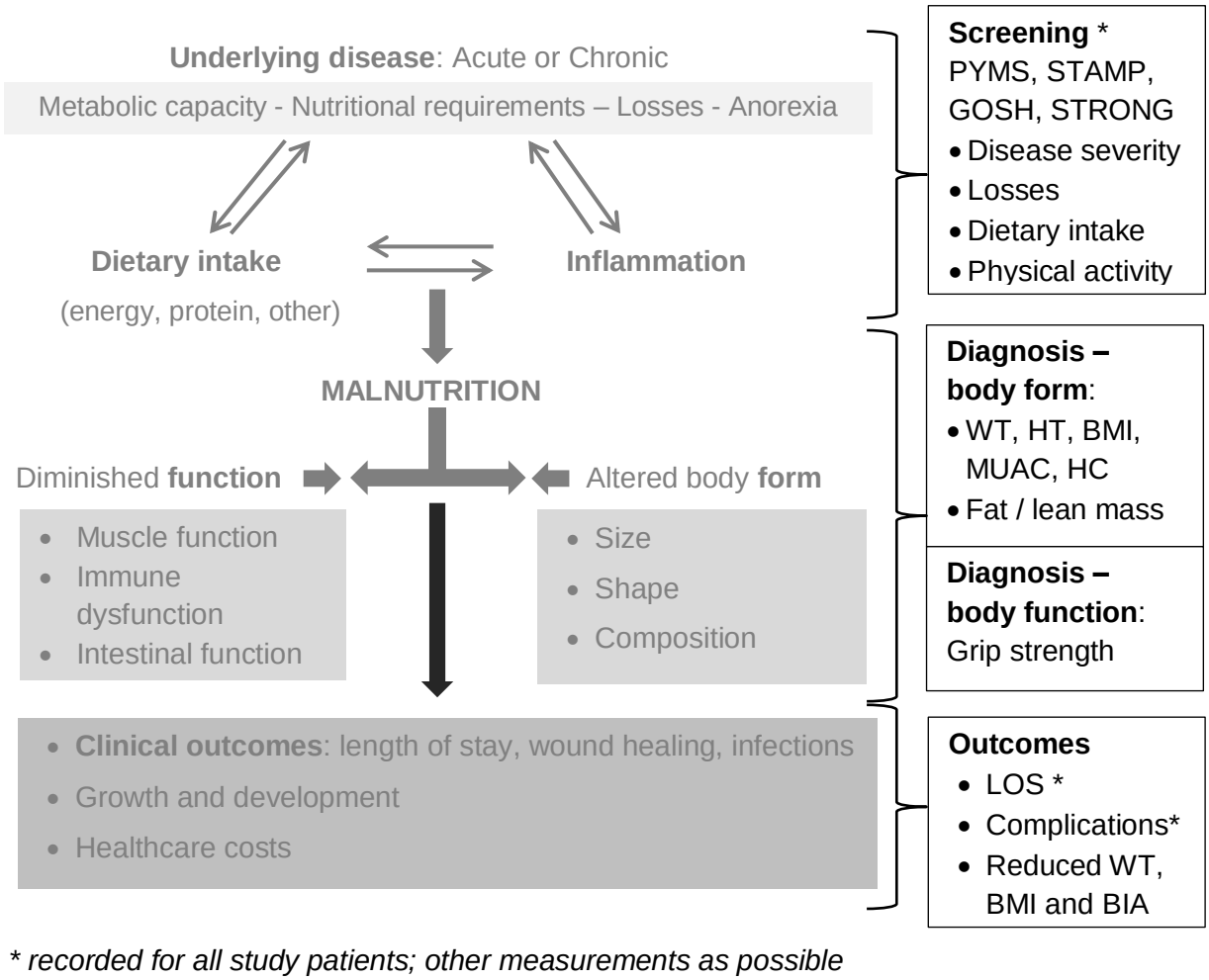


Figure 3.3. Screening, diagnostic parameters and other variables collected in the study with regards to the pathophysiology of malnutrition

3.6. Statistics & data analysis overview

The initial statistical plan included an analysis of the complete patient dataset, and subsequently by individual patient groups. However, the spectrum of patient groups (details on Chapter 7) enrolled into the study was so diverse that this approach was subsequently considered unfeasible. Most patients had multiple and often unique diagnoses and the numbers in each individual diagnostic group, even after re-categorisation, were too small for sub-group analysis. The variable “Admission group” was calculated to broadly categorise patients into medical and surgical admissions, and the different parameters (e.g. steroid use, diet, physical activity) that could influence the predictors and outcomes were adjusted for in the analyses. Some general considerations regarding the reporting of data and statistical tests are outlined below (further details within each result chapter).

3.6.1. Data summary and associations

Data was tested for normal distribution using plots and the Kolmogrov-Smirnov and Shapiro-Wilk (with Lilliefors correction) tests. Descriptive statistics were presented for each anthropometric and BC measurement. Categorical data were presented as frequency and/or percentage. Continuous data was presented as mean and 95% confidence interval (*CI*) or median and inter-quartile range (*IQR*), depending on the distribution of the data. SDS for each anthropometric and BC variables were presented as continuous variables and as categorical/ binary, with SDS <-2 or >2 taken as the cut-off points to indicate abnormality. Relationships between variables were analysed using statistical tests with a 5% level of significance (p<0.05), unless otherwise indicated. Usually, both the parametric and non-parametric tests were run in parallel to make sure there was no difference due to the data distribution. When the resulting *p*-values between the parametric and non-parametric tests differed, the non-parametric was reported and this was indicated in the results.

3.6.2. Validity testing of techniques

Agreement between techniques or tools was assessed for continuous numeric variables using Bland Altman analysis. The mean bias (*MB*), upper limits of agreement (*ULOA*), lower limits of agreement (*LLOA*) and their respective 95% *CI* were calculated as described in the original papers by Bland & Altman (1999; 1986):

$$LOA = MB \pm 1.96 * SD_{\text{mean bias}}$$

$$95\%CI_{\text{mean bias}} = MB \pm 1.96 * SE_{\text{mean bias}}, \text{ where } SE_{\text{mean bias}} = SD_{\text{mean bias}} / \sqrt{n}$$

$$95\%CI_{LOA} = LOA \pm 1.96 * SE_{LOA}, \text{ where } SE_{LOA} = \sqrt{(3 * SD^2_{\text{mean bias}})} / n$$

The *MB* was tested for significance (one sample t-test, H_0: *MB*=0) and the effect of the magnitude on the differences between tools was assessed by calculating the significance of the Pearson's correlation coefficient (*r*). If significant, adjustments to the *MB* and limits of agreement (*LOA*) were performed using linear regression models with the difference as dependent variable and the mean as independent. The SD of the residuals was then used to calculate the new *LOA*. Unstandardized residuals were then regressed to the mean to confirm the variance was constant along the regression line and no further adjustment was needed.

Agreement between categorical variables was tested by calculating the % agreement and Cohen's kappa (κ), where a value of 1 indicates perfect agreement between techniques. The *p*-value for kappa was calculated and interpreted in terms of its clinical rather than purely statistical significance, as suggested by McHugh (2012).

3.6.3. Reliability of techniques

The reliability of each technique was determined by calculating the Intraclass correlation coefficient (*ICC*) of repeated measurements. Additionally, the mean difference between repeated measurements was calculated using an analysis derived from the same principles of Bland Altman analysis of differences between techniques (Myles & Cui 2007). The repeatability coefficient (*CR*) was calculated as follows:

$$\text{Repeatability coefficient} = (1.96\sqrt{2}) * SD_{differences}$$
$$= 2.77 * SD_{differences}$$

The effect of measurement magnitude on the mean difference between measurements was also tested using correlation analysis. If the *r* was significant, both the mean measurement and mean difference variables were included in a linear regression model and the SD of the residuals used to calculate the *CR* using the equation described above.

3.6.4. Regression models and other general considerations

The predictive value of baseline anthropometry, BC and MSTs for later clinical outcomes was assessed using regression models. These parameters were entered into the models both independently and in combination; adjusting for sex, age, admission group and other confounding variables (Section 3.4) suggested to be significant from the univariate analyses. Univariate analyses included correlation coefficients, one-way ANOVAs, independent samples t-tests, and chi-squared tests; or their non-parametric equivalents depending on the data distribution and nature of the variables being tested.

Corrections for multiple testing (Bonferroni correction) were considered to adjust the level of significance in those cases where multiple outcomes were being tested simultaneously (Bender & Lange 2001). However, most of the analyses performed involved many independent parallel tests rather than inclusion of numerous predictive variables, making it unclear if this adjustment is strictly necessary. Thus, the corrected *p*-value for the new significance level (*alpha* / # of variables tested) is considered when interpreting the results, but not used as a rigid new cut-off point. Instead, when possible the exact *p*-value was reported to allow for a more flexible interpretation of the significance.

SDS for BC and anthropometric variables were calculated in Microsoft Excel, using the LMS Growth add-in function (LMS Chart Maker, Medical Research Council, UK). Statistical analysis was performed using SPSS Statistics 21.0 software (SPSS Inc., USA).

3.7. Ethical considerations

Participation in the study BodyBasics study was completely voluntary and the children and their families received no financial incentives or compensation for taking part. Patients were given a certificate of appreciation (Appendix 7) for their participation on the study. The patients were transferred when possible to the Radiology department and later to a room within GOSH, designated for research measurements on body composition, accompanied by a parent or guardian. When transfer was not possible, measurements were performed in the admission ward using bed-side techniques only. Data collection and measurements took an average of 45 min-1 hr depending on the number of measurements being performed and the patient's clinical condition. Times and schedules for consent procedures, measurements and other data collection were planned to cause as little discomfort as possible to the patient and their families, and avoid interference with any planned medical procedures and clinical care.

3.7.1. Ethical approval and consent procedures

Ethical approval for the BodyBasics study was granted by the NRES Committee London-Central (Appendix 8). After approaching the patients and their families, enough time was given for them to consider the study (1-2 hrs). Age-appropriate consent forms were signed by the parent and/or child prior to data collection (see recruitment procedures 3.2.3). A signed copy was kept in a secure file cabinet within the Dietetics department at GOSH, a copy was included in the patient's medical notes, and another given to the families.

Ethical approval for the mixed-methods study (Aim 7) was granted by the University College London Research Ethics Committee (Chair's action) (Appendix 8). Consent procedures and other ethical considerations are detailed in Chapter 11. Face-to-face interviews followed appropriate consent procedures, while the online survey data collection was set-up to allow implied consent by completing the anonymised questionnaire.

3.7.2. Data protection & confidentiality

Collected data was treated per UK Data Protection Act and stored in a secure location within the GOSH and /or Institute of Child Health, University College London. The first page of the data collection forms containing the patient's personal data was kept together with their consent form(s) in a secure location requiring badge access within the Dietetics department at GOSH. The rest of the collection forms containing anonymised data were scanned and the originals kept in a locked cabinet in a floor requiring badge access at the Institute of Child Health. All data analysis and reporting from this point forwards was done using the electronic anonymised data to maintain the patient's confidentiality.

4 Measuring body composition in paediatric patients: practical aspects and validation of different techniques

4.1. Introduction

The measurement of body composition (BC) can be undertaken by a range of different techniques. As Chapter 1 describes, these vary from simple anthropometric measurements estimating BC from different body properties, to more complex multi-technique methods used almost exclusively for research purposes. The 4-component model (4C model), while largely considered the best approach for measuring BC, is generally unsuitable to assess this in non-research settings due to its complexity, the time, equipment and resources needed; as well as the conditions the subjects need to fulfil to perform the measurements. Thus, studies have focused on validating the use of more simple techniques to assess FM and LM and determining if the different techniques could be used interchangeably (Aguirre & Salazar 2014; Fuller et al. 2001; Williams et al. 2006).

Currently, the measurement of BC in paediatric clinical practice is not routinely undertaken, due in part to an uncertainty over which technique(s) would be most suitable to assess the FM and LM of individual patients (Cederholm et al. 2016). Most validation studies of these 'simpler' techniques have been performed in healthy children or adults, making it difficult to know how they could translate to children with complex diagnoses (Ejlerskov et al. 2014; Hosking et al. 2006). In addition, they often validate a single technique at a time and use a range of different approaches to handle the measurement outputs; which can still leave the reported bias between techniques influenced by issues such as age, sex, body size, and disease state (Alicandro et al. 2015; Lintsi et al. 2004; Michels et al. 2013).

With the publication of BC reference data obtained from healthy UK children (Wells et al. 2012), SDS can be calculated from measurements performed by a range of techniques, providing a way to consistently assess how different methods perform. A study by Atherton et. al (2013) validated several techniques against the reference method 4C model in a group of healthy children and patients (mostly children with Cystic Fibrosis) using this reference data, and concluded that DXA was the most accurate and precise method to assess FM and LM. However, the authors noted that the limits of agreement for both FM and LM SDS were still fairly wide, and DXA should therefore not be considered interchangeable with the 4C model, especially in subjects with low FM. Despite this caution, because these limits of agreement were the lowest of any of the tested techniques, and considering it performed well

for identifying subjects with abnormal FM and LM SDS (> 2SDS, <-2 SDS), they conclude DXA would be the best technique to use in clinical practice when the 4C model is unfeasible. Thus, despite its limitations, DXA was selected as the clinical reference method for BC measurement in this study (BodyBasics study).

Regarding BIA comparison to the 4C model for the assessment of LM, the results were similar to those observed for DXA LM across all patient groups, performing at its best in normal and overweight children (Atherton et al. 2013). For FM assessment, other techniques that could identify children with abnormal SDS, although performing poorly to assess FM in individual patients, were measurements of BMI and Triceps SFT. Results overall suggested the agreement between techniques performed differently in healthy children, obese and underweight patients (Atherton et al. 2013). Thus, further analysis into how these measurements perform in a diverse group of patients might be useful for translation into clinical practice.

In addition to the validity of the different techniques, if BC measurements are to be implemented in routine practice in the future, their use in a clinical setting must also consider aspects of acceptance and practicality, since several issues related to the patient's condition (e.g. mobility, fluid shifts, metal implants, contractures) and the setting (e.g. time constraints and scheduling conflict from other medical procedures) could interfere with the measurements. Considering not all techniques might be suitable for all patients at all times, it is important to identify which are acceptable and practical in different situations and the likely barriers to their use.

Thus, this chapter will explore the practicalities and validity of different anthropometric and BC techniques, identified as possible suitable candidates in clinical practice (Atherton et al. 2013), in a diverse sample of patients with complex diagnoses admitted to a tertiary paediatric referral hospital.

4.2. Chapter objectives

1. Determine the acceptability of the different anthropometric and BC measurements when performed on admission and/or discharge, and analyse any change in scores to establish if repeated exposure to the techniques might improve or decrease their acceptance.

2. Explore the practicality of the different anthropometry and BC techniques on admission, by recording successful measurements and reasons for refusal or failed measurements.

3. Measure the reliability of techniques, where repeated measurements were performed on every patient.
4. Corroborate the validity of more 'simple' BC techniques to assess FM and LM, using DXA as the clinical reference method.
5. Establish the optimal adjustments for FM and LM to normalise for body size (remove the effect of height), and the suitability of fat and lean mass indices in the study population.

4.3. Methods

4.3.1. Study population and recruitment

The chapter objectives were investigated using data collected from patients enrolled into the BodyBasics study at Great Ormond Street Hospital. Children 5-18yr old admitted to any inpatient ward were approached for recruitment to the study, provided a member of their clinical team confirmed it was acceptable to talk to the family and that no major medical procedure had already taken place (e.g. surgery, start of chemotherapy, dialysis or other large-volume infusions). Details on patient recruitment and consent procedures are further described in Chapter 3, Section 3.1.

A total of 152 children were recruited to the study, and 64% of them were also able to be approached at the time of hospital discharge. The study population was evenly distributed between admission groups (medical and surgical) and male/female (details in Chapter 7).

4.3.2. Data collection tools

Patients were asked to complete acceptability scales for the different techniques on admission and discharge, and a record was kept with details on any measurements not completed or those performed under sub-optimal conditions (unable to be taken according to the protocol). Measurements of WT, HT, MUAC, HC, grip strength, 4-site SFTs, BIA and DXA were performed on admission on all patients where possible. All techniques, apart from DXA, were repeated at the moment of discharge. A description of each technique, as well as the acceptability scales and other data collection tools relevant to this chapter can be found in Chapter 3 Section 3.3, and Appendices 3 and 6. The measurement protocols and handling of technique outputs were performed in a similar manner to that reported for the UK BC reference data (Wells et al. 2012) and the study by Atherton et al. (2013).

4.3.3. Data analysis and statistics

All data was analysed for normal distribution, summarised using mean and SD or median and interquartile range (*IQR*), and either parametric or non-parametric inference tests as appropriate. The obtained measurements by each of the BC techniques were used to calculate SDS as described in Chapter 3 (Section 3.3) using the UK 1990 reference data (Freeman et al. 1995; Cole et al. 1995) for anthropometric measurements (including BMI), and the UK BC reference data (Wells et al. 2012). The cut-offs ±2SDS were also used to calculate the categorical variables for 'abnormal' SDS: 'normal', '≤ -2SDS', '≥ 2SDS'.

The acceptability score (0-100%) for each technique (details in Chapter 3, Section 3.3.7.) was described on admission and discharge, and any changes assessed using paired samples t-test. The percentage of patients giving an unfavourable score on admission and discharge, defined as a score ≤50%, was also described; as was the percentage of patients changing their scores between admission and discharge by ≥10%.

The reliability of techniques in which repeated measurements were performed: WT, HT, MUAC, HC and 4-site SFTs; was evaluated with *ICC* testing and by calculating the Coefficients of repeatability (*CR*) (details in Chapter 3, Section 3.6.3). For SFTs, where 3 repeated measurements were performed, the first and second measurements were used for the *CR* calculations.

The validity of the techniques was tested by comparing the agreement of the more 'simple' techniques to DXA, defined as the clinical reference method for measuring FM and LM in this study. Numeric variables (each technique SDS) were assessed using Bland-Altman analysis of agreement, and categorical variables ('abnormal' SDS) tested with absolute % agreement and Cohen's kappa (Details in Chapter 3, Section 3.6.2).

The optimal adjustments for removing the effect of height in fat and lean mass measurements was also explored using the approach detailed by Wells & Cole (2002). The suitability of expressing FM and LM as fat mass index (FMI = FM/HT^2) and lean mass index (LMI = LM/HT^2) to account for height in the study sample was tested by regression analysis, and subsequently a log-log regression of height to FM and LM was performed to find the optimal power by which both parameters should be raised in the study sample (further details in Chapter 3, Section 3.3.3).

4.4. Acceptability of techniques

Most of the anthropometric and BC techniques performed in the study had a good acceptability in the patient cohort. Figure 4.1 shows the median score and *IQR* for each technique on admission and at the moment of discharge.

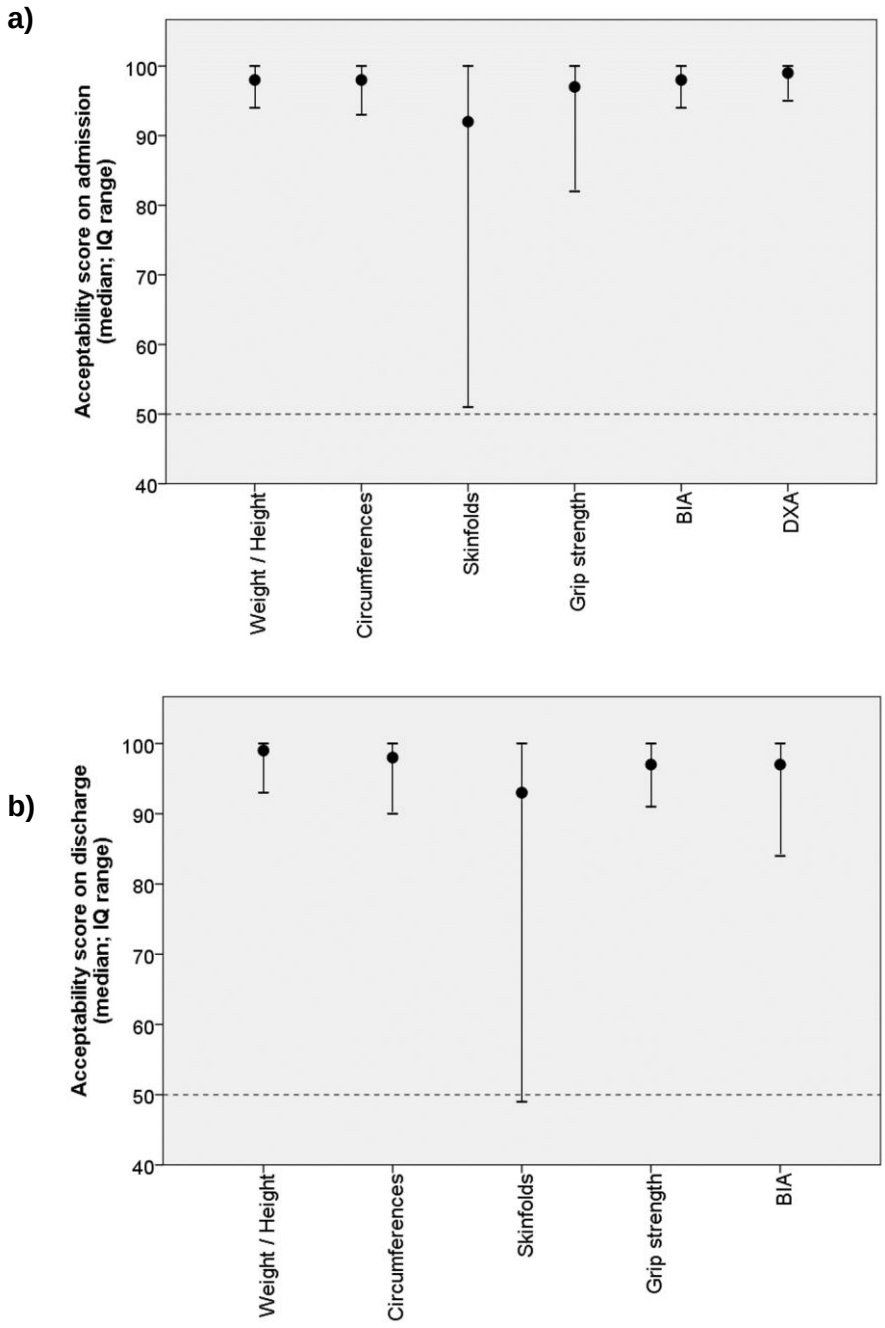


Figure 4.1. Acceptability scores for techniques on admission and discharge

Graphs show median score (0-100%, where 100% corresponds to the best score) and interquartile range. Dotted line indicates cut-off for an unfavourable score (<50%). (a) admission; (b) discharge

Measurements of acceptability at the moment of discharge showed a similar pattern, although with a wider spread and lower inferior-limit ranges than on admission. It should be considered however, that the measurements were performed just before discharge when families and patients were often keen to get home and children were often in more discomfort post-surgery. Additionally, the number of patients completing the measurements and acceptability scales was much lower than on admission (approximately 30 vs 100).

When considering the number of patients who gave an unfavorable score on admission, as can be seen in Table 4.1, SFTs had a much higher percentage of negative scores (25%) compared to the other techniques, where this was rare (4-9%). As can be seen from the *CI*, it is expected that between 17% and up to 33% of all admitted patients in the population could be uncomfortable with SFT measurements on admission. For all other techniques, this is only expected to happen in less than 15% of admitted patients.

Once again, the pattern is not much different for measurements on discharge. However, while the percentage of unfavorable scores decreased slightly for most techniques, those for SFTs and BIA increased. This resulted in 14% of unfavorable scores for BIA, and 29% for SFTs. It should be noted that although the number of unfavorable BIA scores increased by discharge, most of these negative scores were close to the 50%-score cut-off mark, whereas for SFTs some of the scores were extremely low (close to 0%). Once again, the reduced sample on discharge must be considered as it could affect the precision of the estimates, especially for BIA and the SFTs.

	Admission				**Discharge**			
	n [a]	*%* [b]	*CI* [c]		*n* [a]	*%* [b]	*CI* [c]	
WT/HT	105	4	0	7	40	3	0	7
Circumferences	109	7	2	12	36	3	0	8
SFTs	100	25	17	33	28	29	12	45
Grip strength	100	9	3	15	34	3	0	9
BIA	99	5	1	9	35	14	3	26
DXA	83	7	2	13	-	-	-	-

Table 4.1. Unfavourable acceptability scores on admission and discharge

(a) Number of patients completing the acceptability scales – sample size; (b) Percentage of patients giving an unfavourable score (<50%); (c) 95% CI for the percentage of patients giving an unfavourable score.

When the changes in score between admission and discharge were analysed, the significance tests showed no difference between them (Table 4.2), although the power to detect significant differences was low for some measurements (e.g. Power of 45% for SFTs). For WT/HT and circumferences, the large majority of patients did not change their score and the few that did were evenly spread between higher and lower scores. For BIA, a higher percentage (34%) changed their scores but again this was evenly distributed between improvements and decreases in scores. Contrarily to the other techniques, scores for SFTs showed a greater change (40% of patients changed their scores) and a higher number of children gave a worse score by discharge. This suggests that repeated exposure in this limited timeframe might not necessarily improve the acceptance of this technique.

	n	**Differences in score**		**Change in score** [c]	
		Mean difference [a]	*p* [b]	Lower score	Higher score
WT/HT	36	-0.21 (-4.66, 4.22)	0.922	6 (0, 13)	8 (0, 17)
Circumferences	31	0.97 (-4.93, 6.88)	0.739	10 (0, 20)	13 (1, 25)
SFTs	25	-6.22 (-17.24, 4.80)	0.256	24 (7, 41)	16 (2, 30)
Grip strength	29	6.31 (-2.67, 15.29)	0.161	7 (0, 16)	17 (4, 31)
BIA	30	-1.80 (-9.76, 6.159)	0.647	17 (3, 30)	17 (3, 30)

Table 4.2. Difference in acceptability scores between admission and discharge
(a) Mean difference between discharge and admission scores (95% CI); (b) Paired-samples t-test for significance of difference between discharge and admission scores ($p<0.05$), also confirmed non-significant using Related-Samples Wilcox Rank Test; (c) % of patients (95% CI) giving a higher or lower score (≥10% difference) at discharge compared to admission.

4.5. Practicality of techniques

The practicality of the techniques on admission was assessed by the number of successful measurements performed at this time-point. As can be seen from Figure 4.2a, all measurements were successful in more than half the patients recruited to the study. Most patients had a measurement of WT, HT, MUAC and HC. About 80% were still able to get a DXA scan performed, and Triceps and Biceps SFTs measured. The number of successful measurements for Subscapular and Suprailiac SFTs were lower, as was the measurement for standing BIA.

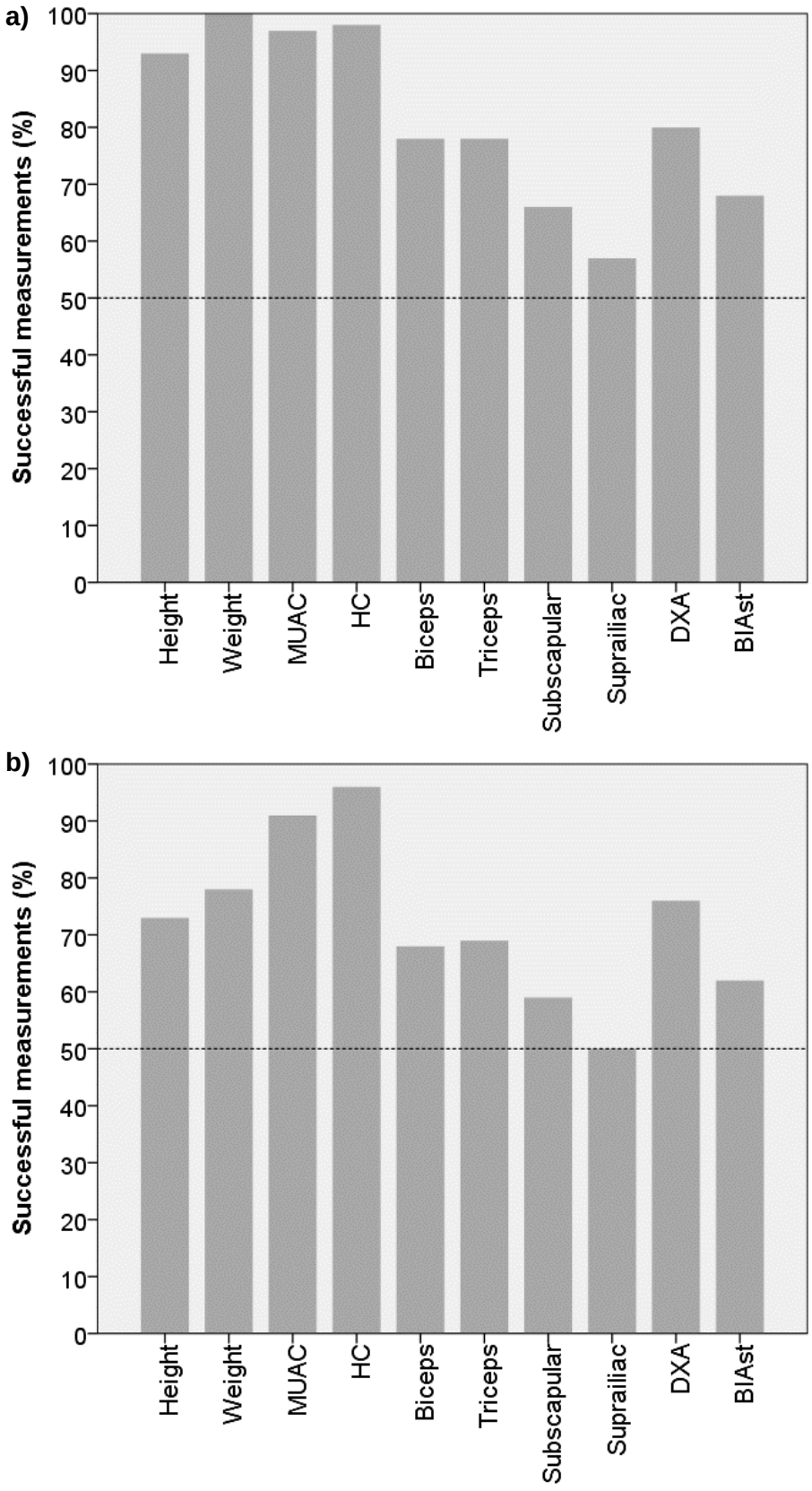


Figure 4.2. Successful measurements performed on admission

(a) percentage of patients measured by each of the techniques; (b) % of patients measured only under adequate conditions and accurate technique on admission.

Unlike a research setting where conditions are tightly controlled, strictly adhering to the technique's measurement protocols in a clinical setting was often challenging. Thus, it was decided that rather than excluding any measurements not performed under ideal conditions and technique, all measurements would be attempted adhering to the protocols as much as possible and any deviations (e.g. measurement performed on the right rather than the left side, while sitting rather than standing, with clothes or artefacts such as cannulas and plasters) would be noted in the data collection forms. This resulted in the creation of a separate restricted database that excluded all those measurements that could be considered inaccurate. Analyses were then re-run for the restricted databases to confirm the results were not markedly different from those of the whole database.

Reasons for exclusion for each of the techniques were:

- HT: measured lying down with a tape measure, or standing but not completely straight (e.g. patients with spinal scoliosis).
- WT: abdominal distension, oedema, ongoing large-volume IV's, renal or fistula losses.
- MUAC: measurement on the right side.
- HC: sub-optimal position (e.g. lying down in bed), or artefact (e.g. head frames for craniofacial surgery).
- SFTs: measured on right side, unable to access exact anatomic sites (e.g. in bedridden patients).
- DXA: out of position or missing small sections in the scan, metal artefact (e.g. metal rods in spinal patients), spinal scoliosis, movement while performing the scan.
- BIA: abdominal distension, oedema, renal dialysis, spasticity of limbs (e.g. children with cerebral palsy).

As can be seen from Figure 4.2b, this restriction of 'inaccurate' measurements resulted in a lower percentage of successful measurements. Accurate HT measurements decreased to just over 70%, with a slightly higher number of accurate weights. DXA and BIA decreased only slightly, with still over 70% and 60% of patients measured by each technique respectively. MUAC and HC had the lowest decrease, with approximately 90% of measurements still successful; and SFTs decreased so that suprailiac SFT measurements were successful in only approximately half of the patients.

When estimating the percentage of successful measurements expected in the population (Table 4.3), WT, HC, and even HT and MUAC measurements are expected to be possible in at least 90% of patients on admission. DXA, Biceps and Triceps SFTs are expected in at least 70% of children, while standing BIA, subscapular and suprailiac SFTs are only expected to be possible in about 55%. When considering only accurate measurements, despite lower expected success rates, all measurements are expected to be possible in at least 50% of patients, with the exception of suprailiac SFT.

	Successful measurements (%)	
	Whole sample	Accurate measurements only
HT	89 - 97	66 - 80
WT	100	72 - 85
MUAC	94 - 100	87 - 96
HC	100	93 - 99
Biceps SFT	71 - 84	61 - 76
Triceps SFT	72 - 85	61 - 76
Subscapular SFT	59 - 74	51 - 66
Suprailiac SFT	49 - 65	42 - 58
DXA	74 - 87	53 - 69
BIA	61 - 89	54 - 70

Table 4.3. Estimated percentage of successful measurements in the population from whole sample and only accurate measurements

Values shown are the 95% CI for the percentage of successful measurements expected on admission using the different techniques.

When the reasons for the unsuccessful measurements were analysed (Table 4.4), it is evident that in agreement with the results from the acceptability scores, 'Patient refusal' was very rare except for the case of SFTs. More patients refused the Subscapular and Suprailiac SFTs simply because of the sequence in which the sites were usually measured (Biceps, Triceps, Subscapular and Suprailiac). Of the 9 patients who refused to have a DXA scan, most were related to parental concerns over radiation exposure in chemotherapy patients, where this is already a sensitive issue. A few others were from parents of children with learning difficulties or cerebral palsy who felt they would be unable to keep still or in the right position for the duration of the scan.

	Reasons for unsuccessful measurements		
	Patient refusal	Unavailable equipment	Failed
HT	-	1	10
WT	-	-	-
MUAC	1	-	4
HC	1	-	2
Biceps SFT	20	-	14
Triceps SFT	19	-	14
Subscapular SFT	26	-	25
Suprailiac SFT	30	-	35
DXA	9	8	13
BIA	3	16	29

Table 4.4. Reasons for failed and missing measurements on admission
Table shows number of failed measurements.

'Unavailability of the equipment' was only an issue for DXA and standing BIA, since they were the only techniques requiring the patient to leave the ward and be transferred to the Radiology department and/or a room for BC assessment. Some of these patients were already under isolation procedures (e.g. for Bone Marrow Transplantation, BMT), connected to infusions, or had other scheduled procedures that impeded them from leaving their rooms. When patients were in isolation, HT measurements were taken in the patient's room using the ward's portable stadiometer; and in only one case was the equipment missing from the ward and a reason for an unsuccessful measurement.

The 'Failed' category encompassed several issues connected to the patient's clinical condition or scheduled medical procedures, such as barium swallow preventing DXA scans, inability to stand for height measurements or standing BIA, inability to access anatomic site for SFTs due to surgical incision or wound, damaged or sensitive skin interfering with anthropometry and BIA, etc. For the restricted database, excluded measurements were counted towards this category. 'Failed' was almost always the main reason for not being able to perform the measurements, and this highlights the need to have a variety of techniques available in these complex patients.

4.6. Reliability of measurements

The reliability of anthropometric measurements was evaluated using the Bland Altman analysis-based approach of plotting the mean against the difference between two repeated measurements. As can be observed in Figure 4.3, the spread of the difference between repeated measurements was narrow for HT, WT, MUAC and HC with limits of agreement (*LOA*) below 0.5 SDS; and wider for SFTs (*LOA* of approximately 1.0 SDS). None of the techniques showed a significant correlation between the difference and mean of repeated measurements, indicating a constant difference and no effect of the magnitude of the measurements.

As can be observed from Table 4.5, the mean differences between repeated measurements were all non-significant. The calculated *CRs* indicate that the absolute difference between two repeated tape measurements of MUAC and HC is expected to be ≤ 0.3 cm with 95% probability. In the case of HT, this was calculated to be ≤ 0.4 cm, ≤0.2 kg for WT, and approximately ≤1mm for SFTs. Calculated *ICC* was very good and significant for all the measurements. Analysis on the restricted database using only measurements performed under adequate conditions and technique (see Appendix 12. Table 1) showed minimal differences compared to the results described using the complete dataset for the calculated mean differences, *CR*s and *ICC* analysis.

	n	***ICC*** [a]	**mean difference** [b]	***CR*** [c]
HT	136	1.000	0.02 (-0.02, 0.06)	0.4 cm
WT	144	1.000	0.00 (-0.02, 0.01)	0.2 kg
MUAC	146	0.999	-0.03 (-0.10, 0.10)	0.3 cm
HC	149	0.999	0.02 (0.00, 0.04)	0.3 cm
Biceps SFT	118	0.992	0.07 (-0.04, 0.17)	1.3 mm
Triceps SFT	119	0.995	-0.03 (-0.13, 0.07)	1.1 mm
Subscapular SFT	101	0.996	0.07 (-0.01, 0.15)	0.8 mm
Suprailiac SFT	86	0.998	0.00 (-0.20, 0.40)	1.3 mm

Table 4.5. Reliability of the different anthropometric measurements

(a) ICC type 3, all values significant (H_0: ICC=0, p<0.001); (b) Mean difference between repeated measurements (95% CI), One sample t-test of the mean differences (H_0: MB=0, p<0.05) all non-significant; (c) Repeatability coefficient using the Bland Altman method for repeated measurements.

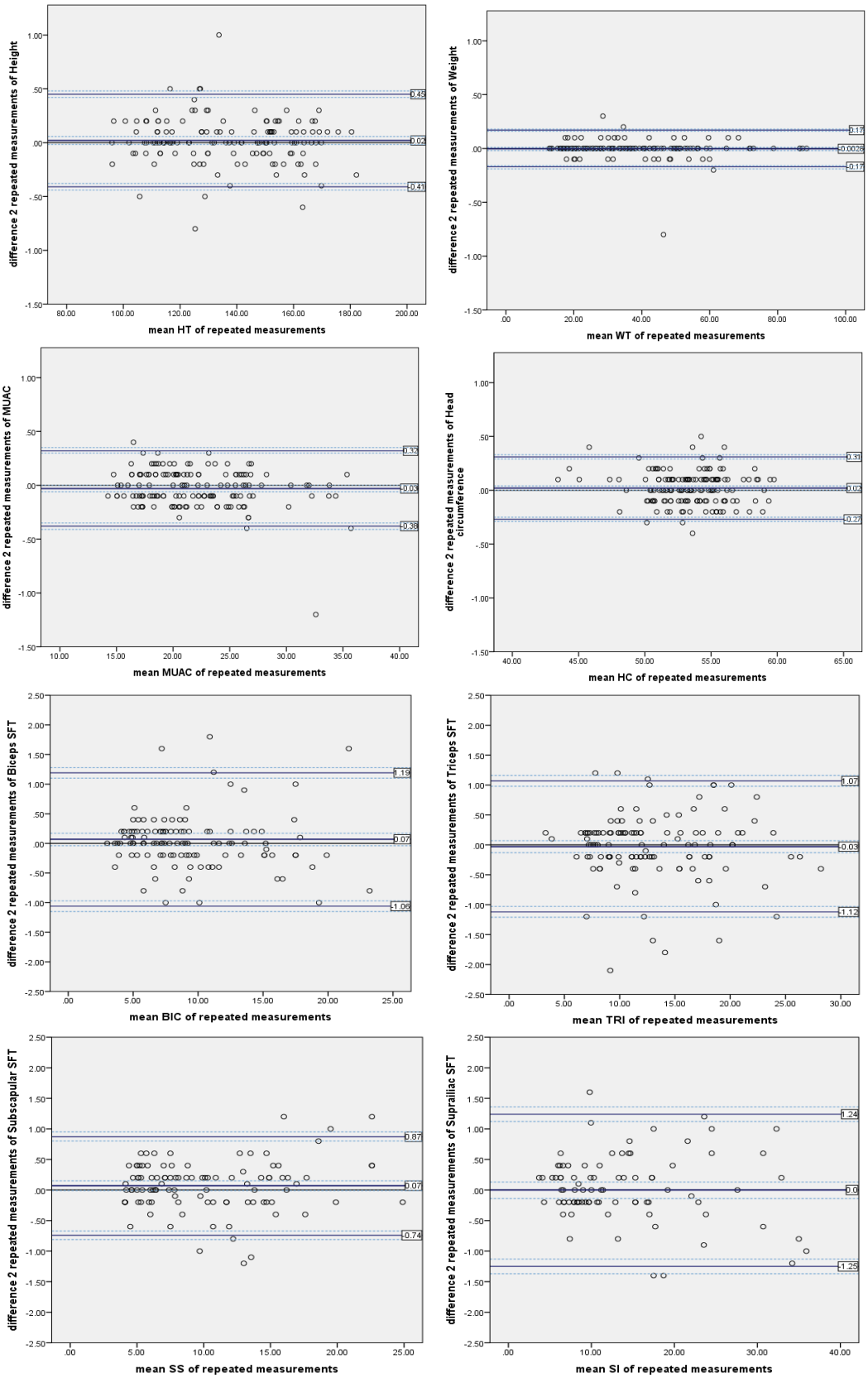


Figure 4.3. Differences between two repeated measurements of HT, WT, MUAC and SFTs *Bland Altman repeatability analysis: continuous line indicates mean bias (MB), segment lines indicate upper and lower limits of agreement (LOA), and dotted thin lines indicate 95% CI for MB and LOA.*

4.7. Validation of techniques against DXA

4.7.1. Fat mass assessment

Fat mass was assessed in the sample of patients using the SDS derived from the more 'simple' measurements: 4-site SFTs and BMI, against DXA FM. FMI SDS were also calculated from DXA fat mass measurements to adjust for body size, and this parameter's SDS compared to DXA FM SDS to identify if this adjustment made a substantial difference for the assessment of FM in this patient population.

The analysis of the agreement showed a significant negative correlation between the difference and mean SDS (Figure 4.4 and Table 4.6), indicating the differences between techniques/parameters and DXA FM are greater in patients with lower FM SDS. BMI was the only parameter that had a non-significant correlation, indicating a constant difference compared to DXA FM SDS.

A closer analysis of the mean bias (*MB*) and *LOA* (Table 4.6) showed there was a significant mean difference for all SFTs compared to DXA FM (approximately 0.35 SDS); with the exception of Triceps SFT, which had a non-significant *MB* of 0.10 SDS. BMI had a slightly lower, though still significant, mean difference (*MB*=0.25 SDS) compared to what was observed for SFTs. However, as it can also be seen from the summary graph (Figure 4.5), all SFTs and BMI SDS had wide *LOA*, sometimes overestimating FM by more than 1.5 SDS compared to DXA FM. Suprailiac SFT had only a slightly narrower *LOA* compared to other SFTs, however this is likely the result of performing the measurement in a smaller number of patients (greater number of 'failed' measurements) that excluded children who would likely have had abnormal measurements (e.g. overweight teenage girls).

Adjusting DXA FM for height resulted in significant differences between the resulting DXA FMI and DXA FM SDS (*MB*=0.12 SDS), with *LOA* ± 0.48 SDS, indicating higher relative amounts of fat mass for their body size. Only DXA measurements of fat and lean mass were analysed as indices because there is no BC reference data (Wells et al. 2012) to obtain SDS for indices using any of the other 'simple' techniques. The reference data for FMI and LMI was developed using absolute values of FM and LM obtained using the 4C model (Wells et al. 2012), but given the close agreement between both techniques and the fact that DXA generates absolute values for FM and LM, this reference was considered suitable to analyse the indices derived from DXA FM and LM measurements.

Considering only accurate measurements, a re-run of the analysis in the restricted database resulted in very similar results (see Appendix 12. Table 2). All techniques, except

for Triceps SFTs (*MB*=0.10SDS), significantly overestimated FM compared to DXA FM. They also all had wide *LOA* of about ± 1-1.3 SDS, and slightly more narrow for FMI (± 0.48 SDS).

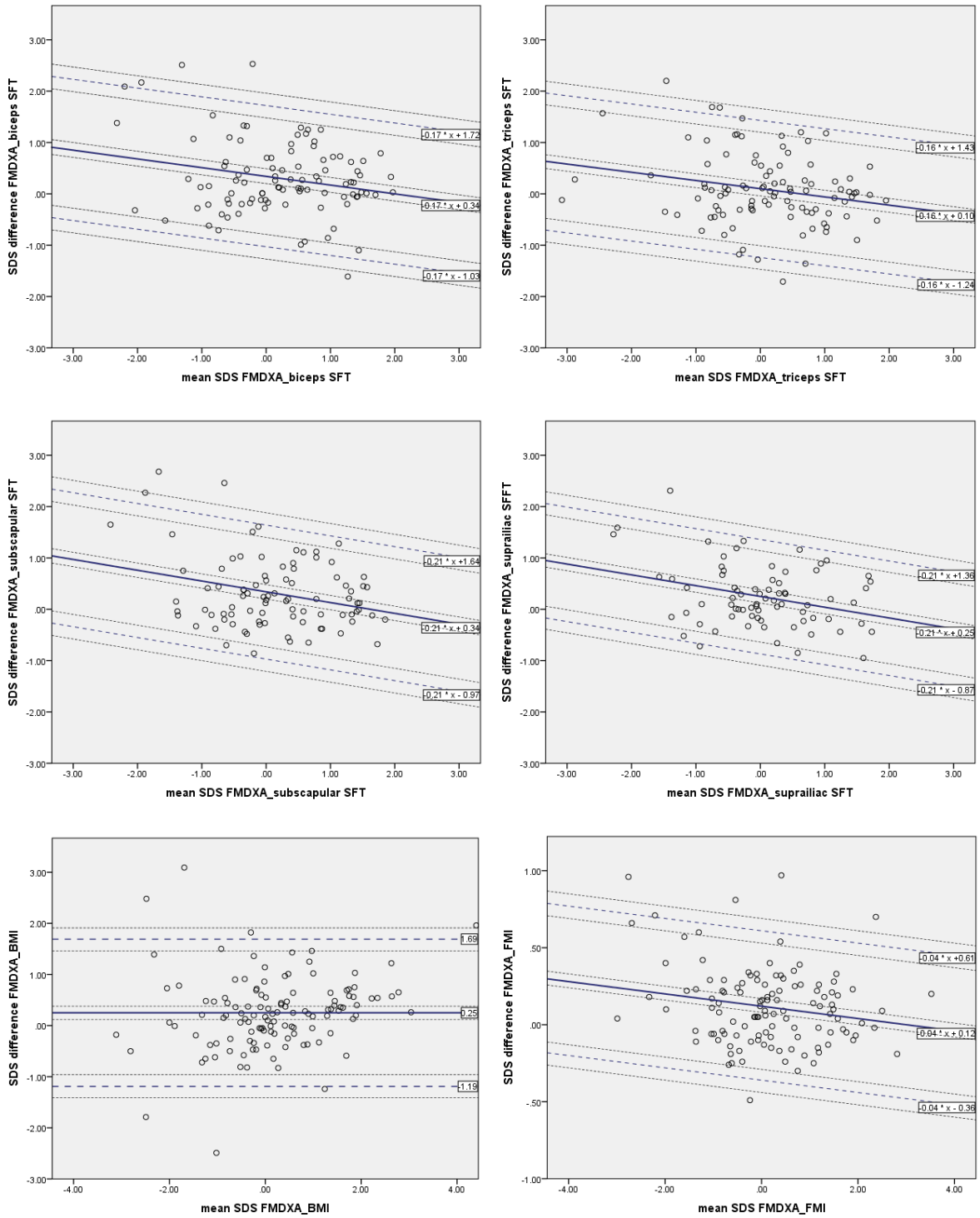


Figure 4.4. Validity of BMI, SFTs and FMI SDS compared to DXA fat mass SDS

Bland Altman analysis of agreement: continuous line indicates MB, segment lines indicate upper and lower LOA, and dotted thin lines indicate 95% CI for MB and LOA.

	n	*MB* [a]	*p* [b]	*LLOA*	*ULOA*	*r* [c]	*p* [d]
BMI	122	0.25	0.000*	-1.19	1.69	0.17	0.064
Biceps SFT	99	0.34	0.000*	-1.03	1.72	-0.23	0.023*
Triceps SFT	100	0.10	0.169	-1.24	1.43	-0.22	0.027*
Subscapular SFT	89	0.34	0.000*	-0.97	1.64	-0.28	0.009*
Suprailiac SFT	74	0.25	0.000*	-0.87	1.36	-0.32	0.006*
FMI	118	0.12	0.000*	-0.36	0.61	-0.21	0.021*

Table 4.6. Mean bias, LOA and correlation coefficients for BMI, SFT and FMI SDS compared to DXA fat mass

(a) Mean bias of the measurements SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

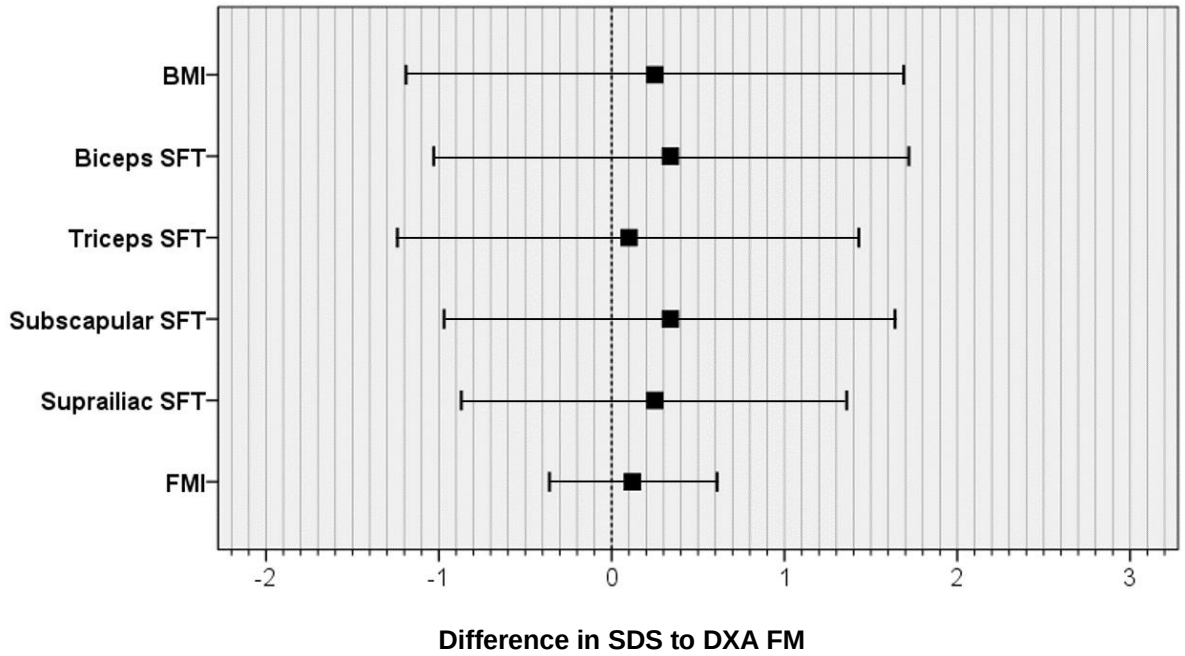


Figure 4.5. Summary of MB and LOA for BMI, SFT and FMI compared to DXA fat mass

(■) MB; (|) LOA; dotted line indicates no mean difference in SDS between techniques.

The results from the analysis on the agreement between techniques using the categorical variables for abnormal SDS is summarised in Table 4.7. There was good absolute agreement between different measurements compared to DXA FM, with >90% agreement for most measurements, with the exception of BMI (87% agreement). FMI and Triceps SFT had the highest absolute agreement of all measurements.

Cohen's kappa values (κ), which unlike absolute agreement also consider the effect of random chance, showed Subscapular, Suprailiac and Biceps SFTs had almost no association to DXA FM; thus, suggesting these techniques alone are likely to miss most patients with abnormal SDS compared by the clinical reference method. The kappa values for BMI and Triceps SFTs were statistically significant, although these were still κ<0.5 for both, indicating only fair/moderate agreement. Some authors have highlighted the need to evaluate kappa values on their clinical relevance, rather than purely on statistical significance, and suggest a value of κ >0.7 could be more relevant as a 'cut-off' to indicate an acceptable agreement (McHugh 2012). Based on this consideration, the kappa for both BMI and Triceps SFT could be classified as poor compared to DXA FM, despite their statistical significance. Additionally, the *CI* of kappa also showed a wide range of expected kappa values for the population and, in the case of Triceps SFT, a lower limit of almost no association. On the other hand, FMI showed an almost perfect agreement (κ=0.86) to DXA FM with narrow *CI*.

The analysis of the agreement between abnormal SDS using the restricted database (see Appendix 12. Table 3), indicated a very similar absolute agreement for all measurements. Kappa values for BMI were slightly higher (κ=0.59) but with similarly wide range of expected values in the population. Once again, there was no agreement between Biceps, Subscapular and Suprailiac SFTs; and no differences in the results for Triceps SFTs. The kappa for FMI was still high, although slightly lower than with the whole dataset, and with wider *CI* from the decreased sample size.

	n	**Agreement** [a]	***κ*** [b]	***p***
BMI	122	87	0.46 (0.24, 0.69)	0.000*
Biceps SFT	99	93	-0.02 (-0.05, 0.00	0.750
Triceps SFT	100	96	0.49 (0.06, 0.91)	0.000*
Subscapular SFT	89	94	-	-
Suprailiac SFT	74	93	-0.01 (-0.04, 0.0)	0.818
FMI	118	97	0.86 (0.70, 1.00)	0.000*

Table 4.7. Agreement of abnormal SDS for BMI, SFTs and FMI compared to DXA fat mass
(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

4.7.2. Lean mass assessment

Standing BIA SDS were tested against DXA SDS, the lean mass index was calculated from DXA LM measurements to adjust for body size, and LMI SDS were then compared to DXA LM SDS. There was no observed correlation between the difference and the magnitude of the measurements for either parameter (Figure 4.6), suggesting a constant difference between techniques. The mean difference in SDS for BIA (Figure 4.7 and Table 4.8) was non-significant and very close to zero, with *LOA* just over 1.0 SDS. However, the use of LMI resulted in significantly higher SDS than those for DXA LM, and wide *LOA* over 1.5 SDS.

Analysis using the restricted database (see Appendix 12. Table 4), showed similar results. Standing BIA was still not significantly different on average from DXA LM and maintained *LOA* close to 1.0 SDS. Measurements of LMI also were significantly higher that DXA LM and maintained the observed wide *LOA*. The correlation of the differences to the magnitude of the measurement, however, was significant in this case suggesting there was a greater difference between techniques in children with lower mean SDS for LM.

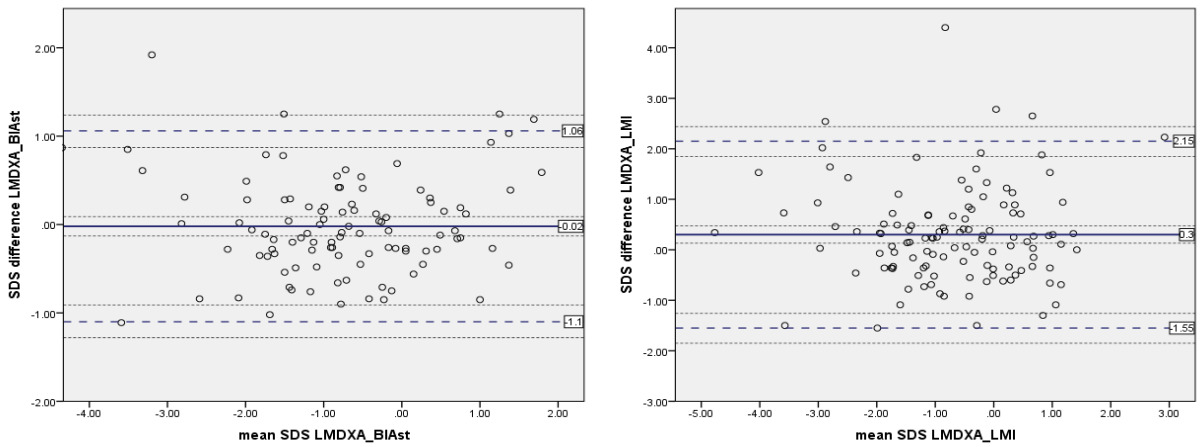


Figure 4.6. Validity of BIA and LMI SDS compared to DXA lean mass

Bland Altman analysis of agreement: continuous line indicates MB, segment lines indicate upper and lower LOA, and dotted thin lines indicate 95% CI for MB and LOA.

	n	*MB* [a]	*p* [b]	*LLOA*	*ULOA*	*r* [c]	*p* [d]
BIA	102	-0.02	0.699	-1.10	1.06	0.02	0.826
LMI	118	0.30	0.001*	-1.55	2.15	-0.01	0.902

Table 4.8. MB, LOA and correlation coefficients for BIA and LMI compared to DXA LM

(a) Mean bias of the measurements SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

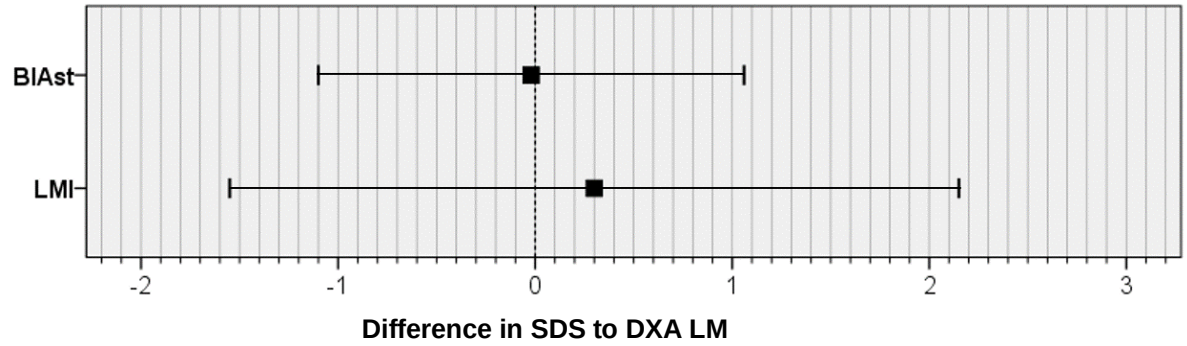


Figure 4.7. Summary of MB and LOA for BIA and LMI compared to DXA lean mass
(■) MB; (|) LOA; dotted line indicates

When analysing the agreement of abnormal SDS (Table 4.9), standing BIA had a high absolute agreement to DXA LM (92%) and a kappa value denotating substantial agreement (κ=0.65) between techniques, although slightly lower than was considered to be clinically relevant by some authors (McHugh 2012). In addition, the lower limit expected kappa value for the population was still showing moderate agreement (κ=0.43). Results from the restricted database (see Appendix 12. Table 5) indicate that excluding 'inaccurate' measurements made almost no difference for the agreement of abnormal SDS compared to DXA LM.

In the case of LMI, the parameter showed a lower absolute agreement of 87%, with a kappa of 0.55 denotating only moderate agreement. The use of the restricted database resulted in a slightly lower agreement and kappa value, with the expected population lower limit close to only a slight agreement (κ=0.15).

	n	Agreement [a]	*κ* [b]	*p*
BIA	102	92	0.65 (0.43, 0.87)	0.000*
LMI	118	87	0.55 (0.35, 0.74)	0.000*

Table 4.9. Agreement of abnormal SDS for BIA and LMI compared to DXA lean mass
(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

4.8. LMI and FMI: an exploration of the optimum adjustment of body composition for height in the study population

There has been some debate about the best way to present BC data, especially when making comparisons among different groups or the same individuals over time. Studies reporting BC measurements handle the data in a variety of different ways, even when the same technique is being used to obtain the measurements. For example, an argument has been made that presenting fat mass as a percentage might not be optimal, since this value can be altered both by changes in fat and lean mass (Wells & Cole 2002).

Even when measurements of fat and lean mass are compared against reference data to obtain SDS, as is the approach followed in this thesis, these SDS would be normalised by sex and age but might still be influenced by body size. This situation might be particularly problematic in patients with complex chronic conditions, such as those included in the present study, because their linear growth might have been affected and comparing them to healthy normal children of the same age and sex might not always be sufficient to normalise the measurement SDS. As can be seen from Table 4.10, the children in this study were on average low for their age and sex in height and weight compared to healthy children. This was still the case after considering only accurate measurements from the restricted database (see Appendix 12. Table 6).

Similarly to how BMI is calculated, it has been suggested that LM and FM could be adjusted to remove the effect of height by dividing LM and FM by the square of height to obtain the new parameters LMI and FMI (VanItallie et al. 1990). However, the use of height squared might not always be appropriate to describe the relationship of LM and especially FM to height, and thus may not adequately adjust for body size (Wells & Cole 2002).

For the study, LMI and FMI were calculated using HT^2, as the reference data used to obtain the FMI and LMI SDS was also calculated in this manner. As Table 4.10 shows, the mean LM SDS was low in this population (-1.0 SDS), but adjusting using HT^2 made the mean SDS increase to -0.6 SDS. For FM, the use of FMI resulted in only a slight increase in SDS compared to FM (0.1 vs 0.2 SDS). Again, these SDS did not change much after the use of only accurate measurements from the restricted database (see Appendix 12. Table 6) and there were also no significant differences between male and female patients. Although the use of the indices in this sample makes a difference for the resulting SDS, especially in the case of lean mass, the decision about whether LM / FM or LMI / FMI should be used to assess the patient´s BC in clinical practice should ideally be made on the basis of how both parameters relate to clinical outcomes, something that will be explored further in Chapter 8.

This chapter section will describe how these indices perform in this particular study population, and explore if other adjustments would have been more appropriate to remove the effect of height from FM and LM measurements.

	n	***mean***	***SD***	**Male**			**Female**			
				n	*Mean*	*SD*	*n*	*Mean*	*SD*	*p* [a]
Age (yr)	152	10.7	3.6	76	10.1	3.9	76	11.4	3.3	0.04*
HT (m)	141	1.4	0.2	72	1.3	0.2	69	1.4	0.2	0.14
LM (kg)	122	26.8	10.6	60	27.1	12.1	62	26.5	9.1	0.75
FM (kg)	122	10.7	8.9	60	9.4	9.0	62	12.0	8.8	0.12**
LMI (kg/m^2)	118	13.5	1.8	58	13.8	2.0	60	13.2	1.6	0.05
FMI (kg/m^2)	118	5.1	3.6	58	4.5	3.6	60	5.7	3.5	0.08**
HT SDS	141	-0.7	1.5	72	-0.6	1.5	69	-0.8	1.5	0.64
WT SDS	152	-0.3	1.7	76	-0.3	1.8	76	-0.4	1.6	0.67
BMI SDS	141	0.2	1.4	72	0.3	1.5	69	0.2	1.3	0.81
LM SDS	122	-1.0	1.5	60	-0.9	1.5	62	-1.0	1.5	0.70
FM SDS	122	0.1	1.2	60	0.3	1.3	62	-0.2	1.2	0.04*
LMI SDS	118	-0.6	1.4	58	-0.6	1.5	60	-0.5	1.2	0.50
FMI SDS	118	0.2	1.2	58	0.4	1.2	60	0.02	1.1	0.09

Table 4.10. Summary of WT, BMI, FM, LM, FMI, LMI values and SDS on admission
(a) 2-samples t-test comparing the mean values and SDS between male and female, (*) significant p<0.05, (**) significant for non-parametric Mann-Whitney test (p=0.03 for FM, p=0.01 for FMI).

4.8.1. Relationship between height and indices of fat and lean mass.

The associations of the calculated LMI and FMI to height were explored to determine if these parameters still had any bias when comparing groups or children of different heights, or in this case between the patient sample and a reference group of healthy children. As Figure 4.8 shows, there was still some positive correlation between the calculated indices and height in this patient sample. This association was stronger for LMI (r =0.55), but nonetheless also significant for FMI (r = 0.36) (Table 4.11). Calculation of the percentage variation in FMI and LMI due to differences in height indicated 6% variation for FMI and 16.2% for LMI.

Analysis using the restricted database with only accurate measurements (see Appendix 12. Table 7), showed a stronger correlation between height and the indices. This was especially true for FMI, and resulted in very similar significant positive associations to height for both (r =0.54 and 0.57 for FMI and LMI respectively). The percentage variation due to differences in height also increased to 16% for FMI and 18% for LMI.

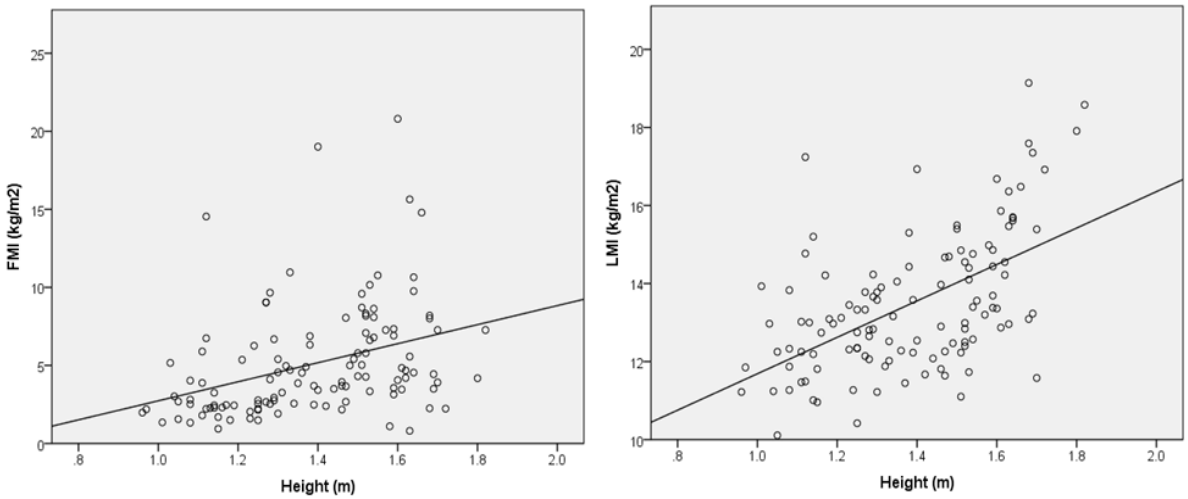


Figure 4.8. Relationship between height and indices of fat and lean mass

n =118	**Correlation coefficient** [a]	***p*** [b]	**% variation** [c]
FMI	0.36	0.000	6.6
LMI	0.55	0.000	16.2

Table 4.11. Correlation of FMI and LMI to height

(a) Pearson's correlation coefficient (r); (b) significance of r (H_0: r=0, p<0.05); (c) % of variation in FMI or LMI due to differences in height.

4.8.2. Relationship of LM and FM to height in the patient sample and the calculation of new indices

The relationship between FM and LM to height in the study sample was analysed to enable the calculation of new indices which were uncorrelated to height. FM, LM and HT values were transformed using natural logs and plotted as observed in Figure 4.9. LogFM or logLM were each regressed to logHT, and the resulting gradient (regression coefficient for HT) corresponded to the power (P) by which HT should be raised to calculate the new indices (LM/HT^P and FM/HT^P). This analysis was performed using the entire database, as well as per sex and admission groups (Table 4.12).

The results indicated that the optimal *P* for the calculation of the new index of LM was 2.4 for the entire sample of patients, with slightly higher values for male and surgical admissions (*P*=2.5). For FM, the calculated *P* was 3.8 for all patients, but higher for girls and patients admitted for medical investigations and procedures (*P*=4.2 and 4.5 respectively) and slightly lower for surgical and male patients. It should also be noted that the lower limit in the *CI* of the regression coefficients excluded 2 for FM, suggesting the optimal *P* is different than that used to calculate FMI (HT^2).

With the restricted database (see Appendix 12. Table 8), the resulting values for *P* in LM were identical to those obtained from the entire set of measurements. However, the observed *P* values for FM were higher using the restricted database. This resulted in a *P* of 4.4 in the entire sample, although the rest of the coefficients still had the same expected pattern of higher values for girls and medical admission groups (*P*=4.7 and 4.4 respectively) and lower for surgical admissions (*P*=4.2) and male patients (*P*=3.9)

To test the new calculated *P,* the new indices ($LMI_{new}=LM/HT^{2.4}$ and $FMI_{new}=FM/HT^{3.8}$) were analysed for associations to height. As Table 4.13 shows, the new indices resulted in almost no association to height as expected, and a percentage variation of only 0.4 for LMI_{new} and cero for FMI_{new}. The calculations of LMI_{new} and FMI_{new} in the restricted database resulted in slightly higher values for the correlations to height and percentage variation. However, these associations were still non-significant for both indices, and with a percentage variation of only 0.2 for FMI_{new} and 1.6 for LMI_{new}. (see Appendix 12. Table 9).

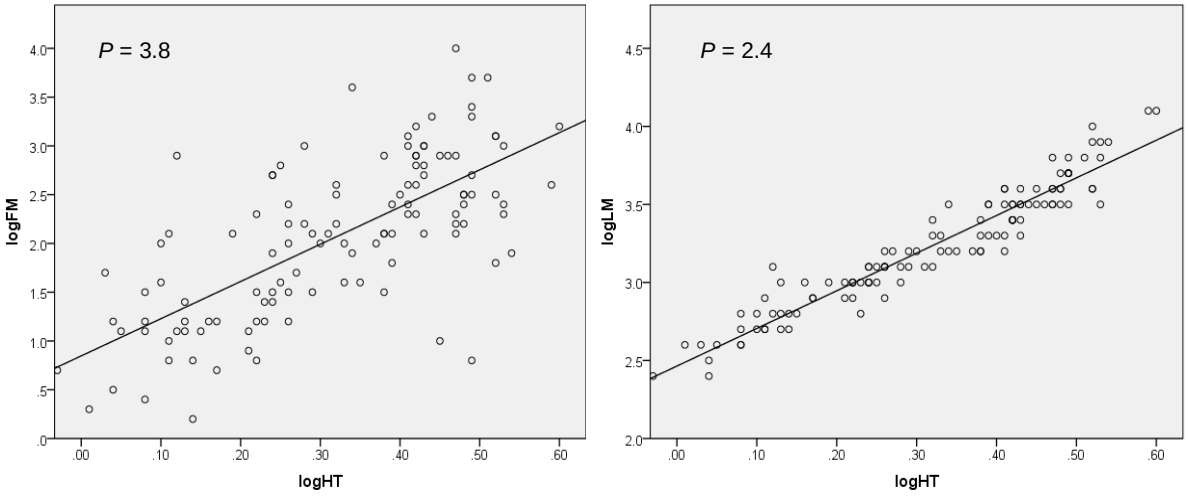


Figure 4.9. Relationship between the log of height and logs of fat and lean mass
Graphs show regression line and P (gradient of the regression).

	n	Gradient [a]	*CI* [b]	
FM				
All patients	118	3.8	3.1	4.5
Boys	58	3.4	2.3	4.4
Girls	60	4.2	3.3	5.1
Medical	64	4.5	3.6	5.4
Surgical	54	3.1	2.0	4.2
LM				
All patients	118	2.4	2.3	2.6
Boys	58	2.5	2.3	2.7
Girls	60	2.4	2.2	2.6
Medical	64	2.4	2.2	2.5
Surgical	54	2.5	2.2	2.7

Table 4.12. Regression gradients to calculate new indices of FM and LM for all patients, and per sex and admission group

(a) resulting gradient (corresponding to P) from regressing logHT on logFM and logLM; (b) 95% CI of the regression gradient.

n =118	Correlation coefficient [a]	*p* [b]	% variation [c]
FMI_{new}	0.00	0.990	0.0
LMI_{new}	0.08	0.369	0.4

Table 4.13. Correlation of new indices of fat and lean mass to height

(a) Pearson's correlation coefficient (r) between HT and the new indices of fat and lean: $FM/HT^{3.8}$ and $LM/HT^{2.4}$; (b) significance of r (H_0: r=0, p<0.05); (c) % of variation in in the new indices attributed to differences in height.

4.9. Summary of main findings

- Measurements by all the anthropometric and BC techniques were overall acceptable and successful in the clear majority of patients.
- SFTs was the only technique with more limited acceptability, which did not seem to improve with repeated exposure (by discharge).
- Most children could have at least one BC measurement for FM and LM performed on admission, although the number of failed measurements and analysis of the restricted database highlight the different practical limitations of each technique and the advantages of having a range of options to assess BC in paediatric patients.
- The repeatability of anthropometric measurements was good, with approximate *CR* of 0.3 cm for circumferences and HT, 0.2 kg for WT, and 1.0 mm for SFTs.
- 'Simple' BC techniques (SFTs and BMI) had a tendency to overestimate FM compared to DXA FM. Triceps SFTs and BMI were the measurements with the best overall agreement to FXA FM SDS, but with wide *LOA* and showing only moderate/ fair agreement for identifying patients with abnormal DXA FM SDS.
- Standing BIA had a good agreement to DXA LM, both in terms of SDS and for identifying patients with abnormal SDS.
- Adjusting DXA FM for size (FMI) resulted in higher average SDS, but still maintained an almost perfect agreement to DXA FM for identifying children with abnormal SDS.
- Size adjustment had a greater effect for DXA LM (LMI), resulting in higher SDS on average and only a moderate agreement to DXA LM for identifying patients with abnormal SDS.
- The calculated FMI and LMI (using HT^2) maintained some of their correlation to height, however the variation percentage was only 6% for FMI and 18% LMI.
- In the patient sample, analysis showed a *P* of 2.4 and 3.8 for DXA LM and DXA FM respectively would result in an optimal adjustment to height.
- Thus, the calculated index for LM using *P*=2 is likely to be suitable in this population, while FM should ideally use a higher *P* for adjusting to height.

4.10. Discussion

4.10.1. Acceptability and practicality of BC measurements in a tertiary centre

There has been increasing interest in using BC parameters to identify malnutrition in paediatric patients more effectively than using the current anthropometric criteria (WT and BMI) (Wells & Fewtrell 2008; Cederholm & Jensen 2016). However, there is a prevailing opinion that, despite their possible advantages, BC measurements are difficult to obtain in routine practice (Becker et al. 2014; Cederholm et al. 2015). My results indicate, for the first time as far as I am aware, that BC assessment by a range of different techniques is both acceptable and practical in a diverse group of children admitted to a tertiary referral centre.

It was encouraging to find that the acceptability and success of a more 'complicated' technique such as DXA was still comparable to the more 'simple' techniques for measuring BC. SFTs was the only technique that, in agreement with the general opinions of clinicians and dietitians, was not as acceptable as other anthropometric and BC techniques. Furthermore, my results on acceptability scores by discharge suggest acceptance does not improve with repeated exposure, at least in the short term. The study was limited in the number of measurements that could be repeated at discharge, meaning analysis of the change in acceptability scores is likely under-powered to detect any significant difference. Furthermore, this population sample included children accustomed to taking part in research and had likely been exposed before to many of the techniques tested; thus, the acceptability observed in this study might not be comparable to that in other centres. Additionally, with regards to SFT measurements, there were slight differences in the way the researchers approached patients to explain the measurements and their confidence in performing the measurements. Although no overt differences were detected in the data between acceptability scores and the researcher performing the measurement, it is suggested further training might address any apprehension for performing the SFT measurements and improve on the acceptability and practicality of the technique. This should be considered, however, in the context of the advantage of measuring SFTs in routine clinical practice (e.g. by evidence of association to clinical outcomes, which will be explored in Chapter 9) to justify the investment in resources.

The study highlighted the difficulties of obtaining accurate measurements of WT and HT in a substantial number of patients. This has been previously reported in other studies in this (Pichler et al. 2014) and other settings (Larsen et al. 2014; Sarni et al. 2009). Considering HT measurements are also required to calculate a number of BC parameters (e.g. BIA, FMI,

LMI) and their importance for the routine clinical management of patients, different approaches for estimating height in these patients will be explored in Chapter 6.

Regarding the practicality of measuring BC, considering this population included children with complex diagnoses and undergoing various surgical and medical procedures, it was not uncommon to find contraindications for some of the techniques. This supports previous statements (Atherton et al. 2013; Wells & Fewtrell 2006) on the advantages of having a range of techniques available in clinical practice. While the main limitation for SFTs was their acceptability, my results show that DXA and BIAst measurements could be difficult to obtain in some cases due to the need to transfer the patients out of the wards to access the equipment. Thus, the use of equipment that allows bedside measurements, which is potentially the case for BIA, might improve the success of the measurements (Mehta et al. 2013), and will be explored in more detail in the following chapter. Furthermore, as reported by other authors (Atherton et al. 2013; Hauschild et al. 2016), fluid shifts and oedema were somewhat common contraindications for some of the techniques in this patient population.

The practicality of BC techniques showed in this study could differ from what is expected in a general hospital setting or less specialised centres, where access to equipment might sometimes be an issue. Additionally, resources in terms of staff training and time available to implement these measurements in routine practice might also be limited. Chapter 10 will address these issues using a mixed-methods approach exploring the current practice, views and opinions of paediatric dietitians in the UK and USA.

4.10.2. Validity of BC: techniques for clinical practice

Several studies have looked at validating some of the more ‘simple’ BC techniques against the 4C reference method model. However, as described in Chapter 1, evidence from these studies has been limited in terms of study population (adults, healthy children) as well as differences in the sets of techniques compared, and how measurement outputs are analysed (e.g. as absolute values, comparisons with standard reference values, use of prediction equations to estimate fat and lean mass amounts). The publication of UK BC reference data (Wells et al. 2012) now provides a way to systematically assess BC measurements using different techniques by calculating SDS that can be assessed similar to WT, HT and BMI assessment, addressing an important limitation for the implementation on BC into practice (Atherton et al. 2013; Kotnik et al. 2015). Thus, the use of this approach is likely to improve and unify evidence from different BC studies in the future.

Despite its limitations, DXA has often been considered the best reference method technique to assess BC, especially in clinical settings (Elberg et al. 2004; Cederholm et al.

2015; Eston et al. 2005; Eisenmann et al. 2004). The present study considered DXA as the reference method BC technique for several reasons: 1) it has shown good agreement to the 4C model, particularly for the UK BC reference data (Wells et al. 2012) and a subsequent in a study using this same reference data and measurement protocols (Atherton et al. 2013) as the ones used for this study; 2) the equipment is available in this setting for clinical and research purposes; 3) the use of other techniques such as BodPod and TBW by deuterium dilution are likely to be difficult to obtain routinely in clinical practice.

The observed agreement between 'simple' BC techniques and DXA in this study, confirm that BIA is a good alternative to DXA LM for the assessment of lean mass in paediatric patients (Eisenmann et al. 2004; Atherton et al. 2013; Thomson et al. 2007). BIA SDS showed a non-significant bias (± 1 SDS *LOA*) to DXA LM SDS, and a substantial agreement in identifying patients with abnormal SDS. This is a promising result, considering BIA is more common in clinical settings, and the flexibility in machines and techniques (standing, bedside) could facilitate its routine measurement in certain groups of patients. However, differences might exist between different machines and measurement protocols (Andreoli et al. 2002) that could affect the agreement of BIA to DXA LM reported here; something that will be further explored in the next chapter.

Considering the validity of the different parameters to assess FM, none of the more 'simple' techniques seemed to have a very good agreement to assess individual patients compared to DXA FM; and, especially for some of the SFTs, agreement is expected to be quite poor. Similar to what was reported by Atherton et al. (2013), Triceps SFT and, to a lesser degree, BMI could be considered the best alternatives for estimating FM when DXA FM measurements are not possible, but with limitations. Triceps SFTs had the least and only non-significant bias compared to DXA FM SDS, but with wide *LOA*, suggesting this measurement might be able to estimate fat in groups but caution should be taken in assessing and tracking individual patients. This is also supported by the poor agreement of all SFTs to DXA FM for identifying patients with abnormal FM SDS. In the case of BMI, there is the possibility that this parameter could significantly overestimate FM in groups and individual patients, as evidence by the significant mean bias compared to DXA FM SDS.

Issues of practicality would suggest BMI and Triceps SFTs (the most successfully measured SFT site in this study) as the most suitable 'simple' techniques when DXA FM measurements are not possible. Additionally, SFTs do have the advantage that they can be repeated as sequential measurements over time (Watts et al. 2006); something that is generally unfeasible using DXA; and that they are an alternative when an accurate measurement of WT and/or HT, which are needed to calculate BMI, is not possible.

Limitations for the use of BMI as a measurement of fatness have now been described by several studies (Siervogel et al. 2000; Demerath et al. 2006; Wells, Coward, et al. 2002). Patients in this study had several clinical conditions (e.g. oncology patients, long-term PN on intestinal failure, wheelchair dependent children with neuromuscular conditions) that might have caused shifts in BC, as suggested by observations of children with similar conditions (Sullivan et al. 2006; Murphy et al. 2010; Pichler, Chomtho, et al. 2014; Rashid et al. 2006; Mastrangelo et al. 2013), limiting its use as a parameter of FM in this population. The heterogeneity of the patient diagnoses and characteristics included in the study (further described in Chapter 7), likely also translate into a wide variance in SDS for FM parameters, making discerning patterns and significance analysis challenging. Future studies targeting specific sub-sets of patients could clarify the advantages of the techniques in different conditions.

4.10.3. Adjusting BC for size: FMI and LMI

The comparison of DXA FM and LM SDS and their indices (FMI and LMI) showed that LM seems to be more affected/related to height than FM. This agrees with observations of LM being closely related to linear growth and bone mass. Further analysis of FMI and LMI, indicated that calculating these indices using HT^2 still maintains some if the associations of FM and LM to height, and could introduce a significant bias when comparing children of different heights or groups of children with different mean heights. The percentage variation however, was only 6% for FMI, which is similar to the value reported in the study by Wells & Cole (2002) and indicates that the majority of the variation in the parameter would be due to variations in fat mass rather than height. For LMI, the results showed a higher variation of 18%. This is different to the results reported by Wells et al. (2002) and suggests this sample of patients has a higher variability in LM relative to height than the sample of healthy 8yr old children analysed in the cited study. Additionally, this difference could also have been in part an artefact of age, as the study analysed the relationships of LM to height in patients 5-18yr rather than focusing on a group of children of the same age. Children in this study are also likely more variable in height compared to healthy reference children, as evidenced from the differences in agreement between DXA LM and LMI SDS.

When analysing the *P* needed to normalise both LM and FM for height, this was higher for FM, which was expected considering children usually vary in fat more than height or lean mass (Wells & Cole 2002; Wells et al. 1999). In this study, a *P* of 2.4 was needed to normalise LM in the sample of patients, and 3.8 was needed for FM. There were some small variations between admission groups and sex. However, all calculated coefficients for HT excluded 2 in their *CI* for FM, suggesting the use of HT^2 will not entirely normalise the measurements for

the children in this population. However, considering the practical implications of using a different coefficient to normalise FM and LM to height, this could be very difficult to implement without the use of automated spreadsheets or programs, especially considering the concept of using a different adjustment is not something most clinicians would be familiar with. Given the variability in the coefficients in different populations, particularly for FM (Wells & Cole 2002), it might be unfeasible to suggest an alternative way of routinely calculating these indices in clinical practice other than using HT^2. These observations, however, might be something to consider when analysing the different associations of FM and LM compared to their indices with regards to clinical outcomes (Chapter 8).

4.11. Conclusions

Overall, the study results show BC can be measured in paediatric inpatients using a range of techniques, each with their own advantages and limitations. BIA seems to be good alternative to assess LM when it is not possible to measure DXA LM. While none of the more 'simple' techniques to assess FM were really comparable to DXA FM. Triceps SFTs, and possibly BMI, could be the best alternatives but should be used with care considering they might introduce a significant bias and overestimate FM in individual patients compared to DXA FM. Although I have used DXA as the clinical reference method, as had been the case with many other studies, it should be remembered that this technique and the 'true gold-standard' 4C model are not entirely interchangeable (Atherton et al. 2013). The decision to support the routine measurement of a BC parameter in clinical practice, whether or not it is accurately assessing FM and LM, should ideally depend on how well they are able to relate to clinical outcomes and their ability to detect changes in the patient's condition that can influence those outcomes. The associations of the different anthropometric and BC parameters to clinical outcomes will be further analysed in Chapter 8.

Ultimately, it is likely that, as authors have highlighted in previous studies (Wells & Fewtrell 2006; Atherton et al. 2013; Van Loan 2003), no one technique will be suitable for all children at all times, and flexibility in choosing the right measurement for individual patients is one of the major steps towards implementing BC into routine practice. In this regard, the study has shown that contrarily to persistent views, BC measurements can be acceptable and practical in a tertiary paediatric centre with a heterogenous group of patients, following the approach of (Wells et al. 2012) of generating SDS using raw measurements to allow comparisons between techniques.

5 Bioelectrical impedance analysis: cross-validation of supine to standing measurements

5.1. Introduction

Bio-electrical impedance analysis (BIA) is a technique that has been validated in several settings, including in the present patient sample (Chapter 4), for the assessment of LM. This method has potential practical advantages over more complex methods, such as deuterium dilution and DXA, outside of controlled research conditions. The principles and limitations underlying this technique have been discussed in previous sections (Chapter 1, Section 1.4; and Chapter 3, Section 3.3). Despite its advantages, BIA measurements are currently not a part of routine nutritional assessment for paediatric patients in most clinical settings.

Recently, the availability of UK paediatric reference data (Wells et al. 2012) has allowed the potential to assess BIA impedance measurements and obtain SDS adjusted for age and sex for individual patients; similar to how WT and HT are currently assessed in clinical practice. This constitutes an advantage and a step towards potentially implementing these measurements in practice. The use of this reference has the added advantage that by comparing the impedance values, as impedance index (HT^2/Z) to those of healthy children of the same age and sex, the compounded error of the estimate is less than that resulting from the use of predictive equations for LM incorporated in the machine software (Wells et al. 2012; Montagnese et al. 2013; Atherton et al. 2013).

The reference data was obtained using a standing Tanita BIA machine, which as discussed in the previous chapter, can be difficult to use in a tertiary referral hospital such as GOSH where isolation procedures and the clinical condition of the patients limit access to the machine and the ability to perform the measurements. My results (Chapter 4) support the idea that bedside techniques in general are easier to implement and would result in higher success rates on admission. The QuadScan multifrequency analyser is a portable BIA machine that allows the measurement of impedance with the child in a supine position.

There are a small number of studies indicating BIA measurements from different machines can have systematic differences. A study by Nuñez et al. (1997) measured foot-to-foot BIA in adults using different machines (one standing and one lying-down) and found a significant mean difference of 15 ohms between them. Similarly, a study in adolescent girls also confirmed differences between two BIA machines in their agreement to DXA for the assessment of fat mass (Nichols et al. 2006). A third study performed specifically in children

measured BIA using a leg-to-leg standing Tanita machine and a hand-to-foot electrode BIA supine machine (BodyStat 1500) and showed a mean difference between machines of 100 ohms (Rowlands & Eston 2001). These results suggest there could be systematic differences between the readings of the two BIA machines used in the BodyBasics study, which could affect the resulting SDS.

Consequently, this chapter will look to determine if both BIA techniques can be used interchangeably, or if adjustments to supine QuadScan impedance measurements are needed to make them comparable to standing Tanita values and allow the use of the mentioned UK reference data to obtain SDS for LM in a larger number of children.

5.2. Chapter objectives

1. Compare the practicality of performing bioelectrical impedance measurements using standing and supine BIA techniques.
2. Determine the reliability of repeated supine BIA measurements using a QuadScan multifrequency analyser.
3. Explore the agreement between standing and supine BIA measurements, and determine the best adjustment to make supine impedance measurements comparable to standing BIA, thus allowing the use of UK reference data to calculate SDS to assess LM.
4. Test the agreement of supine BIA, before and after adjustments, for assessing LM compared to the study´s clinical reference method DXA LM.
5. Corroborate the agreement of the identified supine BIA adjustments in two larger cohorts, separate to the BodyBasics study: patients with Cystic Fibrosis and healthy children.

5.3. Methods

5.3.1. Study population and recruitment

The chapter aims 1-4 were investigated using the data collected from patients enrolled in the BodyBasics study at Great Ormond Street Hospital. 152 children aged 5-18yr (50% male, mean age 10.7 yr.) with a range of complex diagnoses and from all inpatient wards (admission groups: 51.3% surgical and 47.7% medical investigations/procedures) were recruited and measured. Details on consent procedures are detailed in Chapter 3 (Section 3.1), and a full description of the study population characteristics is included at the start of Chapter 7.

The last aim was investigated using data from a cohort of children with Cystic Fibrosis (CF) and healthy children recruited for other studies on body composition conducted by our research group (Williams et al. 2010; Wells et al. 2012). The first group consisted of 140 patients with CF (ages 7 to 19yr; mean age 13±2yr) under the care of Great Ormond Street Hospital who were clinically stable 14 days prior to recruitment. Children in the healthy cohort (ages 8-20yr; mean age 14±3yr) were recruited for another study via schools and adverts in two London newspapers. The study started in February 2002 and measured children born at term (>37 weeks gestation), with a birth WT >2.5 kg and no medical condition or medication that could affect the body composition measurements.

5.3.2. Data collection tools

Children in the BodyBasics study were measured on admission using two different BIA machines/techniques:

1) Standing BIA (BIA_{st}): measured using a Tanita BIA machine with 4-electrodes. The machine uses a single frequency of 50kHz to measure the resistance to the flow of electricity, and thus estimate total body water and LM. A single measurement was performed on every patient enrolled in the study.

2) Supine BIA (BIA_{sup}): measurements were taken using a multi-frequency QuadScan machine, with the subject lying down flat and electrodes placed over the left hand and foot. The machine uses frequencies of 5kHz, 50kHz, 100kHz and 200kHz, which potentially allows discerning between different body water compartments depending on the resistance to the flow of electricity with increasing frequencies. Only the impedance results using the 50kHz frequency were used in the analysis to make them comparable to the impedance results obtained using BIA_{st}. Two repeat measurements were taken for each study subject, one straight after the other with no re-positioning of the electrodes or change in the child's position.

A summary of the principles and underlying assumptions of BIA can be found in Chapter 1 (Section 1.5.2), and a complete description of the measurement conditions for the study can be found in Chapter 3 (Section 3.3.4). BIA SDS were calculated using the impedance index (HT^2/Z) for both techniques. The impedance value changed between techniques but the HT measurements used in the calculations were the same for BIA_{st} and BIA_{sup}.

In addition to BIA measurements, data on the patient's age, sex, HT and WT was collected on admission, and a DXA scan was performed when possible to serve as the clinical

reference method to assess LM. These variables and parameters were used in the data analysis to either adjust BIA_{sup} impedance values or test the agreement to BIA_{st} and DXA LM.

Children from the healthy and CF cohorts were also measured using the same BIA techniques, equipment and measurement protocols as those described for the BodyBasics study patients (Chapter 3) (Wells et al. 2012; Williams et al. 2010).

5.3.3. Data analysis and statistics

Raw impedance values from both BIA techniques were used for the analysis. HT for each subject was used to calculate the impedance index (HT^2/Z), as described in Chapter 3 (Section 3.3.4) (Atherton et al. 2013) and used to calculate SDS using the UK BC Reference data (Wells et al. 2012). The impedance indices and calculated SDS were then analysed for normal distribution and the data was summarised using means and SD, and parametric or non-parametric inference tests as appropriate.

The practicality, defined as the percentage of successful measurements performed, on admission was described for both BIA techniques. The reliability of repeated BIA_{sup} measurements was analysed using *ICC* testing and calculation of the Repeatability Coefficient (*CR*) (details on Chapter 3, Section 3.6.3).

The agreement between BIAst and BIAsup in all databases (BodyBasics, CF and healthy children cohorts) was examined using Bland Altman analysis of agreement on raw impedance values and derived SDS. Several adjustments using age and/or sex were tested using linear regression analysis on BIA_{sup} to improve on the agreement to BIA_{st} measurements. Agreement between both techniques was then assessed with % agreement and Cohen´s kappa comparing the classification of patients with 'abnormal' SDS (≥2 SDS or <-2SDS). Details on the statistical tests can be found on Chapter 3 (Section 3.6.2). Agreement of both BIA techniques compared to DXA for the assessment of LM was also tested using the agreement analysis as described above.

5.4. Practicality of standing and supine BIA techniques

As shown in Chapter 4, several patients were unable to have a standing BIA measurement on admission because they were unable to be transferred out of the wards and into the BC measurement room. Although the Tanita BIA_{st} machine could potentially be moved to the wards to measure standing BIA on patients unable to be transferred, this would still depend on the availability of the equipment for the entire hospital. For example, in this study, it was not feasible to carry the machine to each hospital ward and move it several times a day. Additionally, many of the missed measurements on admission (categorised as 'failed') involved patients unable to stand to perform the measurement (e.g. spinal surgery patients). These observations, in addition to the success of bedside techniques such as MUAC and HC, suggested that a BIA technique that could be performed in isolated and bedridden patients would be much more practical in the study population.

Multifrequency QuadScan BIA_{sup} is a machine that is portable, thus allowing beside and in-ward measurements, and it does not require the patient to stand to perform the measurement. Thus, this technique was also performed on all possible patients on admission alongside all other anthropometric and BC measurements. As Table 5.1 shows, the practicality of BIA_{sup} was much higher than that for BIA_{st} (93 vs 68% respectively).

	All successful measurements	**Successful measurements with adequate technique/conditions**
	%	*%*
BIA_{st}	68	62
BIA_{sup}	93	72

Table 5.1. Successful measurements performed on admission, including those performed only under adequate conditions and accurate technique

As was the case with all other measurements (Chapter 4, Section 4.5), a restricted database containing only those measurements performed under adequate conditions and strictly adhering to the technique's protocol was generated. Reasons for excluded measurements of BIA_{sup} were similar to those described for BIA_{st} in Chapter 4: patients with abdominal distension, oedema, and renal dialysis. In addition, because this technique was used on spinal patients with various neurological and musculoskeletal disorders, spasticity of limbs (e.g. children with cerebral palsy) and measurements taken with the patient sitting in a

wheelchair rather than lying down flat were also excluded. On occasions, patients also had hand/foot plasters and skin lotions that interfered with the placement of the electrodes and resulted in abnormal readings. The number of successful measurements in this restricted database was approximately 20% lower than with the full database, but still the percentage of successful measurements was higher compared to BIA_{st} (Table 5.1).

Table 5.2 describes the reasons for failed measurements by both techniques. Patient refusal was usually not a problem for either, while 'unavailability of the equipment' was only an issue for BIA_{st} as expected. The number of 'failed' measurements was also higher for BIA_{st}, mainly reflecting the number of patients who were unable to stand to perform the measurement, and who in contrast were able to have a BIA_{sup} measurement. The 9 failed BIA_{sup} measurements corresponded to patients where there were problems attaching the electrodes due to skin conditions/sensitivity or the presence of bandages and skin lotions.

After excluding the inaccurate measurements (see Appendix 13. Table 1), the number of failed measurements using BIA_{st} increased by 10 cases, while for BIA_{sup} this was increased by 38 cases. The exclusions for BIA_{sup} corresponded mainly to spinal surgery patients, who presented with muscle contractures, were unable to lie flat for the measurement and a small number of cases were the measurements had abnormal readings from the machine (mostly from those patients on whom the electrodes were not able to be properly attached).

	Reasons for unsuccessful measurements [a]		
	Patient refusal	Unavailable equipment *	Failed
BIA_{st}	3	16	29
BIA_{sup}	1	0	9

Table 5.2. Failed and missing measurements. *(a) number of failed measurements*
(a) number of failed measurements; (*) category refers to cases when the patient was unable to be transferred to the room where the standing BIA machine was setup to perform the measurements.

5.5. Reliability of BIA_{sup} measurements

Analysis of the reliability of BIA_{sup} measurements was determined by Bland Altman-based analysis of the difference between the two measurement impedance values, and the calculation of the *CR*.

As can be observed from Figure 5.1, most repeated BIA_{sup} measurements of impedance had a small difference between them, except for some outliers. These outliers corresponded to cases of patients with lotions or other skin conditions that caused the electrodes to detach slightly by the time of the second measurement, giving different results. These measurements were excluded for the analysis in the restricted database.

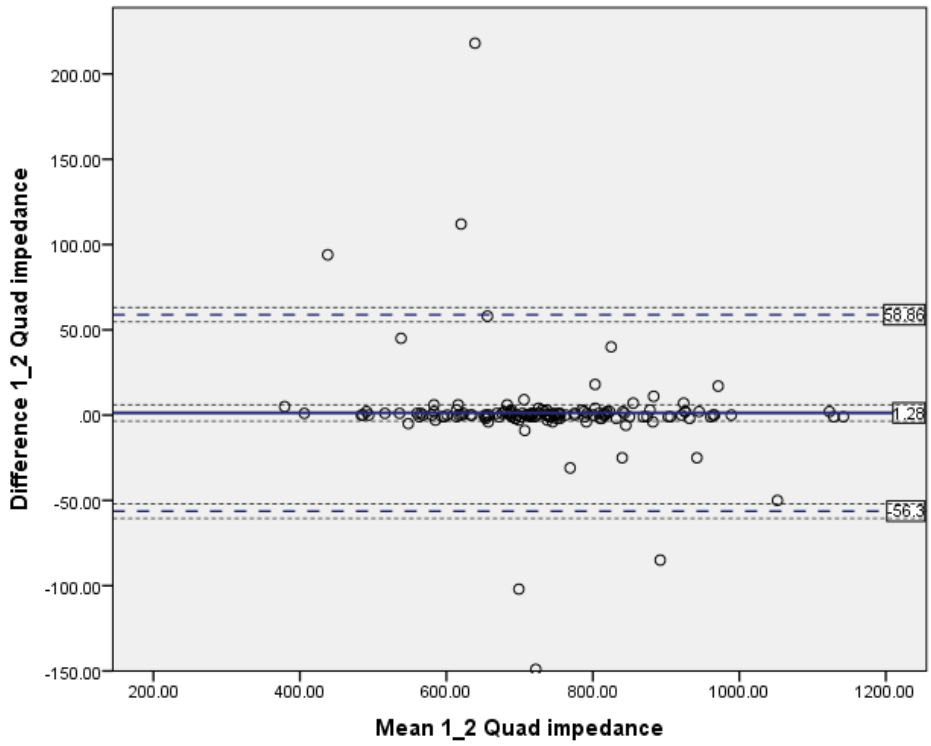


Figure 5.1. Differences between two repeated impedance measurements using BIA_{sup}
Bland Altman repeatability analysis: continuous line indicates mean bias (MB), segment lines indicate upper and lower limits of agreement (LOA), and dotted thin lines indicate 95% CI of MB and LOA.

An analysis on the *ICC* of the repeated measurements showed a significant high agreement (Table 5.3). The calculated *CR* for the whole set of measurements was 77.2 ohms (Ω). However, analysis on the restricted database that removed outlier values, where measurements had been taken with the wrong position or electrodes had been slightly detached for the second reading, resulted in an improved and much more sensible agreement between measurements (mean difference 1.3 Ω; *CR* of 3.9 Ω).

	n	*ICC* [a]	mean difference [b]	*CR* [c]
All measurements	142	0.978	1.3 (-3.6, 6.1)	77.2 Ω
Measurements taken with adequate conditions/technique	110	0.984	1.3 (1.1, 1.6)	3.9 Ω

Table 5.3. Reliability of BIA_{sup} using all measurements and only those obtained under adequate conditions/technique

(a) ICC type 3, all values significant (H_0: ICC=0, p<0.001); (b) Mean difference (Ω) between repeated measurements with 95% CI, One-sample t-test of the mean differences (H_0: MB=0, p<0.05) all non-significant; (c) Repeatability coefficient using the Bland Altman method for repeated measurements.

5.6. Comparison of impedance values and derived SDS between standing and supine BIA measurements

BIA measurements using both machines were compared to determine if both could be used interchangeably with the UK reference data to obtain SDS. The following sections describe the results testing whether BIA_{sup} impedance values and derived SDS differed from those obtained using BIA_{st} on admission, and explores different adjustments to make both techniques comparable in the BodyBasics study cohort of patients.

5.6.1. Accuracy and precision of BIAsup impedance and SDS before and after adjustments to make them comparable to BIAst

As Figure 5.2a shows, there was a strong linear correlation between both techniques, both for the raw impedance values and SDS. The Bland Altman analysis of agreement (Figure 5.3a) showed there was a significant constant difference in impedance between techniques (mean bias; *MB*= -65Ω, *p*=0.000), indicating that on average BIA_{sup} impedance values are lower than those obtained using BIA_{st}. Comparison of the calculated SDS in turn indicated significantly higher SDS for BIA_{sup}, which is explained considering the SDS are calculated using the impedance index (HT^2/Z). A significant correlation was observed between the mean SDS and the difference in SDS, indicating a greater difference between techniques in those children with higher SDS.

Different adjustments were tested to correct for the observed difference between machines. The first adjustment consisted of simply adding the observed *MB* (-65 Ω) between techniques to the raw impedance values from BIA_{sup}. There was a strong correlation between the impedance and SDS of MB-adjusted BIA_{sup} compared to BIA_{st} (Figure 5.2.b), and as can be seen from Figure 5.3b, this also resulted in a constant non-significant mean difference in raw impedance values (*MB*=0.05 Ω, *p*=0.989) and SDS (*MB*=0.01 SDS, *p*=0.715).

To explore whether the simple adjustment using *MB* could be improved further, other adjustments to the raw impedance values of BIA_{sup} were tested using age, sex, and/or WT. The resulting linear regression models are summarised in Table 5.4. However, these new adjustments did not result in a substantial improvement over the more-simple approach using the *MB*. The results for the agreement analysis using age are shown here for comparison and, as can be seen from Figures 5.2c and 5.3c, the resulting BIA_{sup} impedance values were strongly correlated to BIA_{st} and showed a non-significant constant mean difference in SDS (*MB*=0.02 SDS, *p*=0.477) compared to BIA_{st}.

Table 5.5 shows the details for the observed differences and limits of agreement (*LOA*) for the unadjusted BIA_{sup} and the two described adjustments. The precision for BIA_{sup} SDS after both adjustments was improved, in both cases resulting in narrower *LOA* of just over 0.5 SDS compared to the unadjusted values of BIA_{sup} (*LOA*=0.7 SDS). This difference in *LOA*, as well as the improvement in agreement with the adjustments, can be easily appreciated in the summary graph (Figure 5.4). The use of the restricted database values resulted in very similar results (see Appendix 13, Table 2).

Furthermore, a comparison of the observed mean impedance and SDS for this patient cohort on admission using both techniques before and after adjustment are shown in Table 5.6. The results are presented for all measurements obtained by each technique to show 'real-life' comparisons for what the assessment of the patient group would have been using wither BIA_{st} or BIA_{sup}. All mean SDS were significantly low (different from zero), indicating this patients sample would have been classified as having low average LM SDS on admission using both techniques. However, after adjustment, the BIA_{sup} mean impedance and SDS were much more similar to those observed using BIA_{st}. Some differences were still expected, considering BIA_{sup} was measured in a larger number of patients whose assessment of LM could be selectively different by including patients unable to stand and with clinical conditions affecting BC (e.g. spinal surgery patients with muscle dystrophy). The use of only accurate measurements (see Appendix 13, Table 3) resulted in mean values very similar to those observed using the entire set of measurements, but with slightly narrower *CI*.

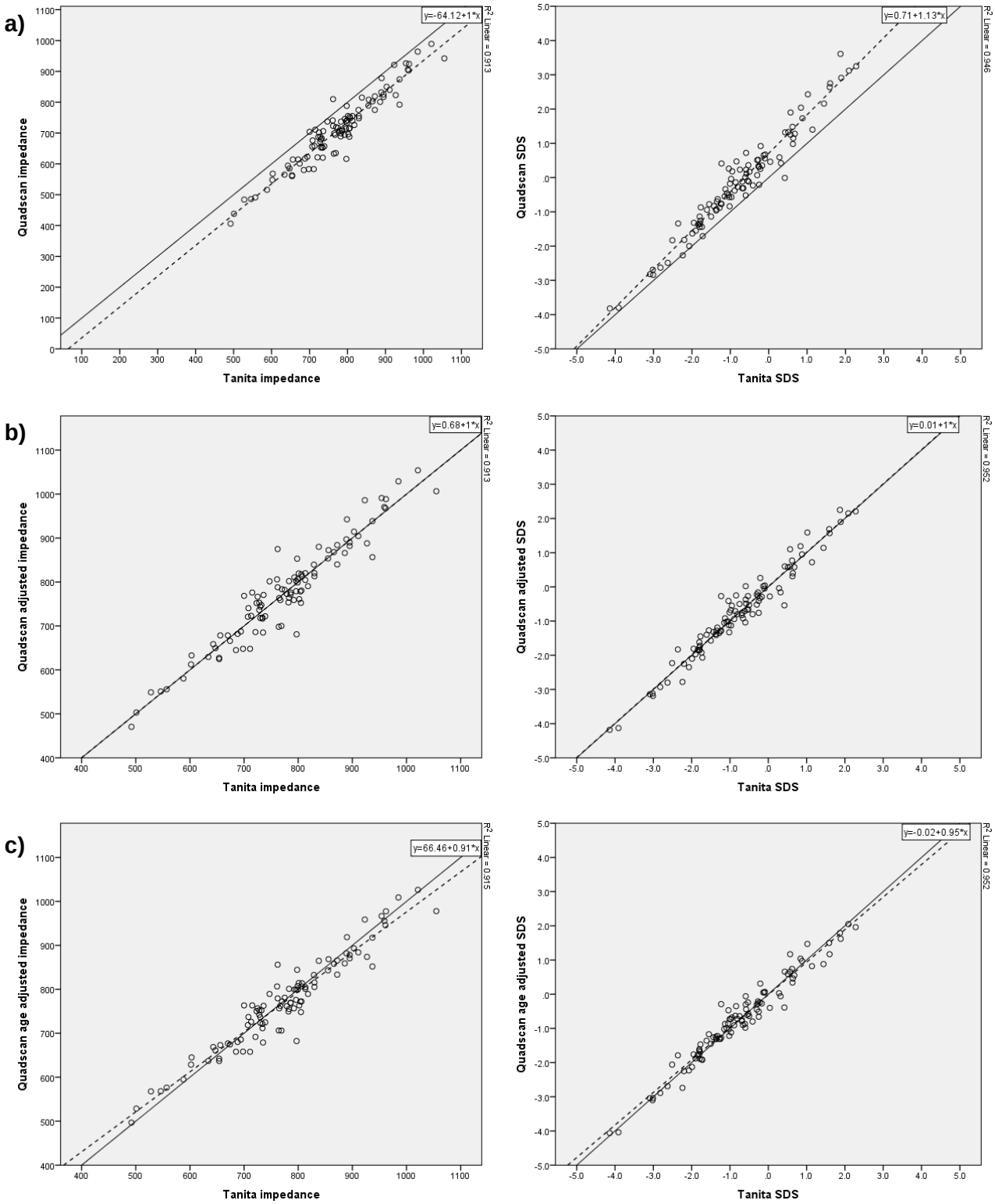


Figure 5.2. Correlations between BIA_{st} and BIA_{sup} impedance values and SDS

a) with unadjusted BIAsup, b) MB-adjusted BIAsup, and c) age-adjusted BIAsup.

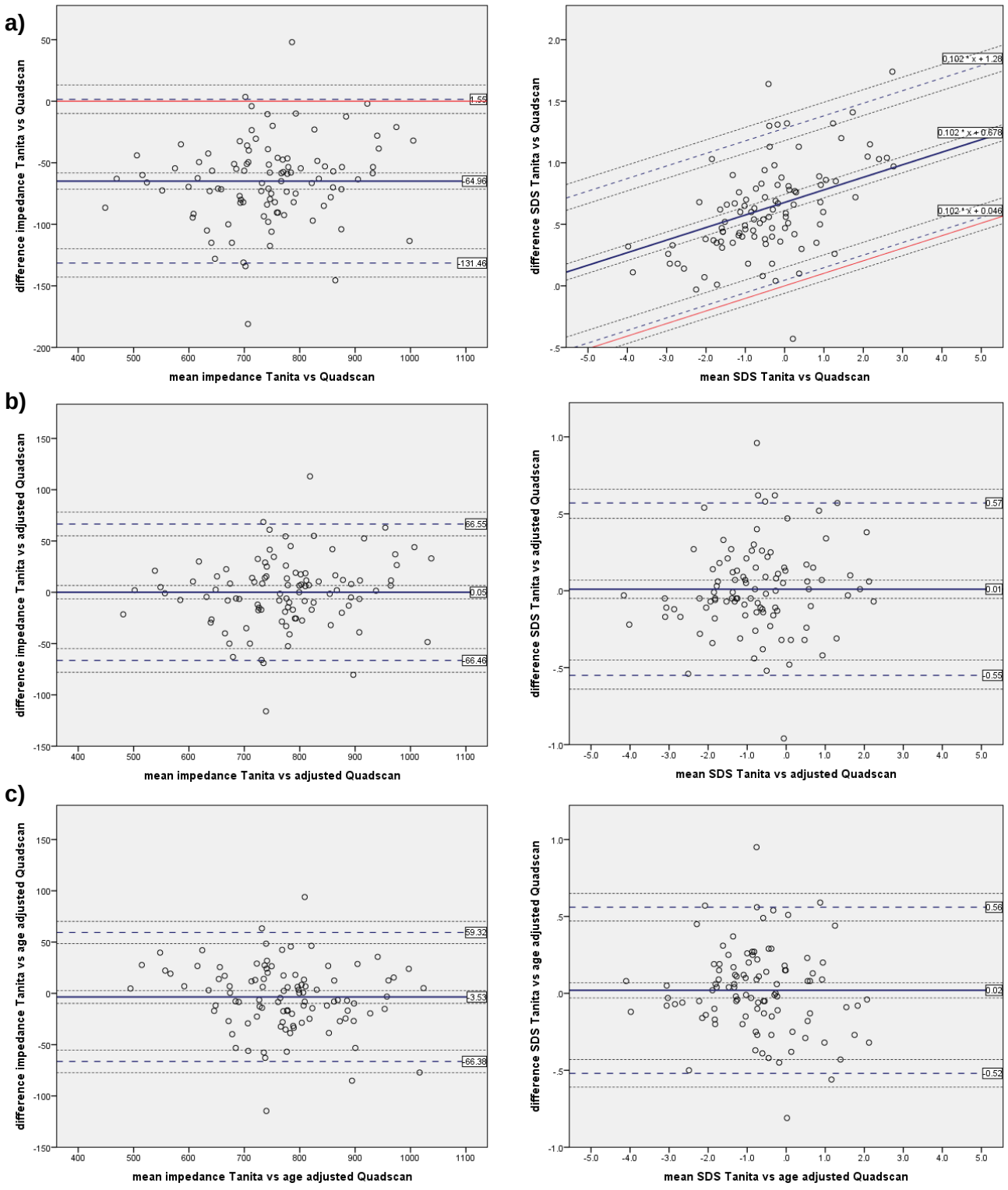


Figure 5.3. Agreement of unadjusted, MB-adjusted and age adjusted BIA_{sup} compared to BIA_{st} impedance and SDS

Bland Altman analysis of agreement: continuous line indicates mean bias (MB), segment lines indicate upper and lower limits of agreement (LOA), and dotted thin lines indicate 95% CI of MB and LOA. Red line shows MB=0. (a) with unadjusted BIAsup, (b) MB-adjusted BIAsup, and (c) age-adjusted BIAsup.

n =100	**Predictors**	***B*** [a]	***CI*** [b]	***p*** [c]	***Adjusted R^2***
Age-adjusted BIA_{sup}	Constant	94.42	36.2, 152.6	0.002	0.913
	BIA_{sup} impedance	0.93	0.9, 1.0	0.000	
	Age	1.53	-0.5, 3.5	0.137	
Adjusted BIA_{sup} by sex	Constant	125.36	84.8, 165.9	0.000	0.913
	BIA_{sup} impedance	0.91	0.9, 1.0	0.000	
	Sex (1=female)	8.50	-4.5, 21.5	0.198	
Age and sex-adjusted BIA_{sup}	Constant	99.82	40.3, 159.3	0.001	0.913
	BIA_{sup} impedance	0.93	0.9, 1.0	0.000	
	Sex (1=female)	6.09	-7.5, 19.7	0.377	
	Age	1.24	-0.9, 3.4	0.248	
WT-adjusted BIA_{sup}	Constant	112.1	41.4, 182.7	0.002	0.911
	BIA_{sup} impedance	0.93	0.8, 1.0	0.000	
	WT	0.13	-0.4, 0.7	0.631	

Table 5.4. Regression models predicting BIA_{st} impedance using BIA_{sup} impedance measurements adjusted for age, sex and/or WT

(a) Coefficients; (b) 95% CI, (c) p-value for significance of coefficient (p<0.05).

n =100	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Raw impedance						
Unadjusted BIA_{sup}	-65.0	0.000	-131.5	1.6	0.15	0.137
MB-adjusted BIA_{sup}	0.05	0.989	-66.5	66.6	0.15	0.137
Age-adjusted BIA_{sup}	-3.5	0.274	-66.4	59.3	-0.17	0.091
SDS						
Unadjusted BIA_{sup}	0.61	0.000*	-0.12	1.34	0.53	0.000*
MB-adjusted BIA_{sup}	0.01	0.715	-0.55	0.57	0.11	0.268
Age-adjusted BIA_{sup}	0.02	0.477	-0.52	0.56	-0.11	0.257

Table 5.5. Mean bias, limits of agreement and correlation coefficients for the different BIA_{sup} impedance adjustments using all available measurements

(a) Mean bias of SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

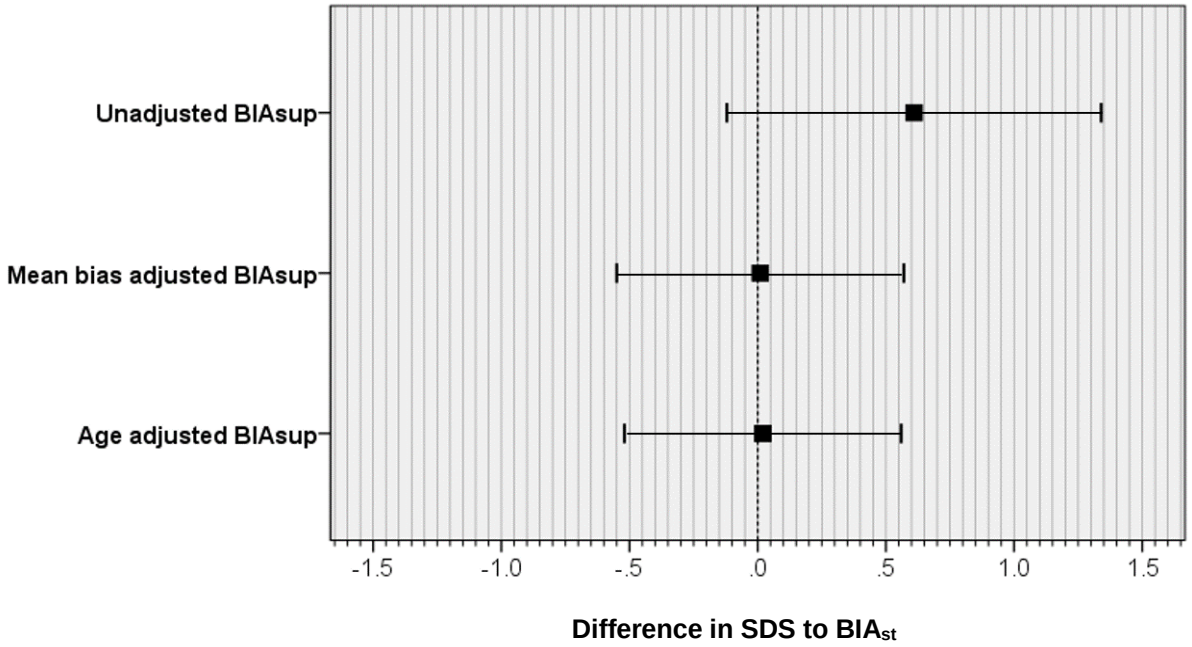


Figure 5.4. Summary of MB and LOA for BIA_{sup} to BIA_{st}

(■) MB; (|) LOA; dotted line indicates no mean difference in SDS between techniques.

	n	*mean*	*CI* [a]	
Raw impedance values				
BIA_{st}	104	776	755	797
BIA_{sup}	142	737	714	760
MB-adjusted BIA_{sup} [b]	142	802	779	824
Age-adjusted BIA_{sup}	142	796	775	817
Standard deviation scores				
BIA_{st}	104	-0.74	-0.98	-0.50
BIA_{sup}	131	-0.37	-0.65	-0.09
MB-adjusted BIA_{sup} [b]	131	-0.95	-1.20	-0.70
Age-adjusted BIA_{sup}	131	-0.94	-1.18	-0.70

Table 5.6. Mean impedance values and SDS on admission using BIA_{st} and BIA_{sup} in the BodyBasics study patient cohort

(a) 95% CI for the mean; (b) BIAsup adjusted by adding the observed MB between measurements (65 impedance).

5.6.2. Agreement of the classification of abnormal SDS between BIA_{st} and BIA_{sup} before and after adjustments

The agreement between BIA_{sup} and BIA_{st} was further tested by comparing the classification of patients with abnormal SDS (<2 SDS or <-2 SDS) between techniques. As can be seen in Table 5.7, the overall agreement between techniques was >90%, with adjustments using *MB* and age resulting in a better agreement (96% and 97% respectively).

Kappa analysis also showed an improved agreement between the techniques for the identification of abnormal SDS cases after adjusting BIA_{sup} for *MB* or age. Although all kappa values proved to be statistically significant, as was discussed in Chapter 4, the clinical significance should probably be assessed more conservatively ($\kappa>0.8$). The use of unadjusted BIA_{sup} impedance would result in moderate/substantial agreement, with expected kappa values of up to 0.84 indicating substantial agreement, but also as low as 0.45 indicating only a fair agreement in this population. On the other hand, the use of adjusted BIA_{sup} impedance values, either using *MB* or age, would result in an almost perfect agreement ($\kappa=1.0$), and a still substantial agreement ($\kappa=0.7$) as the lower expected value in this population.

The use of accurate measurements in the restricted database (see Appendix 13, Table 4) resulted in a slightly better overall agreement between techniques (93-98%), and higher kappa values (0.74, 0.91, and 0.9 for unadjusted, MB-adjusted and age-adjusted respectively), indicating substantial agreement for unadjusted BIA_{sup} and an almost perfect agreement for both adjusted BIA_{sup}.

Regarding what this would mean for the number of patients classified as having abnormal SDS on admission in this patient cohort, Table 5.8 shows that about 13% and 23% of patients were classified as having abnormal SDS using BIA_{st} and BIA_{sup} respectively, with the percentages for BIA_{sup} resembling more those of BIA_{st} after both adjustments. Again, it should be noted that BIA_{sup} was measured in a larger number of patients and the difference in the percentages indicate BIA_{sup} was able to measure more children with abnormal SDS, further supporting the use of this technique in clinical practice to identify the patients who have abnormal BC and likely to benefit from nutritional support. Results from the restricted database (see Appendix 13, Table 5) show very similar results, although all observed percentages were slightly reduced, as expected considering the exclusion of abnormal/ outlier measurements of impedance.

n =100	**Agreement** [a]	**κ** [b]	***p***
Unadjusted BIA_{sup}	90	0.65 (0.45, 0.84)	0.000*
MB-adjusted BIA_{sup}	96	0.85 (0.70, 0.99)	0.000*
Age-adjusted BIA_{sup}	97	0.87 (0.73, 1.00)	0.000*

Table 5.7. Agreement of abnormal SDS classification using unadjusted and adjusted BIA_{sup} measurements against BIA_{st} measurements

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

	n	**Patients with abnormal BIA SDS** *(%)*		
		overall	≤ -2SDS	≥ 2SDS
BIA_{st}	104	13.4	11.5	1.9
BIA_{sup}	131	25.2	16.0	9.2
MB-adjusted BIA_{sup}	131	23.7	20.6	3.1
Age-adjusted BIA_{sup}	131	21.4	19.8	1.5

Table 5.8. Patients with abnormal BIA SDS on admission using BIA_{st} or BIA_{sup}, unadjusted and after adjustments, in the BodyBasics study patient cohort

5.7. Agreement of BIA_{st} and BIA_{sup} adjusted measurements compared to DXA for the assessment of lean mass

5.7.1. Accuracy and precision of lean mass SDS

The different BIA SDS obtained using the different techniques and adjustments were tested against DXA LM SDS to determine the accuracy for the assessment of LM in this population. As Chapter 4 describes, the use of DXA has limitations but is generally considered the reference method technique for assessing FM and LM in clinical practice, considering other more advanced techniques and models such as the 4C model and deuterium dilution are generally unfeasible in these conditions.

As can be seen in Figure 5.5, there was a significant constant difference between the SDS from DXA LM and BIA_{sup} before adjusting, indicating BIA_{sup} measurements would on average overestimate LM. After adjusting BIA_{sup} for *MB* or age, the mean difference between SDS became non-significant in both cases. However, in all instances the *LOA* for the differences were over 1.0 SDS, indicating a large variance in the precision of the estimates of LM compared to the selected clinical reference method.

Table 5.9 gives the details on the agreement analysis for all BIA_{sup} measurements and BIA_{st}. In all cases, there was no significant effect of the magnitude of the measurement on the differences observed to DXA LM SDS (non-significant correlation coefficients). Furthermore, after adjusting BIA_{sup} using *MB* or age, the agreement to DXA LM SDS was comparable to what was observed for BIA_{st} with just slightly wider *LOA*, as can also be easily observed from Figure 5.6. The use of the restricted database (see Appendix 13. Table 6) containing only accurate measurements for BIA and DXA LM resulted in a very similar agreement as that observed using all obtained measurements, only again with slightly more narrow limits of agreement.

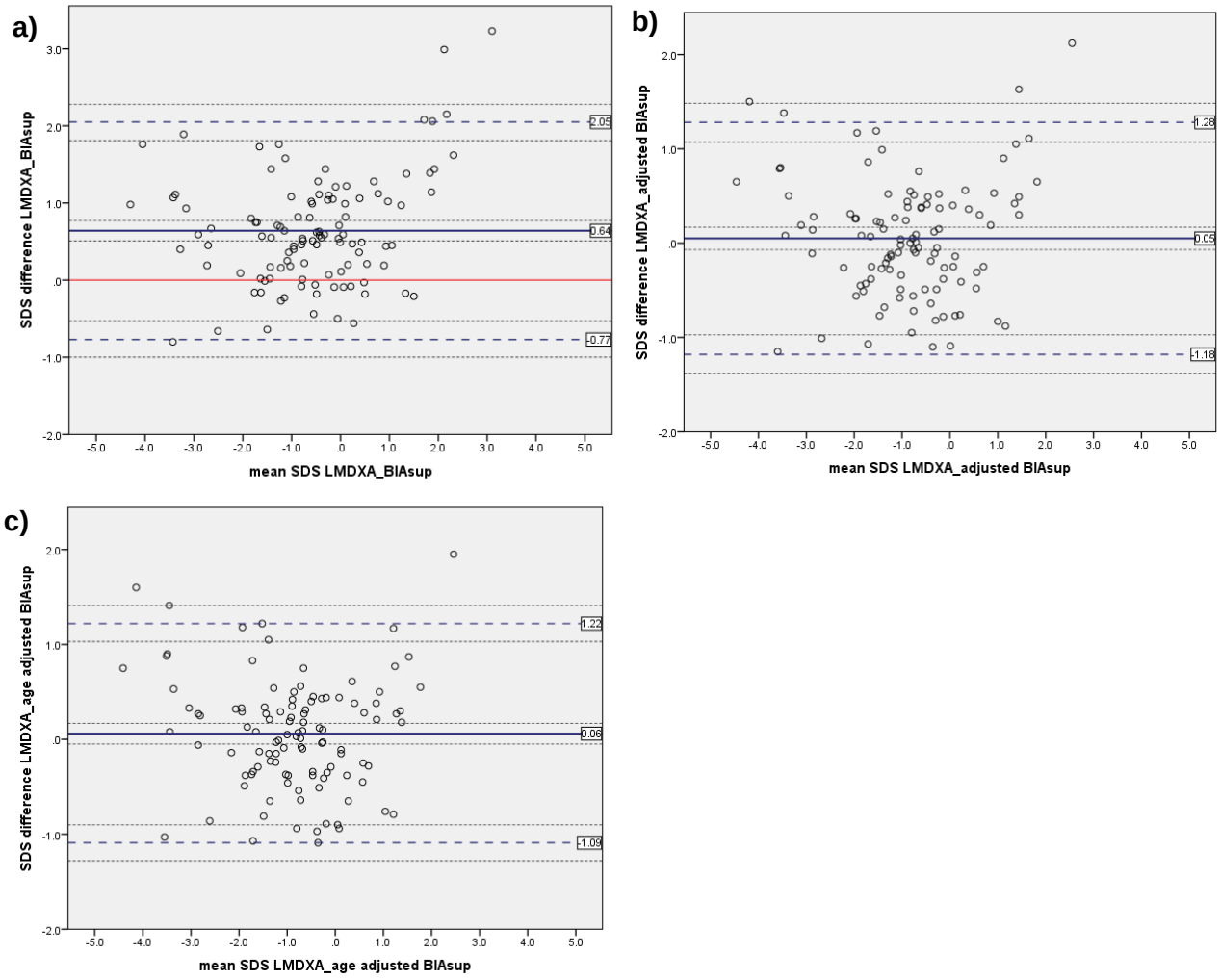


Figure 5.5. Agreement of BIA_{sup} before and after adjustments compared to DXA LM

Bland Altman analysis of agreement: continuous line indicates MB, segment lines indicate upper and lower LOA, and dotted thin lines indicate 95% CI for MB and LOA. (a) with unadjusted BIAsup, (b) MB-adjusted BIAsup, and (c) age-adjusted BIAsup.

	n	*MB* [a]	*p* [b]	*LLOA*	*ULOA*	*r* [c]	*p* [d]
Unadjusted BIA_{sup}	110	0.64	0.000*	-0.77	2.05	0.18	0.058
MB-adjusted BIA_{sup}	110	0.05	0.403	-1.18	1.28	0.04	0.714
Age-adjusted BIA_{sup}	110	0.06	0.267	-1.09	1.22	-0.07	0.460
BIA_{st}	102	-0.02	0.699	-1.10	1.06	0.02	0.826

Table 5.9. Mean bias, LOA and correlation coefficients for the different BIA measurements SDS compared to DXA LM SDS

(a) Mean bias of the measurements SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

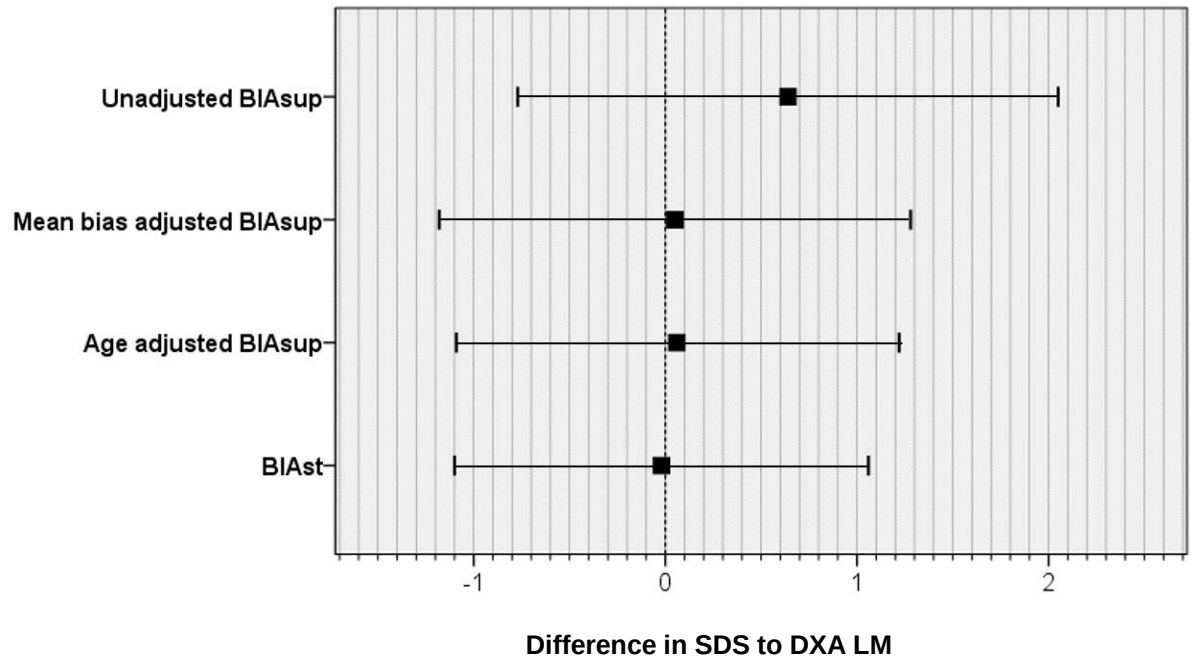


Figure 5.6. Summary of MB and LOA for BIA_{sup} and BIA_{st} SDS with different adjustments compared to DXA LM SDS

(■) MB; (\|) LOA; dotted line indicates no mean difference in SDS between techniques..

5.7.2. Agreement of abnormal lean mass SDS

The agreement between DXA LM and BIA for identifying patients with abnormal SDS (<-2 SDS or >2 SDS) was good overall, as can be observed in Table 5.10. The overall agreement for BIA_{sup} increased from 85% to 87% and 90% after adjusting the measurements for *MB* and age respectively. The kappa values showed also an increased agreement after the adjustments, up to κ=0.66.

The observed agreement and kappa values for both BIA_{sup} adjustment showed a similar agreement to that observed for BIA_{st} (92% agreement, κ=0.65). Thus, the use of either BIA_{st} or BIA_{sup} adjusted by *MB* or age, is expected to give an overall good assessment of LM compared to DXA at a population level, although with somewhat variable expected results for the assessment of individual patients. Results from the restricted database (Appendix 13. Table 7) were very similar to those described above using the complete set of measurements.

	n	Agreement [a]	*κ* [b]	*p*
Unadjusted BIA_{sup}	110	85	0.57 (0.39, 0.75)	0.000*
MB-adjusted BIA_{sup}	110	87	0.60 (0.41, 0.78)	0.000*
Age-adjusted BIA_{sup}	110	90	0.66 (0.48, 0.84)	0.000*
BIA_{st}	102	92	0.65 (0.43, 0.87)	0.000*

Table 5.10. Agreement of abnormal SDS by BIA_{st} and BIA_{sup} with different adjustments compared to DXA LM

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

5.8. Test of BIA supine adjustments in a cohort of children with Cystic Fibrosis

The proposed adjustments of BIA_{sup} to make the measurements comparable to those obtained using BIA_{st} was verified in a different population of paediatric patients. The agreement was tested using data collected from a sample of CF patients managed at GOSH, and recruited and measured as part of another study on body composition carried out by our research group (Williams et al. 2010). The dataset contained anonymised data from 140 CF patients with a mean WT of 44.2±12 kg and a HT of 151.9±13.5 cm. These children were measured using the same BIA equipment and measurement protocols as those used for the BodyBasics study. The same adjustments to the raw impedance of BIA_{sup} (MB-adjustment: add 65Ω; age-adjustment: equation described on Table 5.4) were also used.

5.8.1. Accuracy and precision of BIA_{sup} impedance and SDS before and after MB and age adjustments

As Figure 5.7 shows, there was a significant constant difference between impedance measurements obtained using BIA_{st} and BIA_{sup}, both before and after both adjustments. Table 5.11 shows in detail the resulting *MB* and *LOA* for the raw impedance values and SDS of BIA_{sup} compared to BIA_{st}. The mean difference between techniques was significant for all cases, however the adjustments did result in an improvement of the agreement (*MB*=0.15SDS and 0.12SDS, for MB and age-adjusted BIA_{sup} respectively) and, although statistically significant, the bias for the MB-adjusted and age-adjusted BIA_{sup} were small (0.15 and 0.12SDS respectively) and unlikely to be clinically significant.

Similar to observations in the BodyBasics patient cohort, the difference in SDS between unadjusted BIA_{sup} and BIA_{st} measurements was affected by the magnitude of the measurement, with a larger difference between techniques observed in those children with higher SDS. After the adjustments on BIA_{sup}, however, there was an improvement in the agreement to BIA_{st} SDS and a non-significant effect of the magnitude of the measurement on the difference between techniques. The *LOA* were also slightly narrower after adjustment (approximately 0.6 SDS unadjusted and 0.5 SDS for adjusted BIA_{sup}). Thus, as Figure 5.8. clearly shows, in agreement to observations in the BodyBasics study cohort, both adjustments similarly improved on the accuracy and precision of the derived BIA SDS using BIA_{sup} compared to BIA_{st}.

n =115	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Raw impedance						
Unadjusted	-81.72	0.000*	-139.04	-24.41	0.04	0.691
MB-adjusted	-16.72	0.000*	-74.04	40.59	0.04	0.691
Age-adjusted	-14.61	0.000*	-71.56	42.35	-0.32	0.001*
SDS						
Unadjusted	0.88	0.000*	0.30	1.47	0.59	0.000*
MB-adjusted	0.15	0.000*	-0.40	0.70	0.14	0.137
Age-adjusted	0.12	0.000*	-0.41	0.64	0.02	0.832

Table 5.11. Mean bias, LOA and correlation coefficients for the different BIA_{sup} impedance adjustments in a cohort of Cystic Fibrosis patients

(a) Mean bias of SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

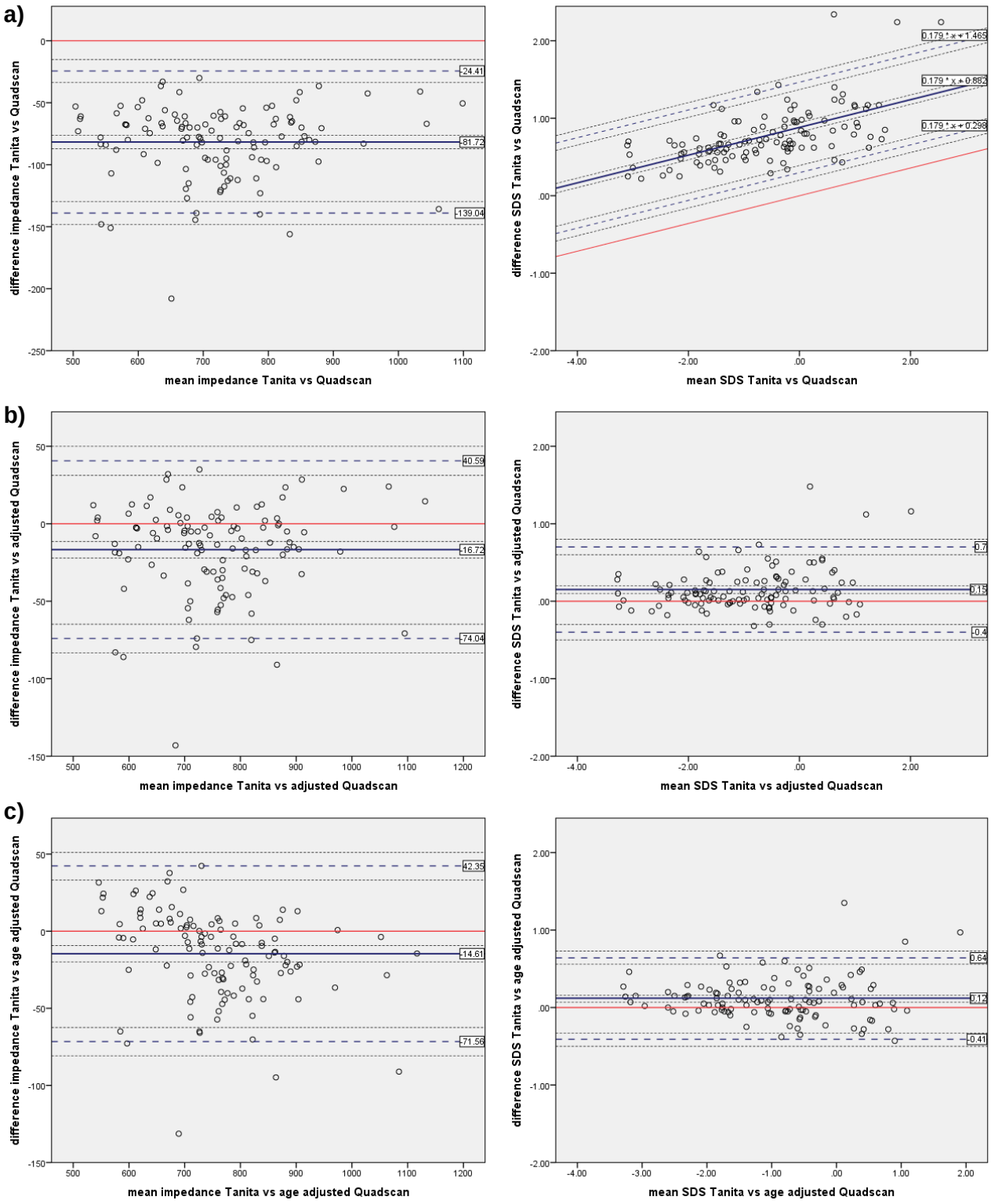


Figure 5.7. Agreement of unadjusted, MB-adjusted and age adjusted BIA_{sup} compared to BIA_{st} impedance and SDS in a cohort of Cystic Fibrosis patients

Bland Altman analysis of agreement: continuous line indicates MB, segment lines indicate upper and lower LOA, and dotted thin lines indicate 95% CI for MB and LOA. (a) with unadjusted BIAsup, (b) MB-adjusted BIAsup, and (c) age-adjusted BIAsup.

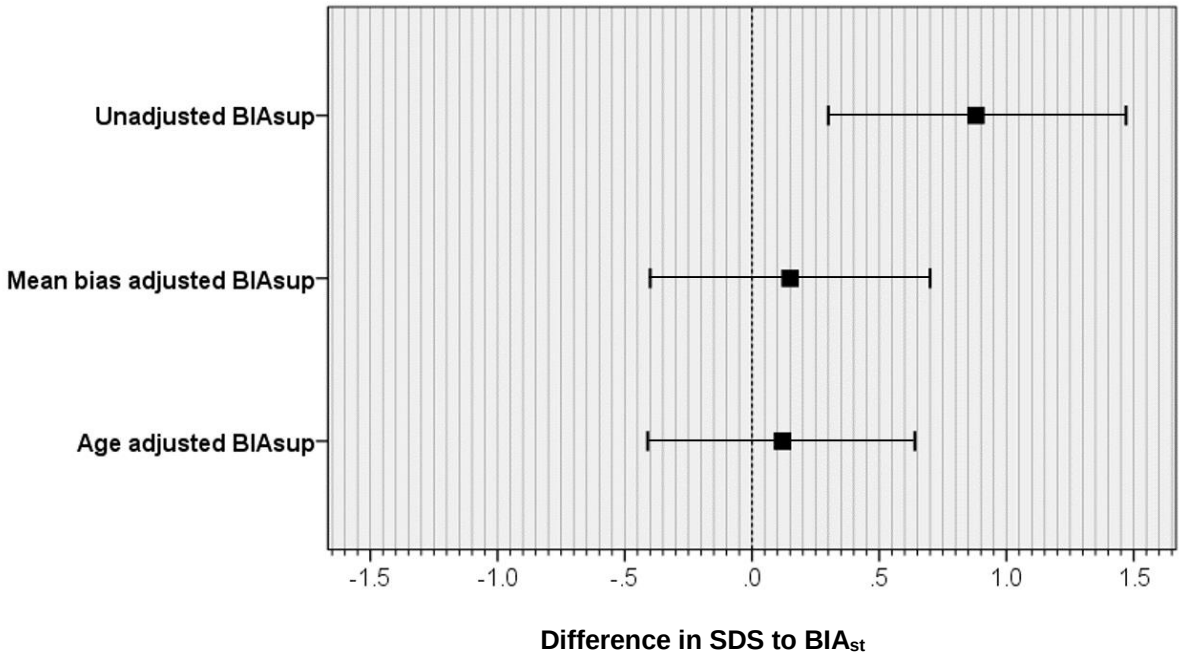


Figure 5.8. Summary of mean bias and LOA for the SDS of unadjusted and different adjustments of BIA_{sup} compared to BIA_{st} in a cohort of Cystic Fibrosis patients
(■) MB; (|) LOA; dotted line indicates no mean difference in SDS between techniques.

5.8.2. Agreement of abnormal SDS before and after BIAsup adjustments

The agreement between techniques for identifying children with abnormal SDS (>2 SDS or <-2 SDS) is summarised in Table 5.12. After adjusting for *MB* or age, the overall agreement between techniques increased from 88% to 96 and 97% respectively. There was also a substantial improvement in kappa values (from κ=0.51 to 0.85/0.87), indicating the agreement improved from only a moderate to a near perfect agreement. These results were very similar to those observed in the BodyBasics study, suggesting these adjustments would correct for the difference in technique/equipment and allow the use of either for the assessment of LM in several populations of paediatric patients.

n =115	**Agreement** [a]	***κ*** [b]	***p***
Unadjusted	88	0.51 (0.72,0.29)	0.000*
MB-adjusted	96	0.85 (0.98,0.72)	0.000*
Age-adjusted	97	0.87 (0.99,0.76)	0.000*

Table 5.12. Agreement of abnormal SDS using unadjusted and adjusted BIA_{sup} measurements against BIA_{st} abnormal SDS in a cohort of Cystic Fibrosis patients
(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

5.9. Test of BIA supine adjustments in a cohort of healthy children

The proposed BIA_{sup} adjustments were lastly tested in a sample of 362 healthy children (mean WT 52.1±14.8 kg, HT 159.2±13.5 cm) measured by both BIA techniques. The analysis used the anonymised data collected for these children recruited and measured for another study performed by our research group (Wells et al. 2012).

5.9.1. Accuracy and precision of BIA_{sup} impedance and SDS before and after MB and age adjustments

As Figure 5.9 and Table 5.13 show, once again the agreement between BIA_{st} and unadjusted BIA_{sup} showed a significant difference, with lower BIA_{sup} impedance values and resulting higher SDS. There was also a greater difference between techniques for those children with higher BIA SDS, but with slightly more narrow *LOA* compared to the BodyBasics study.

After adjusting BIA_{sup} measurement using the *MB* or age, the difference between techniques improved substantially. The adjustment using age was the most accurate and precise, as this resulted in non-significant differences between techniques and narrow LOA of approximately 0.5 SDS. The adjustment using the *MB* resulted in a statistically significant bias, but one that was only slightly higher than 0.1 SDS and unlikely to be clinically significant. Thus, both adjustments seem to correct for the use of another technique/equipment in this sample of healthy children and, as can be appreciated from Figure 5.10, result in consistently similar patterns of improved agreement to those observed for paediatric patients with CF and those enrolled in the BodyBasics study.

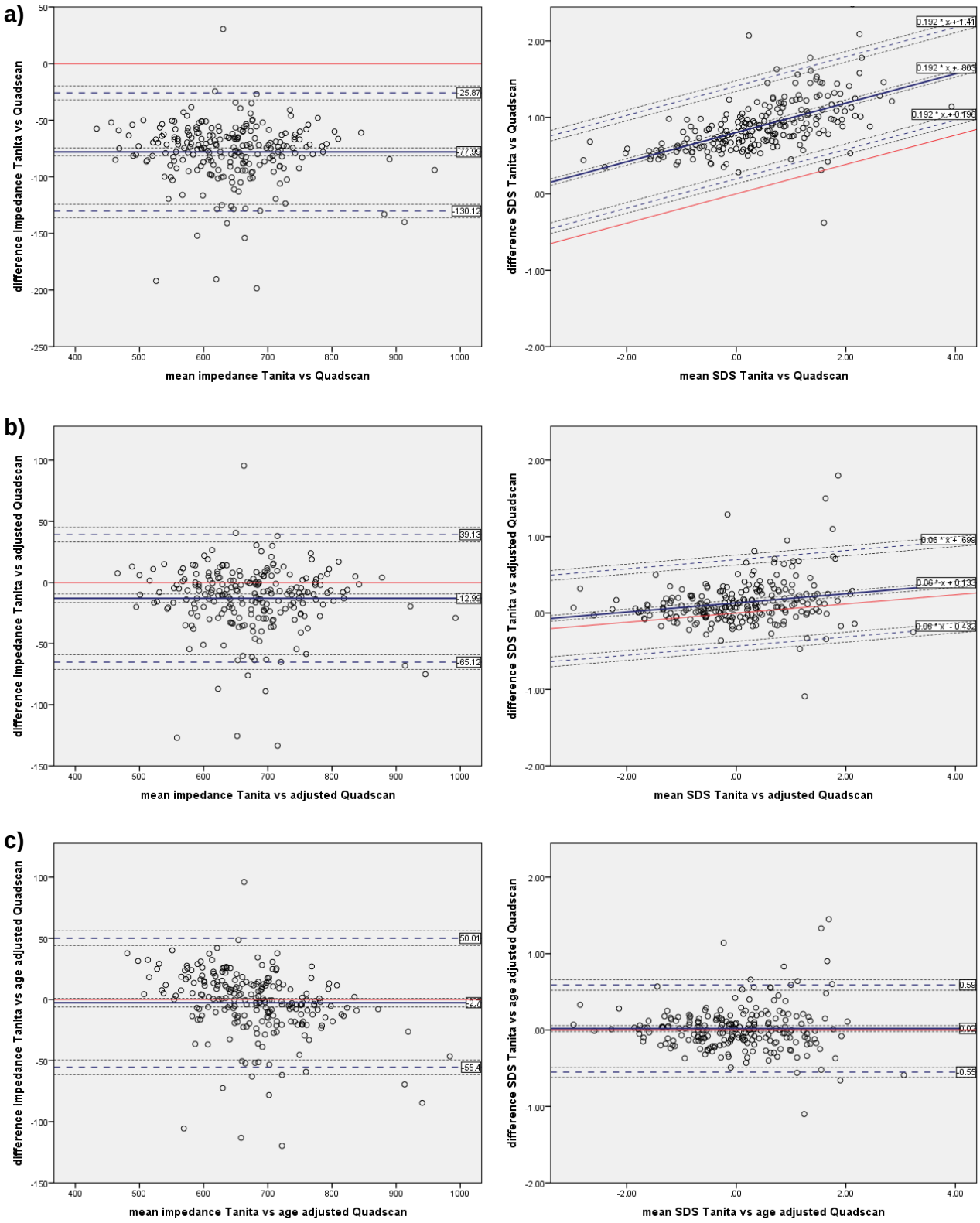


Figure 5.9. Agreement of unadjusted, mean bias adjusted and age adjusted BIA_{sup} compared to BIA_{st} impedance and SDS in a cohort of healthy children

Bland Altman analysis of agreement: continuous line indicates MB, segment lines indicate upper and lower LOA, and dotted thin lines indicate 95% CI for MB and LOA. (a) with unadjusted BIAsup, (b) MB-adjusted BIAsup, and (c) age-adjusted BIAsup.

n =228	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Raw impedance						
Unadjusted	-77.99	0.000	-130.12	-25.87	-0.08	0.246
MB-adjusted	-12.99	0.000	-65.12	39.13	-0.08	0.246
Age-adjusted	-2.70	0.132	-55.40	50.01	-0.35	0.000*
SDS						
Unadjusted	0.80	0.000*	0.20	1.41	0.56	0.000*
MB-adjusted	0.13	0.000*	-0.43	0.70	0.21	0.002*
Age-adjusted	0.02	0.354	-0.55	0.59	0.02	0.787

Table 5.13. Mean bias, LOA and correlation coefficients for the different BIA_{sup} impedance adjustments in a cohort of healthy children

(a) Mean bias of SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

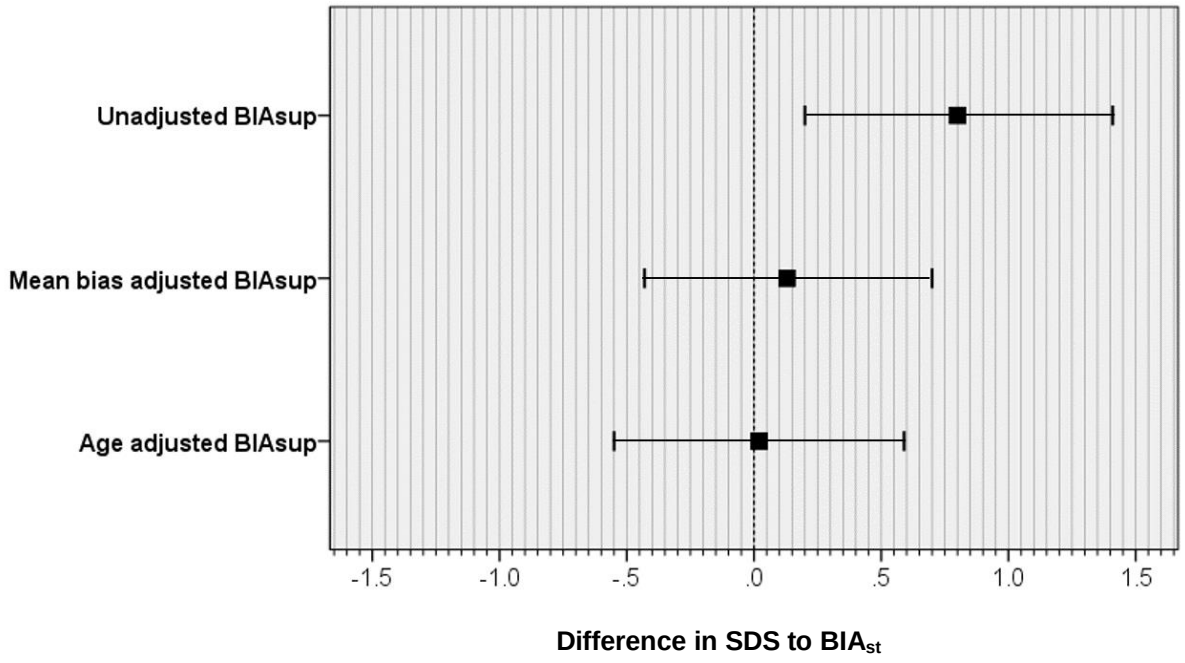


Figure 5.10. Summary of mean bias and LOA for the SDS of unadjusted and different adjustments of BIA_{sup} compared to BIA_{st} in a cohort of healthy children

(■) MB; (\|) LOA; dotted line indicates no mean difference in SDS between techniques.

5.9.2. Agreement of abnormal SDS before and after BIAsup adjustments

The agreement between BIA_{st} and BIA_{sup} techniques in identifying children with abnormal SDS once more showed a very similar pattern to that observed in the cohort of BodyBasics and CF patients. Unadjusted BIA_{sup} measurements resulted in an agreement of 82%, which was improved substantially to 97% after adjusting the measurements using *MB* or age (Table 5.14). Similarly, the kappa values improved after both adjustments, with the highest kappa values observed for the MB-adjustment (κ=0.66). This further supports the idea that the bias between MB-adjusted BIA_{sup} and BIA_{st} in this sample of children is unlikely to be significant in practice, especially when identifying children with abnormal. However, all kappa values were lower than those observed in the agreement analysis of CF and BodyBasics patients, achieving only a kappa of 0.66 maximum using MB-adjusted BIA_{sup} measurements. This difference could be explained due to differences in the percentage of children with abnormal SDS between both groups, since as expected this was much lower in the sample of healthy children (3.1% compared to 13.4% in the BodyBasics study, both using BIA_{st}).

n =228	**Agreement** [a]	***κ*** [b]	***p***
Unadjusted	82	0.16 (0.03, 0.30)	0.000*
Mean bias adjusted	97	0.66 (0.42, 0.89)	0.000*
Age adjusted	97	0.58 (0.29, 0.86)	0.000*

Table 5.14. Agreement of abnormal SDS using unadjusted and adjusted BIA_{sup} measurements compared to BIA_{st} in a cohort of healthy children

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

5.10. Summary of main findings

- BIA bedside measurements using a QuadScan machine (BIA_{sup}) were more practical than standing Tanita (BIA_{st}) measurements in this sample of patients with complex diagnoses (93% vs 68% of patients measured on admission).
- Several of these measurements were performed in patients with fluid shifts, contractures and other small deviations from the measurement protocols. However, even excluding these possibly inaccurate measurements, a higher number of patients were still able to be measured by BIA_{sup} compared to BIA_{st}.

- Repeated BIA_{sup} measurements were reliable, with a *CR* of 3.9 Ω using the restricted database with accurate measurements.
- Agreement analysis showed BIA_{sup} was significantly different to BIA_{st} in terms of impedance values, SDS and categorising patients with abnormal SDS.
- A simple adjustment using the observed MB between techniques (65 Ω) resulted in a good agreement for impedance values, SDS and abnormal SDS.
- Further corrections using age also corrected for the difference between techniques, but did not improve substantially on the described more-simple adjustment using MB.
- The agreement between unadjusted and the MB/age-adjusted BIA_{sup} measurements to BIA_{st} was also confirmed in other samples of CF patients and healthy children.

5.11. Discussion

5.11.1. Practicality and reliability of standing and supine BIA measurements

The results confirmed the practical advantages of performing BIA measurements using a bedside machine such as the QuadScan analyser, and particularly one that can be performed in patients unable to stand. The study population includes many children with mobility issues, such as those with neuromuscular conditions, and/or unable to be transferred off the ward due to isolation procedures as happens before BMT. Thus, it is particularly helpful to have available a technique that is simple, quick and flexible in the conditions of measurement. With this equipment, it is expected that up to 97% of patients could have a measurement of BIA performed on admission.

As expected, the use of a restricted database with only those measurements performed with strict adherence to the measurement protocol, resulted in fewer successful measurements. However, even in this case, the results show that more than half (and up to 80%) of the patients in this population would be able to be measured in admission to hospital. Considering this restricted database excluded many of the abnormal extreme measurements, the repeatability and precision of the measurements were improved.

The analysis examining the reliability of BIA_{sup} measurements also indicated a good agreement, with a non-significant mean difference between repeated measurements of only 1.3 Ω. However, there was variability leading to *LOA* over 50 Ω, mainly due to the effect of some outlier measurements that corresponded to patients where the electrode attachment was problematic.

5.11.2. Validity and adjustments of supine BIA measurements to assess lean mass in paediatric patients and healthy children

Considering one of the imitations to the routine use of BIA and other BC measurements in clinical practice is the lack of appropriate reference data (Atherton et al. 2013; Wells & Fewtrell 2008), it was important to determine if the same reference data used to calculate SDS using BIA_{st} measurements could be used for BIA_{sup} measurements. My results showed that BIA_{sup} measurements resulted in consistently lower impedance readings compared to BIA_{st}, which in turn translated to higher SDS. This could be the result of differences in the way each machine measures and detects the electric current and resistance, or differences in the position of the patient and the resulting redistribution of body water. Nevertheless, adjusting for this mean difference between techniques (*MB*=65 Ω) greatly improved the agreement to BIA_{st}. Further adjustments using age also resulted in a good agreement compared to BIA_{st}, but did not improve much upon the initial more-simple adjustment using *MB*. Similarly, with both adjustments, the resulting kappa for abnormal BIA SDS was very significant, indicating an almost perfect agreement between techniques. The agreement analysis using the restricted database with 'accurate' measurements did not result in overtly different observations, aside from less variance and narrow LOA as expected; supporting the overall use of measurements that might deviate just slightly from the measurement protocols, as is likely to occur in routine clinical practice, for BIA assessment in groups of patients but with caution still warranted at the individual level.

The observed difference between techniques was only influenced by the magnitude of the measurements when comparing the derived SDS of unadjusted BIA_{sup} to BIA_{st}; with patients with higher SDS showing a larger difference between techniques. Considering this was not observed for the agreement analysis of the impedance values or any other adjusted BIA_{sup} SDS, it is likely that this positive correlation can be related to the LMS curve fitting process when calculating the SDS from the raw impedance index values (Wells et al. 2012) and is an artefact arising from the fact that the reference data was not design for use with supine BIA readings, rather than a true association. This pattern was subsequently confirmed using different population samples of CF and healthy children.

When assessing the implications of the different unadjusted and adjusted BIA_{sup} SDS for the assessment of patients in the BodyBasics cohort on admission as normal or abnormal, the percentage of patients with abnormal scores (particularly >2 SDS) decreased to more comparable levels as those observed for BIA_{st} after BIA_{sup} impedance values were adjusted using the MB or age. However, BIA_{sup} measurements could be performed in a greater number of patients, especially those unable to stand for BIA_{st} measurements, and based on the

results, a number of them had abnormal BIA SDS. The fact that more supine BIA measurements could be performed in patients with abnormal SDS, further supports its usefulness for identifying patients in clinical practice who might benefit from referral to a comprehensive nutritional assessment and management.

Subsequent comparisons of BIA_{st} and adjusted BIA_{sup} to DXA LM SDS gave further evidence that these adjustments would correct BIA_{sup} impedance measurements to make them comparable to BIA_{st} specifically for the assessment of LM in this population. The accuracy and precision to DXA LM SDS was slightly better for BIA_{st} SDS, but it should be highlighted again that more BIA_{sup} measurements were performed and that some of these corresponded to patients with more extreme SDS (and thus 'abnormal' SDS), and could thus be introducing greater variance in the distribution of the measurements.

To ensure the adjustments to BIA_{sup} were also valid in other populations, they were tested in other samples of patients and healthy children. The resulting observations confirm the improved agreement of the techniques using the proposed adjustments. The precision of the estimates was better for the CF patients and healthy children compared to the BodyBasics study, which could be explained from the fact that the subjects were likely more homogenous and the subjects likely had less conditions affecting the accuracy of the measurements (e.g. severe contractures, fluid overload and abdominal distention, difficulty positioning to take the measurement, etc.). The advantage of performing the analysis on a very diverse sample compared to that of the present study, is that the precision is likely to be similar or better in other settings, as confirmed by the results.

Considering issues of practicality in clinical settings, MB-adjustments for supine BIA measurements are likely the best option, as they provide a simple and fast way to correct for the observed bias. The suggested adjustment(s) between these techniques, however, might still be influenced by the specific make and model of BIA machines and this should be also considered when contemplating their implementation in practice. Thus, although it has been shown that these two machines can be used after a simple adjustment; it is not guaranteed this would still be the case for other standing and supine BIA machine models.

Previous studies, performed in different populations and using different BIA machines (standing, lying-down, hand-to-foot, leg-to-leg), have consistently reported the presence of bias between measurements (Rowlands & Eston 2001; Nuñez et al. 1997; Nichols et al. 2006). The results from this study are in line with these reports, and the differences observed in the assessment of BIA SDS and abnormal SDS in this patient cohort using unadjusted BIA_{sup} measurements, similarly support the need to validate the use of different BIA machines

(compared to standing Tanita if using the UK BC reference data), especially when making longitudinal comparisons in individuals or groups, and for comparisons between studies.

A last important issue regarding BIA assessment in practice relates to obtaining accurate measurements of HT. As described, SDS were calculated using the impedance index (HT^2/Z). The HT measurements used to calculate these indices and SDS presented in this chapter, were analysed using the database of only accurate measurements. However, the complete study database contained, especially for the case of BIA_{sup}, many non-ambulant patients and the collected data was a mixture of accurate standing measurements, patient-reported HT and estimates from arm-span or lying-down in bed tape measurements. Analysis of this complete database did not show very different results to the 'accurate' measurements only, but although average group results might be similar, this does not dismiss the possibility of differences and inaccuracies at the individual level. As my own results in Chapter 4 and many other studies have reported (Pichler, Hill, et al. 2014), HT measurements on admission are often difficult to obtain; meaning even if BIA_{sup} measurements are available for the assessment of LM in bed-ridden patients, these measurements might not be useful if an accurate estimate of HT is not available to calculate the impedance index. This highlights the importance of measuring or accurately estimating HT in clinical practice, not just for the assessment of growth, but for the assessment of BC in patients who are also likely to have the more complex clinical conditions and the highest risk of sub-optimal nutritional status. Different approaches to estimate HT will be explored in the following Chapter.

5.12. Conclusion

The measurement of BIA_{sup} using the multifrequency QuadScan analyser, is overall a practical and reliable technique that can be easily adjusted to make it a valid alternative to assess BIA and estimate LM SDS in children who are unable to stand to use the Tanita BIA_{st} machine. The different adjustments showed good accuracy and precision, both in terms of derived SDS and for identifying patients with abnormal BIA SDS (<-2 SDS or >2 SDS). Furthermore, they also showed a good agreement to the clinical reference method method for assessing LM, comparable to what was observed using BIA_{st}. Considering the simplicity of adding a constant value of impedance (65 Ω) compared to other more complicated adjustments necessitating the use of equations, this seems to be the best alternative for clinical practice. Finally, the results indicate that patients on whom a standing BIA measurement was not possible to obtain, were often those who had a low SDS measured by BIA_{sup}, suggesting they had low amounts of LM and potentially those patients who would benefit the most from this assessment.

6 Estimating height in paediatric patients using segmental bone measurements: validity of ulna and tibia lengths

6.1. Introduction

Height (HT) is an important anthropometric measurement in clinical practice that is especially relevant for paediatric patients, as it is used not only to assess the normal growth of the child, but also forms a key component of nutritional assessment (Aurangzeb et al. 2012; Leite et al. 1993; Motil 1998). In terms of nutritional assessment, the calculation of BMI (WT/HT^2) requires a measurement of HT, as does the calculation of BC parameters such as the impedance index (HT^2/Z), FMI and LMI (Atherton et al. 2013; Wells 2001). Most hospitals and health authorities have procedures and guidelines indicating patients should have a measured HT (length in children <2 yr.) on admission (Velandia et al. 2016; Pichler, Hill, et al. 2014). Furthermore, the importance of performing this measurement has been supported by evidence of poor agreement between measured and self/parent-reported HT (Bryant et al. 2014; Van Cauwenberghe et al. 2014; Geurden et al. 2012; Wen & Kowaleski-Jones 2012).

Despite its importance, there are limitations in clinical practice that can interfere with the accurate measurement of HT (Bunting & Weaver 1997; Milani et al. 2013; Pichler, Hill, et al. 2014). Chapter 4 has described that, in this diverse sample of paediatric patients, a substantial proportion of children were unable to stand to be measured as required by the study protocol. Different patient conditions (critical illness, bedridden patients with neuromuscular, spinal or developmental disorders) might be common barriers to taking an accurate measurement (Milani et al. 2013; Gauld et al. 2003; Haapala et al. 2014); as was the case in our patient sample. Additionally, the availability of equipment that is properly calibrated in the wards, staff training, procedures on admission and the resulting constraints in time could all make the measurements difficult to execute (Bunting & Weaver 1997; Bouma 2017; Restier et al. 2015). All these factors can result in inaccurate or low reporting rates of HT in patient medical records (Pichler, Hill, et al. 2014; Sissaoui et al. 2013; Larsen et al. 2014).

In view of the difficulties in obtaining a measurement of HT, especially in the context of a patient's clinical condition interfering with their ability to stand, alternative measurements have been proposed. Published studies have analysed different body surrogate measurements to estimate HT, especially in adult patients (Madden et al. 2012; Sancho-Chust et al. 2010; Duyar & Pelin 2003) or children with specific clinical conditions (e.g.

cerebral palsy) (Bell & Davies 2006; Oeffinger et al. 2010; Spender et al. 1989; Yousafzai et al. 2003); with only a few studies focusing on estimating HT in paediatric patients with a range of clinical conditions (Gauld et al. 2004; Abrahamyan et al. 2008; Neyestani et al. 2011).

Surrogate measurements often involve different long bone measurements such as ulna or tibia lengths, or segmental body measurements like knee height or arm span, which could lead to significantly different estimates (Froehlich-Grobe et al. 2011). The studies have also either generated reference data to evaluate growth directly from some of these surrogate measurements (Dangour et al. 2002; Fredriks et al. 2005), or have calculated prediction equations to estimate HT (Gauld et al. 2004; Weidauer et al. 2014; Neyestani et al. 2011). Because different populations can vary in their body proportions, especially during the growth period of childhood and with several chronic and stress conditions that affect the growth rates of different bones and body proportions (Abitbol et al. 1990; Li et al. 2007; Pomeroy et al. 2012; Engstrom et al. 1981), it becomes important to have population-appropriate references and/or predictive equations to ensure the accuracy of the HT assessment.

Considering the available evidence comes from measurements in a variety of different populations and using different surrogate measurements and protocols, it is unclear which surrogate measurement is the most accurate to estimate HT in UK paediatric patients with a range of clinical conditions. Additionally, practicality is especially relevant in implementing these measurements in clinical settings, and some of these measurements require the use of specialised equipment (anthropometers, knee height calipers) and varying degrees of challenge in the measurement body position (e.g. for arm span, the child needs to be standing, back to the wall, arms straight angle from body) that might be difficult to achieve.

In the context of a tertiary paediatric hospital, where many children have chronic conditions and growth alterations, it is important to know if references/equations generated in a healthy population of children using different surrogate measurements can be used in clinical practice to assess their growth and nutritional status. Thus, this chapter will focus on assessing the use of segmental bone measurements for estimating HT and using this estimate to calculate other anthropometric and BC parameters in children with a range of complex conditions admitted to a tertiary paediatric hospital.

Ulna and tibia length measurements were chosen as they were commonly reported surrogate measurements for HT, and two studies in children in Australia and France (Gauld et al. 2004; Abrahamyan et al. 2008) had reported predictive equations using similar measurement protocols as those used in this study (see methods section in this chapter). They were additionally considered to be practical and easy to obtain in children with a range of clinical conditions, especially for those bedridden or with developmental delay.

6.2. Chapter objectives

1. Generate HT prediction equations using tibia and ulna length tape measurements from a sample of healthy UK children.
2. Analyse the accuracy of the derived equations (objective 1) to estimate HT and other parameters using tape measurements of ulna and tibia lengths in paediatric patients with a range of clinical conditions.
3. Test the accuracy of the derived equations (objective 1) to estimate HT and other parameters using DXA whole-body scan measurements of ulna and tibia lengths in paediatric patients with a range of clinical conditions.
4. Assess the agreement between ulna and tibia lengths obtained with the standard tape measurement technique and DXA whole-body scan measurements.
5. Compare the estimates of HT obtained using different published paediatric equations and those calculated in the study (objective 1), and determine if estimates can be improved using a 'wisdom of crowds' approach using the different prediction equations.

6.3. Methods

6.3.1. Study population and recruitment

Prediction equations from ulna and tibia length measurements (objective 1) were calculated using anonymised data from healthy UK children enrolled for other studies at our department (Fewtrell et al. 1999, and unpublished data). The generated prediction equations to estimate HT and other parameters were tested in our cohort of 152 patients enrolled to the BodyBasics study (objectives 2-5). Recruitment procedures for the BodyBasics study have already been detailed (Chapter 3, Section 3.1) and study group characteristics will be further described at the start of Chapter 7.

6.3.2. Data collection tools

Ulna and tibia measurements for both UK healthy reference children and BodyBasics paediatric patients were obtained using a non-stretchable tape, with measurements performed by duplicate on the left side to the nearest 0.1cm. Standing HT was obtained by duplicate to the nearest 0.1cm using a wall-mounted stadiometer. The protocol procedures for these measurements are detailed in Chapter 3, Section 3.3.5.

Additionally, another measurement technique for long-bones using custom-analysis (in Lunar encore software regions-of-interest ROI analysis) of whole-body DXA scans (Lunar Prodigy scanner) was used as described in a study by Abrahamyan et al. (2008). Considering that tape measurements for ulna and tibia lengths were not commenced from the start of recruitment to the BodyBasics study, the retrospective analysis of the DXA scan database of BodyBasics patients allowed the number of measurements obtained for ulna and tibia lengths to increase (*n*=113) compared to those obtained using the standard tape-measurement technique (*n*=26). Arm span measurements were also attempted together with the ulna and tibia lengths, but were abandoned (data not presented in the thesis) once it became clear that the measurement was difficult to obtain even in relatively healthy children, and more so in patients with contractures and other neuromuscular conditions.

6.3.3. Data analysis and statistics

For objective 1, ulna and tibia length measurements of healthy children were analysed using linear regression models to generate prediction equations for measured height. Adjustments for age, sex and weight were performed, and the model fit assessed using the adjusted R^2 and the significance of the coefficients in the model.

The reliability of tape and DXA whole-body scan measurements was assessed using *ICC* and the Bland Altman analysis *CR*s, as detailed in Chapter 3, Section 3.6.3. Agreement between estimated HT and standing HT measurements was assessed with Bland Altman analysis for the differences in HT (cm) and HT SDS, and agreement of 'abnormal' SDS (<-2 SDS or > 2SDS) was tested using Cohen's kappa and absolute % agreement (details in Chapter 3, Section 3.6.2). Similar analyses were performed to test the agreement for BMI (as kg/m^2 and SDS) and BIA SDS obtained using the measured and the estimated HT values. A validation of the technique based on DXA whole-body scan analysis of ulna and tibia lengths compared to the standard tape-measurement technique was also performed using Bland Altman analysis of agreement for the measured ulna and tibia lengths (cm) and the resulting HT SDS.

An approach known as the 'wisdom of crowds' (Surowiecki 2004) was used in the study, which maintains that the aggregate (average) of several individual predictions, no matter how individually 'flawed', can lead to a more accurate estimate of a parameter (Wells et al. 2009). To perform the analysis, the HT estimates calculated from different published equations (Abrahamyan et al. 2008; Gauld et al. 2004) and our own predictive equations (objective 1) were used, and an agreement analysis (as detailed above) was performed for each individual estimate and for the average of all the estimated HT values ('aggregate').

6.4. Height prediction equations from ulna and tibia lengths in heathy UK children

6.4.1. Height estimates using ulna length

Data from a cohort of healthy children (*n*=700) was analysed to generate equations to predict standing HT from ulna length measurements. Table 6.1 describes some of the main subject characteristics. The children were aged 4-14yr, with 362 boys and 338 girls measured. The SDS for weight, height and BMI were calculated using UK reference data (Freeman et al. 1995; Cole et al. 1995). As expected, the mean weight, height and BMI of the children (both boys and girls) was within 'normal' ranges (± 2 SDS from zero), although the SDS for girls were slightly lower than those for boys. The observed range included a very small number of children with low SDS (-3 to -4 SDS).

	Boys (*n=362*)				**Girls** (*n=338*)			
	mean	*SD*	*Range*		*mean*	*SD*	*Range*	
Age (*yr*)	10.5	1.9	4.3	14.2	10.5	1.8	4.4	14.6
Weight (*kg*)	34.3	9.8	15.2	99.1	34.5	10.4	15.2	79.4
Height (*cm*)	139.3	12.1	104.6	171.5	138.5	12.2	102.0	168.0
BMI (kg/m^2)	17.4	2.9	12.5	38.9	17.6	3.0	12.8	28.4
Weight SDS	-0.10	1.28	-4.12	2.71	-0.24	1.11	-4.60	3.97
Height SDS	-0.31	1.07	-3.74	2.70	-0.30	1.07	-4.93	2.85
BMI SDS	0.12	1.26	-3.08	3.51	-0.17	1.10	-3.57	3.77

Table 6.1. Subject characteristics of ulna measurement cohort of healthy children

The relationship between ulna length and height was assessed, and a strong correlation was found between the two measurements (Figure 6.1), with a R^2 of 0.79. Prediction equations were then calculated using linear regression analysis. As Table 6.2 shows, several predictors including age, sex and weight were tested in the models to improve their accuracy. The best model (adjusted R^2=0.87) included age and weight in addition to ulna length. Sex (1=female), although significant as a predictor of ulna length, did not significantly improve the accuracy of the estimates after age and weight were also added into the model. Additionally, generating separate prediction equations for male and female, as has been performed for most published equations including those by Gauld et al. (2004), did not improve the fit of the model (still an adjusted R^2=0.87).

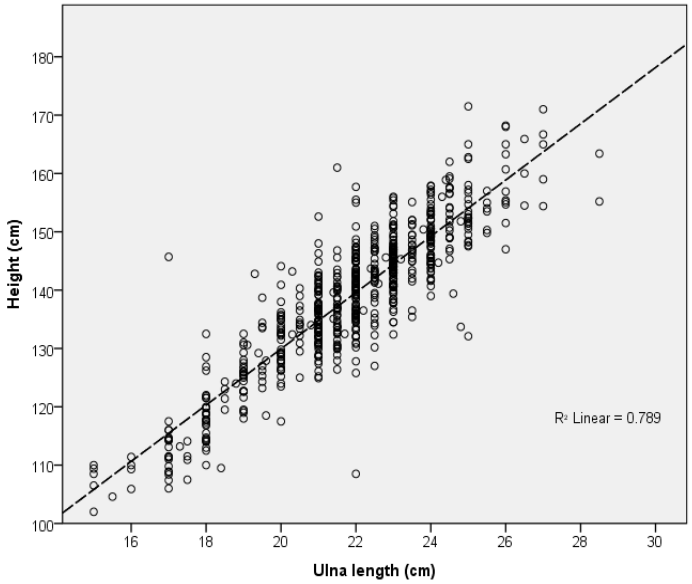


Figure 6.1. Relationship between height and ulna length

Predictors	*B* [a]	*CI* [b]		*p* [c]	adjusted R^2
(Constant)	33.48	29.41	37.56	0.000	.789
Ulna	4.82	4.64	5.01	0.000	
(Constant)	32.46	28.34	36.59	0.000	.790
Ulna	4.84	4.66	5.03	0.000	
Sex	1.13	0.30	1.96	0.008	
(Constant)	39.91	36.14	43.69	0.000	.830
Ulna	3.56	3.31	3.81	0.000	
Age	2.01	1.71	2.31	0.000	
(Constant)	48.98	44.82	53.15	0.000	.836
Ulna	3.49	3.25	3.74	0.000	
Weight	0.40	0.34	0.45	0.000	
(Constant)	53.72	49.97	57.48	0.000	.871*
Ulna	2.44	2.17	2.70	0.000	
Age	1.84	1.57	2.10	0.000	
Weight	0.37	0.32	0.41	0.000	
(Constant)	53.37	49.52	57.22	0.000	.871
Ulna	2.45	2.19	2.72	0.000	
Sex	0.27	-0.38	0.93	0.411	
Age	1.83	1.57	2.09	0.000	
Weight	0.36	0.32	0.41	0.000	

Table 6.2. Height prediction models using ulna length measurements

n=700; (a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). (*) Chosen as best model.

6.4.2. Height estimates using tibia length

Prediction equations using tibia length measurements were also calculated. The database for the measurements from healthy children in this case was smaller than the one used for ulna length measurements (*n*=133), with an age range of 10-17yr. Table 6.3 shows the subject characteristics from this cohort. As expected, the mean SDS from weight, height and BMI were all within the 'normal' ranges, but in this case slightly higher for female subjects.

	Boys (*n=69*)				**Girls** (*n=64*)			
	mean	*SD*	*Range*		*mean*	*SD*	*Range*	
Age (*yr*)	13.9	2.0	10.0	17.5	13.8	2.1	9.6	18.2
Weight (*kg*)	50.6	16.1	26.6	107.3	53.0	10.9	25.5	76.9
Height (*cm*)	160.4	15.3	128.0	189.1	158.8	8.5	135.6	173.1
BMI (kg/m^2)	19.1	3.1	14.3	31.6	20.9	3.6	12.5	31.0
Weight SDS	0.33	1.01	-2.65	3.08	0.80	0.92	-2.02	2.80
Height SDS	0.36	1.02	-1.77	2.06	0.72	0.83	-1.16	2.46
BMI SDS	0.18	0.98	-2.84	2.70	0.56	1.17	-3.31	2.86

Table 6.3. Subject characteristics of tibia measurement cohort of healthy children

As with the case of ulna length, the correlation between height and tibia length measurements was high (R^2=0.79) (Figure 6.2).

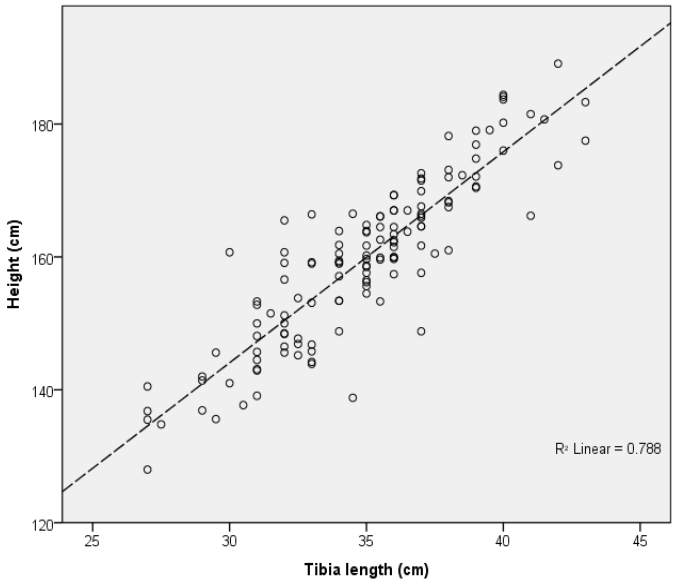


Figure 6.2. Relationship between height and ulna length

Linear regression models were once more calculated, this time using tibia length together with sex, age and/or weight to improve on the accuracy of the prediction. As can be seen in Table 6.4, sex (1=female) was not a significant predictor in the model, neither on its own or together with age and weight. The best model, as with the case of the ulna length prediction equation, included age and weight together with tibia length (adjusted R^2=0.87).

Predictors	***B*** [a]	***CI*** [b]		***p*** [c]	**adjusted R^2**
(Constant)	48.85	38.88	58.82	0.000	.787
Ulna	3.17	2.89	3.46	0.000	
(Constant)	47.28	37.08	57.48	0.000	.788
Ulna	3.20	2.91	3.49	0.000	
Sex	1.37	-0.62	3.35	0.176	
(Constant)	47.59	39.00	56.18	0.000	.842
Ulna	2.47	2.15	2.79	0.000	
Age	1.86	1.32	2.40	0.000	
(Constant)	63.67	54.35	72.98	0.000	.848
Ulna	2.28	1.94	2.62	0.000	
Weight	0.32	0.23	0.40	0.000	
(Constant)	58.60	49.56	67.64	0.000	.866 *
Ulna	2.08	1.74	2.41	0.000	
Age	1.22	0.66	1.78	0.000	
Weight	0.23	0.14	0.32	0.000	

Table 6.4. Height prediction equations using tibia length measurements

n=133; (a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). (*) Chosen best as model.

The final prediction equations for ulna and tibia lengths are described below (Table 6.5).

	n	**Ages** *(yr)*	**Height prediction equation**	R^2	***RMSE*** [a]	**Ref range** [b]
Ulna	700	4.3 - 14.2	HT=53.722 + 2.438U + 1.837A + 0.367WT	0.87	4.4	8.5
Tibia	133	10.0 - 17.5	HT=58.602 + 2.075T + 1.219A + 0.226WT	0.87	4.6	8.9

Table 6.5. Prediction equations for height estimation using ulna and tibia lengths

(a) root mean square of the error (cm). (b) 95% reference range (cm). U=ulna length (cm); T=tibia length (cm); A=age (yr); WT=weight (kg).

6.5. Validation of estimated height and derived parameters calculated using tape measurements of ulna and tibia lengths

6.5.1. Reliability of tibia and ulna length tape measurements

The accuracy of using tibia and ulna length measurements to estimate height was tested in our patient cohort enrolled in the BodyBasics study. Ulna and tibia length measurements were taken in 25 patients in the study using a non-stretchable tape measure, considering this equipment is common and likely to be available in clinical settings. Additionally, the data from healthy children used to generate the prediction equations in the previous section also measured ulna and tibia lengths using this equipment. This section details the analysis for the reliability of these tape measurements performed in duplicate on each patient.

As can be seen from Table 6.6, the reliability of the repeated measurements for ulna and tibia was similarly high assessed by the *ICC.* There was also a non-significant bias between repeated ulna length measurements and a significant but very small difference of 0.1 cm for tibia lengths. The *CR* was 0.4 cm for ulna lengths and 0.6 cm for tibia lengths.

	n	***ICC*** [a]	**mean difference** [b]	***CR*** [c]
Ulna measurements	26	0.999	0.0 (-0.1, 0.1)	0.41
Tibia measurements	25	0.999	-0.1* (-0.2, -0.1)	0.58

Table 6.6. Reliability of ulna and tibia length tape measurements
(a) ICC type 3, all values significant (H_0: ICC=0, p<0.001); (b) Mean difference (cm) between repeated measurements (95% CI), One sample t-test of the mean differences (H_0: MB=0), (*) significant (p<0.05) (c) Repeatability coefficient (cm) using the Bland Altman method for repeated measurements.

6.5.2. Agreement to standing height measurements

Height was estimated in our sample of BodyBasics patients using the ulna and tibia length equations described in the first section of this chapter. Table 6.7 shows the main descriptives for HT (cm and SDS), measured and estimated from ulna and tibia, in this cohort. Both HT estimates using ulna and tibia resulted in mean values that were higher than that of the measured HT. Consequently, the SDS were also on average higher. The mean SDS for measured HT was -1.2 SDS, but this increased to -0.6 in the ulna-estimated HT and then further to 0.0 SDS for tibia-estimated HT. Unsurprisingly, the number of patients with abnormal SDS decreased as well using the estimated HT (from 5 to 3 and 0 patients).

	n	*mean*	*SD*	*range*		*Abnormal SDS* [a]	
						Freq.	*%*
HT [b] (*cm*)	23	147.8	19.6	105.8	172.0		
Ulna-estimated HT (*cm*)	26	150.8	19.1	115.2	181.1		
Tibia-estimated HT (*cm*)	26	155.5	16.3	123.1	183.4		
HT [b] SDS	23	-1.2	1.3	-4.6	0.4	5	21.7
Ulna-estimated HT SDS	26	-0.6	1.0	-2.8	0.9	3	11.5
Tibia-estimated HT SDS	26	-0.0	0.9	-1.9	1.2	0	0.0

Table 6.7. Height, ulna and tibia length descriptives

(a) SDS <-2 or >2, Freq=number of patients; (b) measured standing height.

In agreement with these observations, the Bland Altman analysis (Table 6.8) showed both HT estimates had a significant bias to measured HT. This bias was larger for tibia-estimated HT (7.4 cm and 1.1 SDS) than for ulna-estimated HT (4.4cm and 0.3 SDS), with also slightly wider *LOA* (±1.75 SDS for ulna and ±1.86 SDS for tibia estimates of HT). There was no effect of the magnitude of the measurement on the difference between estimated and measured HT.

n = 22	*MB* [a]	*p* [b]	*LLOA*	*ULOA*	*r* [c]	*p* [d]
Height *(cm)*						
Ulna-estimated	4.4	0.006 *	-8.6	17.3	0.01	0.953
Tibia-estimated	7.4	0.000 *	-3.3	18.2	-0.3	0.133
Height SDS						
Ulna-estimated	0.3	0.005 *	-1.46	2.04	-0.46	0.058
Tibia-estimated	1.1	0.000 *	-0.73	2.98	-0.35	0.111

Table 6.8. Mean bias, limits of agreement and correlation coefficients between measured and estimated heights using ulna and tibia lengths

(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements of height, all non-significant.

Agreement was also tested using the categorical variable of abnormal SDS (<-2 or >2 SDS). As Table 6.9 indicates, the overall percentage agreement was good, although slightly higher for the ulna-estimated HT than for the tibia-estimated HT. However, the kappa for ulna-estimated HT, although statistically significant, only showed a moderate agreement to measured HT for the classification of patients with abnormal SDS. The kappa for tibia-estimated HT could not be calculated because this estimate failed to identify any cases of abnormal SDS.

n =22	**Agreement** [a]	***κ*** [b]	***p***
Ulna-estimated HT	86.4	0.51 (0.06, 0.96)	0.006 *
Tibia-estimated HT	81.8	-	-

Table 6.9. Agreement of abnormal SDS between measured and estimated height using ulna and tibia lengths

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

6.5.3. Agreement of BMI

The use of the estimated HT was further tested to determine if these values could be used to calculate other anthropometric and BC parameters accurately. This section describes the agreement analysis for BMI (kg/m^2 and SDS). Table 6.10 shows the main descriptives for the BMI values calculated using measured HT, ulna-estimated HT and tibia-estimated HT. In agreement with the patterns observed for the HT agreement analysis in the previous section, the mean ulna-derived BMI was lower than the BMI calculated using measured HT. The mean BMI from the tibia-estimated HT was even lower. The calculated SDS followed the same pattern, with lower average SDS for BMI derived from ulna, and even more so those derived from tibia lengths. Considering the BMI SDS were lower with tibia and ulna estimates of HT, the observed percentage of patients with abnormal (low) BMI SDS increased for tibia estimates, and to a lesser degree for ulna estimates.

The agreement analysis (Table 6.11), indicated there was a significant difference between BMI values (both kg/m^2 and SDS) obtained using measured HT compared to BMI values derived from ulna and tibia estimates of HT. The *MB* for the BMI SDS was of approximately 0.6 SDS and had wide *LOA* (approximately ±1.8 SDS), with greater bias and wider *LOA* observed for tibia-derived BMI SDS. Only BMI SDS from tibia-estimated HT was significant for the effect of the magnitude of the measurement on the difference, indicating

that children with higher BMI SDS had a greater difference between BMIs derived from measured HT and tibia-estimated HT.

	n	*mean*	*SD*	*range*		Abnormal SDS [a]	
						Freq.	*%*
BMI [b] (*kg/cm²*)	23	18.6	4.4	12.4	34.6		
Ulna-derived BMI (*kg/cm²*)	26	17.3	3.6	11.0	28.2		
Tibia-derived BMI (*kg/cm²*)	26	16.8	4.0	9.5	30.5		
BMI [b] SDS	23	-0.3	1.4	-3.2	3.1	3	13.0
Ulna-derived BMI SDS	26	-0.94	1.62	-4.92	2.21	9	34.6
Tibia-derived BMI SDS	26	-1.49	2.16	-8.49	2.60	10	38.5

Table 6.10. Descriptives of BMI values obtained from measured and estimated heights using ulna and tibia lengths

(a) SDS <-2 or >2, Freq=number of patients; (b) calculated using measured standing height.

n = 22	*MB* [a]	*p* [b]	*LLOA*	*ULOA*	*r* [c]	*p* [d]
BMI *(kg/m²)*						
Ulna-derived [e]	4.4	0.006	-8.6	17.3	0.01	0.953
Tibia-derived [f]	7.4	0.000	-3.3	18.2	-0.33	0.133
BMI SDS						
Ulna-derived [e]	-0.6	0.008	-2.4	1.3	0.40	0.069
Tibia-derived [f]	-0.7	0.001	-2.6	1.2	0.72	0.000*

Table 6.11. Mean bias, limits of agreement and correlation coefficients between BMIs calculated using measured and estimated heights from ulna and tibia lengths.

(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements; (*) significant (p<0.05); (e) BMI calculated using ulna-estimated height, and (f) tibia-estimated height.

The agreement of 'abnormal' categorisation of the BMI SDS is summarised in Table 6.12. The absolute agreement and kappa values indicate better agreement for BMI calculated using ulna-derived HT compared to tibia. In both cases the kappa values, although statistically significant, only show a moderate/weak agreement to BMI calculated from measured HT values.

n =22	**Agreement** [a]	***κ*** [b]	***p***
Ulna-derived BMI	81.8	0.51 (0.12, 0.89)	0.006 *
Tibia-derived BMI	77.3	0.43 (0.07, 0.79)	0.014 *

Table 6.12. Agreement of abnormal BMI SDS calculated using measured and estimated heights from ulna and tibia lengths

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

6.5.4. Agreement of BIA SDS

Measured HT and estimated HT values were used to calculate the index of impedance (HT^2/Z) for BIA assessment (measured using a multifrequency QuadScan analyser and the resulting BIA_{sup} impedance values adjusted using MB as described in Chapter 5) and SDS calculated using the UK reference for BC (Wells et al. 2012). Table 6.13 summarises the resulting mean BIA SDS, and Table 6.14 summarises the results for the analysis of agreement. The mean SDS using HT estimated using ulna were higher (closer to zero), and even more so for tibia-estimates of HT, compared to the mean BIA SDS calculated using measured HT. There was a significant bias between the BIA SDS from estimates of HT compared to measured HT no greater than 0.5 SDS, with *LOA* of ±1.0 and 0.7 for ulna and tibia-derived BIA SDS respectively. Once more, BIA SDS derived from tibia-estimates of HT was the only one significant for the effect of the magnitude on the differences, in this case it indicated patients with lower BIA SDS had a greater difference between tibia-derived BIA SDS and measured HT BIA SDS.

	n	***mean***	***SD***	***range***		***Abnormal SDS*** [a]	
						Freq.	*%*
BIA [b] SDS	23	-1.43	1.19	-3.60	1.19	7	30.4
Ulna-derived BIA SDS	26	-1.26	1.23	-2.97	1.73	7	26.9
Tibia-derived BIA SDS	26	-1.14	1.00	-2.45	1.17	7	26.9

Table 6.13. Descriptives of BIA SDS obtained from measured and estimated heights using ulna and tibia lengths

(a) SDS <-2 or >2, Freq=number of patients; (b) calculated using measured standing height (for the index Ht^2/Z).

n = 22	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Ulna-derived [e]	0.4	0.008 *	-0.7	1.4	0.03	0.908
Tibia-derived [f]	0.6	0.000 *	-0.4	1.0	-0.55	0.008 *

Table 6.14. Mean bias, limits of agreement and correlation coefficients between BIA SDS calculated using measured and estimated heights from ulna and tibia lengths

(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements; (*) significant (p<0.05); (e) BIA SDS calculated using ulna-estimated height (for the index HT^2/Z), and (f) tibia-estimated height.

The analysis of the agreement of abnormal BIA SDS (Table 6.15) indicated a good overall agreement (approximately 86%) and higher kappa values than those observed for HT SDS and BMI SDS, reaching a substantial/moderate agreement for tibia-derived abnormal BIA SDS (κ=0.65) compared to abnormal BIA SDS calculated using measured HT.

n =22	**Agreement** [a]	***κ*** [b]	***p***
Ulna-derived	86.4	0.59 (0.20, 0.98)	0.002 *
Tibia-derived	86.4	0.65 (0.30, 0.99)	0.001 *

Table 6.15. Agreement of abnormal BIA SDS calculated using measured and estimated heights from ulna and tibia lengths

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

Figure 6.3 summarizes the observed MB and LOA for HT SDS, BMI SDS and BIA SDS calculated using tibia and ulna lengths compared to measured HT.

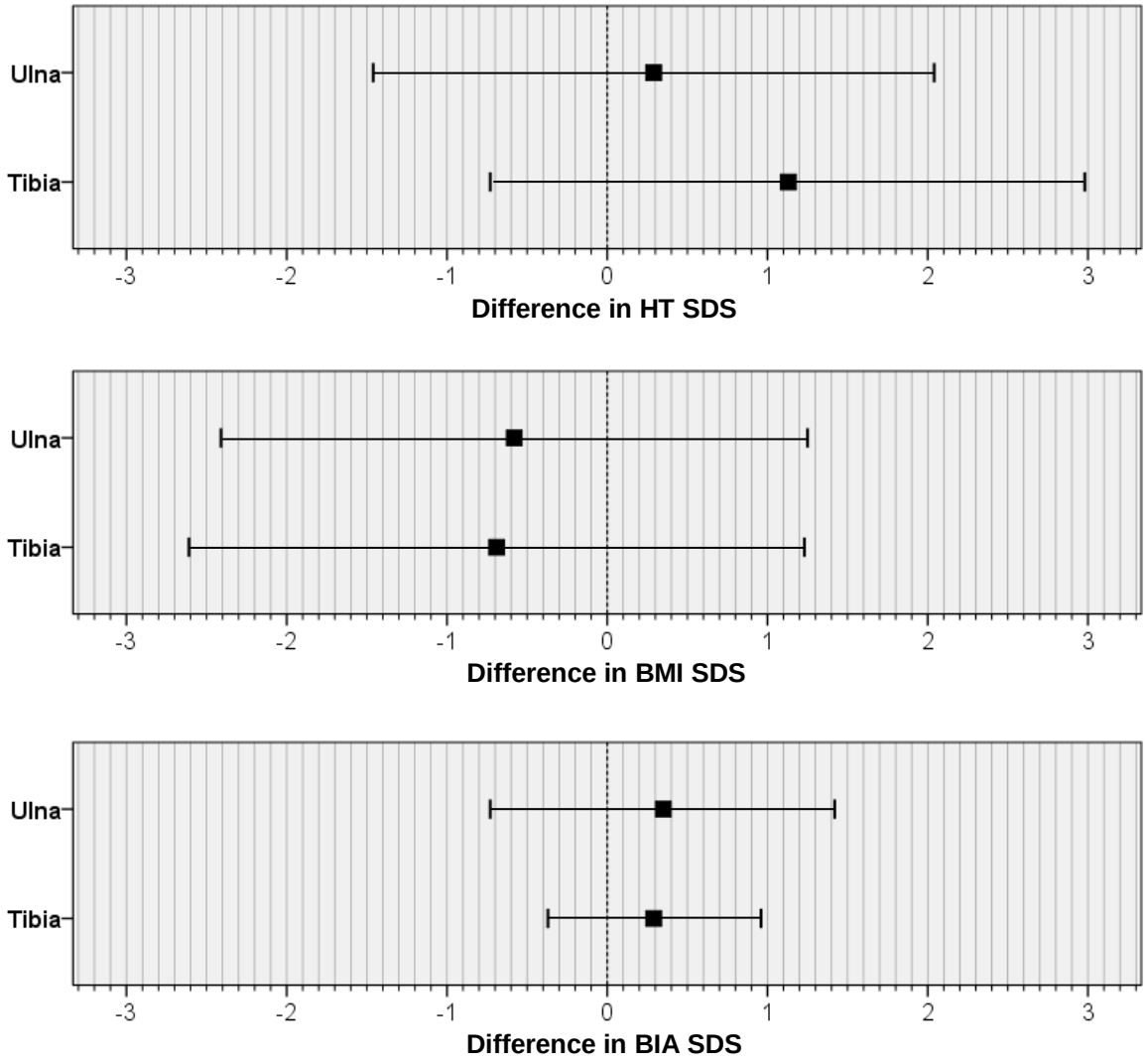


Figure 6.3. Summary of MB and LOA for HT, BMI and BIA SDS between measured and estimated height using ulna and tibia lengths

(■) MB; (|) LOA; dotted line indicates no mean difference in SDS between techniques (MB=0).

6.6. Validation of estimated height and derived parameters calculated using DXA whole-body scan measurements of ulna and tibia

A study by Abrahamyan et al. (2008) proposed the use of whole-body DXA scans to measure long-bones and estimate the height of children. Considering only a small number of patients enrolled to the BodyBasics study had tape measurements of ulna and tibia lengths performed, analysis of the whole-body DXA scan database of recruited patients allowed the measurement of ulna and tibia lengths in a much larger number of children. This section describes the reliability of these DXA-scan measurements, their agreement to standard tape measurements and the agreement of the DXA-scan ulna and tibia-estimated HT, BMI and BIA parameters to those calculated using measured HT.

6.6.1. Reliability of tibia and ulna length measurements using DXA whole-body scans

The reliability of repeated ulna and tibia length measurements in DXA whole-body scans was good, as evidenced by the high *ICC* and small mean difference between measurements (Table 6.16). The difference was smaller and non-significant (-0.01 cm) for tibia measurements, while ulna lengths had a greater and significant difference of approximately -0.6 cm. This also resulted in *CR* of 1.2 cm for ulna lengths and 1.0 cm for tibia lengths. The lower reliability of repeated measurements for ulna is likely the result of increased difficulty in identifying the anatomical sites for the measurement on the screen, especially in younger children where smaller bones are more difficult to observe in the scan.

	n	***ICC*** [a]	**mean difference** [b]	***CR*** [c]
Ulna measurements	113	0.993	-0.63 * (-1.14, -0.12)	1.17
Tibia measurements	113	0.998	-0.01 (-0.07, 0.06)	0.97

Table 6.16. Reliability of ulna and tibia length measurements from DXA whole-body scans
(a) ICC type 3, all values significant (H_0: ICC=0, p<0.001); (b) Mean difference (cm) between repeated measurements (95% CI), One sample t-test of the mean differences (H_0: MB=0), (*) significant (p<0.05) (c) Repeatability coefficient (cm) using the Bland Altman method for repeated measurements.

6.6.2. Agreement between tape and DXA whole-body scan measurements of ulna and tibia lengths

The agreement analysis between ulna and tibia measurements using the standard tape technique compared to DXA whole-body scan measurements is summarised in Table 6.17. The comparison was possible in 17 patients who had both tape measurements of ulna and tibia lengths as well as a DXA scan (performed in the study to assess FM and LM). There was a significant difference between techniques (DXA measurement - tape measurement) of 0.6 cm for ulna and -1.9 cm for tibia lengths. After calculating HT using the predictive equations generated in the first section of this chapter, the resulting HT SDS differed significantly between measurement techniques (-1.0 SDS for ulna and -0.6 SDS for tibia length). This was similarly reflected in the low non-significant kappa value (minimal agreement) for ulna-estimated HT SDS (Table 6.18). The kappa value for tibia-estimated HT SDS was not possible to analyse because there were no cases of abnormal SDS identified.

n = 17	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Ulna (*cm*)	0.6	0.000 *	-3.9	5.1	-0.49	0.050
Ulna-estimated HT SDS	-1.0	0.000 *	-2.1	0.1	0.01	0.974
Tibia (*cm*)	-1.9	0.001 *	-6.1	2.2	-0.25	0.309
Tibia-estimated HT SDS	-0.6	0.001 *	-1.8	0.6	-0.37	0.128

Table 6.17. Mean bias, limits of agreement and correlation coefficients between tape and DXA whole-body scan measurements of ulna and tibia lengths

(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements, all non-significant.

n =17	**Agreement** [a]	***κ*** [b]	***p***
Ulna-estimated HT [c]	82.4	0.34 (-0.17, 0.85)	0.063
Tibia-estimated HT [d]	100.0	-	-

Table 6.18. Agreement of abnormal height SDS classification between tape and DXA whole-body scan ulna and tibia lengths

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05); (c) abnormal SDS (<-2 SDS or >2 SDS) for height, calculated using ulna lengths, or (d) tibia lengths.

6.6.3. Agreement to standing height measurements

The agreement to measured HT was tested again for the ulna and tibia-estimated HT values, this time using the lengths measured from whole-body DXA scans. Table 6.19 shows the descriptives for these new calculations and Table 6.20 summarises the results from the agreement analysis.

Once more, there was a significant bias between measured and estimated HT values and SDS. Ulna-estimated HT differed on average by -4.7cm, while tibia-estimated HT was 3.7 cm on average higher than measured HT. This difference was reflected in a similarly significant bias for the SDS: -0.97 SDS for ulna-estimated HT and 0.6 SDS for tibia-estimated HT, with wide *LOA* (approximately ±1.5 SDS). There was a significant negative correlation between the magnitude of the measurement and the difference between estimates of HT using ulna (HT SDS) and tibia (HT in cm and SDS) lengths. This suggests a larger difference between estimated and measured HT for those children who are shorter in HT.

The agreement of abnormal HT SDS is shown on Table 6.21, and shows an only moderate/weak agreement between estimated and measured HT abnormal SDS (κ=0.5 for ulna and 0.4 for tibia estimates).

	n	***mean***	***SD***	***range***		***Abnormal SDS*** [a]	
						Freq.	*%*
HT [b] (*cm*)	118	138.7	20.9	96.1	182.2		
Ulna-estimated HT [c] (*cm*)	113	133.3	20.6	97.6	177.3		
Tibia-estimated HT [c] (*cm*)	113	141.7	19.4	104.3	178.4		
HT [b] SDS	118	-0.5	1.3	-4.8	2.3	18	15.3
Ulna-estimated HT [c] SDS	113	-1.36	1.15	-4.12	1.23	29	25.7
Tibia-estimated HT [c] SDS	113	0.05	1.13	-3.44	2.19	9	8.0

Table 6.19. Descriptives of measured height, and ulna and tibia length measurements using DXA whole-body scans

(a) SDS <-2 or >2, Freq=number of patients; (b) measured standing height; (c) measured from DXA whole-body scans.

n = 110	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Height *(cm)*						
Ulna-estimated	-4.7	0.000 *	-15.6	6.1	0.012	0.899
Tibia-estimated	3.7	0.000 *	-3.9	11.3	-0.31	0.001 *
Height SDS						
Ulna-estimated	-0.97	0.000 *	-2.63	0.69	-0.28	0.003 *
Tibia-estimated	0.59	0.000 *	-0.61	1.79	-0.41	0.000 *

Table 6.20. Mean bias, limits of agreement and correlation coefficients between measured and estimated heights using DXA whole-body scan ulna and tibia lengths.
(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements of height; (*) significant (p<0.05).

n =110	**Agreement** [a]	***κ*** [b]	***p***
Ulna-estimated HT	83.6	0.50 (0.30, 0.69)	0.000 *
Tibia-estimated HT	87.3	0.40 (0.15, 0.65)	0.000 *

Table 6.21. Agreement of abnormal height SDS classification between measured and estimated heights using DXA whole-body scan ulna and tibia lengths.
(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

6.6.4. Agreement of BMI

The average values and other descriptive statistics for the calculated BMIs are shown in Table 6.22. The mean BMI values in the patient sample using the estimates of HT resulted in lower values using tibia length, and higher values using ulna lengths compared to measured HT. Similarly, the mean BMI SDS was higher using ulna-estimated HT and lower using tibia-estimated HT. All mean BMI SDS were, however, within the 'normal' cut-offs (>-2 and <2 SDS).

The agreement analysis (Table 6.23) showed a significant bias between BMI values obtained using measured HT and estimated HT values from ulna (*MB*= 0.7 SDS) and tibia (*MB*= -0.6 SDS) lengths, with wide *LOA* (>1.0 SDS). The agreement in identifying patients with abnormal SDS (Table 6.24) was better for ulna-derived BMI (95% agreement, κ=0.8 indicating substantial/strong agreement) than for tibia-derived BMI (85% agreement, κ=0.5 indicating moderate/weak agreement).

	n	*mean*	*SD*	*range*		*Abnormal SDS* [a]	
						Freq.	*%*
BMI [b] (*kg/cm²*)	118	18.9	4.5	12.2	35.8		
Ulna-derived BMI (*kg/cm²*)	113	20.1	3.9	12.3	30.9		
Tibia-derived BMI (*kg/cm²*)	113	17.8	4.2	10.6	30.9		
BMI [b] SDS	118	0.3	1.4	-3.4	5.4	18	15.3
Ulna-derived BMI SDS	113	0.9	1.3	-3.2	5.2	21	18.6
Tibia-derived BMI SDS	113	-0.2	1.7	-6.1	4.8	23	20.4

Table 6.22. Descriptives of BMI values obtained from measured and estimated heights using DXA whole-body scan ulna and tibia lengths.

(a) SDS <-2 or >2, Freq=number of patients; (b) calculated using measured standing height.

n = 110	*MB* [a]	*p* [b]	*LLOA*	*ULOA*	*r* [c]	*p* [d]
BMI *(kg/m²)*						
Ulna-derived [e]	-4.8	0.000	-15.5	6.0	0.00	0.998
Tibia-derived [f]	3.6	0.000	-4.0	11.1	-0.16	0.089
BMI SDS						
Ulna-derived [e]	0.69	0.000	-0.44	1.82	-0.29	0.002 *
Tibia-derived [f]	-0.56	0.000	-1.70	0.59	0.43	0.000 *

Table 6.23. Mean bias, limits of agreement and correlation coefficients between BMIs calculated using measured and estimated heights from DXA whole-body scan ulna and tibia lengths.

(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements; (*) significant (p<0.05); (e) BMI calculated using ulna-estimated height, and (f) tibia-estimated height.

n =110	**Agreement** [a]	*κ* [b]	*p*
Ulna-derived BMI	94.5	0.81 (0.66, 0.96)	0.000 *
Tibia-derived BMI	85.5	0.51 (0.31, 0.72)	0.000 *

Table 6.24. Agreement of abnormal BMI SDS calculated using measured and estimated heights from DXA whole-body scan ulna and tibia lengths.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

6.6.5. Agreement of BIA SDS

Continuing the observed pattern for HT and BMI estimates using ulna and tibia length measurements from DXA scans, the mean BIA SDS were lower using ulna-estimated HT and higher using tibia-estimated HT (Table 6.25). Since all SDS were on average low (<0 SDS), this then translated to BIA SDS derived from ulna HT estimates to identify more patients with abnormal (low) SDS, and tibia-estimates to identify less patients with abnormal BIA SDS.

Agreement analysis (Table 6.26) indicated there was a significant difference between BIA SDS calculated using measured HT and using estimates of HT from ulna (*MB*= -0.6 SDS) and tibia (*MB*=0.3 SDS) lengths. The *LOA* were also wide, although less so than those observed for BMI SDS (previous section). The agreement of abnormal BIA SDS (Table 6.27) showed that there was a substantial/moderate agreement for both estimates using ulna (87% agreement, κ=0.6) and tibia (91% agreement, κ=0.7) lengths.

	n	***mean***	***SD***	***range***		***Abnormal SDS*** [a]	
						Freq.	*%*
BIA [b] SDS	110	-0.84	1.39	-4.18	3.61	22	20.0
Ulna-derived BIA SDS	102	-1.31	1.32	-4.39	2.71	29	28.4
Tibia-derived BIA SDS	102	-0.53	1.31	-3.44	3.13	17	16.7

Table 6.25. Descriptives of BIA SDS obtained from measured and estimated heights using DXA whole-body scan ulna and tibia lengths.
(a) SDS <-2 or >2, Freq=number of patients; (b) calculated using measured standing height (for the index Ht^2/Z).

n = 22	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
BIA SDS						
Ulna-derived [e]	-0.56	0.000 *	-1.45	0.34	-0.25	0.011 *
Tibia-derived [f]	0.25	0.000 *	-0.38	0.89	-0.37	0.000 *

Table 6.26. Mean bias, limits of agreement and correlation coefficients between BIA SDS calculated using measured and estimated heights from DXA whole-body scan ulna and tibia lengths.
(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements; (*) significant (p<0.05); (e) BIA SDS calculated using ulna-estimated height (for the index HT^2/Z), and (f) tibia-estimated height.

n =22	**Agreement** [a]	***κ*** [b]	***p***
Ulna-derived BIA SDS	87.3	0.62 (0.46, 0.78)	0.000 *
Tibia-derived BIA SDS	91.2	0.66 (0.49, 0.83)	0.000 *

Table 6.27. Agreement of abnormal BIA SDS calculated using measured and estimated heights from DXA whole-body scan ulna and tibia lengths.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

The graphs below (Figure 6.4) summarizes the agreement for HT, BMI and BIA SDS.

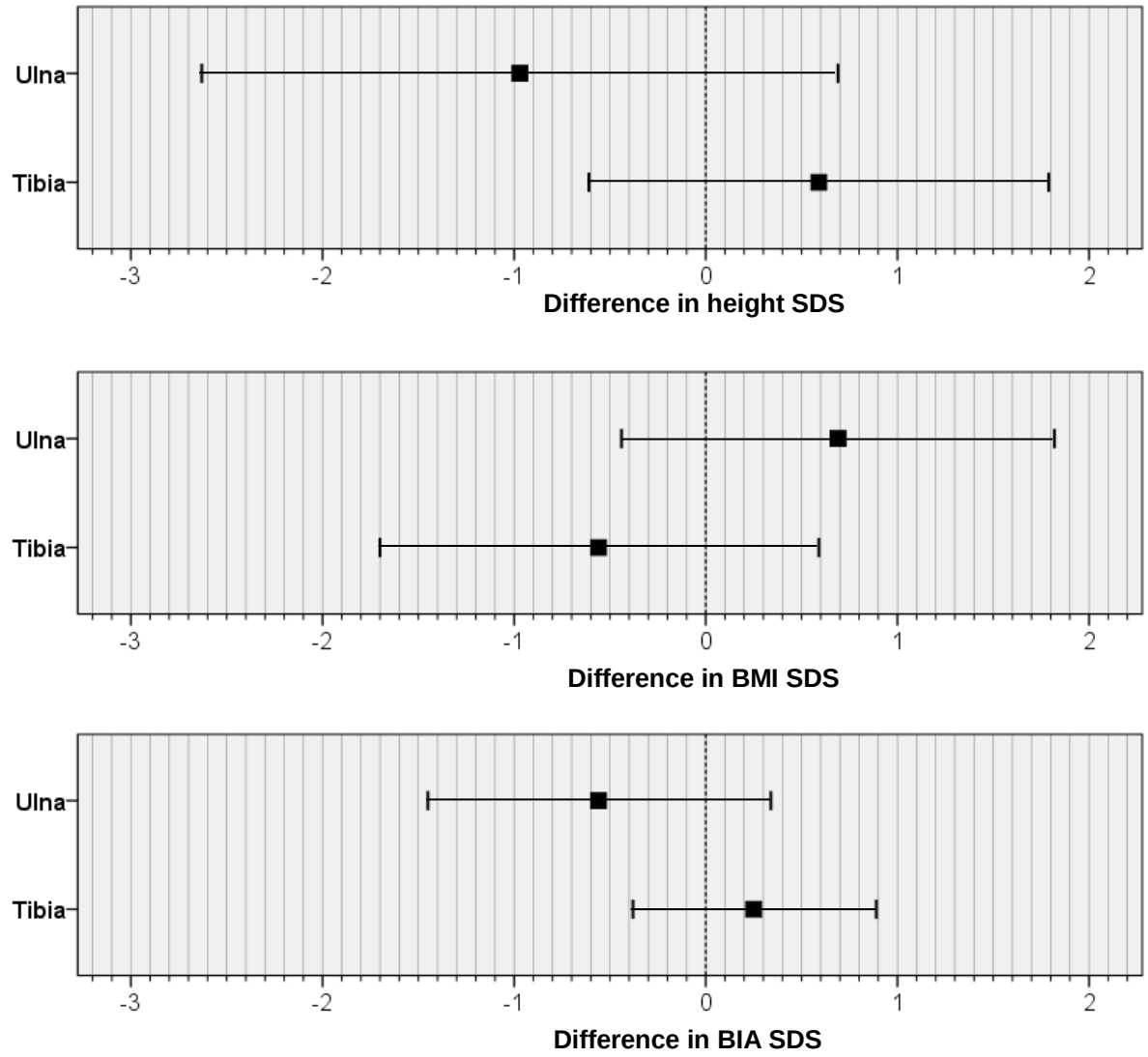


Figure 6.4. Summary of MB and LOA for HT, BMI and BIA SDS between measured and estimated HT using DXA whole-body scan ulna and tibia lengths.

(■) MB; (\|) LOA; dotted line indicates no mean difference in SDS between techniques (MB=0).

6.7. Aggregate predictions to estimate height in paediatric patients

The approach of 'wisdom of crowds' (Wells et al. 2009; Surowiecki 2004) was applied to determine if this would improve the accuracy of the estimates, which as can be seen from the results in the previous sections resulted in a significant bias. Estimates of HT were calculated using the equations generated in this study ('Calculated') and other published equations, using the average of tibia and ulna length measurements obtained by DXA and tape measurements. The different estimates of HT were then averaged ('Aggregate'). Table 6.28 summarises the equations used to estimate HT from ulna and tibia length measurements.

	Age range *(yr)*	***n***	**Height prediction equation**	R^2
Using ulna length				
Calculated	4.3-14.2	700	HT=53.722 + 2.438U + 1.837A + 0.367WT	0.87
Gauld et al. (2004)	5-19	1144	Male: HT=28.003 + 4.605U + 1.308A	0.96
		1199	Female: HT=31.485 + 4.459U + 1.315A	0.94
Using tibia length				
Calculated	10.0-17.5	133	HT=58.602 + 2.075T + 1.219A + 0.226WT	0.87
Gauld et al. (2004)	5-19	1144	Male: HT=36.509 + 2.758T + 1.717A	0.96
		1199	Female: HT=37.748 + 2.771T + 1.457A	0.95
Abrahamyan et al. (2008)	5.9–18	170	Male: HT=3.196(1.012T + 1.729) + 31.774	0.901
	6.1–18	243	Female: HT=3.348(0.999T + 2.436) + 25.847	0.921

Table 6.28. Calculated and published prediction equations for height estimation using ulna and tibia lengths in children.

6.7.1. Aggregate estimates of height using ulna length

The estimates of HT derived from ulna length measurements are summarised in Table 6.29. The mean HT SDS for all estimates was low (<0 SDS), even more so using the predictive equation by Gauld et al. (2004). Thus, the percentage of patients identified as having abnormal (low) SDS for height was also higher using the Gauld et al. (2004) equation.

The agreement analysis (Table 6.30) indicated all estimates were significantly lower than measured HT, both in terms of raw values (cm) and SDS. The 'Calculated' estimates had a lower *MB* than that of the Gauld et al. (2004) estimates, but similarly wide *LOA* (>1.5 SDS).

n =122	**Height (cm)**				**Height SDS**				**Abnormal SDS** [a]	
	mean	*SD*	*Range*		*mean*	*SD*	*Range*		*Freq.*	*%*
Calculated	134.2	20.9	97.6	177.3	-1.3	1.2	-4.1	1.2	34	27.9
Gauld et al. (2004)	131.7	21.9	89.7	177.9	-1.8	1.4	-5.3	1.5	50	41.0
Aggregate	132.9	21.2	93.8	175.9	-1.6	1.2	-4.7	0.9	40	32.8

Table 6.29. Calculated heights, height SDS and abnormal SDS of individual and aggregate prediction equations using ulna length.
'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

n =113	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Height *(cm)*						
Calculated	-4.1	0.000 *	-15.3	7.1	0.10	0.304
Gauld et al. (2004)	-7.5	0.000 *	-20.4	5.4	0.19	0.050
Aggregate	-5.8	0.000 *	-17.1	5.5	0.14	0.154
Height SDS						
Calculated	-0.7	0.000 *	-2.5	1.1	-0.25	0.007 *
Gauld et al. (2004)	-1.3	0.000 *	-3.3	0.8	0.05	0.581
Aggregate	-1.0	0.000 *	-2.8	0.8	-0.14	0.134

Table 6.30. Mean bias, limits of agreement and correlation coefficients between individual and aggregate prediction equations using ulna length.
(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements; (*) significant (p<0.05). 'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

The agreement for classifying patients with abnormal HT SDS (Table 6.31) indicated 'Calculated' HT estimates had a better agreement (85% agreement, κ=0.5) than the estimates using the equation by (Gauld et al. 2004) (69% agreement, κ=0.3).

n =113	**Agreement** [a]	**κ** [b]	***p***
Calculated	85.0	0.52 (0.32, 0.71)	0.000 *
Gauld et al. (2004)	69.0	0.29 (0.13, 0.44)	0.000 *
Aggregate	77.0	0.37 (0.19, 0.56)	0.000 *

Table 6.31. Agreement between abnormal height SDS calculated with the individual and aggregate prediction equations using ulna length.
(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05). 'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

6.7.2. Aggregate estimates of height using tibia length

The mean HT and HT SDS using the different predictive equations based on tibia length are summarised in Table 6.32. The use of both published equations resulted in lower estimates of HT (both in cm and as SDS). This was more pronounced for the (Abrahamyan et al. 2008) equation than for the equation by (Gauld et al. 2004).

The agreement to measured HT indicated that there was a significant bias between the estimates and measurements of HT for all equations, with wide *LOA* (>1.0 SDS). The mean difference, however, was smaller for the Gauld et al. (2004) equation estimates. The 'Calculated' and the Abrahamyan et al. (2008) equations both over and under estimated measured HT, respectively, to approximately the same degree (*MB*=4 cm and -4.3 cm). The aggregate estimate, for the first time, resulted in a non-significant bias (*MB*= -0.6 cm and -0.1 SDS) compared to measured HT, although the *LOA* remained wide.

n =122	**Height (cm)**				**Height SDS**				**Abnormal SDS** [a]	
	mean	*SD*	*Range*		*mean*	*SD*	*Range*		*Freq.*	*%*
Calculated	142.3	19.4	104.3	178.4	0.0	1.2	-3.4	2.2	12	9.9
Gauld et al. (2004)	137.2	21.3	93.9	179.0	-0.9	1.2	-5.3	1.3	20	16.5
Abrahamyan et al. (2008)	134.3	19.2	92.3	172.6	-1.3	1.5	-6.0	1.4	33	27.3
Aggregate	137.9	19.9	96.9	175.6	-0.7	1.2	-4.9	1.5	18	14.9

Table 6.32. Calculated heights, height SDS and abnormal SDS of individual and aggregate prediction equations using tibia length.
'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

n = 113	***MB*** [a]	***p*** [b]	***LLOA***	***ULOA***	***r*** [c]	***p*** [d]
Height *(cm)*						
Calculated	4.0	0.000 *	-3.7	11.6	-0.25	0.007 *
Gauld et al. (2004)	-1.6	0.000 *	-10.6	7.3	0.19	0.040 *
Abrahamyan et al. (2008)	-4.3	0.000 *	-13.7	5.2	-0.27	0.004 *
Aggregate	-0.6	0.092	-8.5	7.2	-0.13	0.161
Height SDS						
Calculated	0.68	0.000 *	-0.63	1.99	-0.42	0.000 *
Gauld et al. (2004)	-0.31	0.000 *	-1.73	1.11	-0.19	0.045 *
Abrahamyan et al. (2008)	-0.68	0.000 *	-2.14	0.78	0.11	0.260
Aggregate	-0.10	0.091	-1.35	1.14	-0.23	0.012 *

Table 6.33. Mean bias, limits of agreement and correlation coefficients between individual and aggregate prediction equations using tibia length.

(a) Mean bias (cm or SDS); (b) One-sample t-test of mean bias (H_0: MB=0), (*) significant (p<0.05); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between measurements; (*) significant (p<0.05). 'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

The agreement analysis for identifying patients with abnormal HT SDS (Table 6.34) showed once more that the estimates using the Gauld et al. (2004) equation had the best agreement (95%, κ=0.8 indicating substantial agreement). The use of the aggregate estimate also resulted in a good agreement (93%, κ=0.7 indicating substantial/moderate agreement).

n =113	**Agreement** [a]	***κ*** [b]	***p***
Calculated	87.6	0.40 (0.15, 0.65)	0.000 *
Gauld et al. (2004)	94.7	0.79 (0.63, 0.95)	0.000 *
Abrahamyan et al. (2008)	86.7	0.59 (0.41, 0.77)	0.000 *
Aggregate	92.9	0.69 (0.50, 0.89)	0.000 *

Table 6.34. Agreement between abnormal height SDS calculated with the individual and aggregate prediction equations using tibia length.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05). 'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

The graphs below (Figure 6.5) summarise the agreement analysis for the individual and aggregate estimates of HT using ulna and tibia length measurements.

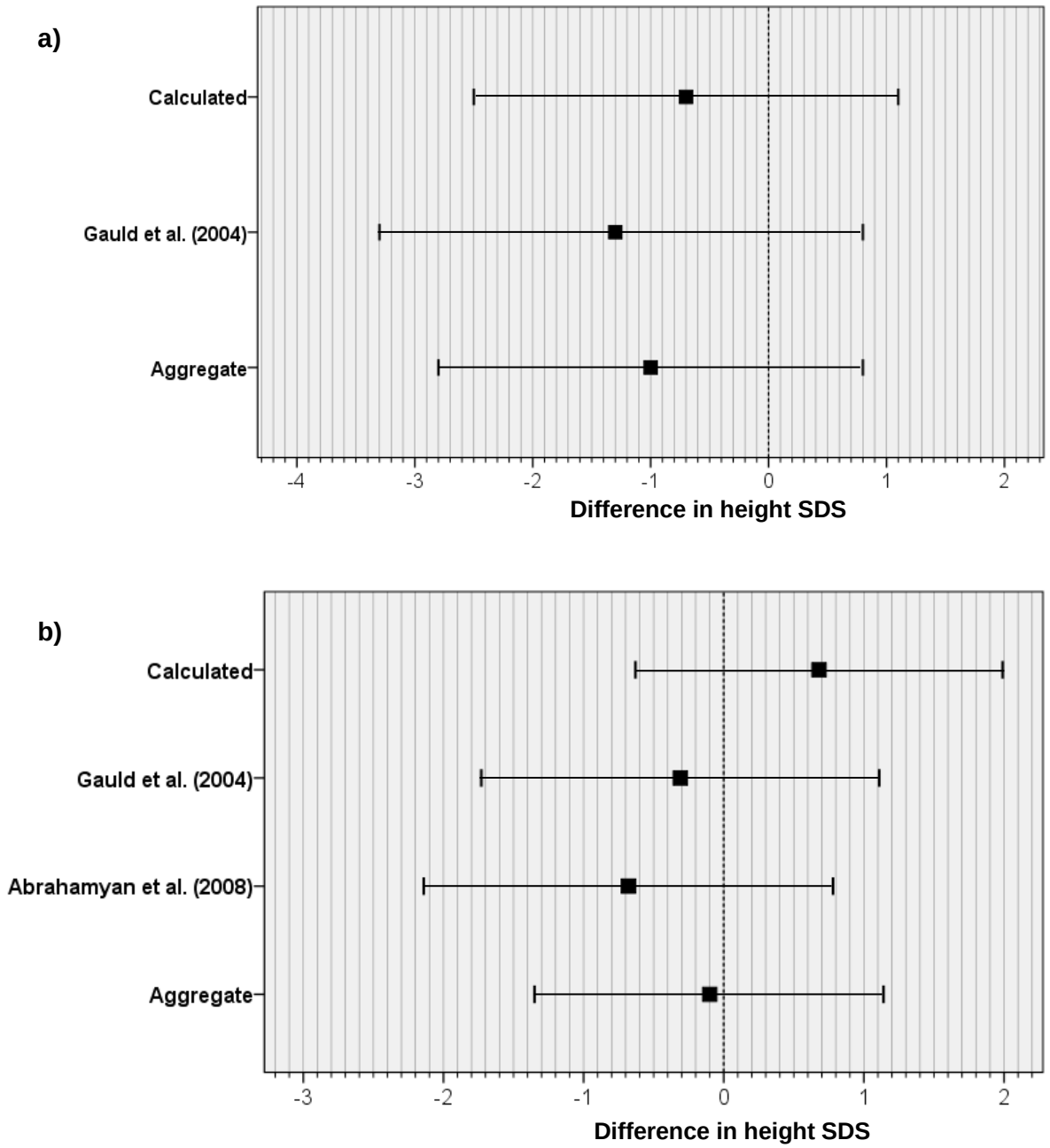


Figure 6.5. Summary of MB and LOA of individual and aggregate prediction equations for height.

(■) MB; (|) LOA; dotted line indicates no mean difference in SDS between techniques (MB=0).; Height estimated using (a) ulna and (b) tibia lengths. 'Calculated' refers to predictive equations generated in the first section of this chapter, 'Aggregate' is the average of all estimates of height by the different equations.

6.8. Summary of main findings

- Prediction equations using ulna and tibia length measurements from healthy UK children were generated to estimate HT. These equations included variables of age and weight to improve the accuracy of the estimates.
- Tape measurements were reliable, with a *CR* of 0.4 cm and 0.6 cm for ulna and tibia duplicate measurements respectively.
- Both ulna-estimated HT and tibia-estimated HT from tape measurements overestimated the measured HT in this patient sample, with an observed *MB* of 0.3 SDS and 1.1 SDS for ulna and tibia respectively. This also meant the estimates of HT identified less children with abnormal (low) HT SDS.
- Agreement of BMI indicated ulna-estimated and tibia-estimated HTs resulted in BMI SDS that were significantly lower than those calculated using measured HT (*MB*= -0.6 SDS and -0.7, for ulna and tibia respectively). Thus, these estimates resulted in a larger number of patients classified with abnormal (low) BMI SDS.
- Agreement of BIA SDS showed a significant overestimation using ulna (*MB*=0.4 SDS) and tibia (MB=0.6 SDS) estimates of HT for the calculation of the impedance index compared to measured HT. This led to the identification of slightly fewer children with abnormal (low) SDS for BIA.
- The *LOA* for estimates of HT, BMI and BIA SDS using ulna and tibia lengths were generally wide (>1.0 SDS).
- Reliability of ulna and tibia length measurements using DXA whole-body scans was overall acceptable, but with higher *CR* for ulna (1.2 cm) and tibia (1.0 cm) lengths than those observed using tape measurements.
- Agreement between the two techniques for measuring ulna and tibia lengths in 17 patients indicated generally a poor agreement, with a *MB* of -0.6cm for ulna and -1.9cm for tibia lengths; which then also translated into poor agreement to measured HT SDS (*MB*= -1.0 SDS for ulna and -0.6 SDS for tibia).
- DXA whole-body scan measurements of ulna length resulted in an underestimation of HT and BIA SDS (*MB*= -1.0 SDS and -0.6 SDS respectively), also meaning more patients were classified with abnormal (low) scores for HT and BIA; and an overestimation of BMI SDS (*MB*=0.7 SDS). The opposite was found for tibia lengths, which resulted in an

overestimation of HT and BIA SDS (*MB*=0.6 SDS and 0.3 SDS respectively) and an underestimation of BMI SDS (*MB*= -0.6 SDS).

- The observed *LOA* were also wide (>1.0 SDS), although slightly narrower for tibia estimates than for ulna estimates.
- The 'calculated' equation for ulna had the best agreement to measured HT, although still underestimating HT (significant bias, wide *LOA* and low kappa); while the equation by Gauld et al. (2004) underestimated HT to a larger degree. Because both equations underestimate HT, the use of the aggregate did not improve the accuracy of the estimate.
- For estimating HT using tibia length, the aggregate estimate resulted in the correction of bias with a non-significant mean difference compared to measured HT, and a substantial agreement for identifying patients with abnormal SDS. The 'calculated' equation overestimated HT, while the equations by Abrahamyan et al. (2008) and Gauld et al. (2004), to a lesser degree, underestimated HT in our patient sample. However, the *LOA* were still wide (>1.0 SDS).

6.9. Discussion

Despite the importance of HT assessment in paediatric patients, there are many conditions that might interfere with these measurements in clinical practice, resulting in poor reporting rates in the patient's medical notes. There are currently studies proposing the use of surrogate measurements to estimate height in patients unable to stand, but contrarily to the case in adults, there is less evidence from studies estimating HT in children, other than perhaps in the case of children with specific clinical conditions (e.g. cerebral palsy) that might not be suitable to assess the growth and nutritional status in a wider population of paediatric patients. There is also the complication that predictive equations or reference data for surrogate measurements should be appropriate and specific for the population being assessed, and that the measurement protocols (anatomic sites, equipment) vary in the few studies available.

Ulna and tibia measurements were chosen as surrogate measurements in this study because: a) they are some of the most commonly-reported measurements in these studies; b) are relatively easy and quick to measure; 3) can be performed without the need for the patient to stand, which is the main reason for the need to perform these measurements. Although some studies advocate the accuracy of measuring body segments using an anthropometer, my aim was to identify suitable measurements that could be performed easily in routine clinical practice. Thus, it was decided that tape-measurements would be more

practical, as this equipment is usually available in most clinical settings. Additionally, our research group had anonymised databases of healthy UK children that included tibia and ulna length measurements obtained precisely using a non-stretchable tape, which could be used to generate new predictive equations for height.

Two published studies were found which could be of use to estimate HT in our population, but both had limitations. The first by Gauld et al. (2003) was performed in a large number of Australian children 5-20 years of age, and reported predictive equations for height using ulna and tibia lengths. However, it is unclear how these predictions would perform for the assessment of paediatric patients in the UK, especially in a tertiary paediatric centre such as GOSH where children have a large range of clinical diagnoses. Additionally, ulna and tibia lengths were measured using an anthropometer. The second study by Abrahamyan et al. (2008) was performed in a sample of French children (6-18yr of age) who had DXA whole-body scans, ulna and tibia (among other bone measurements) were taken using the ruler tool for custom analysis in the manufacturer's software, and prediction equations for HT were generated. Once more, it was unclear how these equations would perform in our sample from a different population and using different measurement protocols. However, the present study did use the methodology described by these researchers to validate ulna and tibia measurements using DXA whole-body scans to provide an alternative to tape measurements, especially when children already have or are scheduled for routine DXA scans as part of their clinical management.

Analysis of our databases of healthy UK children resulted in predictive equations using ulna and tibia lengths, both with a R^2 of 0.87. These equations also included age (yr) and weight (kg) to improve the estimates of HT. The variable 'sex' (1=female) was also entered into the linear regression models, but this was non-significant after the inclusion of the weight variable. Thus, it was considered unnecessary to both include it in the model or generate separate predictive equations for males and females, as had been done in other studies. The study by (Gauld et al. 2004) included age and separate equations for males and females; while the study by (Abrahamyan et al. 2008) just provided different equations for male and female adding no other predictors. The practical advantage of our approach is that it involves the use of a single equation, but on the other hand is dependent on accurate measurements of weight that, similar to height, might be lacking in clinical settings. Although these equations provide an alternative to estimate height specifically in UK children, a major limitation for the equation using tibia length is that the database only included children from ages 10-18yr, meaning the accuracy of the estimates in younger patients cannot be ensured. No reasons were found to explain why some healthy children in the ulna-derived equations cohort had

low SDS (-3 to -4 SDS), this was only observed in a very limited number of children and unlikely to significantly influence the derived equations.

The generated predictive equations were tested in the BodyBasics study sample of recruited children to analyse their use in a clinical setting with a large variety of patients. However, tape measurements of ulna and tibia lengths began after the study had already started recruiting, and many were taken initially in disabled children where there was also not a measurement of standing HT for the analysis of agreement. This resulted in a small set of measurements (*n*=25), that nonetheless provided information on the reliability of the technique and agreement to measurements of standing HT.

Ulna tape measurements were more reliable, and their estimates had better agreement to measured HT, as well as to the derived parameters of BMI and BIA, compared to tibia measurements. However, there was still a significant bias (overestimating HT) from the estimates using both ulna and tibia, with wide *LOA*. This might be explained by the fact that more than half the measurements were taken in patients undergoing spinal surgery (with a diagnosis of adolescent scoliosis); they might have been able to stand for a measurement of HT but this might have underestimated their 'true' HT due to the curvature of their spine. Thus, using these predictive equations in this small and heterogenous group of patients might lead to an inaccurate assessment of HT and other anthropometric parameters; whilst it might be the only alternative if standing HT measurements are unfeasible, it is important that the limitations are recognised. Additionally, some diseases could have cause the disproportionate growth of certain bones, making the predictions of HT based on these bone measurements inaccurate (Pomeroy et al. 2012).

To assess the validity of the predictive equations in a larger group of patients, measurements of ulna and tibia lengths were performed retrospectively for patients enrolled in the BodyBasics study who already had a whole-body DXA scan as part of their assessment in the study. The reliability of these measurements was lower than using the tape measure technique (higher *CR*), especially for ulna lengths. This could be explained considering it was sometimes difficult to identify clearly anatomical markers to measure the bone. DXA scans do not provide the same detail as, for example, X-rays, and the ulna (especially the distal portion of the bone) was often not discernible in the scan of small children. This is further supported by the observed correlation between the difference of repeated measurements and the mean length of the ulna (r = -0.206, p=0.029), which was furthermore non-significant for tibia lengths.

In terms of the agreement analysis, the use of ulna lengths derived from DXA scans resulted in lower mean HT estimates, while tibia resulted in higher HT estimates. The

agreement was generally better for tibia lengths, although the MB was significant in both cases and both had wide *LOA*. The same pattern was observed for BIA SDS and the reverse for BMI, explained by considering how both parameters are calculated (BMI as WT/HT^2, impedance index as HT^2/Z). These results in a larger and more diverse group of patients, compounded by the larger measurement error, likely resulted in the wide variance and *LOA*.

Comparison of the tape and DXA-scan techniques for measuring ulna and tibia lengths was assessed and results show a generally poor agreement between both. However, this analysis was only possible in a restricted number of patients (n=17). Furthermore, all the DXA measurements were performed by myself, without much prior practice or training. Thus, if these measurements were to be used in practice, it is likely that standardization of measurements and training might improve on the reliability of the measurements and the agreement between techniques. However, this highlights the consequences of differences in measurement protocols, and this should be considered when selecting and implementing predictive equations found in the literature for the assessment of HT in different settings.

Observing the agreement results for measured HT, BMI and BIA using both techniques, similar patterns can be recognised. The use of ulna length generally resulted in lower estimates of height compared to tibia, similarly lower estimates of BIA SDS and higher estimates for BMI. Both ulna and tibia tape measurements overestimated (*MB*>0) measured HT, while DXA-scan tibia and ulna estimates seem to have increased overall, with ulna now underestimating measured HT and tibia still overestimating it. However, this might simply be the effect of tape measurements performed in patients with spine curvatures (see explanation above). Thus, using the aggregate (average) of both ulna and tibia length estimates could improve the accuracy of the estimated HT (calculated non-significant *MB*=0.0 SDS, *LOA* ± 1.4 SDS – analysis not shown in results) although still observing wide *LOA*.

Finally, the advantage of using aggregate estimates to improve accuracy of HT was investigated using the two published equations described above in addition to the generated equations for UK children in this study ('calculated'). A study by Wells et al. (2009) has suggested the use of this approach when different prediction equations are available to estimate metabolic variables, each with their own bias, showing that the average of the different predictions might improve on the accuracy of the estimate. For ulna, because both estimates using the 'calculated' and (Gauld et al. 2003) prediction equations resulted in an underestimation of measured HT, the aggregate estimate did not improve on the accuracy. The 'calculated' estimate was indeed the best, although still showing a significant *MB* and wide *LOA* as has been described in the results above. For estimates using tibia length, equations by both (Abrahamyan et al. 2008) and (Gauld et al. 2003) resulted in an

underestimation of measured HT but, as it has been described above, the 'calculated' estimate resulted in an overestimation of HT. Thus, the aggregate estimate resulted in a non-significant bias and was thus the best alternative to estimate HT in this patient sample. It should not be forgotten, however, that in all cases the wide LOA mean estimates will vary greatly in the patient population and this may be the result of the heterogeneity in the patient characteristics and underlying diagnoses affecting the relationship of these bone lengths to height.

6.10. Conclusion

Overall, the results highlight the importance of the choice of surrogate measurement, the measurement protocol, and the use of different prediction equations for the accuracy of HT estimates. This study has generated prediction equations for UK children, using a simple and reliable tape measurement technique of ulna and tibia lengths to estimate HT. The alternative use of DXA whole-body scans to obtain ulna and tibia length measurements is promising but should be investigated further to assess its reliability; and seems to require more training and practice to reduce the measurement error.

The generated equations perform similarly, and slightly better for tibia lengths, than other published equations for children in other populations (Gauld et al. 2003; Abrahamyan et al. 2008). The use of aggregate estimates from all these three equations improve on the accuracy of tibia estimates of HT. Considering ulna measurements with our generated equation tend to underestimate measured HT, while tibia tends to overestimate it; the average of both could also result in a better prediction of HT. In any case, the wide *LOA* indicate the accuracy at the individual level is very variable; likely from the wide range of patient diagnoses and underlying conditions in our population.

There is still limited evidence on the most appropriate way to estimate HT in a diverse population in a specialised clinical setting such as GOSH. The use of the estimates tested in this study could be helpful, but can have important limitations for the assessment of individual patients and cannot be recommended for routine clinical practice without further analysis. Ultimately, equations developed for specific patient groups might improve on the accuracy of HT, or aggregate measurements could be used if the former are unavailable. Future studies should investigate this further, including the generation of prediction equations for different populations and settings. At this stage, the explored estimates were also not considered to be accurate enough to impute the missing HT values in the BodyBasics study database, which would be used in the following chapters of the thesis, as this would have introduced additional error in the analyses.

7 Nutritional parameters and associated factors on admission, discharge and during hospitalisation: quantifying malnutrition prevalence in paediatric patients

7.1. Introduction

Despite overall agreement that malnutrition in paediatric patients is an ongoing concern in both developing and developed countries, its prevalence is still unclear; with studies reporting figures from 6% up to 60% (Joosten & Hulst 2008). As has been discussed in previous chapters (see Chapter 1, Section 1.1), one of the main issues hindering a reliable assessment of prevalence is the lack of consensus on the diagnostic parameters that should be used (Cederholm et al. 2015; Becker et al. 2014). Studies have used a wide range of measurements, cut-offs, references, and population characteristics that do not allow comparisons between different studies and deter from a full characterisation of the problem.

In view of these inconsistencies, the work in this thesis has made use of the reference data developed to assess BC in UK children by a range of different techniques (Wells et al. 2012); which will provide a chance to systematically assess and compare the prevalence of malnutrition using different BC parameters, as well as the more established anthropometric parameters of WT, HT and BMI (Cole et al., 1995; Freeman et al., 1995). This will not only help quantify the extent of paediatric 'malnutrition', but also identify the variables associated with these measurements on admission and during hospitalisation. An analysis on how the different parameters perform with regards to their associations to clinical outcomes, and thus their potential use as diagnostic parameters for malnutrition, will be further explored in the next chapter (Chapter 8).

7.2. Chapter objectives

1. Describe the study subject characteristics (BodyBasics study).
2. Calculate SDS for the different anthropometric and BC parameters on admission, and quantify the number of patients categorised with abnormal SDS.
3. Summarise the predictor variables on admission concerning 4 domains: steroid prescription, fluid restriction, physical activity, and dietary intake.
4. Determine which variable(s) best predict the different anthropometric and BC SDS on admission.

5. Describe the treatment procedures during hospitalisation and other subject characteristics at the moment of hospital/study discharge.
6. Determine the SDS for the different anthropometric and BC parameters at discharge, and the number of patients categorised with abnormal SDS.
7. Explore the change in SDS between admission and discharge for the different anthropometric and BC parameters.
8. Summarise the predictor variables at discharge: steroid prescription, fluid restriction, and dietary intake.
9. Determine which predictor variable(s) best predict the change in anthropometric and BC SDS during hospitalisation.

7.3. Methods

7.3.1. Study population and recruitment

The chapter objectives were investigated using data collected from patients enrolled in the BodyBasics study. This chapter describes the study subject characteristics, as well as the admission and diagnosis groups. Full details on the inclusion/exclusion criteria, as well as the recruitment and consent procedures can be found in Chapter 3, Section 3.1.

7.3.2. Data collection, analysis and statistics

The SDS for the different anthropometric and BC parameters on admission and discharge were calculated as detailed in Chapter 3, Section 3.3. The SDS for each parameter were obtained using the average of repeated measurements (if relevant) and subsequently comparing these values to relevant reference data for healthy UK children (Wells et al. 2012; Freeman et al. 1995). SDS were summarised with the *mean* and 95% *CI*, and each mean SDS tested using One sample t-tests to determine if the value was significantly different from zero. The percentage of patients with abnormal SDS (defined as ≥2 SDS or ≤-2 SDS) was also calculated. Any differences in SDS between sexes and admission groups (medical, surgical) were explored using Independent samples t-tests, and the effect of age on mean SDS was determined by calculating the Pearson's Correlation Coefficient (*r*).

For BIA, results are presented separately for those measurements obtained using the standing (BIA_{st}) and supine (BIA_{sup}) techniques, considering there was some difference in the patients that could be measured using the different machines (e.g. spinal surgery patients

with musculoskeletal abnormalities), and this distinction contributed to the interpretation of results. BIA_{sup} values had been adjusted using *MB* as detailed in Chapter 5. BIA_{all} was also calculated as the average between BIA_{st} and BIA_{sup} (when both measurements were available) or just BIA_{sup}.

Additionally, after the SDS for the parameters on admission and at discharge were obtained, the change in SDS was calculated (discharge-admission SDS), and the variable 'decreased SDS' (no/yes) generated.

Analyses of the parameters SDS and abnormal SDS were performed taking all available measurements into account, meaning the number of observations often differ between techniques. In other words, different (types of) patients might have been measured by different techniques. However, it was decided to present the results in this manner, rather than restricting analyses to only those patients who had all measurements performed, because this first approach is more pragmatic, and shows how the population would have been characterised in real life, with the use of the different techniques. Additionally, the validation of the techniques (how they compare to each other) had already been performed in Chapter 4, and this helped with the interpretation of the results in this chapter.

The predictor variables on admission and discharge were summarised using percentages, and the effects of sex, admission group and age were also explored using Chi-squared and One-way ANOVA tests. These analyses included several variables (categorical and binary) describing each of the domains being assessed: steroid use, fluid restriction, physical activity/mobility and dietary intake. For subsequent analyses, however, only binary variables for each of the domains were selected, as the univariate analyses showed the statistical limitations (e.g. expected cell count below 5 for Chi-squared tests) for using variables with increasing number of categories.

The associations between the SDS for each parameter and the predictor variables were explored using univariate analyses (Independent samples t-test or Chi-squared/Fisher's exact test), and subsequently linear regression models were constructed based on all observed significant associations between the parameters and predictor variables, adjusted for age, sex and/or admission group as appropriate.

The level of significance before ($p<0.05$) and after Bonferroni adjustment for multiple testing (details in Chapter 3, Section 3.6.4) are both indicated in the results table footnotes.

7.4. Study subject characteristics

7.4.1. Age and sex

The study enrolled children aged 5-18yr, considering this is the age range available for the UK BC reference data (Wells et al. 2012) used to calculate the SDS for BIA, DXA and SFTs measurements. Table 7.1 describes the study characteristics in terms of age and sex. The sample had equally distributed numbers of male and female patients, however female patients were significantly older (mean age 11.4 yr) than males (mean age 10.1 yr).

	n	***mean*** [a]	***min***	***max***
Age (*yr*)	152	10.7 (3.6)	5	18

Sex	***n***	***%***	**Age**	
			mean [b]	*p* [c]
male	76	50	10.1 (3.9)	0.037*
female	76	50	11.4 (3.3)	

Table 7.1. Study subject characteristics.
(a) Mean age in years (SD) for the entire sample; (b) Mean age in years (SD) per sex; (c) Independent samples t-test for difference in age between sexes, (*) significant (p<0.05).

7.4.2. Diagnoses and admission specialties

Initially, all wards and specialties at GOSH were targeted for recruitment to the study. This included the following medical wards: Respiratory, Gastroenterology, Dermatology/ Rheumatology, Oncology, Neurology, Urology (Dialysis); and surgical wards: Spinal, Gastroenterology (stoma closures, intestinal resections), Cardiac, Renal, Cranio-facial and Neurology. Figure 7.1 shows the number of recruited patients from each specialty on admission.

The largest groups of patients recruited into the study were admitted for spinal surgery, mainly spinal fusion procedures, and to the Gastroenterology wards. For Spinal surgery admissions, two groups of patients were identified: those with Adolescent Idiopathic Scoliosis and patients with more complicated syndromes and neuromuscular/neurological impairments (e.g. Cerebral Palsy; CP). Similarly, most Gastroenterology patients were admitted for short-term investigations such as gastrointestinal (GI) motility studies, and a smaller number had longer admissions to conduct feeding trials or start Enteral nutrition (EN) feeds or Parenteral

nutrition (PN). Other patient groups recruited in smaller but still somewhat significant numbers were: Cystic Fibrosis (CF) patients admitted for routine antibiotic treatment, patients scheduled for Bone Marrow Transplantation (BMT), and those admitted for investigations or treatment on the Dermatology/Rheumatology ward.

Recruitment in the surgical wards was initially difficult to coordinate, since a large proportion of the children were admitted on the same day that their surgery was scheduled, leaving limited time to enrol them in the study and perform the measurements. After contacting the admission teams in each specialty, we were able to identify pre-assessment clinics which provided an opportunity to approach patients and their families to inform them about the study and give them time to consider it before their admission. This was especially successful for the spinal surgery service, as families often came back to the hospital one more time before their admission to sign surgery consent forms, giving us the chance to enrol them and perform the measurements just 1-2 days before their actual admission/surgery (in this case, this date was considered their 'admission date'). If families came from abroad or outside London, they often arrived to stay at the patient hotel one day before, again giving us the chance to perform the measurements before the day of the surgery. Cardiac surgery pre-assessment clinics also provided an opportunity to approach families and give them information on the study. However, surgery was usually scheduled further ahead, meaning we could not perform the measurements in clinic and consider this as their 'admission' measurements; and there was still a chance we could be too late to enrol and measure them on the day of their surgery/admission.

In terms of diagnoses, all recruited patients had multiple (often up to five) different diagnoses. Thus, primary diagnoses were identified for each patient, and an attempt was then made to classify these into common categories. However, they were so diverse that this still resulted in a large number of categories, some unique to a single patient. Figure 7.2 shows some of the main categories for primary diagnosis in our patient sample. In agreement with the number of recruited children in each specialty/ward, most patients had a GI (e.g. constipation) or Orthopaedic (e.g. scoliosis) diagnosis, followed by patients with CF, Oncological/Haematological conditions (most with diagnosis of Leukemia admitted for BMT), inflammatory GI, and neuromuscular conditions (most with CP or Muscular Dystrophy admitted for spinal surgery).

Considering the large range of admission and diagnosis groups, I decided to use the more robust classification of 'medical/surgical', as has been used in the previous chapters already. The number of patients classified as 'medical' and 'surgical' (Table 7.2) were 48.7% and 51.3% respectively.

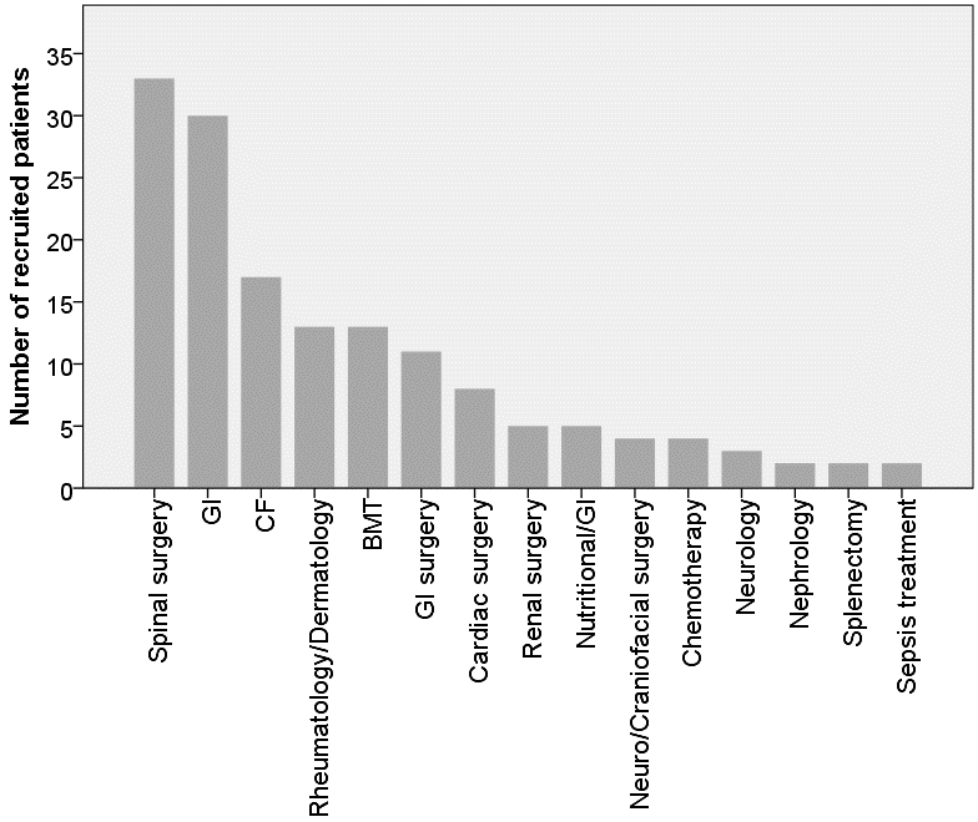


Figure 7.1. Admission specialties and scheduled procedures for recruited patients.

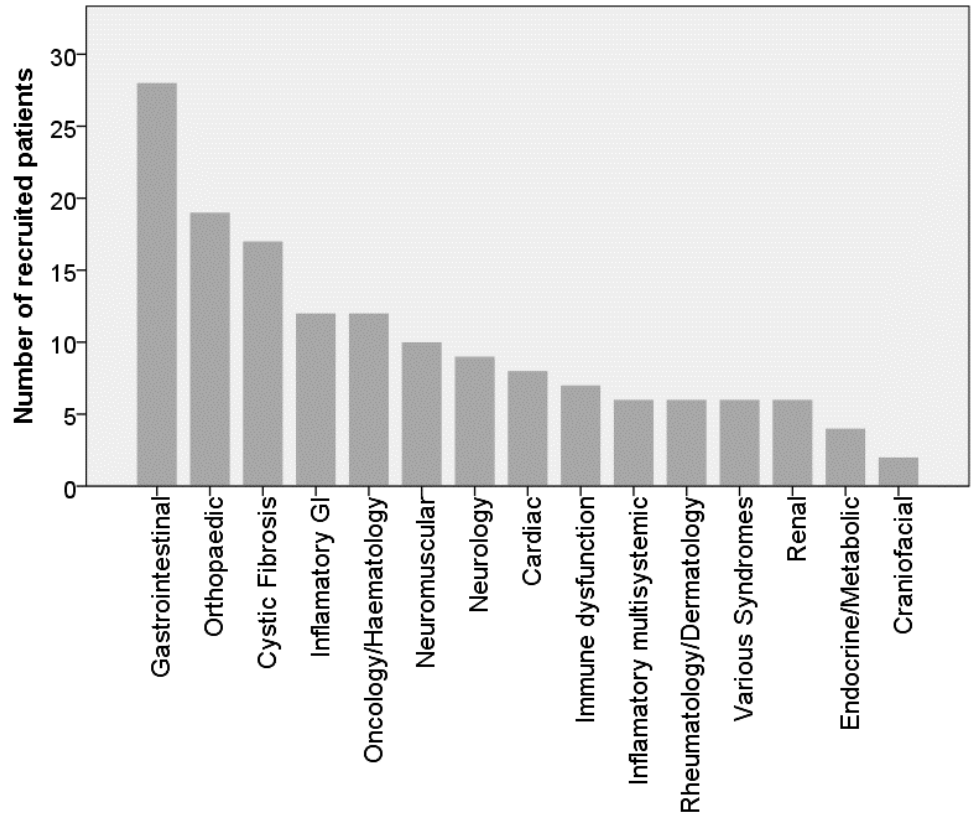


Figure 7.2. Diagnosis categories of recruited patients.

Differences in age and number of male/female patients between admission groups were explored, and there was a significant difference in the mean age between groups, surgical patients being 1 year older on average compared to medical patients (Appendix 14, Table 1). The groups, however, were evenly distributed between male and female for both groups of patients.

7.5. Anthropometric and body composition parameters on admission.

7.5.1. Simple anthropometric parameters

Calculated mean SDS for the anthropometric parameters of HT, WT, MUAC and HC are summarised in Table 7.2. Patients in our sample had on average low SDS for all parameters. These values were all significantly different from zero, meaning as evidenced from their calculated 95% *CI*s, that our population as a whole has negative mean SDS on admission. HT and HC had the lowest mean SDS, both below -0.5 SDS, with the higher *CI* limit for HT close to -1.0 SDS. WT and MUAC had similar mean SDS of approximately -0.3 SDS. WT had a slightly lower mean SDS but larger variation, resulting in a wider *CI* compared to MUAC.

Calculated SDS using only 'accurate' measurements obtained adhering to each technique's protocol (Appendix 14, Table 2), showed very similar results for WT and MUAC, both having mean SDS significantly different (lower) from zero. WT also had a lower SDS, close to -0.5 SDS, and a narrower *CI*. HC showed only a small change, as expected considering only three measurements were excluded from the analysis. HT, however, changed to a significant mean SDS just below -0.5 SDS. This was unsurprising considering 30 measurements were excluded from the analysis, many of these from spinal surgery patients who had low HT SDS.

	n	**SDS** [a]	***CI*** [b]		***p*** [c]
HT	141	-0.70	-0.45	-0.95	0.000**
WT	152	-0.34	-0.07	-0.60	0.015*
MUAC	147	-0.29	-0.10	-0.48	0.003*
HC	148	-0.64	-0.36	-0.91	0.000**

Table 7.2. Anthropometric parameters SDS on admission.

(a) Mean Standard Deviation Score; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0: mean SDS=0), (*) significant ($p<0.05$), (**) significant even after correction for multiple testing ($p<0.003$).

Analysis on the percentage of children with abnormal SDS on admission indicated approximately 20% of patients had either a SDS ≥ 2 or ≤ -2 (Table 7.3). The percentage was lower for the case of MUAC (10.9%). As evidenced from the *CI*s, up to 26% of patients admitted to GOSH could be expected to have abnormal SDS for HT, WT and HC (16% for patients assessed using MUAC). The vast majority of abnormal SDS for HT were cases of low SDS (≤ -2 SDS). For WT and HC, most cases were also low SDS, but about 5% of patients also had SDS ≥ 2. MUAC identified a lower percentage of children with abnormal SDS (both low and high) compared to WT.

When considering only accurate measurements (Appendix 14, Table 3), the percentage of patients with abnormal SDS did not change much for WT, MUAC or HC. HT, on the other hand, showed a lower percentage of patients with abnormal SDS; indicating, as expected, that a good number of excluded values were patients with abnormally low SDS for HT.

	n	**abSDS [a]**	***CI* [b]**		**≤ -2SDS [c]**	**≥ 2SDS [d]**
HT	141	19.9	13.3	26.4	18.4	1.4
WT	152	19.7	13.4	26.1	13.8	5.9
MUAC	147	10.9	5.8	15.9	8.8	2.0
HC	148	20.3	13.8	26.7	15.5	4.7

Table 7.3. Abnormal SDS for anthropometric parameters on admission.
(a) Percentage (%) of patients with abnormal standard deviation scores (abSDS) on admission for each parameter; (b) 95% CI for the % of patients with abSDS; (c) % of patients with ≤-2 SDS; (d) % of patients with ≥2 SDS.

Differences in mean SDS between male and female patients (Appendix 14, Table 4) were all non-significant, although there was a trend for female patients to have lower SDS for all parameters. Similarly, there was no significant difference between medical and surgical patients, although surgical patients also had a tendency towards lower mean SDS for all parameters. There was no significant correlation of age with mean SDS for any of the parameters (data not shown).

Analysis using only accurate measurements (Appendix 14, Table 5) resulted in similar non-significant differences between male/female patients and admission groups. The tendency for surgical patients to have lower mean SDS, however, changed for the case of HT. This confirms again that most of the excluded HT were likely surgical (spinal) patients.

7.5.2. Body composition: FM and LM parameters

The mean SDS for FM parameters (Table 7.4) were all positive (above zero), although they were non-significant in most cases, except for biceps and subscapular SFTs. This indicates patients had a tendency to present with higher mean SDS for FM on admission, although some patients are still expected to have negative SDS compared to healthy children of the same age and sex.

The SDS for DXA FM, considered the clinical reference method in our study, showed a mean SDS very close to zero and a *CI* spanning both positive and negative SDS. This suggests children admitted in our population have varying amounts of FM, both higher and lower than those expected for healthy children of the same age and sex.

For BMI, it is particularly interesting to note how the mean of this index is higher than zero, and higher than the average SDS for WT. This is explained considering our patient population had low average SDS for both WT and HT. Thus, the use of BMI alone to assess the patient's nutritional status in our population would likely miss many children with low WT and HT, that might nonetheless benefit from nutritional assessment and management. Its use for the assessment of FM, resulted in an overestimation compared to DXA FM, as was expected considering the results from the parameter's validation against DXA (Chapter 4).

LM parameters, on the other hand, showed consistently very significant negative mean SDS on admission. Considering the lower limit of the *CI*, the mean SDS in our population could be close or even lower than -1.0 SDS. The mean SDS for DXA LM, BIA_{sup}, and BIA_{all} were approximately -0.95 SDS; while the mean SDS for BIA_{st} was around -0.75 SDS. This reflects how many of the patients unable to be measured by BIA_{st}, but who had measurements of BIA_{sup} (or DXA), were likely to have low SDS. The mean SDS for BIA_{all} and DXA LM were very similar, overall confirming the good agreement between techniques as explored in Chapters 4 and 5.

Results from the restricted measurements database (Appendix 14, Table 6) showed very similar results to those described above, but with narrower *CI*s. This suggests measurements in clinical practice obtained with a technique that deviates slightly from the protocol guidelines, could still give a good assessment of FM and LM, at least for group estimates.

	n	SDS [a]	*CI* [b]		*p* [c]
FM parameters					
BMI	141	0.22	-0.01	0.45	0.058
Biceps SFT	118	0.43	0.26	0.60	0.000*
Triceps SFT	119	0.12	-0.06	0.29	0.191
Subscapular SFT	101	0.32	0.15	0.50	0.001*
Suprailiac SFT	87	0.15	-0.04	0.33	0.127
DXA FM	122	0.07	-0.15	0.29	0.532
LM parameters					
BIA_{st}	104	-0.74	-0.98	-0.50	0.000*
BIA_{sup}	131	-0.95	-1.20	-0.70	0.000*
BIA_{all}	135	-0.94	-1.18	-0.70	0.000*
DXA LM	122	-0.97	-1.23	-0.70	0.000*

Table 7.4. BC parameters SDS on admission.
(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS ($H_{0:}$ mean SDS=0), (*) significant (p<0.05, and corrected p<0.003 for multiple testing).

The percentage of patients with abnormal SDS for FM and LM parameters can be observed in Table 7.5. Considering DXA for the assessment of FM, our sample showed that around 12% of patients had abnormal SDS, with the *CI* indicating that up to 17% of patients in our population could be expected to have abnormal FM SDS on admission. This percentage was similarly distributed between patients with high and low SDSs (≥2 SDS and ≤-2 SDS respectively).

For BMI, the percentage of patients with abnormal SDS was slightly higher (13.5%), but most importantly, a higher percentage of abnormal SDS were found in patients classified as having high SDS (≥2 SDS) rather than low. This observation further confirms how the use of BMI can overestimate FM (observed in Chapter 4), and can result in both an overestimation of the number of patients with abnormally high SDS and an underestimation of those with abnormally low SDS compared to our clinical reference method of DXA FM. Some of the high SDS cases could have also been spinal surgery patients, whose' HT might have been underestimated (due to curvature of spine) resulting in inaccurate higher BMI SDS. This is supported by the slightly decreased percentage of patients with abnormal high SDS in the restricted database, which excluded these HT measurements and their resulting BMIs.

All SFTs showed a low percentage of abnormal SDS (0% for subscapular SFT). Biceps SFTs seemed to identify a similar percentage of patients with high SDS as DXA FM, however the use of this parameter to assess FM seemed to miss all patients with abnormal low SDS identified by other techniques. This suggests Biceps SFT would be the 'best' option among the different SFT sites to assess FM, although this measurement is still expected to misclassify some patients with abnormal high SDS, and miss almost all patients with low SDS below the cut-off -2 SDS.

	n	abSDS [a]	*CI* [b]		≤ -2SDS [c]	≥ 2SDS [d]
FM parameters						
BMI	141	13.5	7.8	19.1	2.8	10.6
Biceps SFT	118	4.2	0.6	7.9	0.8	3.4
Triceps SFT	119	1.7	0.0	4.0	1.7	0.0
Subscapular SFT	101	0.0	0.0	0.0	0.0	0.0
Suprailiac SFT	87	2.3	0.0	5.4	1.1	1.1
DXA FM	122	11.5	5.8	17.1	6.6	4.9
LM parameters						
BIA_{st}	104	13.5	6.9	20.0	11.5	1.9
BIA_{sup}	131	23.7	16.4	30.9	20.6	3.1
BIA_{all}	135	23.0	15.9	30.1	20.0	3.0
DXA LM	122	19.7	12.6	26.7	19.7	0.0

Table 7.5. Abnormal SDS for BC parameters on admission.
(a) Percentage (%) of patients with abnormal standard deviation scores (abSDS) on admission for each parameter; (b) 95% CI for the % of patients with abSDS; (c) % of patients with ≤-2 SDS; (d) % of patients with ≥2 SDS.

Regarding LM, our results show that approximately 20% of patients in our sample had abnormal SDS. The percentage of abnormal SDS for DXA LM was just slightly lower than those observed for BIA_{sup} and BIA_{all} (19.7% compared to approximately 23%), which could be explained by the fact that more patients (with abnormal low SDS) were measured using BIA_{sup} (21 patients). These patients are likely to be mostly spinal surgery patients, since they were also similarly unable to have BIA_{st} measurements; which also showed a smaller percentage of patients with abnormal SDS. It should be considered that these low LM SDS in spinal patients could result from both children having genuinely low lean (muscle) mass, but also might have been the result of an underestimated HT on admission in patients with

spinal curvature (e.g. adolescent scoliosis). Considering BIA SDS are calculated using the impedance index (HT^2/Z), this could have resulted in lower BIA SDS.

The results from the restricted database (Appendix 14, Table 7) showed very similar percentage of abnormal SDS for FM and LM parameters, and only a slight decrease in all percentages, indicating an exclusion of measurements classified as abnormal (both ≥2 SDS and ≤-2 SDS).

7.5.3. Indices of FM and LM

Calculation of the indices for DXA FM and LM (FMI and LMI respectively), resulted in a higher mean SDS for both parameters (Table 7.6). The effect of size adjusting was greater, however, for LM than for FM. The use of the restricted database resulted in very similar results (data not shown).

	n	**SDS** [a]	***CI*** [b]		***p*** [c]
DXA FM	122	0.07	-0.15	0.29	0.532
FMI	118	0.19	-0.02	0.41	0.076
DXA LM	122	-0.97	-1.23	-0.70	0.000*
LMI	118	-0.56	-0.80	-0.31	0.000*

Table 7.6. DXA FM, LM and BC indices on admission.
(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0: mean SDS=0), (*) significant (p<0.05, and corrected p<0.003 for multiple testing).

	n	**abSDS** [a]	***CI*** [b]		**≤ -2SDS** [c]	**≥ 2SDS** [d]
DXA FM	122	11.5	5.8	17.1	6.6	4.9
FMI	118	9.3	4.1	14.6	3.4	5.9
DXA LM	122	19.7	12.6	26.7	19.7	0.0
LMI	118	11.0	5.4	16.7	10.2	0.8

Table 7.7. Abnormal SDS for DXA FM, LM and BC indices on admission.
(a) Percentage (%) of patients with abnormal standard deviation scores (abSDS) on admission for each parameter; (b) 95% CI for the % of patients with abSDS; (c) % of patients with ≤-2 SDS; (d) % of patients with ≥2 SDS.

In agreement to the previous observations, the percentage of patients with abnormal SDS was lower after adjusting for size in both FM and LM (Table 7.7). Just as mean SDS for FMI shifted towards higher SDS, the percentage of patients with SDS ≥2 SDS increased, while those with SDS ≤-2 SDS decreased.

7.5.4. BC differences by admission group, sex, and associations with age

Appendix 14, Table 8 shows the observed differences between mean SDS of FM and LM parameters between male/female patients and medical/surgical admission groups. Female patients had a non-significant tendency for lower SDS for FM parameters. This was significant (p=0.024) only for DXA FM mean SDS, but became non-significant after adjustment for size (mean FMI SDS). Similarly, females had a tendency for lower DXA LM SDS compared to male patients, but the mean SDS also shifted to a higher value after adjustment for size (LMI SDS). Surgical patients on the other hand, had a non-significant tendency for higher FM SDS and lower LM SDS. The lower LM probably reflects the fact that this group included a significant proportion of spinal surgery patients. This is further supported by observations of BIA. The BIA_{st}, which excluded this group of spinal surgery patients, showed a mean SDS that was even slightly higher than that of medical patients; while BIA_{sup} and BIA_{all} that included these children admitted for spinal surgery had an almost-significant lower mean SDS compared to medical patients.

Analyses performed using the restricted database (Appendix 14, Table 9) showed the same trends as those described for the complete database, including the significantly lower DXA FM SDS for females compared to males. Furthermore, mean SDS for BIA_{sup} and BIA_{all} now became significantly and near-significantly lower in surgical patients compared to medical admissions. Mean FMI SDS was also significantly higher for surgical patients.

There was no significant correlation between SDS for all BC parameters and age, both with the complete and restricted databases (data not shown). Analysis of the percentage of abnormal SDS (both categorical: normal, ≥2SDS, ≤-2SDS; and binary variables: normal, abnormal) per sex and admission group showed no significant associations for both databases, but still showed the same trends as those described above for the mean SDS (data not shown).

7.6. Description of predictor variables on admission

Data on variables considered as potential predictors of baseline nutritional status were recorded on admission. These variables included: steroid medication known to affect appetite and possibly impact FM, fluid restrictions that could also affect oral intake, physical activity impacting mainly on LM, and factors related to dietary intake. This section gives a description of these variables and explores any differences per admission group, sex and age.

7.6.1. Steroid prescription

A description of the number of patients receiving steroid medication at the moment of admission is shown on Table 7.8. The clear majority of patients (78%) did not report taking steroid medication of any type within the past 6 months, while little over 10% had taken some steroid medication, but this was usually not routine and/or low dose (e.g. topical creams for skin condition flare-ups, asthma inhalers). Only 9% of patients were reported to be on routine (high dose) medication containing steroids.

Considering the heterogeneity in patient diagnoses and clinical conditions, the classification of steroid prescription was discussed at length and the decision was made to a use a robust classification of ‘low’ or ‘high’ as described by the parents. Only a small number of patients were taking any steroid medication and the range of dosis, prescription schedules and duration was additionally highly variable and, as with the patient diagnoses, it was not possible to classify these into more-detailed groups for analysis.

	Frequency	%
Steroid prescription		
no	119	78
low	19	13
high	14	9
High steroids		
no	138	91
yes	14	9

Table 7.8. Summary of steroid medication prescription on admission.

Differences in steroid prescription between male/female and admission groups were explored (Appendix 14, Table 10). Results indicated no significant difference in the number of patients between admission groups, although there was a near-significant trend for a higher number of medical patients to be on steroid medication compared to surgical patients. There was no significant difference between male and female patients, and similarly there was no significant difference in age between patients with and without steroid medication prescription.

7.6.1. Fluid restriction

The degree of fluid restriction at the moment of admission is summarised in Table 7.9. Most patients reported no restrictions in fluid intake. From those who were limited in how much they could drink, just over half of them were restricted in preparation for a medical/surgical procedure (nil by mouth; NBM) and the rest were reported to be on a more long-term restriction due to their clinical condition (e.g. renal patients).

There was no difference in the percentage of restricted patients between admission groups, and no difference in mean age between those who were on restrictions and those who were not (Appendix 14, Table 11). There was however, a significantly higher proportion of male patients with restrictions, especially due to an underlying medical condition.

	Frequency	%
Fluid restrictions		
no	132	87
NMB	12	8
limited	8	5
Restricted fluid		
no	132	87
yes	20	13

Table 7.9. Summary of fluid restrictions on patients at the moment of admission.

7.6.1. Physical activity

The degree of mobility and physical activity of the patients prior to admission was assessed by asking the parents to rate their child's level of activity, and asking about school attendance/use of wheelchair.

As Table 7.10 shows, half the children in our study were assessed as having a lower level of activity compared to their peers and only 19% of them had a higher active physical activity. However, most patients (70%) were ambulatory and reported being active and attending mainstream school. Children using wheelchairs (11%) were evenly divided between those reporting some level of activity/physiotherapy and those almost completely immobile.

There was no significant difference between the proportions of male/female patients between categories of physical activity (Appendix 14, Table 12); and no differences in age either. However, as expected, there was a non-significant tendency for surgical patients to be less active, assessed by their parents, compared to medical patients; and a significant difference in the proportion of patients on wheelchairs (18% vs 4% in surgical and medical groups respectively). Even for those patients who were ambulatory, surgical patients tended to be less active compared to children admitted for medical procedures.

Many of the wheelchair dependent patients were being admitted for spinal surgery, and they constituted a group of interest due to their relatively large numbers and particular characteristics, as has been mentioned in previous sections.

	Frequency	%
Activity level by parent		
much less	36	24
less	39	26
same	47	31
more	16	11
much more	12	8
Activity level		
wheelchair not active	8	5
wheelchair active	9	6
walk not active	28	18
walk active	107	70
Wheelchair user		
no	135	89
yes	17	11

Table 7.10. Summary of physical activity on patients at the moment of admission.

7.6.2. Diet-related factors

Several aspects related to the children's diets were assessed on admission to give an overall picture of the adequacy of their nutritional intake. Such aspects were related to the mode of feeding (oral, enteral, parenteral), the range of foods in the diet (dietary restrictions), how much is eaten (changes in appetite and reported problems with intake), and need for previous nutritional management/guidance (prior dietetic advice). Table 7.11 gives details about these variables on admission.

Most of the patients recruited to the study were orally self-fed (72%), a lower but still important percentage (20%) reported needing help from a carer either with the full oral feeds or to help administer EN and/or PN alongside the oral intake. Less than 10% were completely dependent on a carer to supply either full EN/PN feeds or together with some oral feeding. Only two patients reported being on self-administered EN/PN and oral feeds. Around 20% of patients were on some form of EN/PN feeds, and of those only about one third required full artificial nutrition support (EN and/or PN). Additionally, more than half (56%) of the patients reported having seen a dietitian within the last 6 months.

Restrictions in the diet were common, with more than 50% of children reporting some form of limitation in the foods consumed. About 20% of children had a minor restriction, mainly due to personal preference ('picky' eater) or necessary changes in food texture; but almost 35% had a more significant restriction due to their clinical condition (e.g. food allergies and sensitivity, or following special diets for renal disease and other medical diagnoses). This last category also included children requiring some form of artificial nutrition support.

Regarding appetite, this was measured as the change in a continuous Likert scale comparing the level of appetite 6 weeks previously vs. the week before admission. Considering this assessment sometimes resulted in a minimal (even when the patients tried to make the score the same) difference between both appetite scores, a variable was calculated considering only those cases reporting a decrease equal or greater than 10% between both scales. This level of decreased appetite was reported by 26% of patients. The assessment of intake problems (limit in the amount of food intake) showed that 17%, were limited in their intake, mostly due to scheduled medical procedures (NBM). A variable was then calculated combining appetite and intake and this resulted, as expected, in large overlap between the two, so that 28% of patients were classified as having problems with intake and/or reduced appetite.

	Frequency	%
Feeding categories		
oral self	110	72
oral carer	13	9
oral + EN/PN self	2	1
oral self + EN/PN carer	16	11
oral + EN/PN carer	3	2
EN/PN carer	8	5
EN/PN feeding regime		
no	123	81
partial	21	14
full	8	5
EN/PN feeding		
no	123	81
yes	29	19
Dietary restrictions		
none	68	45
minor	32	21
very restricted	52	34
Restricted diet		
no	100	66
yes	52	34
Loss of appetite		
no	108	74
yes	38	26
Intake problems		
none	127	84
NBM	18	12
limited by clinical condition	7	5
Intake / appetite problems		
no	109	72
yes	43	28
Prior dietetic advice		
no	67	44
yes	85	56

Table 7.11. Summary of diet-related factors on admission.

Appendix 14, Table 13 shows associations between diet-related factors and admission groups, sex and age. There was no significant difference in the proportion of male and female patients within each category. However, there was an overall significant difference between the medical and surgical groups regarding these diet-related factors on admission.

A higher number of surgical patients required help by their carer with oral feeds. Several of these children were spinal surgery admissions of children with diagnoses of CP or other syndromes causing developmental delay and/or musculoskeletal abnormalities. On the other hand, a higher number of medical admission patients were feeding orally by themselves but were on EN/PN feeds that required the help of the carer. This was reflected in the near-significant differences in the proportion of patients on artificial nutrition support (p=0.08). Similarly, the proportion of patients on a restricted diet (which included artificial nutrition support) was significantly greater in the medical group (42%, p=0.038); as was the percentage of patients with loss of appetite (34%, p=0.029) and/or intake problems (38%, p=0.009); and those who had received previous dietetic advice (65%, p=0.023).

There was also evidence of a difference in age between groups, with patients on dietary restrictions on average 1 year younger than those on minor or no restrictions (approximately 10yr vs 11yr). Younger patients, understandably, were also more dependent on their carers for their nutrition (oral and/or EN/PN); while older children (and adolescents) were more likely to also be in charge of their artificial nutrition. The case should be highlighted for children on part oral feeds and artificial nutrition, both administered by the carer. Unlike the pattern described above for younger children depending on their parents/carers, these children are on average older (13yr) and thus likely include a large proportion of children with developmental delays and neuromuscular conditions affecting their motor function.

7.7. Variables predicting the parameter SDS on admission

7.7.1. Predictor variables for anthropometric parameters

The significance for the univariate analyses between anthropometric SDS and prediction variables on admission are summarized in Table 7.12 (further details in Appendix 14, Tables 14 and 15). Only predictive binary variables were selected for the analyses in this and the following sections because of the observed statistical limitations on variables with more categories (expected and observed cell counts per cell), as is indicated in the footnotes of the tables in the previous sections. There were no significant effects of steroid medication prescription or fluid restriction prior to admission on the mean SDS. Patients who were wheelchair dependent however, had a significantly lower mean SDS for all anthropometric

parameters, especially for those related to linear growth and development: HT and HC. Regarding the diet-related variables, patients on EN/PN feeds, on a restricted diet or those who had received previous dietetic advice by a dietitian had significantly lower mean SDS for WT, HT, MUAC and HC. There were no differences in the significance of these parameters with the restricted measurements database (Table 7.13)

7.7.2. Predictor variables for FM and LM parameters

Analyses for the associations between potential predictors and mean FM and LM SDS are also summarised in Table 7.12 (further details in Appendix 14, Tables 16 and 17). Once more, there was no significant effect of steroid medication prescription, but patients on fluid restriction had a significantly higher mean SDS for FM and FMI.

Wheelchair dependent children had variable mean SDS for FM according to the different parameters, and only Triceps SFT SDS was significantly higher compared to ambulatory patients. Conversely, they had consistently low mean SDS for all LM parameters including DXA LM and LMI. There was a difference in significance with the restricted measurements database (Table 7.13), where most LM parameters were no longer significantly different between ambulatory and wheelchair-bound patients, as many of the excluded measurements corresponded to non-ambulatory patients with low SDS for LM (e.g. spinal surgery patients with CP or other neuromuscular conditions).

Regarding the diet-related variables, patients on EN/PN feeds had lower mean SDS for all FM parameters, although this difference was only significant for BMI, Subscapular SFT and DXA FM. They also had significantly lower LM parameter SDS, although adjusting DXA LM for size (LMI) resulted in a non-significant difference. Similarly, patients on restricted diets had on average lower SDS for all FM and LM parameters, with the exception of Biceps SFTs and LMI; and patients who had prior dietetic advice also had significantly lower SDS for FM assessed by all parameters as well as low LM by all BIA measurements. In the restricted database (Table 7.13), DXA LM SDS (but not LMI SDS), were also significantly lower in those patients with prior dietetic advice. Patients with or without intake/appetite problems had no significant differences in FM or LM parameters.

Overall, the strongest univariate predictors of BC parameters were ‘wheelchair user’, and 3 of the diet-related variables: ‘EN/PN feeding’, ‘restricted diet’, and ‘prior dietetic advice’. However, while FM parameters seemed to be better predicted by whether patients had any prior dietetic advice, LM parameters were more strongly predicted by whether or not they were on EN/PN feeds. These associations were considered when constructing the different linear prediction models described in the next section.

	Steroid prescription	Fluid restriction	Wheelchair user	EN / PN feeding	Restricted diet	Intake/ appetite problems	Prior dietetic advice
Anthropometric parameters							
HT	0.421	0.982	0.000*	0.001**	0.000**	0.155	0.001**
WT	0.410	0.264	0.000*	0.000**	0.000**	0.547	0.000**
MUAC	0.476	0.461	0.490	0.005*	0.001**	0.850	0.000**
HC	0.511	0.884	0.000*	0.001**	0.001**	0.131	0.009*
FM parameters							
BMI	0.154	0.179	0.125	0.004*	0.012*	0.851	0.012*
Biceps SFT	0.833	0.472	0.282	0.194	0.226	0.980	0.008*
Triceps SFT	0.871	0.622	0.024*	0.190	0.029*	0.182	0.018*
Subscapular SFT	0.643	0.148	0.452	0.017*	0.035*	0.662	0.000**
Suprailiac SFT	0.694	0.105	0.541	0.340	0.031*	0.585	0.001**
DXA FM	0.240	0.007*	0.691	0.037*	0.009*	0.976	0.012*
FMI	0.223	0.004*	0.685	0.109	0.035*	0.636	0.025*
LM parameters							
BIA_{st}	0.503	0.960	0.058	0.001**	0.009*	0.814	0.054
BIA_{sup}	0.491	0.971	0.003*	0.000**	0.000**	0.492	0.002**
BIA_{all}	0.425	0.947	0.003*	0.000**	0.000**	0.563	0.002**
DXA LM	0.991	0.548	0.000**	0.000**	0.010*	0.121	0.060
LMI	0.897	0.100	0.001**	0.077	0.855	0.620	0.813

Table 7.12. Associations between mean SDS for all parameters and all predictor variables on admission.

Table shows p-values for independent samples t-test comparing the mean SDS of the anthropometric and BC parameters between patients with and without the predictor variable; (*) Significant (p<0.05) but non-significant after correction for multiple testing (p<0.003), (**) Significant even after correction for multiple testing.

	Steroid prescription	Fluid restriction	Wheelchair user	EN / PN feeding	Restricted diet	Intake/ appetite problems	Prior dietetic advice
Anthropometric parameters							
HT	0.214	0.617	0.002**	0.001**	0.001**	0.363	0.019*
WT	0.371	0.598	0.000**	0.002**	0.000**	0.566	0.001**
MUAC	0.344	0.451	0.512	0.006*	0.001**	0.767	0.000**
HC	0.521	0.755	0.000**	0.001**	0.001**	0.138	0.007*
FM parameters							
BMI	0.242	0.850	0.156	0.101	0.184	0.526	0.015*
Biceps SFT	0.440	0.399	0.409	0.073	0.133	0.885	0.015*
Triceps SFT	0.975	0.623	0.020*	0.187	0.049*	0.125	0.043*
Subscapular SFT	0.571	0.108	0.898	0.029*	0.034*	0.602	0.000**
Suprailiac SFT	0.976	0.091	0.402	0.354	0.057	0.584	0.002**
DXA FM	0.512	0.016*	0.094	0.047*	0.002**	0.905	0.000**
FMI	0.507	0.012*	0.752	0.320	0.042*	0.601	0.001**
LM parameters							
BIA_{st}	0.498	0.826	0.053	0.014*	0.013*	0.637	0.107
BIA_{sup}	0.276	0.500	0.352	0.009*	0.002**	0.318	0.004*
BIA_{all}	0.464	0.836	0.071	0.018*	0.002**	0.552	0.028*
DXA LM	0.925	0.796	0.000**	0.000**	0.001**	0.181	0.016*
LMI	0.639	0.296	0.238	0.546	0.912	0.463	0.815

Table 7.13. Associations between mean SDS for all parameters obtained from accurate measurements and all predictor variables on admission.
Table shows p-values for independent samples t-test comparing the mean SDS of the anthropometric and BC parameters between patients with and without the predictor variable; (*) Significant (p<0.05) but non-significant after correction for multiple testing (p<0.003), (**) Significant even after correction for multiple testing. Highlighted results differ in significance from the complete dataset.

7.7.3. Prediction models for baseline anthropometric and BC SDS

Based on the previous univariate analyses, variables were selected to construct prediction models for the different anthropometric and BC parameter SDS on admission. The main predictor variables considered were: 'wheelchair user', 'EN/PN feeding', 'dietary restriction', and 'prior dietetic advice'. The models were constructed using stepwise multiple regression. Usually, the diet-related variables were entered into the model one by one and then in combination with 'wheelchair user'. Finally, the model was adjusted for sex, age and admission group. Tables 7.14 to 7.16 show the constructed (best) models (assessed by the highest R^2 and significance of coefficients) constructed for the anthropometric, FM and LM parameters respectively. Table 7.17 shows the selected final models for all parameters.

For WT and HT, 'wheelchair user' in combination with either 'restricted diet' or 'prior dietetic advice' were the best predictors for mean SDS on admission. The selected final prediction model indicated that patients in a wheelchair had an average predicted difference in HT of 1.7 SDS lower (with a range of 0.8-2.7 SDS) compared to ambulatory patients, and patients on a restricted diet had 0.5-1.5 lower SDS. For WT, this is expected to be 0.6-2.2 lower SDS for non-ambulatory children, and 0.4-1.5 lower SDS for patients with restricted diets.

MUAC and HC had very similar predictors to those observed for WT and HT. However, further adjustment by sex improved on the adjusted R^2 of the final models. For HC, the mean SDS on admission were 0.8-2.4 SDS, 0.5-1.5 SDS and 0.2-1.2 SDS lower in non-ambulant children, patients with a restricted diet and for females, respectively. MUAC mean SDS on admission were also predicted to be 0.03-0.7 SDS lower for females, and 0.5-1.2 SDS lower in patients who have had prior dietetic advice.

In the case of FM, because SDS on admission were more variable (patients had low and high SDS for FM, while on average having low SDS for LM and anthropometric parameters), models in general had a lower adjusted R^2. The best models included different combinations of 'diet-related' and, only for the case of Triceps SFT, 'wheelchair user' variables. Furthermore, for FM and FMI, the use of 'fluid restriction' and 'sex' variables were also tested. 'Prior dietetic advice' was the best diet-related predictor for all FM parameters, with a predicted 0.1-1.0 lower mean SDS on admission. For Triceps SFT, however, non-ambulatory patients had higher SDS (0.3-1.6 SDS) than ambulatory children. Regarding FM derived from DXA, patients with fluid restrictions had higher FM SDS (0.3-1.6 SDS and 0.4-1.6 SDS for FM and FMI respectively). Although 'sex' was a significant predictor variable for FM and FMI, after accounting for fluid restrictions, this became non-significant in the model.

		Predictors	*B* [a]	*CI* [b]	*p* [c]	adjusted R^2
HT *(n=141)*	Model 1	Wheelchair user	-1.72	-2.66, -0.78	0.000	0.189
		Restricted diet	-0.96	-1.45, -0.48	0.000	
	Model 2	Wheelchair user	-1.88	-2.83, -0.93	0.000	0.159
		Prior dietetic advice	-0.73	-1.20, -0.27	0.002	
WT *(n=152)*	Model 1	Wheelchair user	-0.26	-2.17, -0.58	0.001	0.148
		Restricted diet	-0.27	-1.49, -0.43	0.000	
	Model 2	Wheelchair user	-1.38	-2.18, -0.58	0.001	0.137
		Prior dietetic advice	-0.85	-1.35, -0.34	0.001	
MUAC *(n=147)*	Model 1	Restricted diet	-0.66	-1.04, -0.27	0.001	0.066
		Prior dietetic advice	-0.80	-1.16, -0.44	0.000	0.111
	Model 2	Prior dietetic advice	-0.85	-1.21, -0.50	0.000	0.132
		Sex (1=female) *	-0.39	-0.74, -0.03	0.034	
HC *(n=148)*	Model 1	Wheelchair user	-1.52	-2.37, -0.70	0.001	0.139
		Restricted diet	-0.89	-1.32, -0.35	0.001	
	Model 2	Wheelchair user	-1.53	-2.40, -0.67	0.001	0.109
		Prior dietetic advice	-0.61	-1.13, -0.09	0.023	
	Model 3	Wheelchair user	-1.59	-2.41, -0.76	0.000	0.180
		Restricted diet	-1.01	-1.55, -0.47	0.000	
		Sex (1=female)	-0.74	-1.24, -0.23	0.004	
	Model 4	Wheelchair user	-1.59	-2.44, -0.74	0.000	0.145
		Prior dietetic advice	-0.71	-1.23, -019	0.008	
		Sex (1=female)	-0.69	-1.21, -0.18	0.009	

Table 7.14. Predictor models for anthropometric SDS on admission.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). (*) 'Sex' variable coefficient the model was non-significant considering correction for multiple testing (p<0.025), similarly the model using 'Restricted diet' and 'Sex' was non-significant for the coefficient of 'Sex' (p=0.052; R^2=0.084). Variables entered stepwise in the models. Highlighted values indicate selected best model to predict baseline SDS for each parameter.

		Predictors	*B* [a]	*CI* [b]	*p* [c]	adjusted R^2
BMI *(n=141)*	Model 1	EN / PN feeding	-0.88	-1.47, -0.29	0.004	0.053
	Model 2	Restricted diet	-0.62	-1.10, -0.14	0.012	0.045
Biceps SFT *(n=118)*	Model 1	Prior dietetic advice	-0.46	-0.79, -0.12	0.008	0.052
Triceps SFT *(n=119)*	Model 1	Wheelchair user	0.94	0.29, 1.58	0.005	0.089
		Restricted diet	-0.52	-0.88, -0.16	0.006	
	Model 2	Wheelchair user	0.94	0.30, 1.58	0.004	0.096
		Prior dietetic advice	-0.51	-0.85, -0.17	0.003	
Sub-scapular SFT (*n=101*)	Model 1	EN / PN feeding	-0.58	-1.06, -0.11	0.017	0.047
	Model 2	Prior dietetic advice	-0.63	-0.96, -0.29	0.000	0.114
Suprailiac SFT (*n=87*)	Model 1	Restricted diet	-0.45	-0.85, -0.04	0.031	0.043
	Model 2	Prior dietetic advice	-0.63	-0.98, -0.28	0.001	0.119
DXA FM *(n=122)*	Model 1	Restricted diet	-0.59	-1.05, -0.14	0.012	0.093
		Fluid restriction	0.84	0.22, 1.47	0.009	
	Model 2	Prior dietetic advice	-0.62	-1.04, -0.19	0.005	0.105
		Fluid restriction	0.96	0.34, 1.59	0.003	
	Model 3	Restricted diet	-0.70	-1.15, -0.24	0.003	0.122
		Fluid restriction	0.69	0.06, 1.32	0.033	
		Sex (1=female)	-0.49	-0.92, -0.05	0.029	
	Model 4	Prior dietetic advice	-0.70	-1.13, -0.28	0.001	0.134
		Fluid restriction	0.83	0.20, 1.46	0.010	
		Sex (1=female)	-0.49	-0.92, -0.06	0.027	
FMI *(n=118)*	Model 1	Restricted diet	-0.46	-0.90, -0.01	0.043	0.085
		Fluid restriction	0.86	0.26, 1.46	0.006	
	Model 2	Prior dietetic advice	-0.54	-0.95, -0.13	0.010	0.105
		Fluid restriction	0.962	0.37, 1.56	0.002	
	Model 3	Restricted diet	-0.529	-0.98, -0.08	0.022	0.097
		Fluid restriction	0.752	0.14, 1.37	0.017	
		Sex (1=female)	-0.346	-0.77, 0.08	0.110	
	Model 4	Prior dietetic advice	-0.595	-1.01, -0.19	0.005	0.118
		Fluid restriction	0.866	0.26, 1.47	0.005	
		Sex (1=female)	-0.345	-0.76, 0.07	0.105	

Table 7.15. Predictor models for FM SDS on admission.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). Variables entered stepwise in the models. Highlighted values indicate selected best model to predict baseline SDS for each parameter.

		Predictors	*B* [a]	*CI* [b]	*p* [c]	adjusted R^2
DXA LM *(n=122)*	Model 1	Wheelchair user	-3.08	-4.03, -2.13	0.000	0.327
		EN / PN feeding	-0.97	-1.56, -0.37	0.002	
	Model 2	Wheelchair user	-3.28	-4.23, -2.32	0.000	0.310
		Restricted diet.	-0.64	-1.12, -0.16	0.009	
LMI *(n=118)*	Model 1	Wheelchair user	-2.67	-4.16, -1.17	0.001	0.089
	Model 2	Wheelchair user	-2.48	-4.01, -0.95	0.002	0.091
		EN / PN feeding	-0.36	-1.02, 0.29	0.277	
BIA_{st} ** *(n=104)*	Model 1	EN / PN feeding	-1.06	-1.68, -0.43	0.001	0.090
	Model 2	Restricted diet	-0.69	-1.21, -0.17	0.009	0.055
BIA_{sup} *(n=131)*	Model 1	Wheelchair user	-1.08	-2.12, -0.03	0.044	0.113
		EN / PN feeding	-1.00	-1.66, -0.34	0.003	
	Model 1	Wheelchair user *	-1.26	-2.26, -0.26	0.014	0.132
		Restricted diet.	-0.90	-1.41, -0.39	0.001	
BIA_{all} *(n=135)*	Model 1	Wheelchair user	-1.11	-2.13, -0.08	0.035	0.108
		EN / PN feeding	-0.94	-1.59, -0.30	0.005	
	Model 2	Wheelchair user *	-1.28	-2.26, -0.30	0.011	0.128
		Restricted diet.	-0.85	-1.35, -0.36	0.001	

Table 7.16. Best predictor models for LM SDS on admission.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). (*) 'Admission group' variable near significant in models (p=0.069 for BIA_{sup}; p=0.092 for BIA_{all}), as suggested by the univariate analysis, but association with 'Wheelchair user' variable made coefficient non-significant. (**) Technique had only one measurement on a patient in a wheelchair who could stand briefly to perform the measurement. Variables entered stepwise in the models. Highlighted values indicate selected best model to predict baseline SDS for each parameter.

	Predictors	*B* [a]	*CI* [b]	*p* [c]	adjusted R^2
Anthropometric parameters					
HT	Wheelchair user	-1.72	-2.66, -0.78	0.000	0.189
	Restricted diet	-0.96	-1.45, -0.48	0.000	
WT	Wheelchair user	-0.26	-2.17, -0.58	0.001	0.148
	Restricted diet	-0.27	-1.49, -0.43	0.000	
MUAC	Prior dietetic advice	-0.85	-1.21, -0.50	0.000	0.132
	Sex (1=female)	-0.39	-0.74, -0.06	0.034	
HC	Wheelchair user	-1.59	-2.41, -0.76	0.000	0.180
	Restricted diet	-1.01	-1.55, -0.47	0.000	
	Sex (1=female)	-0.74	-1.24, -0.23	0.004	
FM parameters					
BMI	EN / PN feeding	-0.88	-1.47, -0.29	0.004	0.053
Biceps SFT	Prior dietetic advice	-0.46	-0.79, -0.12	0.008	0.052
Triceps SFT	Wheelchair user	0.94	0.30, 1.58	0.004	0.096
	Prior dietetic advice	-0.51	-0.85, -0.17	0.003	
Subscapular SFT	Prior dietetic advice	-0.63	-0.96, -0.29	0.000	0.114
Suprailiac SFT	Prior dietetic advice	-0.63	-0.98, -0.28	0.001	0.119
DXA FM	Prior dietetic advice	-0.62	-1.04, -0.19	0.005	0.105
	Fluid restriction	0.96	0.34, 1.59	0.003	
FMI	Prior dietetic advice	-0.54	-0.95, -0.13	0.010	0.105
	Fluid restriction	0.96	0.37, 1.56	0.002	
LM parameters					
BIA_{st}	EN / PN feeding	-1.06	-1.68, -0.43	0.001	0.090
BIA_{sup}	Wheelchair user	-1.26	-2.26, -0.26	0.014	0.132
	Restricted diet	-0.90	-1.41, -0.39	0.001	
BIA_{all}	Wheelchair user	-1.28	-2.26, -0.30	0.011	0.128
	Restricted diet	-0.85	-1.35, -0.36	0.001	
DXA LM	Wheelchair user	-3.08	-4.03, -2.13	0.000	0.327
	EN / PN feeding	-0.97	-1.56, -0.37	0.002	
LMI	Wheelchair user	-2.67	-4.16, -1.17	0.001	0.089

Table 7.17. Summary of variables predicting SDS on admission by the different parameters. *(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). Table shows selected best models from Tables 7.21-23.*

The main predictors for LM were 'wheelchair user' combined with diet-related variables, mainly 'EN/PN feeding' or 'restricted diet'. It should be noted, however, that there was some association between 'EN/PN feeding' and 'wheelchair user' variables, as many of the non-ambulatory children with developmental delay and neuromuscular conditions had some form of EN feeds (e.g. partial of full gastrostomy feeds). For LMI, after accounting for 'wheelchair user', the 'EN/PN feeding' variable became non-significant in the model. In the case of DXA LM, when 'wheelchair user' and 'EN/PN feeds' were added to the model, this had a higher adjusted R^2 but the significance of the individual coefficients was stronger for 'wheelchair user' than 'restricted diet'. For BIA_{sup} and BIA_{all}, 'wheelchair user' and 'diet restriction' were the best variables predicting SDS on admission. Both are predicted to result in lower SDS (0.26-2.26 SDS for non-ambulatory patients and 0.36-1.4 for children on restricted diets). Because BIA_{st} was only able to be measured in one wheelchair patient who could stand very briefly to take the measurement, understandably only 'dietary restriction' and 'EN/PN feeding' were significant predictors. SDS are predicted to be lower (0.17-1.2 SDS) for those children on a restricted diet or on EN/PN feeds (0.4-1.7 SDS).

7.8. Anthropometric and body composition parameters at discharge

Patients enrolled in the BodyBasics study were visited and measured again before being discharged from the hospital, or after 3 months from the date of their admission if they were still inpatients. Although every effort was made to see the patients and their families before they left the hospital, many discharges occurred unexpectedly or out-of-hours. Consequently, 23% of patients were missed completely at discharge, while 13% of them were missed but left their patient diary on the wards for collection, which had annotated the discharge patient WT taken by the ward nursing staff. Only 64% of patients were seen prior to their discharge, but time constrictions and patient/parental preference meant only some of the measurements (often the most simple and bedside techniques) were performed. Patients had a median stay of 9 days (IQR: 4-15 days). Details on the length of stay is described in Chapter 8, Section 8.4.1.

Figure 7.3. shows the categorisation of patients according to the treatment/procedure they received while in hospital. This was understandably very similar to the categories observed for the patients at baseline according to the reason for admission (planned procedures or treatment). Considering there was no difference between the categorisation of medical/surgical patients on admission and at the time of discharge, the first variable was still used for adjustments and comparisons in the following sections.

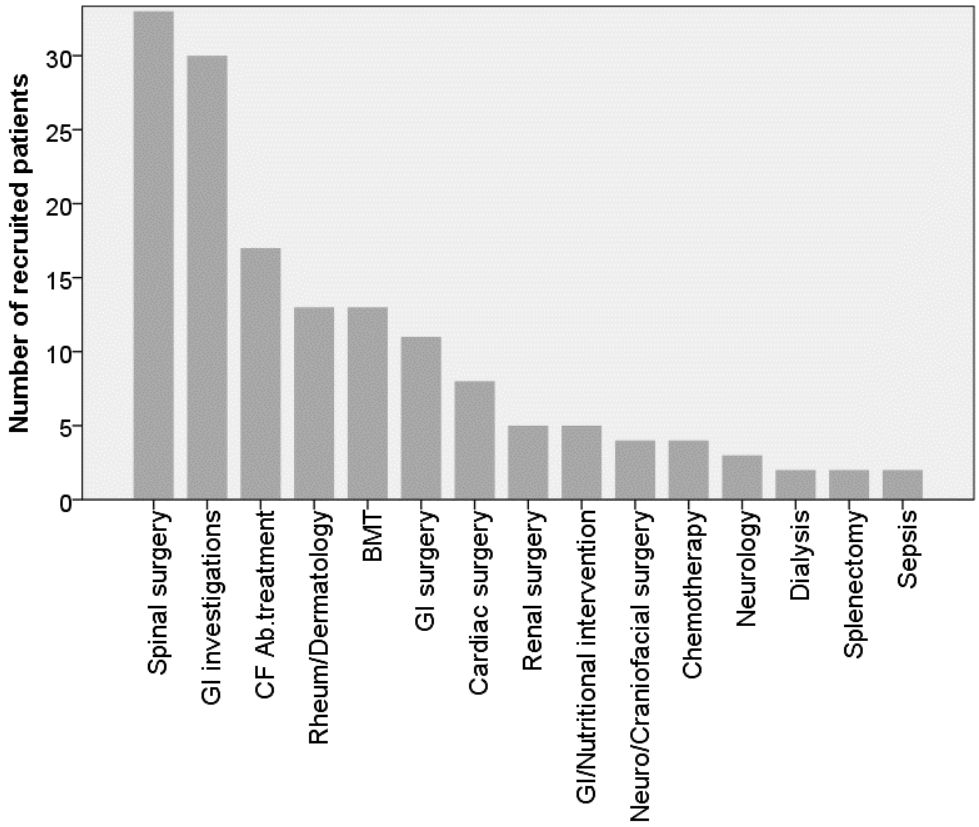


Figure 7.3. Treatment categories for recruited patients at the moment of discharge.

7.8.1. Simple anthropometric parameters

Table 7.18 summarises the mean SDS for the parameters on discharge. WT was, as expected, the most successful measurement recorded for patients on discharge. Only about half of the patients were measured using HT, MUAC or HC. Similar to admission, the mean SDS for all parameters were significantly low (<0 SDS), even more so for HT and HC. The number of patients with abnormal SDS (Table 7.19) was around 20%, most of these cases of patients with low SDS (≤-2 SDS) rather than high (≥ 2 SDS). The mean SDS were analysed for differences and associations to sex, admission group (Appendix 14, Table 18) and age (not shown) but no significant associations were found. The analysis using only accurate measurements (Appendix 14, Tables 19-21) showed understandably a smaller number of measurements, especially for WT, but no major differences in men SDS compared to the results using all of the obtained measurements.

	n	SDS [a]	*CI* [b]		*p* [c]
HT	75	-0.50	-0.83	-0.18	0.003**
WT	114	-0.32	-0.63	-0.01	0.046*
MUAC	80	-0.39	-0.70	-0.08	0.017*
HC	78	-0.58	-0.96	-0.20	0.004**

Table 7.18. Anthropometric parameters SDS at discharge.

(a) Mean Standard Deviation Score; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0=0), (*) significant (p<0.05), (**) significant even after correction for multiple testing (p<0.013).

	n	abSDS [a]	*CI* [b]		≤ -2SDS [c]	≥ 2SDS [d]
HT	75	18.7	9.8	27.5	17.3	1.3
WT	114	18.4	11.3	25.5	12.3	6.1
MUAC	80	16.3	8.2	24.3	13.8	2.5
HC	78	21.8	12.6	31.0	19.2	2.6

Table 7.19. Abnormal SDS for anthropometric parameters at discharge.

(a) Percentage (%) of patients with abnormal standard deviation scores (abSDS) at discharge for each of the parameters; (b) 95% CI for the % of patients with abSDS; (c) % of patients with SDS of -2 or lower; (d) % pf patients with SDS of 2 or higher.

7.8.2. Body composition: FM and LM parameters

The mean SDS for FM parameters at discharge, similar to admission, were positive (>0 SDS) but only significant for Biceps SFT and to a lesser degree for Subscapular SFT (Table 7.20). All BIA SDS at discharge showed a significant negative mean SDS suggesting low amounts of LM in these patients compared to healthy children of the same age and sex.

Regarding identification of children with abnormal SDS (Table 7.21), BMI assessment resulted in 18% of patients measured being classified as abnormal, half due to low SDS (≤-2 SDS) and half due to high SDS (≥2 SDS). Subscapular and Suprailiac SFTs, only measured in a small number of children, failed to identify any children with abnormal SDS; while Biceps SFTs identified a small percentage of children with high SDS, and Triceps SFT a small percentage with low SDS. Considering the results from Chapter 4, BMI and Triceps SFTs, although with limitations, were the best alternatives to assess FM when DXA FM was

unavailable. However, all SFTs either because they were unable to be measured in children that would have abnormal SDS, or because the measurement itself failed to detect it, were not good for detecting and quantifying abnormal FM at discharge. BMI might have also identified more children with abnormal SDS simply because it was measured in a larger number of patients; but suggests that at least that this parameter might be more practical and suitable for sequential (and discharge) measurements, despite its limitations regarding its accuracy for the assessment of FM.

Regarding LM, BIA measurements identified about one quarter of patients with abnormal SDS, most of these with low SDS (≤-2 SDS). BIA_{st} identified a smaller number of patients with abnormal SDS, in line with previous observations that this measurement was not performed in a group of patients with mobility issued but with abnormal low LM SDS (spinal surgery patients with musculoskeletal abnormalities).

Analysis of any differences between admission groups or male/female all resulted in non-significant associations (Appendix 14, Table 22) and correlations to age were similarly non-significant (analysis not shown).

	n	**SDS** [a]	***CI*** [b]		***p*** [c]
FM parameters					
BMI	75	0.13	-0.19	0.46	0.427
Biceps SFT	48	0.52	0.24	0.79	0.001**
Triceps SFT	51	0.17	-0.12	0.46	0.258
Subscapular SFT	35	0.36	0.06	0.66	0.023*
Suprailiac SFT	29	0.07	-0.26	0.39	0.694
LM parameters					
BIA_{st}	44	-0.97	-1.41	-0.52	0.000**
BIA_{sup}	69	-0.92	-1.38	-0.47	0.000**
BIA_{all}	71	-1.04	-1.45	-0.63	0.000**

Table 7.20. BC parameters SDS at discharge.

(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0=0), (*) significant (p<0.05), (**) significant even after correction for multiple testing (p<0.006); BIA_{all} refers to SDS using BIA_{st} and/or BIA_{sup}.

	n	abSDS [a]	*CI* [b]		≤ -2SDS [c]	≥ 2SDS [d]
FM parameters						
BMI	75	18.7	9.8	27.5	9.3	9.3
Biceps SFT	48	4.2	0.0	9.8	0.0	4.2
Triceps SFT	51	2.0	0.0	5.8	2.0	0.0
Subscapular SFT	35	0.0	0.0	0.0	0.0	0.0
Suprailiac SFT	29	0.0	0.0	0.0	0.0	0.0
LM parameters						
BIA_{st}	44	22.7	10.3	35.1	20.5	2.3
BIA_{sup}	69	34.8	23.5	46.0	29.0	5.8
BIA_{all}	71	33.8	22.8	44.8	29.6	4.2

Table 7.21. Abnormal SDS for BC parameters at discharge.
(a) Percentage (%) of patients with abnormal standard deviation scores (abSDS) at discharge for each of the parameters; (b) 95% CI for the % of patients with abSDS; (c) % of patients with SDS of -2 or lower; (d) % pf patients with SDS of 2 or higher.

Analysis of the restricted database containing only accurate measurements (Appendix 14, Tables 23-25) did not indicate any major difference compared to the results described above for the whole set of measurements. The only non-worthy observation was that restriction of BIA_{sup} measurements, many of which corresponded to this selective group of spinal surgery patients (restricted due to slight changes in position, e.g. measured while sitting in wheelchair rather than lying down completely flat), confirmed that this group is responsible for differences to BIA_{st} results since both techniques now identified almost the same number of patients with abnormal SDS.

7.9. Change in anthropometric and BC parameter SDS during hospitalisation

To establish how nutritional status when assessed by the different anthropometric and BC parameters changed during hospitalisation, the difference in SDS between admission and discharge was calculated and is described in the following sections.

7.9.1. Simple anthropometric parameters

Table 7.22 summarises the mean change in SDS for the anthropometric parameters. For HT, there was a significant increase in mean SDS at discharge compared to admission, with HT SDS increasing on average by 0.1 SDS. WT, on the other hand, showed no mean change in SDS, possibly because some patients lost WT while others increased it to a comparable degree. Something similar was observed for MUAC, with a change in SDS just slightly negative (-0.06 SDS) but non-significant. HC was not analysed for change, as it was not expected to alter in children over 5yr of age, especially in this short period of time and any change was likely due to measurement error or after craniofacial surgery.

The analysis of the restricted database (Appendix 14, Table 26) suggests that some of the cases with the largest increase in HT could be from spinal surgery patients where the measured HT on admission likely underestimated their 'true' HT as a result of the curvature of the spine, especially in adolescent scoliosis patients. By discharge, after corrective surgery, increases in HT are expected and likely contributing the greater observed increase in HT SDS by discharge in the whole database of patients.

	n	**Change in SDS** [a]	***CI*** [b]		***p*** [c]
HT	73	0.09	0.04	0.15	0.002**
WT	114	0.00	-0.05	0.05	0.977
MUAC	79	-0.06	-0.15	0.03	0.210

Table 7.22. Change in anthropometric parameters SDS between admission and discharge.
(a) Mean difference in the Standard Deviation Score between admission and discharge; (b) 95% CI for the mean change in SDS; (c) One-sample t-test of the mean change in SDS (H_0: mean change=0), (*) significant (p<0.05), (**) significant even after correction for multiple testing (p<0.013).

Approximately 35% of patients with measured HT had decreased SDS values on discharge compared to admission (Table 7.23). Most of these were small differences that could be attributed to measurement error (<0.1 SDS), as a large proportion of patients had a short admission (<7 days) that is unlikely to affect HT in a substantial manner. For WT, almost half of the measured patients had a decrease in SDS during their hospitalisation. MUAC SDS were similarly decreased in more than half the patients. For both parameters, the range of decrease in SDS was varied (from approximately 0.1 to 1.0 SDS difference). Analysis of the restricted database with only accurate measurements (Appendix 14, Table 27) showed similar results to the ones described for the complete set of measurements.

	n	Frequency [a]	% patients [b]	*CI* [c]	
HT	73	24	32.9	22.1	43.7
WT	114	54	47.4	38.2	56.5
MUAC	79	42	53.2	42.2	64.2

Table 7.23. Percentage of patients with decreased SDS for anthropometric parameters between admission and discharge.

(a) Number and (b) percentage (%) of patients that had a lower standard deviation score at discharge compared to admission for each of the parameters; (c) 95% CI for the % of patients.

There were also no significant differences in the mean change in SDS between male/female and medical/surgical patients for the complete and restricted databases (Appendix 14, Table 28 and 29). Associations between SDS change and age was only significant for WT, with a negative correlation observed for both the whole set of measurements (r = -0.19, p=0.040) and the restricted database (r = -0.33, p=0.009), meaning older children lost more WT during their admission.

7.9.2. Body composition: FM and LM parameters

Table 7.24 below summarises the mean change in SDS for FM and LM parameters. The change in FM was variable, as reflected in the non-significant mean change in SDS for all parameters except BMI. In this last case, BMI was on average decreased by -0.13 SDS. However, this significant decrease in BMI was likely affected by 'inaccurate' HT measurements on admission in spinal surgery patients, since analysis of the restricted database (Appendix 14, Table 20) that excluded these patients showed a non-significant average change in SDS similar to all other FM parameters. Analysis of LM parameters assessed by BIA also showed a non-significant average change in SDS for both the whole (Table 7.24) and restricted databases (Appendix 14, Table 30).

Focusing on the percentage of patients with a decrease in SDS (Table 7.25), almost 50% of the patients had a decrease in the SDS of FM parameters. BMI once again showed a much higher percentage of patients with decreases in SDS, something that changed in the restricted database (Appendix 14, Table 31). For LM, more than half the patients had a decrease in SDS (some up to -1.3 SDS).

	n	Change in SDS [a]	*CI* [b]		*p* [c]
FM parameters					
BMI	73	-0.13	-0.23	-0.03	0.005*
Biceps SFT	45	0.14	-0.05	0.34	0.158
Triceps SFT	50	0.02	-0.16	0.21	0.824
Subscapular SFT	31	-0.05	-0.24	0.14	0.587
Suprailiac SFT	26	0.00	-0.22	0.23	0.987
LM parameters					
BIA_{st}	42	-0.12	-0.25	0.02	0.098
BIA_{sup}	69	0.12	-0.13	0.37	0.353
BIA_{all}	71	0.03	-0.15	0.21	0.733

Table 7.24. BC parameters SDS at discharge.

(a) Mean difference in SDS between admission and discharge; (b) 95% CI for the mean change in SDS; (c) One-sample t-test of the mean change in SDS (H_0: mean change=0), (*) significant even after correction for multiple testing (p<0.006).; BIA_{all} refers to SDS using BIA_{st} and/or BIA_{sup}.

	n	Frequency [a]	% patients [b]	*CI* [c]	
FM parameters					
BMI	73	45	61.6	50.5	72.8
Biceps SFT	45	18	40.0	25.7	54.3
Triceps SFT	50	23	46.0	32.2	59.8
Subscapular SFT	31	18	58.1	40.7	75.4
Suprailiac SFT	26	12	46.2	27.0	65.3
LM parameters					
BIA_{st}	42	25	59.5	44.7	74.4
BIA_{sup}	69	35	50.7	38.9	62.5
BIA_{all}	71	39	54.9	43.4	66.5

Table 7.25. Percentage of patients with decreased SDS for BC parameters between admission and discharge.

(a) Number and (b) percentage (%) of patients that had a lower standard deviation score at discharge compared to admission for each of the parameters; (c) 95% CI for the % of patients.

Differences for the change in SDS between male/female and medical/surgical patients is summarised in Appendix 14, Table 32. Female patients had significantly more of a decrease in Suprailiac SFT SDS and BIA_{st} SDS both in the whole and restricted databases

(Appendix 14, Table 33). Surgical patients also had a significantly greater mean decrease in SDS for Subscapular SFT. There was a similar tendency, albeit non-significant, for surgical patients experiencing a greater mean decrease in SDS for BMI and BIA (all measurements), especially on the restricted database. Associations with age were non-significant for the whole and restricted databases (data not shown).

7.10. Description of predictor variables during hospitalisation

The following section describes the data collected on discharge regarding steroid medication prescription, fluid restriction, and diet-related variables; similar to the 4 domains assessed on admission. These variables reflect changes in these variables during hospitalisation and will be used in the following sections to determine relevant variables predicting the change in the parameters SDS.

7.10.1. Steroid prescription during hospitalisation

As Table 7.26 describes, 9% of patients reported taking steroid medication during their hospitalisation. This percentage corresponded to high dose steroids usually prescribed for inpatient treatment/procedures, for example in patients undergoing BMT or other surgical procedures. Indeed, more surgical patients were prescribed steroid medication (Appendix 14, Table 34), but this did not reach statistical significance. There were no observed differences between male and female patients and, although patients prescribed steroids were younger on average, this was also non-significant.

	Frequency	%
Steroid prescription		
no	93	89
low	2	2
high	9	9
High steroids		
no	95	91
yes	9	9

Table 7.26. Summary of prescription of steroid medication during hospitalisation.

7.10.2. Fluid restriction during hospitalisation

As Table 7.27 describes, 15% of patients were restricted in fluid during their hospital stay. Half of these had to do with preparation for medical procedures (nil by mouth) while the other half were usual restrictions from their underlying medical condition (e.g. patients with renal failure). The analysis of differences between male and female patients (Appendix 14, Table 35) showed that more male patients were restricted in fluid, largely because of their underlying medical condition. Similarly, more surgical patients were on fluid restriction due to their underlying diagnosis. There was no observed difference in age between those on fluid restriction and those without.

	Frequency	%
Fluid restrictions		
no	87	85
NBM	8	8
limited by diagnosis	7	7
Restricted fluid		
no	87	85
yes	15	15

Table 7.27. Summary of fluid restrictions in patients during hospitalisation.

7.10.3. Diet-related factors during hospitalisation

Table 7.28 summarises the variables associated with the patient's dietary intake. 12% of patients were on full EN or PN feeds, with a further 15% of them on partial EN/PN feeds. This translated into slightly more than one quarter of patients having some form of artificial nutrition. For 10% of patients, their dependence on EN/PN increased during hospitalisation (3% of patients on partial feeds had to be placed on full EN/PN, and 8% of patients with normal oral intake had to be prescribed at least some EN/PN).

Regarding dietary restrictions, about a quarter of patients had some form of restriction; half of these patients had restricted their diet due to preparation for a medical procedure (e.g. GI investigations), while the other half was restricted due to their underlying medical diagnosis. Furthermore, almost half the patients had a significant decrease in appetite during hospitalisation (≥10% change between appetite score on admission and discharge).

Additionally, more than half the patients had been referred to a dietitian for nutritional management.

Analysis between female and male patients was non-significant, except for a significantly higher number of male patients being referred for dietetic management (Appendix 14, Table 36). Surgical patients were also more likely to have an increased dependence on EN/PN, to have decreased appetite and intake problems during hospitalisation. Patients on EN/PN feeds (partial) and those referred for dietetic management were also significantly younger.

	Frequency	%
Feeding categories		
oral self	66	62
oral carer	11	10
oral self + EN_PN carer	13	12
oral + EN_PN carer	3	3
EN_PN carer	13	12
EN/PN feeding regime		
no	77	73
partial	16	15
full	13	12
EN/PN feeding		
no	77	73
yes	29	27
Change in artificial nutrition prescription		
no	95	90
oral to partial EN_PN	7	7
partial to full EN_PN	3	3
oral to full EN_PN	1	1
Increased use of EN/PN		
no	95	90
yes	11	10
Dietary restrictions		
none	71	68
minor/hospital food	8	8
for procedure NBM	13	12
by clinical condition	13	12
Restricted diet		
no	79	75
yes	26	25
Loss of appetite		
no	45	56
yes	35	44
Dietary advice during hospitalisation		
no	49	47
yes	56	53

Table 7.28. Summary of diet-factors during hospitalisation.

7.11. Variables predicting the change in anthropometric and BC parameter SDS during hospitalisation

7.11.1. Predictor variables for change in anthropometric parameters

Univariate analysis of the associations between predictor variables and the change in SDS for the different anthropometric parameters: WT, HT and BMI; is summarised on Table 7.29 (further details in Appendix 14, Tables 37 and 38). All of the significant variables were diet-related. There were no significant associations between the change in HT SDS and any of the predictor variables. Patients on EN/PN prescription and those that received dietary advice had increased WT SDS during their admission; while those with low of appetite during hospitalisation had a decrease in SDS. Decreases in MUAC SDS were observed in those patients with intake or appetite problems. Analysis of the restricted database (Table 7.30) showed small differences, with changes in WT now only related to loss of appetite.

Linear regression models were constructed by adding the predictor variables stepwise. Considering there were few associations from the univariate analysis, further prediction models were calculated for male/female and medical/surgical patients to determine if the predictors might be affecting these groups differently. Table 7.31 summarises the significant best models for the anthropometric parameters. Once more, changes in HT were not predicted by any of the variables. Intake or appetite problems predicted decreases in WT SDS for the whole patient sample, while for female and medical subjects the most significant predictor for decreased WT SDS was dietary restrictions; and loss of appetite during admission for surgical patients. Intake/appetite problems and EN/PN feeding was significantly associated with decreases in MUAC SDS during hospitalisation for all patients and female subjects respectively. Lastly, in surgical patients, the change in MUAC was influenced by loss of appetite, dietary and fluid restrictions. Adjustments using the length of stay were performed but were not significant in the models.

7.11.1. Predictor variables for change in FM and LM parameters

For FM parameters, dietary restrictions, intake problems and loss of appetite were the only variables significantly associated with the changes in SDS (Table 7.29 and Appendix 14, Tables 39 and 40). Patients who reported a loss of appetite during hospitalisation had greater decreases in BMI SDS.

	Steroid prescription	Fluid restriction	EN / PN feeding	Increased use of EN/PN	Restricted diet	Intake/ appetite problems	Dietary advice	Loss of appetite
Anthropometric parameters								
HT	0.673	0.678	0.238	0.790	0.966	0.468	0.782	0.072
WT	0.438	0.941	0.030 *	0.186	0.623	0.069	0.028 *	0.047 *
MUAC	0.319	0.373	0.680	0.488	0.737	0.027 *	0.225	0.082
FM parameters								
BMI	0.451	0.947	0.615	0.741	0.565	0.051	0.052	0.005 *
Biceps SFT	0.966	0.090	0.874	0.990	0.035*	0.435	0.679	0.446
Triceps SFT	0.245	0.895	0.891	0.343	0.459	0.641	0.507	0.842
Subscapular SFT	0.996	0.096	0.289	0.128	0.921	0.018 *	0.951	0.048 *
Suprailiac SFT	0.726	0.414	0.847	-	0.733	0.761	0.149	0.376
LM parameters								
BIA_{st}	0.302	0.466	0.798	0.227	0.123	0.079	0.020 *	0.084
BIA_{sup}	0.850	0.404	0.443	0.466	0.148	0.894	0.410	0.505
BIA_{all}	0.626	0.323	0.540	0.468	0.110	0.839	0.867	0.840

Table 7.29. Associations between the change in SDS for all parameters and all predictor variables during hospitalisation.

Table shows p-values for independent samples t-test comparing the mean SDS of the anthropometric and BC parameters between patients with and without the predictor variable; (*) Significant (p<0.05) but non-significant after correction for multiple testing (p<0.006).

	Steroid prescription	Fluid restriction	EN / PN feeding	Increased use of EN/PN	Restricted diet	Intake/ appetite problems	Dietary advice	Loss of appetite
Anthropometric parameters								
HT	0.132	0.709	0.208	0.633	0.445	0.169	0.116	0.723
WT	0.293	0.353	0.511	0.253	0.401	0.154	0.073	0.038 *
MUAC	0.312	0.325	0.794	0.492	0.673	0.047 *	0.099	0.158
FM parameters								
BMI	0.410	0.222	0.905	0.835	0.095	0.395	0.208	0.160
Biceps SFT	0.977	0.298	0.912	0.979	0.094	0.804	0.466	0.453
Triceps SFT	0.295	0.717	0.744	0.311	0.326	0.682	0.389	0.907
Subscapular SFT	0.940	0.062	0.219	0.187	0.779	0.030 *	0.623	0.138
Suprailiac SFT	0.687	0.957	0.378	-	0.546	0.678	0.204	0.693
LM parameters								
BIA_{st}	0.232	0.429	0.953	0.232	0.198	0.073	0.053	0.114
BIA_{sup}	0.922	0.348	0.892	0.615	0.036 *	0.159	0.105	0.112
BIA_{all}	0.969	0.101	0.743	0.604	0.087	0.141	0.122	0.107

Table 7.30. Associations between the change in SDS for all parameters, using only accurate measurements, and all predictor variables during hospitalisation.

Table shows p-values for independent samples t-test comparing the mean SDS of the anthropometric and BC parameters between patients with and without the predictor variable; (*) Significant (p<0.05) but non-significant after correction for multiple testing (p<0.006). Highlighted results differ in significance from the complete dataset.

There was also a trend (non-significant) for patients who had been referred to a dietitian to experience less of a decrease in their BMI SDS. For SFTs, Biceps SDS were more decreased in patients who had a restricted diet, and intake/appetite problems for the case of Subscapular SDS. Changes in Triceps and Suprailiac SDS were not significantly related with any of the predictor variables. As the restricted database analysis shows in Table 7.30, the only significant association was found between patients with intake or appetite problems and reduced SDS for Subscapular SFTs.

Prediction models (Table 7.32) confirmed that loss of appetite was a predictor for decreases in BMI SDS for the whole sample of patients; while for surgical patients, both intake and appetite problems were significantly related with decreases in the SDS. Similarly, intake or appetite were significant in male patients, while dietary restrictions and loss of appetite were significant in female patients. Dietary restrictions were confirmed to be significantly related to decreases in Biceps SDS for the whole sample of patients, and even more so for surgical and male patients. Also in agreement with the univariate analysis, none of the predictors were significant for the change in Suprailiac SDS, but female patients who were referred to a dietitian were more likely to have decreases in their Triceps SDS during hospitalisation.

	Predictors	***B*** [a]	***CI*** [b]	***p*** [c]	**adjusted R^2**
HT (*n=73*)	*No significant predictors*				
WT *(n=114)*	*All patients:* Intake/ appetite problems	-0.168	-0.318 -0.018	0.028	0.050
	Female: Restricted diet	-0.180	-0.312 -0.048	0.009	0.155
	Medical: Restricted diet	-0.163	-0.312 -0.013	0.034	0.094
	Surgical: Loss of appetite	-0.268	-0.500 -0.035	0.025	0.105
MUAC *(n=79)*	*All patients*: Intake/ appetite problems	-0.285	-0.488 -0.082	0.007	0.096
	Female: EN / PN feeding	-0.368	-0.651 -0.085	0.013	0.168

Table 7.31. Best predictor models for the change in anthropometry SDS.
(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). Predictor variables entered stepwise in the models.

	Predictors	*B* [a]	*CI* [b]	*p* [c]	adjusted R^2
BMI *(n=73)*	*All patients*: Loss of appetite	-0.321	-0.543 -0.100	0.005	0.114
	Male: Intake/ appetite problems	-0.476	-0.847 -0.104	0.014	0.158
	Female: Loss of appetite	-0.316	-0.526 -0.107	0.005	0.287
	Restricted diet	-0.278	-0.508 -0.049	0.019	
	Surgical: Intake/ appetite problems	-0.638	-1.235 -0.041	0.037	0.124
Biceps SFT *(n=45)*	*All patients:* Restricted diet	-0.470	-0.911 -0.029	0.037	0.093
	Male: Restricted diet	-0.605	-1.154 -0.055	0.033	0.177
	Surgical: Restricted diet	-0.787	-1.532 -0.043	0.040	0.203
Triceps SFT *(n=50)*	*Female*: Dietary advice	-0.720	-1.347 -0.092	0.027	0.224
Sub-scapular SFT *(n=31)*	*All patients*: Intake/ appetite problems	-0.518	-0.868 -0.169	0.005	0.374
	Fluid restriction	-0.591	-1.038 -0.143	0.012	
	Male: Increased use of EN/PN	1.022	0.177 1.868	0.021	0.443
	Fluid restriction	-0.611	-1.133 -0.089	0.025	
Suprailiac SFT *(n=26)*	*No significant predictors*				

Table 7.32. Best predictor models for the change in FM parameters SDS.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). Predictor variables entered stepwise in the models.

	Predictors	*B* [a]	*CI* [b]	*p* [c]	adjusted R^2
BIA_{st} *(n=42)*	*All patients*: Dietary advice	0.348	0.047 0.648	0.025	0.114
	Medical: Intake/ appetite problems	-0.288	-0.558 -0.019	0.037	0.152
	Surgical: Steroid prescription	1.406	0.187 2.625	0.028	0.312
BIA_{sup} *(n=69)*	*Medical*: Intake/ appetite problems	-0.482	-0.867 -0.096	0.016	0.185
BIA_{all} *(n=71)*	*Medical*: Intake/ appetite problems	-0.400	-0.656 -0.144	0.004	0.265

Table 7.33. Best predictor models for the change in LM parameters SDS.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). Predictor variables entered stepwise in the models.

7.12. Summary of main findings

7.12.1. Admission

- The study recruited patients 5-18yr from a wide range of specialties and with complex and numerous diagnoses. The largest/more defined patient groups were spinal surgery, GI investigations, CF patients, and those being admitted for BMT.
- Patients on admission were on average short and slightly underweight compared to healthy children of the same age and sex.
- The use of WT SDS resulted in almost 20% of patients being classified as 'malnourished', most them under- rather than overweight. The same was true for HT, HC and to a lesser extent for MUAC.
- Patients on admission had on average abnormal BC characterised by low LM SDS and variable amounts of FM. LM parameters resulted in approximately also 20% of patients classified with abnormal SDS (most low SDS). FM assessed by DXA indicated 12% of patients had abnormal FM, about half of them with low and half of them high SDS.
- Adjusting DXA LM for HT (LMI) had much more of an effect than adjusting DXA FM (FMI), in both cases resulting in higher SDS and, in the case of LM, classification of only half the number of patients with abnormal SDS as those before adjustment.
- Around 10% of the patients in the study had steroid medication prescription, fluid restrictions or were wheelchair dependent. 20-30% of patients also had some reported problem with their diet intake (related to mode of feeding, food restrictions or appetite), and half of them had received prior dietetic advice.
- Dietary restrictions and being wheelchair dependent were significant variables predicting low WT, HT and HC SDS on admission. Prior dietetic advice was also a predictor for low MUAC SDS on admission.
- Prior dietetic advice was the most significant predictor for low SDS for FM parameters.
- Being wheelchair dependent and either on a restricted diet or on EN/PN feeds were the most significant predictors for low SDS for LM parameters.

7.12.2. Change during hospitalisation

- 64% of patients were seen and measured on discharge, resulting in a much lower sample size to calculate the change in anthropometric and BC parameters during hospitalisation. Notably, SFTs were performed in a very restricted number of children and detected very few (if any) cases of abnormal FM.
- Mean SDS for the parameters at discharge still showed patients were short and underweight compared to healthy reference children. They also had on average abnormal BC, with low LM and variable amounts of FM SDS.
- Patients during their hospital stay had a tendency to increase in HT SDS. WT and MUAC showed on average no significant change; but about half the patients had experienced a decrease in their SDS during their admission.
- FM and LM also showed no clear average change in SDS, but again about half the patients had experienced some decrease in in their FM and LM SDS.
- A special case was identified for spinal surgery patients, where 'inaccurate' HT measurements on admission (due to curvature of the spine that led to underestimated HT and BIA SDS while overestimating BMI SDS on admission. This, combined with increases in HT after corrective surgery, also resulted in inaccurate assessment of changes in SDS during hospitalisation (large HT / BIA increases, and BMI decreases).
- Associations between predictor variables and the change in the parameters SDS were less clear (and significant) possibly in part due to the limited sample and/or average short length of stay. Only diet-related variables (mainly loss of appetite and dietary restrictions) were predictors for decreases in the anthropometric parameters SDS. Dietary advice was usually a predictor for increases in these parameters SDS, with some exceptions that might reflect patients who experienced decreases in WT SDS and were referred for dietetic management.

7.13. Discussion

7.13.1. Abnormal anthropometric and BC SDS to define malnutrition prevalence

Malnutrition is increasingly recognised to be an important problem in paediatric patients (Corkins 2016; Bouma 2017), leading to the publication of multiple studies looking to quantify the extent of the problem in different countries and settings (Joosten & Hulst 2008; Brinksma et al. 2012; Baxter et al. 2014). However, the range of reported prevalence figures is

extremely wide; reflecting the inherent problem highlighted by several recent consensus statements that perhaps the practical definition of 'malnutrition' (diagnostic criteria) needs revisiting (Bouma 2017; Cederholm et al. 2015; Becker et al. 2014). Although most studies have assessed malnutrition using measurements of WT and HT (and BMI), these outputs are assessed in different ways (e.g. WFA, WFH, HFA, among other indices), using a variety of references and criteria (Joosten & Hulst 2011). Additionally, the role of BC, especially LM, as a contributing diagnostic criteria has more recently been suggested (Becker et al. 2014; Cederholm et al. 2016; Wells & Fewtrell 2008); but so far only measured in a limited number of settings/studies assessing paediatric malnutrition (Pileggi et al. 2016; Inaba et al. 2012; Halpern-Silveira et al. 2010), and no consensus exists on how to measure BC (and LM) routinely in paediatric patients for this effect.

This chapter looked to describe the prevalence of 'malnutrition' using a range of different anthropometric and BC parameters, all assessed in a standardised manner (calculation of SDS, with a cut-off of ±2SDS to indicate abnormality) to allow comparisons between parameters, but also allow comparisons to other studies using similar criteria. The results show 'malnutrition' (SDS <-2 or >2) is relatively common in this population, with an overall approximate prevalence of 20%, most corresponding to cases of low SDS (undernutrition) and a smaller number to high SDS (overnutrition/obesity). This prevalence is similar to reports from another study in the same population (Pichler, Hill, et al. 2014) and another tertiary paediatric centre (Hulst et al. 2004), both of which used SDS of WT as diagnostic criteria; although higher compared to other reports (Dura-Trave et al. 2016) where BMI SDS was used as the diagnostic parameter. This exemplifies the importance of using similar diagnostic criteria to compare prevalence between studies.

These results show children admitted to GOSH are on average short and underweight; but furthermore, have an abnormal BC, characterised by low LM and variable amounts of FM. There have been reports of children with different clinical conditions having abnormalities of FM and/or LM (Murphy et al. 2010; Pichler, Chomtho, et al. 2014; Rashid et al. 2006; Mastrangelo et al. 2013). Considering all patients admitted to GOSH have complex and often chronic diagnoses, the study observations are consistent with these previous observations in selective patient groups; but might not be generalizable to other settings where children present with acute conditions but are otherwise healthy.

Additionally, about half the patients in the study had a decrease in the different parameters SDS between admission and discharge. Some of these changes, however, were very small and could very likely be attributed to measurement error; also, considering half the patients had a length of stay <10 days and large changes were not expected, especially for

HT and HC. A study by Hulst et al. (2004) used a change in >1SDS during admission and discharge as one of the criteria for malnutrition. Using this cut-off, only about 5% of our patients experienced this significant decrease in SDS (for BMI, BIA, MUAC but none for WT), which was similar to the 4% of older children who had a drop in their WFA SDS in the study by Hulst et al. (2004).

7.13.2. Variables related to abnormal SDS on admission and discharge

The analysis of the variables related to SDS on admission showed that the most relevant predictors for all parameters were diet-related: restricted diet, receiving EN/PN feeds and prior dietetic advice. This last variable is likely to identify patients with long-term alterations in nutritional status due to their underlying condition (under the regular care of a dietitian), thus reflecting those patients who are sicker and more at risk. Additionally, being wheelchair-dependent was significantly associated with low SDS for LM and WT, which could be the result of the immobility but also the underlying condition (e.g. neuromuscular) considering this variable was also related to low scores for HC (common in patients with neurological impairments and syndromes who were wheelchair-dependent).

For the change in SDS during hospitalisation, the results showed that loss of appetite and dietary restrictions were the variables most commonly associated with decreases in the parameters SDS. However, the study was limited by the number of measurements performed at the time of hospital discharge, which likely limited my ability to detect significant associations.

7.13.3. Contribution of the results and gaps in evidence

The characterisation of abnormal SDS to define ‘malnutrition’ using these parameters, which are also practical and reliable in a tertiary hospital setting (Chapter 4), shows for the first time as far as I am aware, how the identification and quantifying of malnutrition in a clinical setting can be influenced by the choice of diagnostic criteria from this range of measurements, especially for FM parameters. The results presented in this chapter were analysed using all collected measurements and resulted in a range of prevalence values on admission: approximately 20% for WHT, HT, MUAC and LM parameters; 13% for BMI, and 0-4% for the 4 SFTs. This has the advantage that the mean SDS and % of abnormal SDS are influenced both by the ability of the technique to detect abnormalities (e.g. SFTs have shown to be less accurate and precise for assessing FM than DXA FM) but also the practicality of obtaining the measurements in the population. This was shown to be especially important when following up changes in the parameters (performing sequential measurements) that could not be assessed with the reference technique of DXA. At

discharge, even within the patients who were seen, some measurements (notably SFTs) were only performed in a small number of patients; which then identified a very small (if any) number of 'malnutrition' cases. As concluded in Chapter 4, the agreement between FM parameters in classifying patients with abnormal SDS was generally poor. This means that the use of SFTs to assess 'malnutrition' might lead to large differences compared to other diagnostic criteria. Even though compliance and rates for the measurements could be improved in clinical practice, the agreement between the techniques could still make comparisons between studies and reports of prevalence difficult.

7.14. Conclusion

Malnutrition is prevalent in our tertiary paediatric setting. Diet-related parameters such as dietary restriction, EN/PN feeding and dietetic referral, together with being wheelchair-dependent, influenced the parameters SDS on admission. However, the change in SDS were mostly affected (although weakly) by decreases in appetite and dietary restrictions during the hospital stay, although my ability to detect associations was limited by the relatively small sample size.

The results indicated how the prevalence of 'malnutrition' is influenced by the choice of diagnostic criteria used. Patients in our population are short and underweight on average, and have abnormal BC (low LM and variable FM) compared to healthy children of the same age and sex. Both of the more standard diagnostic criteria of WT and HT indicated a 20% prevalence of malnutrition, mostly due to undernutrition rather than overnutrition. A similar prevalence was found using LM parameters, but FM parameters resulted in variable percentages from 13% for BMI to 0% for some for the SFT measurements.

Ultimately, whether the assessment of BC is relevant and important as part of the diagnostic criteria for malnutrition should ideally depend (among other things) on its ability to predict clinical outcomes better than the established parameters of weight, height and BMI alone. Similarly, to determine which BC technique, perhaps even independently of their accuracy for assessing FM and LM as such, is the best option to diagnose malnutrition in practice, needs to be assessed with associations to clinical outcomes. Chapter 8 will investigate this further.

8 Body composition and anthropometric parameter associations to clinical outcomes: towards a practical definition of malnutrition

8.1. Introduction

Despite consistent reports that malnutrition in paediatric clinical settings is common, it appears that it is often an unrecognised problem (Kelly et al. 2000; Huysentruyt, P Alliet, et al. 2013). Chapter 1 has outlined the prevalence and characteristics of studies on paediatric clinical malnutrition, highlighting the lack of homogeneity, not just in terms of the study population and design, but perhaps more importantly, in the criteria used to define malnutrition. It is logical to assume that this lack of consensus in the practical diagnostic criteria for malnutrition is a key issue that needs to be addressed, not only to better quantify the extent of the problem in different settings and studies, but to enable future studies guiding clinical practice into the possibility of interventions to prevent/treat this condition (Cederholm et al. 2015).

WT and HT are the most frequently used parameters to diagnose malnutrition, however, they are assessed in a variety of ways (cut-off values, indices: weight-for-height, height-for-age, BMI-for-age) that often lead to strikingly different prevalence values (Joosten & Hulst 2008). Although these parameters are the basis for the assessment of growth and might serve as malnutrition parameters in the community, identifying malnutrition in a clinical setting poses additional challenges that might limit the diagnostic accuracy of these measurements. As Chapter 1 has detailed, patients with similar weights or BMIs could have markedly different proportions of FM and LM (Wells, Coward, et al. 2002; Daniels 2009; Demerath et al. 2006; Phan et al. 2012), while nutritional interventions could similarly lead to increases in WT but with differing patterns of FM and LM accretion (Sullivan et al. 2006).

Previous results from the BodyBasics study (Chapter 7) have shown the influence that different diagnostic parameters can have on the quantified prevalence of malnutrition; especially in this population of children with complex diagnoses often presenting with abnormal BC – fat and lean mass - on admission.

Studies and consensus statements have begun to propose the use of BC measurements, mainly LM, to improve on the diagnosis of malnutrition (Cederholm et al. 2016; Cederholm & Jensen 2016; Becker et al. 2014). However, they also mention the predominant idea that these measurements are difficult to perform in clinical practice. Chapter 4 showed that by

using a standardised method of assessing BC (comparing measurements to reference data to generate SDS) by a range of techniques, these measurements were overall practical as well as acceptable in a diverse population of children with complex conditions. Although these results might not be generalizable to other settings, it does suggest they would be possible to implement them in routine practice if there was evidence for the added benefit of measuring BC for the nutritional management of certain patient populations.

This chapter will explore the associations between BC measurements of fat and lean mass and clinical outcomes in our sample of paediatric patients, and determine if there is any additional advantage over the standard measurements of WT, HT and BMI, supporting their use as diagnostic parameters for malnutrition.

8.2. Chapter objectives

1. Describe the clinical outcomes at discharge: length of stay, complications, decreased muscle function, and worsening nutritional status during hospitalisation.
2. Analyse the associations between baseline WT, HT, and DXA FM and LM, to clinical outcomes, either as single or aggregate parameters.
3. Determine if parameters adjusted for size (BMI, FMI and LMI) are better predictors of clinical outcomes in this population.
4. Confirm if the use of other simple anthropometric and BC measurements (HC, MUAC, Biceps SFT and BIA) still show the same associations to clinical outcomes as those described using WT, HT, and DXA FM and LM.

8.3. Methods

8.3.1. Study population and recruitment

The chapter objectives were investigated in the sample of 152 patients recruited to the BodyBasics study at GOSH. The patient characteristics and recruitment procedures have already been described in detail in earlier chapters (Chapters 3, Section 3.1; and Chapter 7).

8.3.2. Data collection tools

Anthropometric and BC measurements were taken within 48 hours of admission, SDS calculated using the appropriate reference data (Freeman et al. 1995; Wells et al. 2012), and the cut-offs ≥2SDS and ≤-2SDS used to define abnormal SDS. A full description of the

measurement protocols can be found in Chapter 3, Section 3.3, and Chapter 7 includes a detailed analysis of the observed measurement SDS for the study on admission, discharge and change during hospitalisation.

Data was also collected for the purposes of defining the clinical outcomes both on admission and discharge. Information for the length of stay (LOS) and complications was collected on admission and discharge. Measurements of grip strength were used as an indicator of muscle function, and were similarly performed on admission and discharge when possible. Changes in the WT, BMI and BIA SDS were also used as markers for worsening nutritional status during admission. The details of how the data was collected and the resulting variables selected for the analyses are described in Chapter 3, Section 3.5.

8.3.3. Data analysis and statistics

Data on the clinical outcomes was summarised using descriptive statistics as appropriate for numeric and categorical/binary variables. When calculating the differences between admission and discharge measurements/SDS, the mean was tested for significance using one sample t-tests or Wilcox signed t-test as appropriate. The clinical outcomes were also analysed for differences depending on sex, admission group and age. Several numerical and categorical/binary variables for each clinical outcome are presented for the purposes of describing them in detail in this first section, however, for all subsequent analyses in the chapter, only the binary/diagnostic variables for each clinical outcome were used.

The associations between diet-related and other variables during hospitalisation (described in Chapter 7) with the clinical outcomes was tested first using univariate analysis. Subsequently, univariate associations between all anthropometric and BC parameters as SDS and as categorical variables (‘abnormal’ scores) were calculated for each clinical outcome. Logistic regression models were constructed for WT, HT, and DXA LM and FM; adjusting for age, sex, admission group, and/or confounders as appropriate. Finally, models using more than one parameter were constructed to establish if the use of more than one measurement (e.g. WT plus DXA LM) could improve the prediction of clinical outcomes.

8.4. Clinical outcomes at discharge

8.4.1. Length of stay: prolonged and greater than expected

Most of the studies exploring the associations of malnutrition with clinical outcomes have focused on LOS (days). However, the heterogeneity in the study subject characteristic meant a wide range of LOS were expected depending on the procedures and interventions scheduled during their hospitalisation. Thus, a decision was taken to assess the number of days in hospital compared to the expected/predicted LOS on admission. This 'predicted' LOS was usually the number of days that ward staff assigned to each planned admission based on the scheduled procedure. For example, the standard stay for a child with CF admitted for a routine course of antibiotics was 2 weeks. When this was not available from the hospital's online system, a member of the patient's clinical team was asked to provide an estimate.

Table 8.1 summarises the predicted, actual and the difference in LOS. Although most of the patients had a short stay of approximately 1 week, there were a small number of patients staying for extended periods of time, notably patients undergoing BMT (expected LOS of a couple of months). There were no significant differences between the predicted and actual LOS on average (mean or median).

n=152	***mean***	***CI*** [a]	***p*** [c]	***median***	***IQR*** [b]	***p*** [d]
Predicted stay	13.8	(10.9, 16.7)	-	8.0	(5.0, 14.0)	-
Actual stay	16.6	(12.1, 21.1)	-	9.0	(4.0, 14.8)	-
Difference LOS	2.8	(-0.9, 6.5)	0.134	0.0	(-2.0, 2.8)	0.793

Table 8.1. Length of stay descriptives.

Length of stay (LOS, days); (a) 95% confidence interval for the mean; (b) Inter-quartile range (25th and 75th) for the median; (c) One sample t-test for the mean difference in length of stay, days (d) and percentage (%) (H_0: mean difference=0, p<0.05); (d) Wilcox signed test (H_0: median=0, p<0.05).

Patients admitted for BMT were classified in the 'surgical' group, considering the complexity of the procedure compared to other more-simple medical interventions and investigations (e.g. GI investigations of motility). Considering they were expected to stay a couple of months as opposed to the more usual expected LOS of 3 days to a week in other wards this resulted in a higher median and wider range in LOS for the 'surgical' group compared to the 'medical' group, although this difference did not reach statistical significance (Appendix 15, Table 1).

Table 8.2 describes the observed frequencies for the 3 categorical variables calculated in relation to this outcome. 22% of patients had the same LOS as predicted, while 41% of them stayed less than predicted and 37% more than predicted. These frequencies were significantly different in surgical patients compared to medical, since most patients (38%) stayed longer than predicted and only 8% stayed less.

Subsequently, two binary variables were calculated to describe LOS for the subsequent statistical analysis of associations. 'Prolonged stay' indicated the number of patients staying longer than the median LOS (9 days), which in this case was 43% of patients. A significantly higher percentage of surgical patients (41%) had prolonged LOS compared to the medical patients. The second binary variable was 'increased LOS' which identified patients staying longer than their predicted LOS, and which resulted in a stay above the median. This was calculated with the intent of avoiding classifying patients as having an 'increased LOS', when this was only for 1-2 extra days due to reasons not associated with the patient's clinical condition (e.g. time to arrange transport, bed rotation schedules).

	Freq.	*%*	**Medical** [d]	**Surgical** [d]	*p* [e]
Difference in LOS [a]					
less	62	40.8	26	8	0.000*
same	34	22.4	30	32	
more	56	36.8	18	38	
Prolonged stay [b]					
no	86	56.6	49	37	0.023*
yes	66	43.4	25	41	
Increased LOS [c]					
no	109	71.7	61	48	0.003*
yes	43	28.3	13	30	

Table 8.2. Length of stay categorical descriptives and differences between medical and surgical admissions.

(a) Different categories depending on the comparison between predicted and actual length of stay (LOS); (b) Patients with a LOS above the median (≥10 days); (c) Patients with a longer than predicted LOS (>1day difference); (d) number of patients; (e) Chi-squared test and Fisher's exact test of significance comparing medical and surgical admissions, (*) significant (p<0.05).

8.4.2. Complications

The clinical outcome of ‘complications’ was calculated by assessing the occurrence of several events. As Table 8.3 details, these were hospital/ward transfer, increased used of EN/PN and ‘other’ complications. Hospital/ward transfers referred to cases when patients were discharged to their local hospital rather than home because of the need to continue monitoring their clinical condition, or when the patient was transferred within the hospital after they developed a complication (e.g. a patient with post-operative complications unable to be extubated was transferred to the PICU and then to the respiratory ward). This occurred in 8.6% of cases, with no difference between surgical and medical groups of patients.

The increased use of EN/PN (unplanned) was calculated as patients requiring either form of nutrition provision during their stay: patients feeding orally now receiving partial of full EN/PN, or patients on partial EN/PN switched to full EN/PN. Cases where the provision of EN or PN was a part of their planned treatment/procedure were excluded. EN referred exclusively to tube feeding (no oral supplements). Nine patients (8.6%) had increased use of EN/PN during their stay, which had then stopped by the time of discharge. 10.4% of patients had increased need for EN/PN that was still ongoing by the time they were discharged from the study/hospital. There was a significant difference between the medical and surgical groups, with surgical patients needing more use of EN/PN, presumably post-operatively.

The third event category of ‘other’ referred mainly to infectious or post-operative complications recorded in the patient’s medical notes, or reported by the family/patient and their clinical team. Considering the large range of patients and clinical specialties, this was not a planned category at the start of the study, but was calculated in patients where information of an event could be obtained with some degree of detail and trusted source (e.g. fever with antibiotic treatment reported by a member of the clinical team, delayed wound healing report in the surgical notes). Thus, these were slightly more often recorded for surgical patients compared to medical, with an overall prevalence of 8.4%.

A category for ‘complications’ was calculated for patients experiencing one or more of the complication events detailed above, which was present in 22% of patients in the study, and significantly more frequent in surgical patients.

	Freq.	*%*	**Medical** [e]	**Surgical** [e]	*p* [f]
Transfer to another ward or hospital [a]					
no	139	91.4	68	71	1.000
yes	13	8.6	6	7	
Increased use of EN or PN during stay [b]					
no	86	81.1	49	37	0.012*
resolved	9	8.5	2	7	
ongoing	11	10.4	2	9	
Other complications [c]					
no	98	91.6	50	48	0.489
yes	9	8.4	3	6	
Complications during stay [d]					
no	119	78.3	64	55	0.019*
yes	33	21.7	10	23	

Table 8.3. Complications during hospitalisation descriptives and differences between medical and surgical admissions.

(a) Patients who were transferred to another ward or discharged to another hospital rather than home; (b) Patients who had a new or increased reliance (from partial to full) on EN/PN nutrition during their hospitalisation (not planned); (c) Periods of infection (fever and antibiotic treatment), delayed wound healing or taken back to surgery due to complications; (d) Patients who either: had a ward/hospital transfer, had increased use of EN/PN, or experienced other complications during their hospitalisation; (e) number of patients; (f) Chi-squared test and Fisher's exact test of significance comparing medical and surgical admissions, (*) significant ($p<0.05$)

8.4.3. Grip strength changes during hospitalisation

Grip strength (GS) was assessed as marker of muscle function in the study. GS measurements on admission were compared to measurements at the time of discharge, with the difference (diffGS) and % difference calculated. Table 8.4 shows the mean values for GS and diffGS. At the time of admission, the average GS was 14.7 newtons (N), decreasing to a mean of 14.6 N at discharge. The mean GP between admission and discharge was not significantly different.

As Table 8.5 shows, however, there was a significant difference between surgical and medical groups, with patients categorised as 'surgical' having lower GS on discharge despite no significant differences to 'medical' patients at baseline (admission). This translated to significant diffGS: medical patients on average increased their GS by 0.6N while surgical

patients decreased it by 1.0N. Although the GS on admission and discharge was positively correlated with age, the diffGS was non-significant. There were no significant differences in GS or diffGS between male and female patients.

	n	***mean***	***CI*** [a]		***p*** [b]
GS on discharge	54	14.6	12.3	17.0	-
GS on admission	108	14.7	13.2	16.3	-
diffGS	53	-0.3	-1.1	0.6	0.540

Table 8.4. Grip strength descriptives.

GS=grip strength, diffGS=difference in grip strength. Units: Newtons (N); (a) 95% confidence interval for the mean; (b) One sample t-test for the mean difference in grip strength between admission and discharge measured as N and percentage (%) (H_0: mean difference=0, p<0.05).

	Medical		**Surgical**		*p* [a]	**Age**	
	mean	*SD*	*mean*	*SD*		*r* [b]	*p*
GS on discharge	17.7	11.2	12.4	5.8	0.048*	0.6	0.000*
GS on admission	14.4	8.8	15.0	7.8	0.692	0.7	0.000*
diffGS	0.6	2.4	-1.0	3.6	0.006*+	-0.1	0.380

Table 8.5. Differences in grip strength between medical and surgical admissions, and correlations to age.

GS=grip strength, diffGS=difference in grip strength. Units: Newtons (N); (a) Independent samples t-test comparing the mean between medical and surgical admissions (H_0: differences between groups=0); (+) Wilcox t-test; (*) significant (p<0.05); (b) Pearson's correlation coefficient (r) between age and grip strength variables, (*) significant (p<0.05).

The calculated categorical variables for GS are summarised in Table 8.6. More than half of the patients had a decrease in their GS measurements between admission and discharge, while almost 40% of them had an increase. There was a significant difference between the surgical and medical groups. In agreement with the observations above, a greater number of surgical patients decreased their GS by the time of discharge. However, considering many of these changes were minimal, another binary category was calculated to identify only those children who had a decrease in GS >10%, resulting in 43% of patients identified as having 'decreased GS'. Furthermore, more than half of surgical patients were classified as having decreased GS, which was still significantly different to medical patients.

	Freq.	*%*	**Medical** [c]	**Surgical** [c]	*p* [d]
Difference in GS [a]					
same	1	1.9	1	0	0.033*
decreased	31	58.5	9	22	
increased	21	39.6	13	8	
Decreased GS [b]					
no	30	56.6	17	13	0.049*
yes	23	43.4	6	17	

Table 8.6. Decrease in grip strength categorical descriptives and differences between medical and surgical admissions.

(a) Different categories depending on the comparison between discharge and admission grip strength; (b) Patients with a decrease of more than 10% in their grip strength between admission and discharge; (c) number of patients; (d) Chi-squared test and Fisher's exact test of significance comparing medical and surgical admissions, (*) significant (p<0.05).

8.4.4. Worsening nutritional status: decreases in weight, BMI and BIA SDS

Changes in WT, BMI and BIA between admission and discharge were also calculated as markers of worsening nutritional status. Table 8.7. summarises the mean differences for these parameters. WT decreased (non-significantly) on average by 0.2kg, BMI decreased significantly by 0.3kg/m^2, while the mean BIA SDS did not change significantly.

The only significant differences between surgical and medical patients was for BMI, with surgical patients showing a decrease of -0.5 kg/m^2. Age was also significantly associated with the difference in WT and BMI, with older children showing the greatest decrease in WT and BMI (Table 8.8).

The categorical variables for worsening nutritional status are summarised in Table 8.9. more than half the patients had some degree of weight loss during their stay, while approximately 40% increased their WT. Because many of these changes were small, a variable for 'decrease in WT during stay' was calculated to include patients who had a weight loss of >2% or any degree of weight loss if they were already classified as underweight. About one third of patients experienced a weight loss like this. For BMI, about 60% of patients had a decrease in this parameter during their hospital stay, but only 40% had a decrease that was considered substantial (>2%). The cases where the decrease in BMI was just the result of changes in HT from an inaccurate measurement on admission in spinal surgery patients (and

subsequent correction post-op) were excluded. Finally, almost 50% of patients had a decrease in their BIA SDS that was at least 0.1SDS to be considered substantial.

Considering that about half of the patients had a short hospital stay of a few days up to a week, the criteria for selecting changes (decreases) in the parameters were not overly strict, while still looking to exclude small spurious differences.

	n	***mean***	***CI*** [a]		***p*** [b]
Difference in WT (kg)	114	-0.2	-0.5	0.1	0.153
Difference in WT (%)	114	0.0	-0.8	0.7	0.924
Difference in BMI (kg/m^2)	73	-0.3	-0.5	-0.1	0.002*
Difference in BMI (%)	73	-1.4	-2.4	-0.4	0.008*
Difference in BIA_{st} SDS	42	-0.1	-0.2	0.0	0.098
Difference in BIA_{sup} SDS	69	0.1	-0.1	0.4	0.353

Table 8.7. Worsening nutritional status during hospitalisation descriptives.
Body Mass Index (BMI), standing Bio-electrical Impedance Analysis (BIA_{st}), supine BIA (BIA_{sup}); (a) 95% confidence interval for the mean; (b) One sample t-test for the mean difference between admission and discharge measurements in original units and as percentage (%) (H_0: mean difference=0), (*) significant (p<0.05).

	Medical		**Surgical**		*p* [a]	**Age**	
	mean	*SD*	*mean*	*SD*		*r* [b]	*p*
Difference in WT (kg)	-0.1	1.1	-0.3	1.7	0.647	-0.25	0.008*
Difference in WT (%)	-0.2	3.1	0.1	5.0	0.742	-0.21	0.026*
Difference in BMI (kg/m^2)	-0.1	0.5	-0.5	1.0	0.016*+	-0.37	0.001*
Difference in BMI (%)	-0.5	3.0	-2.5	5.5	0.019*+	-0.33	0.004*
Difference in BIA_{st} SDS	-0.1	0.3	-0.2	0.6	0.343	-0.09	0.589
Difference in BIA_{sup} SDS	0.0	0.6	0.3	1.3	0.209	0.13	0.272

Table 8.8. Differences in makers of nutritional status between medical and surgical admissions, and correlations to age.
(a) Independent samples t-test comparing the mean between medical and surgical admissions (H_0: differences between groups=0); (+) Wilcox t-test; (*) significant (p<0.05); (b) Pearson's correlation coefficient (r) between age and the differences in weight, BMI and BIA; (*) significant (p<0.05).

	Freq.	%	Medical Freq.	Surgical Freq.	p [e]	Age Mean	Age SD	p [f]
Difference in WT [a]								
same	7	1.9	5	2	0.530	9	3	0.144
decreased	54	58.5	27	27		11	3	
increased	53	39.6	26	27		10	4	
Decrease in WT during stay [b]								
no	77	67.5	56	53	0.676	11	4	0.200
yes	37	32.5	2	3		9	2	
Difference in BMI [a]								
decreased	45	61.6	22	23	0.347	12	3	0.008*
increased	28	38.4	17	11		9	4	
Decrease in BMI during stay [c]								
no	44	60.3	36	30	0.698	11	4	0.193
yes	29	39.7	3	4		12	3	
Decrease in BIA during stay [d]								
no	36	50.7	18	18	0.814	11	4	0.971
yes	35	49.3	16	19		11	3	

Table 8.9. Worsening nutritional status categorical descriptives, differences between medical and surgical admissions, and age.

Freq.=number of patients; (a) Difference at discharge compared to admission; (b) Patients who had >2% weight loss between admission and discharge (or any if underweight on admission); (c) Patients who had a decrease in BMI >2%; (d) Patients with a decrease in SDS>0.1 in either standing or supine BIA by discharge compared to admission; (e) Chi-squared test and Fisher's exact test of significance comparing medical and surgical admissions, all non-significant (p<0.05); (f) Once-way ANOVA and Independent samples t-tests comparing mean age between groups, (*) significant (p<0.05).

8.4.5. Associations between confounding variables and clinical outcomes

The choice of clinical outcomes was limited by the large heterogeneity of the study patient characteristics, meaning it was difficult to find outcomes that would be relevant for the expected range of diagnoses and conditions. The chosen outcomes described above could potentially be measured in any patient being admitted to GOSH. However, they had the disadvantage of being very generic, and as such, likely affected by other factors other than the anthropometric and BC SDS on admission.

To determine other factors that might be related with the clinical outcomes, the associations between predictor variables during hospitalisation (Chapter 7) were analysed

with relation to the outcomes using univariate statistical tests. Table 8.10 summarises the *p*-values of the associations found to be significant for at least one of the clinical outcomes. There were no variables associated with decreases in GS, WT, BMI or BIA. Prior dietetic advice, EN/PN feeding and being wheelchair-dependent were significantly associated with the variables for LOS. For complications, dietetic advice and steroid medication during hospitalisation were significant. Additionally, a significant association was found between the outcome of 'complications' and both LOS outcome variables (p=0.003 for 'prolonged stay', and p=0.005 for 'increased LOS').

These associations, together with the associations to admission group were considered for adjusting the prediction models for the baseline anthropometric and BC SDS.

	Steroids [a]	EN/PN [b]	Dietetic advice [c]	Wheelchair user
Prolonged stay	0.143	0.007	0.000	0.004
Increased LOS	0.122	0.034	0.005	0.018
Complications	0.013	0.058	0.002	0.528
Decrease in GS	0.269	0.279	0.079	-
Decrease in WT	0.486	0.514	0.119	0.584
Decrease in BMI	0.456	0.580	0.173	0.640
Decrease in BIA	0.500	0.475	0.500	0.125

Table 8.10. Associations between confounding variables and clinical outcomes.
Values are p-values for Fisher's Exact Test, highlighted values show significant (p<0.05) associations. (a) on high steroid medication during hospitalisation; (b) on EN/PN feeds during hospitalisation; (c) dietetic advice during hospital stay (referred to dietitian).

8.5. Baseline weight, height and BC: associations to clinical outcomes

8.5.1. Weight, height and BC SDS on admission

Table 8.11. summarises the results from the univariate analysis exploring the differences in mean SDS for WT, HT, DXA LM and DXA FM between the categories (no/yes) of clinical outcomes. Significant associations between variables were only found for the clinical outcomes of 'prolonged stay', 'increased LOS' and 'complications'. Patients who had a prolonged stay or increased LOS in hospital had on average significantly lower HT, WT and DXA LM SDS. They also had a lower, but non-significant, mean DXA FM SDS.

Regarding complications, there was a tendency for lower HT, WT, LM and FM SDS in patients experiencing at least one of the complications assessed during their hospital stay, but was only significant for the case of DXA LM. Patients who experienced complications had a mean DXA LM of -1.6 SDS compared to those who did not (-0.82 SDS).

Although there was a tendency for lower HT, WT, LM and FM SDS in those patients with a decrease in GS, this was non-significant. However, because GS was only able to be measured in approximately 50 patients, both on admission and discharge, it is possible that the reduced sample size would be limiting the ability of the statistical tests to detect a significant difference.

Similarly, patients with a decrease in BIA SDS (>0.1 SDS) during their hospitalisation had a tendency for worse WT, HT, DXA FM and especially DXA LM SDS on admission (all non-significant).

8.5.1. Abnormal weight, height and BC SDS on admission

The associations to the clinical outcomes were also analysed using the binary variables for abnormal SDS (<-2 or >2 SDS) for WT, HT, DXA LM and FM. Figure 8.1 summarises the *RR* for the clinical outcomes between patients categorised with abnormal SDS (abSDS) for these parameters on admission compared to 'normal' parameter SDS (details in Appendix 15, Table 2).

WT, HT, DXA LM and FM abSDS were all associated with a significantly increased risk of a prolonged stay above the median and an increased LOS, although this was non-significant for FM abSDS and prolonged stay. There was also an increased risk for complications, higher for patients with DXA LM abSDS (*RR*=1.8) and FM abSDS (*RR*=1.7) compared to WT and HT abSDS, however this did not reach statistical significance.

The categorisation with abSDS for all parameters also resulted in an increased risk for a decreasing GS during hospitalisation, even more so for HT (*RR*=2.6) and LM (*RR*=2.4). However, again this did not reach statistical significance for any of the parameters.

Abnormal DXA LM SDS were also associated (non-significant) to an increased risk for worsening nutritional status during hospitalisation, assessed by decreases in WT, BMI and BIA (*RR*=1.4, 1.3 and 1.5 respectively). WT abSDS were significantly associated with a decrease in WT during hospitalisation (*RR*=2.1), but not for decreases in either BMI or BIA. DXA FM abSDS on admission increased the risk of weight loss and decreasing BIA SDS during hospitalisation, while HT abSDS only increased the risk for decreasing BIA SDS.

	Prolonged stay					Increased LOS					Complications					Decrease in grip strength				
	No		Yes		p^a	*No*		*Yes*		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
HT	-0.35	1.3	-1.20	1.7	0.001	-0.48	1.3	-1.42	1.9	0.002	-0.67	1.6	-0.80	1.3	0.685	-0.49	1.2	-0.86	1.5	0.321
WT	0.06	1.4	-0.86	1.9	0.001	-0.14	1.5	-1.00	2.1	0.008	-0.25	1.8	-0.64	1.4	0.250	-0.11	1.5	-0.69	1.8	0.212
DXA LM	-0.66	1.3	-1.48	1.6	0.003	-0.82	1.4	-1.54	1.6	0.032	-0.82	1.5	-1.61	1.2	0.020	-1.00	1.4	-1.32	1.4	0.442
DXA FM	0.24	1.1	-0.21	1.4	0.051	0.15	1.1	-0.27	1.6	0.135	0.10	1.2	-0.06	1.4	0.581	0.08	1.2	-0.20	1.3	0.444

Table 8.11. Univariate analysis of the associations between WT, HT and BC SDS on admission with clinical outcomes.

Table shows mean SDS for the parameters on admission. (a) independent samples t-test for the difference in mean SDS between groups (H_0: difference=0), highlighted values show significant ($p<0.05$) associations.

	Decrease in weight					Decrease in BMI					Decrease in BIA				
	No		Yes		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
HT	-0.74	1.4	-0.39	1.6	0.254	-0.54	1.4	-0.52	1.5	0.952	-0.59	1.5	-1.12	1.7	0.173
WT	-0.43	1.5	-0.09	2.0	0.320	-0.20	1.5	-0.01	1.7	0.625	-0.05	1.6	-0.68	2.0	0.149
DXA LM	-0.94	1.3	-0.92	1.9	0.955	-0.72	1.1	-1.12	1.7	0.248	-0.75	1.3	-1.44	1.5	0.062
DXA FM	-0.06	1.2	0.15	1.4	0.457	0.03	1.3	0.28	1.2	0.417	0.23	1.1	-0.07	1.4	0.352

Table 8.11. *(Cont.)* Univariate analysis of the associations between WT, HT and BC SDS on admission with clinical outcomes.

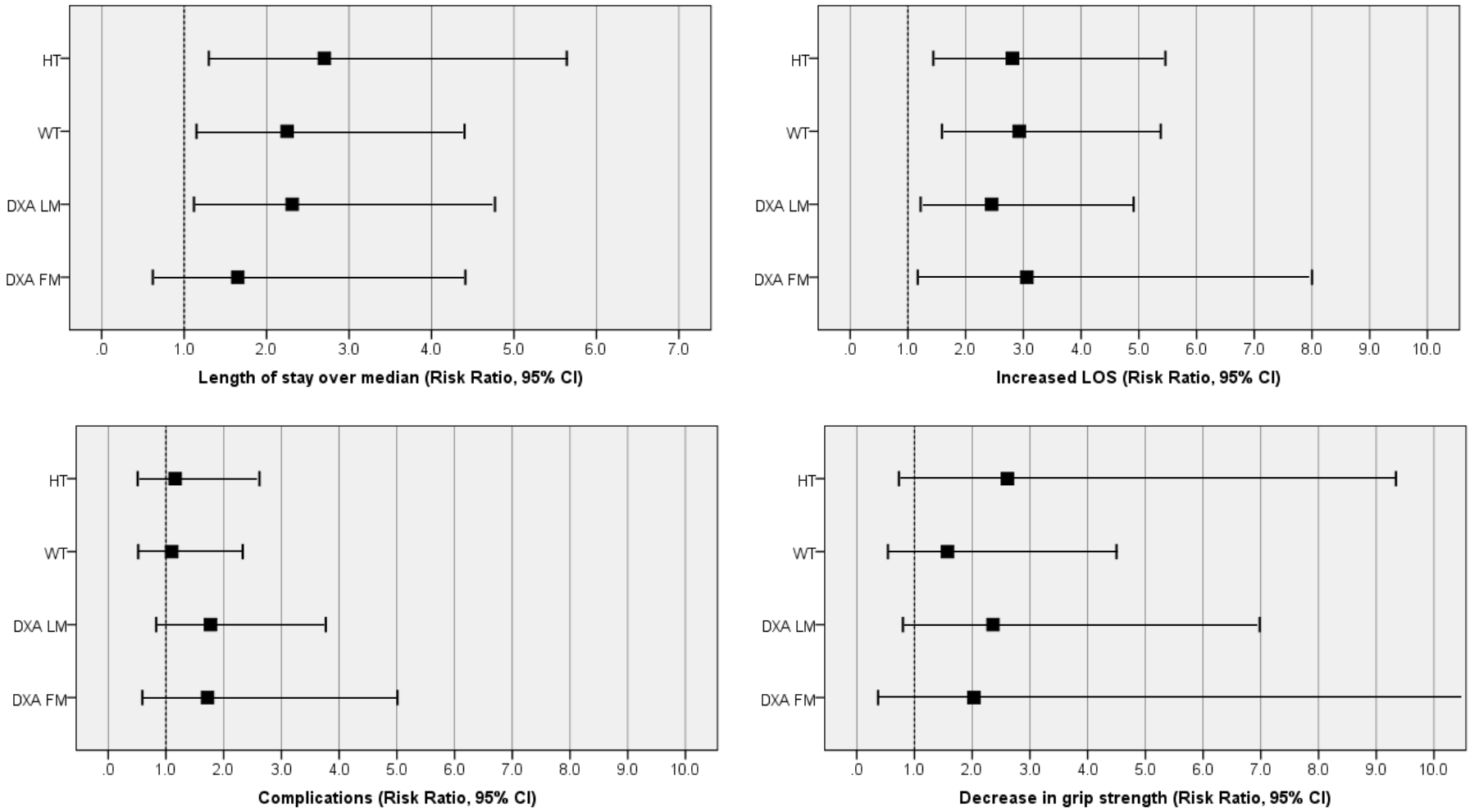


Figure 8.1. Summary of *RR* for worse clinical outcomes in patients with abnormal WT, HT, DXA LM and FM SDS on admission.
Graphs show the RR (■) and 95% CI for the RR (I) for each parameter. Dotted line shows a RR=1 (no risk).

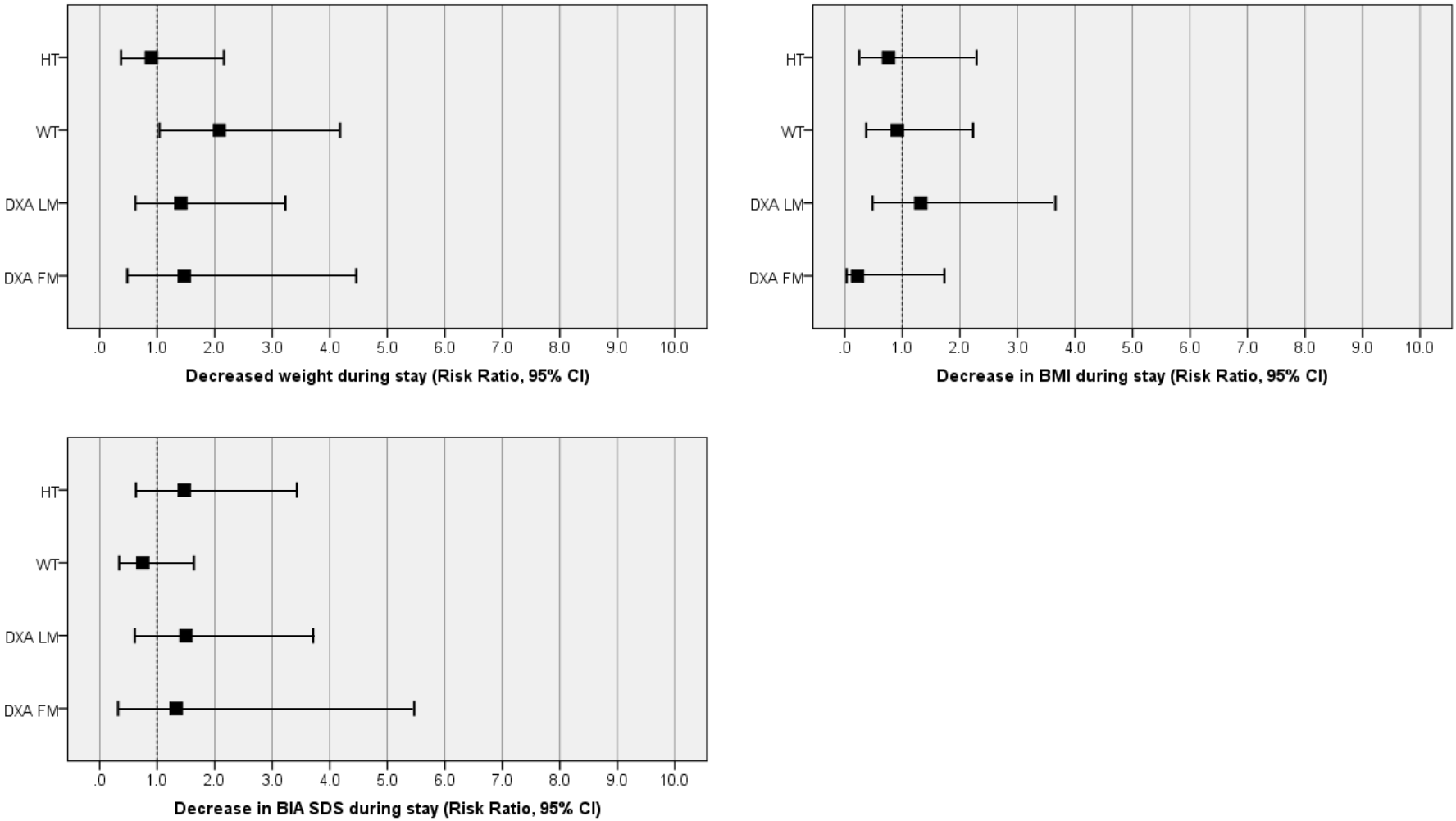


Figure 8.1. *(Cont.)* Summary of *RR* for worse clinical outcomes in patients with abnormal WT, HT, DXA LM and FM SDS on admission.

8.6. Adjusting for size: baseline BMI, FMI and LMI associations with clinical outcomes

8.6.1. BMI, FMI and LMI SDS on admission

The effects of adjusting for HT to obtain the indices of BMI, LMI and FMI, with regards to their associations to clinical outcomes were explored using the mean SDS for these parameters and the binary variables for abnormal BMI, LMI and FMI SDS.

There were no significant differences in the baseline BMI, LMI and FMI SDS between patients who had a decrease in GS, WT, BMI or BIA during their hospitalisation and those who did not (Appendix 15, Table 3), although there was a tendency for lower BMI, LMI and FMI SDS in patients who presented with these negative clinical outcomes.

Focusing on patients who had a 'prolonged stay' or an 'increased LOS', although there was a tendency for them to have lower mean BMI, LMI and FMI SDS on admission, this was only significant for BMI with regards to a 'prolonged stay'. A similar pattern was found for the outcome of 'complications', and in this case those patients with complications had a significantly lower DXA LMI on admission.

8.6.2. Abnormal BMI, FMI and LMI SDS on admission

The risk of presenting worse clinical outcomes in patients with abSDS for BMI, LMI and FMI on admission is summarised in Figure 8.2 (details in Appendix 15, Table 4). Patients with BMI abSDS on admission did not have a significant increased risk for a prolonged stay, an increased LOS, complications, or a decreased GS. However, there was a higher risk for weight loss, BMI and BIA SDS decreases during hospitalisation, but this was only significant for weight loss. This observed RR were not higher/better than those obtained using WT SDS on admission; suggesting the use of BMI would not improve the identification of children who are likely to present with worst clinical outcomes.

Patients with abSDS for FMI on admission had a higher risk for a prolonged stay, an increased LOS, decreased GP and weightless during their hospitalisation. The only significant *RR* however, was for 'increased LOS'. Compared to the results obtained using the unadjusted DXA FM on admission, the adjustment for HT did not improve on the identification of children who would present with worst clinical outcomes; and both parameters would be able to identify children staying longer than predicted (only significant *RR*). These observations are in line with results in previous chapters showing adjustment to HT made more of a difference for LM than FM.

The risk for 'increased LOS', 'prolonged stay', 'complications' and 'decreased GS' in those patients with LMI abSDS on admission was lower (and non-significant) in all instances compared to the observed risk using DXA LM abSDS. However, the risk for worsening nutritional status (decreased WT, BMI and BIA SDS during hospitalisation) was higher using LMI abSDS on admission, although these were all non-significant.

Overall, although BMI, LMI and FMI SDS on admission were associated with increased risk for some of the clinical outcomes, the results suggest there is no advantage on adjusting for height to improve the identification of children who will present with worst clinical outcomes. Identifying children who are short appears to be similarly important as identifying those with low body mass (fat or lean) proportional to their size. This is further supported by the observed significant associations between the HT SDS on admission and the clinical outcomes. Although the indices of LMI and FMI might not perform better as single indicators for worst outcomes, their use in conjunction with each other and with other measurements, such as HT, could prove to be more accurate than unadjusted DXA LM and FM.

8.7. Use of alternative anthropometric and BC parameters to predict clinical outcomes

8.7.1. HC, MUAC, Biceps SFT and BIA SDS on admission

Considering it might not always be possible to measure WT, HT and DXA FM and LM, associations to the more relevant clinical outcomes for these parameters (prolonged stay, increased LOS, complications, and decreased GS) were also tested using surrogate anthropometric and BC measurements: MUAC, HC, BIA, and SFTs (Appendix 15, Table 5).

The univariate analysis showed that patients who had a 'prolonged stay' or 'increased LOS' had significantly lower mean MUAC and HC SDS (non-significant for differences in mean HC SDS between 'increased LOS' categories). There were no other significant differences for these parameters between categories of the clinical outcomes (no/yes). For the assessment of lean mass, the admission BIA SDS (BIA_{st}, BIA_{sup} and BIA_{all}) were all significantly lower in patients who had a 'prolonged stay', an 'increased LOS', and 'complications' during their hospitalisation. Once more, analysis of the other clinical outcomes did not result in any significant observed differences between groups. On the other hand, for FM parameters, Triceps and Subscapular SFT SDS on admission were significantly lower on average for patients who had an 'increased LOS', a 'prolonged stay', and a 'decrease in BMI'.

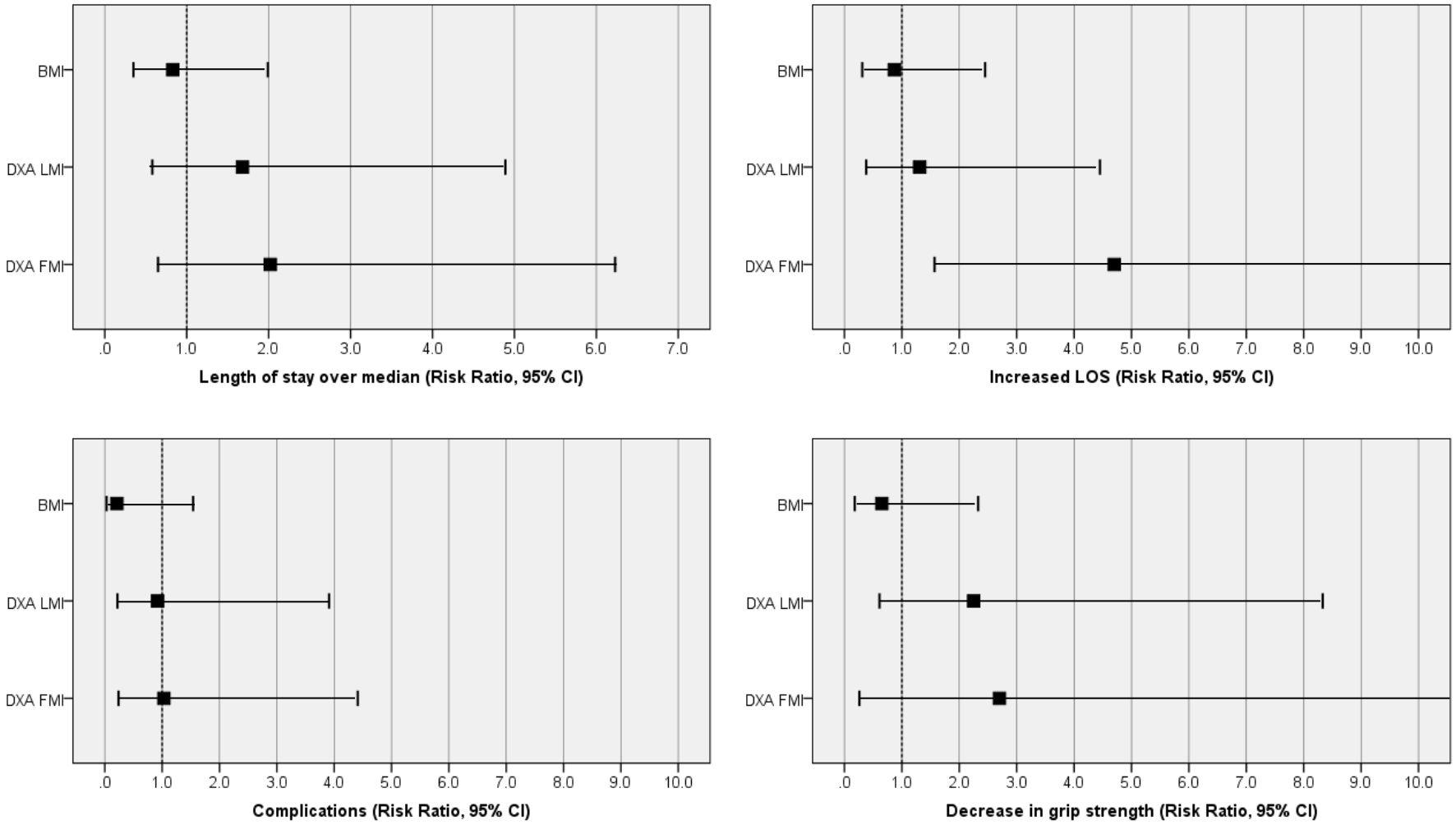
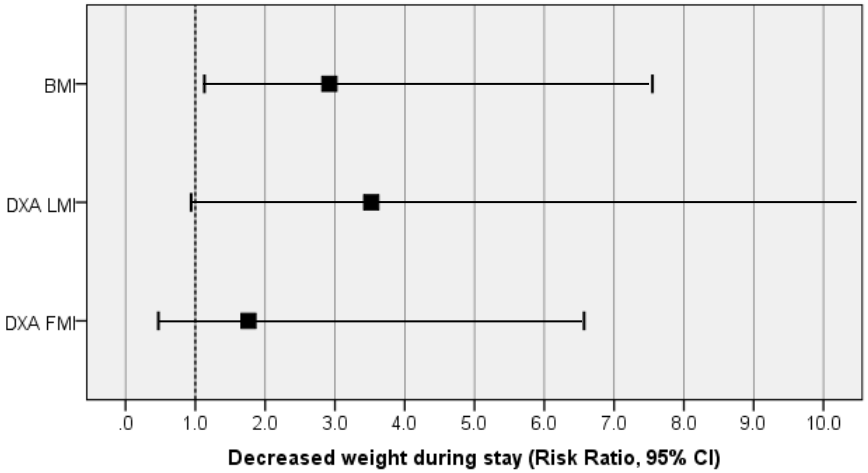
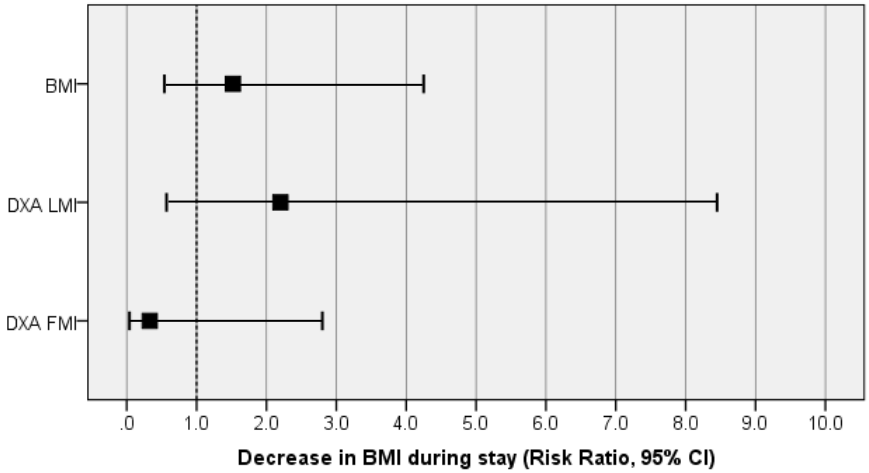


Figure 8.2. Summary of *RR* for worse clinical outcomes in patients with abnormal BMI, LMI and FMI SDS on admission.

Graphs show the RR (■) and 95% CI for the RR (I) for each parameter. Dotted line shows a RR=1 (no risk).





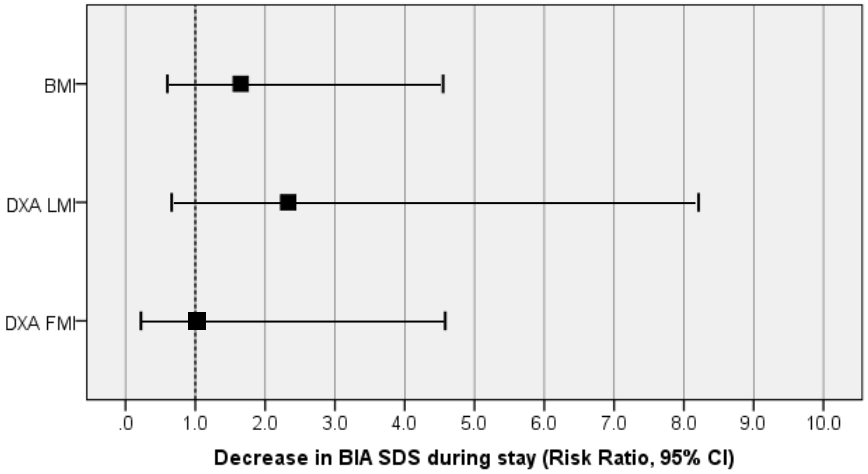


Figure 8.2. *(Cont.)* Summary of *RR* for worse clinical outcomes in patients with abnormal BMI, LMI and FMI SDS on admission.

8.7.2. Abnormal HC, MUAC, Biceps SFT and BIA SDS on admission

The calculation of risk for worse clinical outcomes, (details in Appendix 15, Table 6), showed a significantly increased risk for an 'prolonged stay' in patients with abnormal HC and BIA (all parameters). The risk for an 'increased LOS' was higher in patients with abnormal Biceps and Triceps SFTs, in addition to the abnormal HC and BIA SDS. Other than this, the only significant increased risk was an increased risk for complications in patients with abnormal Biceps SFT. It should be highlighted that SFTs (particularly subscapular and suprailiac) were not able to detect any children with an abnormal SDS <-2 or >2.

Overall, as can be observed from the summary graphs in Figures 8.3-8.5, the risk for worse outcomes in the case of MUAC and HC is similar to WT and HT SDS, while BIA SDS had similar results to those obtained using DXA LM. The similarities, however, were less clear when considering the 4-stes SFTs compared to DXA FM. This suggests that the use of HC. MUAC and BIA as surrogate measurements, particularly for the case of BIA, could still be able to identify children who are likely to develop worst clinical outcomes during their hospital admission.

8.8. Multivariate regression models: parameters to assess malnutrition

The parameters of WT, HT, DXA LM and FM were used to calculated logistic regression models to predict the odds of the clinical outcomes occurring. The clinical outcome chosen for this analysis was 'increased LOS'. This was chosen considering it had the most significant associations (from the univariate analyses described in the previous sections) with the anthropometric and BC parameters SDS on admission. It was also recorded for all the patients in the study. In comparison, the outcomes for the decrease in GS, WT, BMI and BIA during hospitalisation all showed non-significant associations to the baseline anthropometric and BC SDS. This could have been the result of a more limited sample size preventing the detection of significant associations, compounded by the fact that only small changes in the parameters were observed between admission and discharge. Considering many patients had a short stay (<9 days), no large differences were expected, particularly for HT and HC. There were, additionally, some identified cases of children with adolescent scoliosis undergoing corrective spinal surgery, where measurement error for HT on admission led to a large 'false' change in HT and also affected the changes in BMI and BIA SDS. Thus, these outcomes could have also been confounded by the error of the performed measurements on admission and/or discharge.

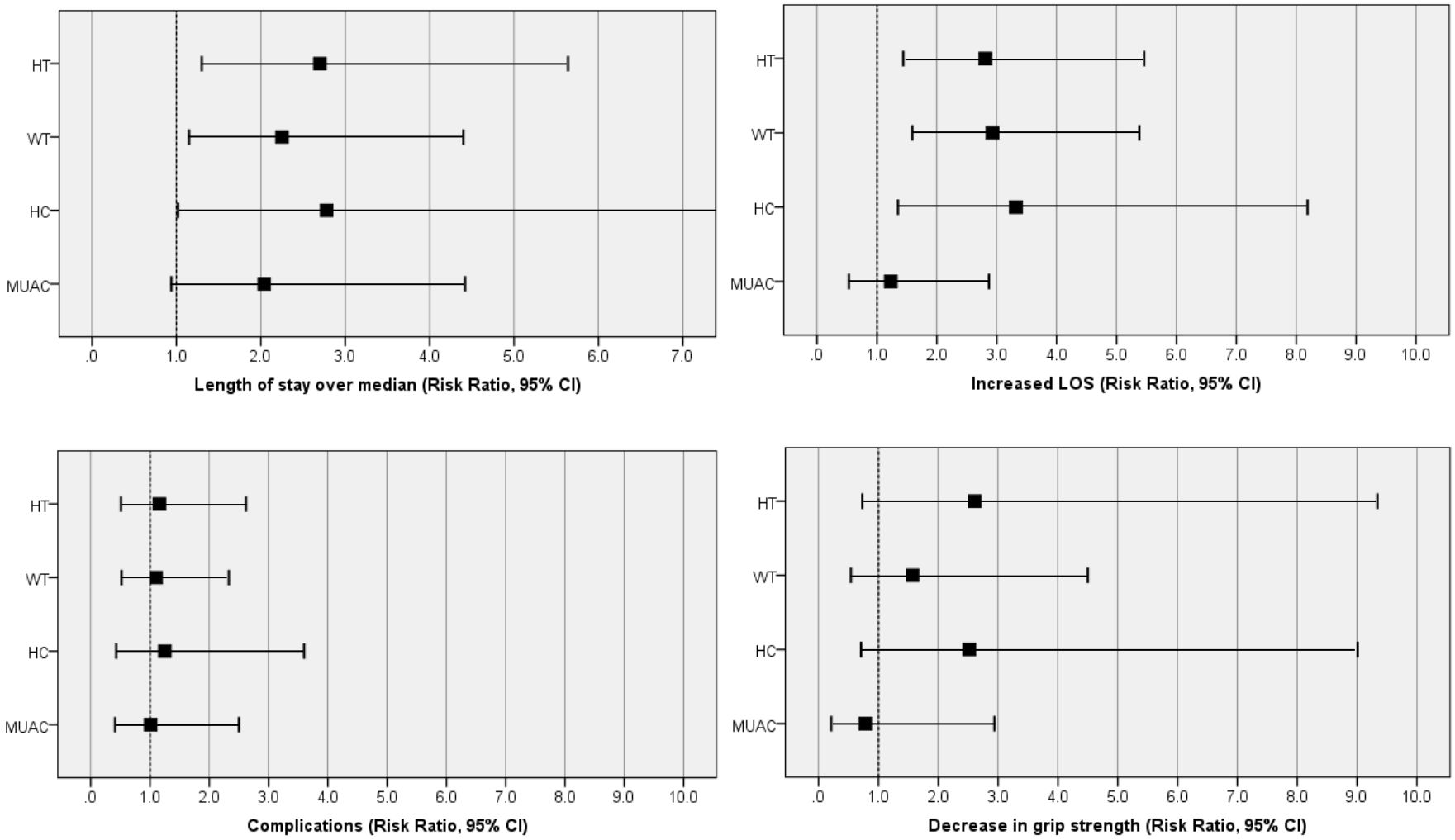


Figure 8.3. Summary of *RR* for worse clinical outcomes in patients with abnormal SDS for anthropometric parameters on admission.
Graphs show the RR (■) and 95% CI for the RR (I) for each parameter. Dotted line shows a RR=1 (no risk).

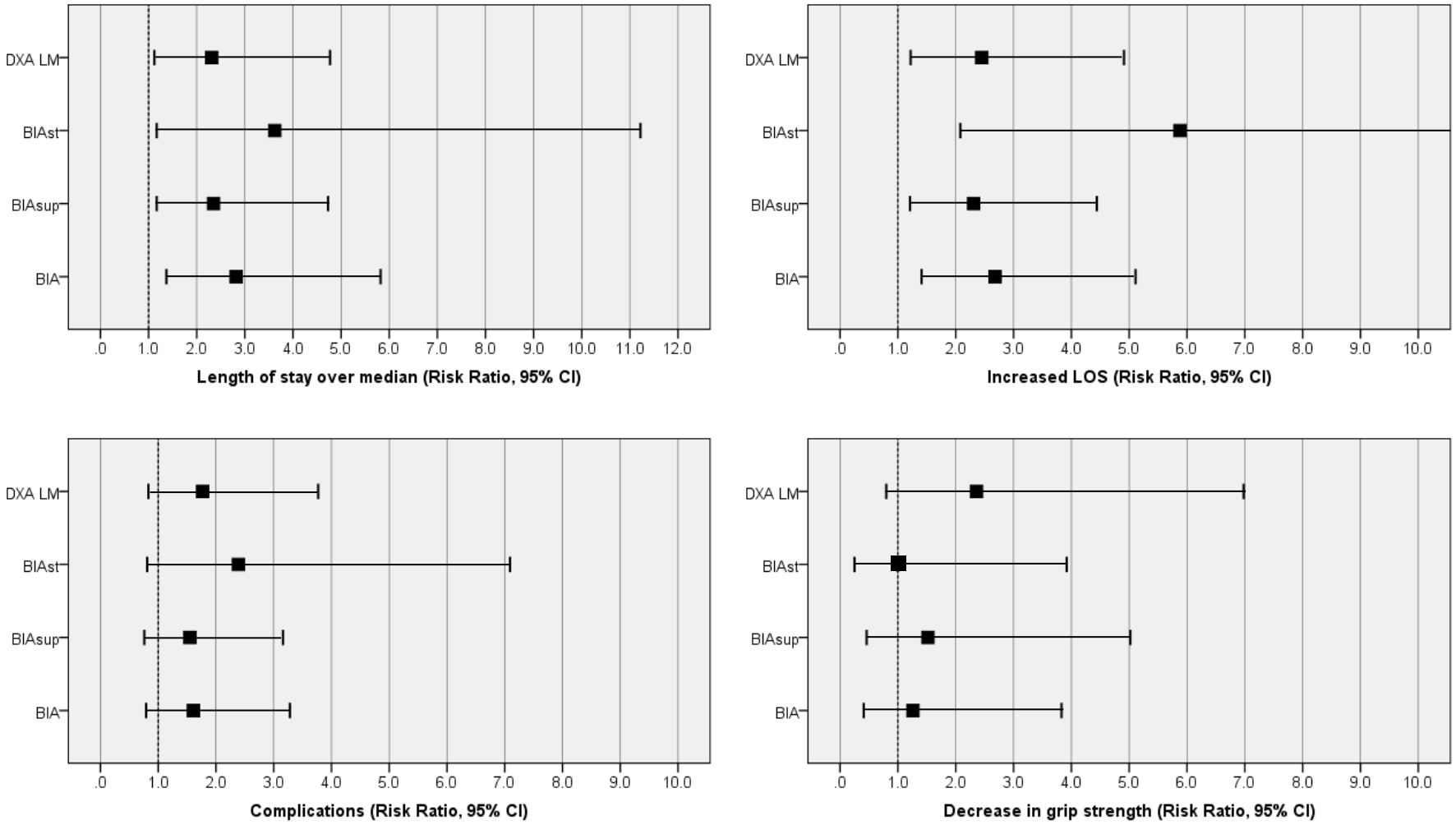


Figure 8.4. Summary of *RR* for worse clinical outcomes in patients with abnormal SDS for lean mass parameters on admission.
Graphs show the RR (■) and 95% CI for the RR (I) for each parameter. Dotted line shows a RR=1 (no risk).

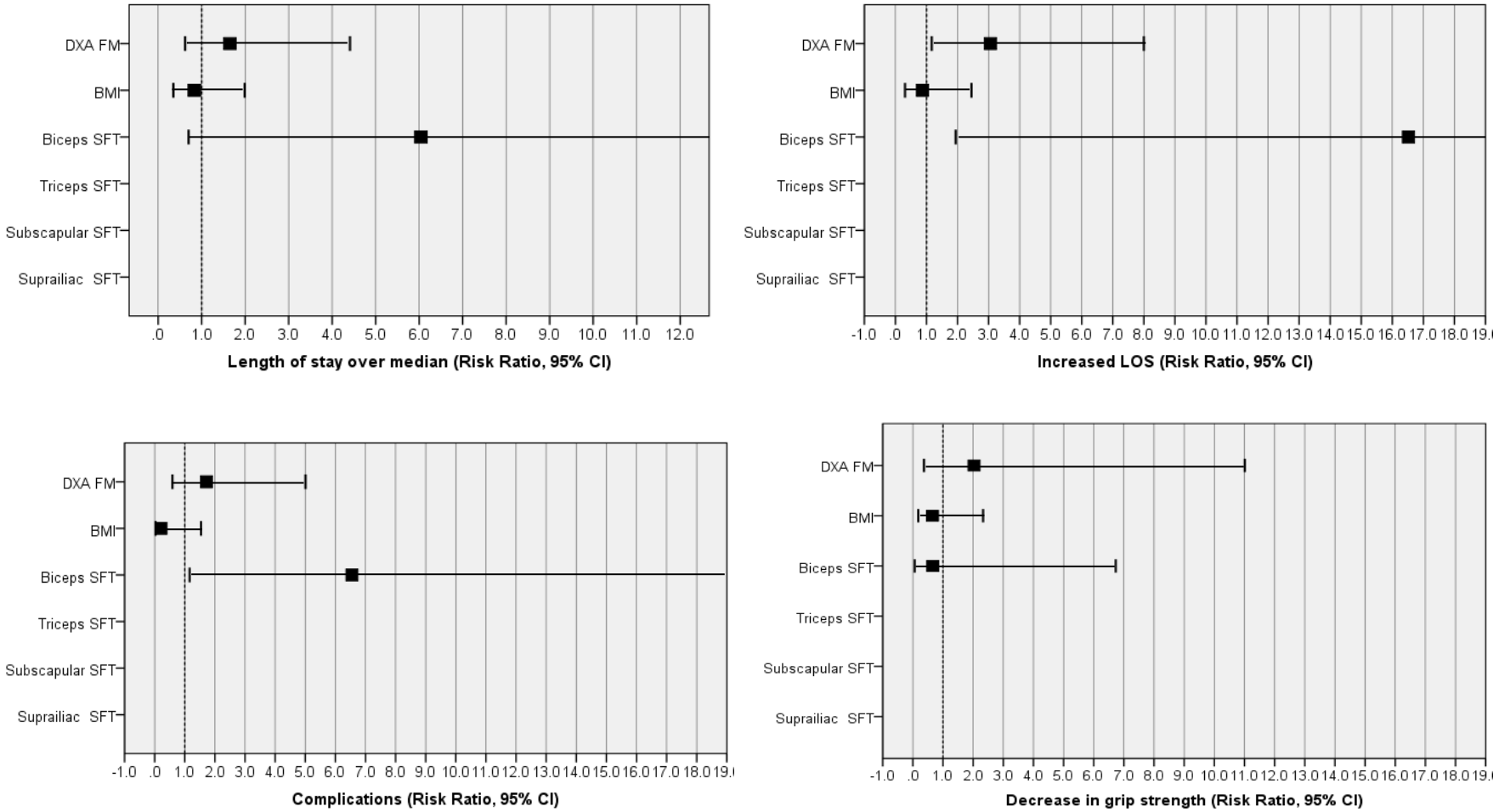


Figure 8.5. Summary of *RR* for worse clinical outcomes in patients with abnormal SDS for fat mass parameters on admission.

Graphs show the RR (■) and 95% CI for the RR (I) for each parameter. Dotted line shows a RR=1 (no risk).

Predictive models for 'increased LOS' were calculated for the abSDS of WT, HT, DXA LM and FM as single predictors; adjusting for admission group, complications, and dietetic referral. These adjustments were selected based on the univariate observations of significant associations with the clinical outcomes. Other variables (steroid medication, decrease in appetite, wheelchair-user) were tested with the final models, and it was confirmed they were not significant predictors.

Table 8.12 shows the best models for each parameter on admission. For WT and HT abSDS, adjusting for complications during the period of hospitalisation improved on the model, while this was not required for LM abSDS. This models indicate that the odds of having an 'increased LOS' increase by 5.6 and 5.2 if the child presents with an abnormal HT SDS or WT SDS respectively. Similarly, the odds of having an increased LOS were 4.6 higher in patients with abnormal (low) LM SDS on admission. For FM, the use of the size-adjusted parameter (FMI) resulted in a better predictive model, with an increase in odds of 5.4 for an increased LOS for patients with abnormal FMI SDS on admission.

Finally, several combinations of these parameters were included in a model to identify the combination of measurements on admission that would best predict de odds of an increased LOS. Table 8.13 summarises the two most significant models using the combination of: WT, HT, DXA LM, DXA FM (or the indices LMI, FMI). It was encouraging to find that the strongest predictive model resulted from the use of LM and FMI abnormal SDS categories (Model 1), which was improved further after adjustment to 'complications' during hospitalisation (Model 2). The use of HT abnormal SDS instead of LM abSDS also resulted in a good model (Model 3), again improved after the inclusion of 'complications' in the model (Model 4).

The clinical outcome of 'complications' was interesting, as it seemed to have a strong association to LM (particularly to LM SDS, rather than abSDS). However, the logistic regression models predicting this outcome using LM abSDS (and LMI abSDS) resulted in non-significant coefficients, suggesting that this cut-off to define 'abnormal SDS' might not be able to detect patients who are likely to have more complications.

Thus, rather than using the binary variables, the continuous numerical variables were included in the predictive model for 'complications'. The measurements of WT, HT, DXA FM, DXA LM and FMI SDS on admission were all non-significant. LMI SDS however, was significant, resulting in a prediction model that explained 8% (Nagelkerke R^2) of the variance in 'increased LOS' and correctly classified 80.5% of cases. In this model, increasing LMI SDS were significantly associated with a decrease in the likelihood of an increased LOS.

n=118		Predictors	*B* [a]	*CI* [b]		*p* [c]	Nagelkerke R^2	% correct
HT	Model 1	HT abSDS	4.87	1.73	13.70	0.003	0.13	75.3
		Constant	0.23					
	Model 2	HT abSDS	5.58	1.84	16.90	0.002	0.23	76.3
		Complications	4.40	1.52	12.70	0.006		
		Constant	0.13					
WT	Model 1	WT abSDS	4.35	1.64	11.52	0.003	0.12	75.2
		Constant	0.21	0.00	0.00	0.000		
	Model 2	WT abSDS	5.17	1.81	14.78	0.002	0.22	76.2
		Complications	4.35	1.57	12.06	0.005		
		Constant	0.12			0.000		
LM	Model 1	LM abSDS	4.58	1.51	13.88	0.007	0.12	77.9
		Constant	0.18			0.000		
FMI	Model 1	FMI abSDS	5.36	1.27	22.56	0.022	0.09	78.3
		Constant	0.23			0.000		

Table 8.12. Best predictor models using the WT, HT, DXA LM or FM abSDS on admission to predict the odds of increased LOS.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05).

n=118	**Predictors**	***B*** [a]	***CI*** [b]	***p*** [c]	**Nagelkerke R^2**	**% correctly classified cases**
Model 1	LM abSDS	4.43	1.50 13.10	0.007	0.18	82.2
	FMI abSDS	5.77	1.49 22.33	0.011		
	Constant	0.14		0.000		
Model 2	**LM abSDS**	4.192	1.391 12.632	0.011	0.22 **	84.7
	FMI abSDS	6.105	1.553 23.989	0.010		
	Complications	3.191	1.051 9.688	0.041		
	Constant	4.192		0.000		
Model 3	HT abSDS	3.49	1.09 11.23	0.036	0.14	82.2
	FMI abSDS	5.34	1.41 20.24	0.014		
	Constant	0.16		0.000		
Model 4	**HT abSDS**	4.101	1.222 13.757	0.022	0.21 *	83.9
	FMI abSDS	5.714	1.448 22.549	0.013		
	Complications	3.913	1.286 11.905	0.016		
	Constant	0.115		0.000		

Table 8.13. Best predictor models using a combination of abSDS for the parameters on admission to predict the odds of increased LOS.
(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05). (**) Best predictor model, (*) second-best predictor model.

8.9. Summary of main findings

- Measurements of WT, HT, DXA LM and FM, either as SDS or using the cut-off of ± 2SDS, were significantly associated with the clinical outcomes of prolonged length of stay (>9 days) and increased LOS.
- BC measurements - particularly LM – were associated with the outcome of complications during hospitalisation; while WT and HT were not.
- Other clinical outcomes: decrease in GS (muscle function), WT, BMI and BIA SDS; were not significant associated in the univariate analyses with any of the baseline anthropometric and BC parameters.
- Parameters that were size-adjusted using HT2 (BMI, LMI and FMI) were no better than the unadjusted parameters (WT, DXA LM and DXA FM) for predicting clinical outcomes, at least as single predictors.
- Abnormal FMI and LMI SDS on admission resulted in a higher risk for most of the clinical outcomes compared to that observed for abnormal BMI SDS. However, these increased risks were not significant, except for DXA FMI abSDS being significantly associated with the risk of an increased LOS.
- The use of surrogate measurements of MUAC and HC instead of WT and HT, resulted in similar associations to the outcomes of prolonged stay, increased LOS, complications and decreased GS. BIA measurements also showed similar associations than those obtained using DXA LM for all the clinical outcomes. SFTs measurements did not have many significant associations to the clinical outcomes, except perhaps Triceps and Subscapular SFTs to both of the outcomes related to length of stay, and overall did not identify many (if any) patients with abnormal SDS that would have been categorised as presenting with the clinical outcomes.
- Constructed regression models showed that adjusting for complications improved the prediction of the likelihood of having an increased LOS, using HT or WT abSDS on admission as the predictors. Other significant prediction models were constructed using the predictors of abnormal LM SDS and abnormal FMI SDS.
- A multivariate logistic regression model was constricted for the outcome of ‘increased LOS’ using abnormal LM and FMI SDS on admission as predictors, and adjusted for ‘complications’ during hospitalisation. The model explained 22% of the variance in

'increased LOS', and correctly classified 82.2% of the cases. Having abnormal FMI and LM SDS on admission were significantly associated with an increased likelihood of an 'increased LOS'.

- The second-best model included HT abSDS and FMI abSDS on admission, together with 'complications'. This model explained 21% of the variance in the clinical outcome of 'increased LOS', and correctly classified 83.9% of the cases.

8.10. Discussion

8.10.1. Predicting LOS: importance of height and BC

The univariate analysis of the associations between the parameters SDS on admission and the categories of 'abnormal' SDS showed that both the standard measurements of WT and HT, as well as the measurements of LM and FM, were significantly associated with LOS (both 'prolonged stay' and 'increased LOS'). The observed associations between low WT and HT to clinical outcomes, especially LOS, are in agreement with previous studies (Aurangzeb et al. 2012; Becker et al. 2014; Hecht et al. 2014; Bechard et al. 2016; Abdelhadi et al. 2016).

Nevertheless, there is limited evidence from previous studies that abnormal BC (mainly low LM) can be associated with clinical outcomes, particularly in paediatrics. The observed results however, were in agreement with the available evidence that low LM is associated with increased LOS in adults (Ursula G Kyle et al. 2005; Pichard et al. 2004). Evidence in paediatrics also show that low fat mass stores in children undergoing surgery for congenital heart defects leads to worse clinical outcomes (Radman et al. 2014), and that CF children with low FM have worse pulmonary function (Chaves et al. 2009; Pedreira et al. 2005). However, these studies were carried out in specific patient populations that might not be comparable or reflect the situation of such a heterogenous sample of patients in this study.

When the parameters BMI, LMI and FMI were analysed, the results suggested these indices as single predictors might be less helpful in identifying the children who were likely to have an increased LOS. LMI and FMI abSDS still seemed to be associated with an increased risk for these outcomes, but the *RR* were usually not significant, except for the case of FMI abSDS. As has been observed in previous chapters of the thesis, where results indicated DXA LM seemed to be more affected (changed to higher SDS values) than DXA FM to adjustments of height, in this case the change in the associations with the clinical outcomes was also more pronounced than for FMI. The observed risk for children with LMI abSDS was lower than that reported using DXA LM abSDS, and suggests that increased LOS is associated to both short stature and low amounts of LM, whereby removing the effect of

height in the calculation of LMI, can lead to a weaker association to the outcome. Indeed, height seemed to be the parameter more strongly associated with LOS in this population.

BMI abSDS on admission was not associated with an increased risk for LOS, and had a lower association than that reported for WT abSDS, further supporting the idea that low height accounts for much of the observed associations to this clinical outcome. Our population is quite unique and different to what might be expected from a general hospital, in that most children have complex chronic conditions affecting their linear growth. Thus, the importance of height in relation to clinical outcomes might not be the same in other clinical settings.

The regression models constructed showed that HT abSDS seemed to be the best predictor for the likelihood of having an increased LOS, even more so after adjusting using the variable of 'complications'. Similarly, models using the predictors of WT or LM abSDS explained 12% of the variance in 'increased LOS', and the model of WT abSDS could also be improved further by adjusting for 'complications' during hospitalisation. FM abSDS was not a significant variable in the model as a single predictor, but FMI abSDS was.

There is no evidence in the literature on the advantages of BC measurements over simple measurements of weight and height for identifying paediatric patients who will develop worse clinical outcomes in a tertiary setting. The constructed multivariate models for the prediction of increased LOS, showed that measurements of LM and FMI abSDS were the best predictors for this clinical outcome. The second-best model included both HT abSDS and FMI abSDS. Addition of low weight SDS in the model was always non-significant after accounting for the effect of abnormal height and/or BC SDS. These results seem to suggest that the assessment of BC (FM and LM), in addition to HT, can be helpful in identifying children who are at risk of having an increased LOS, and should be investigated further.

However, it is possible that the observed associations between BC parameters and clinical outcomes is confounded by other issues such as the underlying diagnosis of the patients. Considering the study sample was very heterogenous, together with the use of generic clinical outcomes, means these results should be interpreted with care. More studies are needed to confirm the advantages of using BC measurements to predict clinical outcomes in select groups of patients using more specific clinical outcomes. Furthermore, evidence that the use of these measurements can help guide nutritional management and improve the clinical outcomes of patients is needed before it can be routinely implemented in practice. Thus, future studies should help identify when and on whom BC measurements provide an advantage over the standard assessment of weight and height.

8.10.2. BC for predicting clinical outcomes: importance of the technique used

As Chapter 1 has summarised, there are limited studies reporting associations between BC parameters and clinical outcomes in children (Wells & Fewtrell 2008), but more importantly, these have all used different measurements and criteria to assess fat and/or lean mass. This heterogeneity in the study characteristics hinder the ability to reach a consensus on the advantages of measuring BC in clinical practice, especially over the established measurements of weight and height. This study has used DXA as the clinical reference method in addition to a number of other more-simple techniques, all measured in a standardised manner (calculation of SDS from using UK BC reference data) that furthermore avoid the compounded error of using predictive equations that might be outdated and/or not be suitable for the population being studied.

The results in this chapter show the importance of the technique used to assess BC in relation to the associations to clinical outcomes. Similar to observed differences in the prevalence of 'malnutrition' by different parameters (Chapter 7), the associations to the various clinical outcomes were not always the same for all anthropometric and BC parameters. On the positive side, in agreement with my results on the validity of BIA SDS to DXA LM (Chapter 4), the associations to clinical outcomes using these parameters assessing lean mass were very similar. Furthermore, both BIA_{sup} and BIA_{st} had similar associations to the clinical outcomes; thus, providing different alternatives for the assessment of LM in clinical practice.

However, for the case of fat mass, SFTs failed to identify most of the children who had worse clinical outcomes during their hospitalisation. These measurements have practical limitations and are reliant on the training and expertise of the assessor. However, considering they are simple and can be measured in a number of settings, in addition to the suggested importance of FM for identifying children with worse clinical outcomes, it might be worth exploring their use further (e.g. as aggregate estimates).

8.11. Conclusion

The results in this chapter highlight a possible role of BC measurements in the diagnosis of hospital malnutrition in this selective group of patients with complex diagnoses. The associations to the clinical outcomes, particularly LOS and complications, suggest implementing BC measurements in practice for certain selective groups, such as the one measured in this study, could confer an advantage over measurements of weight and height.

It also highlighted the importance of the techniques and parameters used to measure BC, as well as the chosen clinical outcomes. The limitations in the selection of clinical outcomes and the observational nature of the study design, mean that the results should be interpreted with care and used as basis for further research into the use of BC measurements in clinical practice. Further evidence on how these measurements perform in different settings, population groups and in relation to different clinical outcomes will help identify when and how best to use them in clinical practice to improve the diagnosis of malnutrition and the nutritional management of paediatric patients.

9 Screening for malnutrition risk in paediatric patients: an appraisal of different tools

9.1. Introduction

Malnutrition screening has the aim of identifying children who are likely to be malnourished on admission, but also to identify those children who are at risk of developing malnutrition during their hospital stay. Thus, the implementation of MSTs in a hospital setting should allow the timely implementation of nutritional referral and support to prevent further deterioration of the patient's nutritional status (Hartman et al. 2012).

A recent paper by Huysentruyt et al., (2016) has outlined a nutritional care algorithm, which combines nutritional screening and assessment, and highlights the importance of combining these two approaches to identify, manage and prevent malnutrition in paediatric patients. The previous chapters of the thesis have focused on describing the nutritional status of patients admitted to a tertiary level paediatric centre, and exploring the best parameters to diagnose malnutrition in these complex children with a range of diagnoses. Now, the aim of the present chapter is to complement this picture with an assessment of different tools available to screen for malnutrition in paediatric patients.

Chapter 1 has summarised some of the main paediatric MSTs available, and the evidence regarding their applicability and validation in clinical settings. Although there is some evidence for how some of the MSTs compare to each other, the patient's nutritional status, and some outcomes (mainly LOS); the studies once more have approached this using a variety of study designs and methods, making it difficult to reach a consensus on their use and applicability to different settings (van den Berg et al. 2010). A recent multi-centre European study on the validation of three MSTs: PYMS, STAMP and STRONGkids (Chourdakis et al. 2016), showed how the risk of malnutrition differed markedly depending on the tool used. They found some associations to the patient's nutritional status on admission (using BMI and HFA SDS), but concluded the tools missed a considerable proportion of children with abnormal anthropometric parameters, and could not recommend the use of one tool over another.

The present study had the advantage of having measured, not just the more-simple anthropometric indicators, but a more diverse range of BC parameters. Considering there is still debate on which parameter should be used to diagnose malnutrition, this provided the

opportunity to validate these three MSTs using measurements of BC, while also relating them to clinical outcomes in a selective population of complex paediatric patients.

9.2. Chapter objectives

1. Describe the risk of malnutrition using different paediatric MSTs, plus the GOSH screening flowchart; and identify the variables predicting malnutrition risk on admission.
2. Compare how the tools compare to each other in their classification of malnutrition risk on admission (Concurrent validity).
3. Determine the associations between malnutrition risk assessed by the different tools and anthropometric/BC parameters on admission (Diagnostic validity).
4. Analyse the associations between malnutrition risk on admission and clinical outcomes at discharge (Predictive validity).

9.3. Methods

9.3.1. Study population and recruitment

The chapter objectives were investigated in the cohort of patients enrolled to the BodyBasics study. Previous chapters have already described the recruitment procedures, study design, (Chapter 3) and patient characteristics on admission (Chapter 7).

9.3.2. Data collection tools

Three MSTs developed for paediatric populations: STAMP, PYMS and STRONGkids in Europe were assessed in all study patients. A detailed summary of the tools and the validation studies was presented in Chapter 1, Section 1.7. At the time of the study design, these were the most widely used/validated tools available in the literature. Chapter 3, Section 3.3.8 details the application of the tools for the study patients on admission and Appendix 5 includes the 3 MSTs used in the study and the GOSH screening flowchart.

The GOSH flowchart differs from the other 3 MSTs, since it simply refers patients (when >12 months old) to a dietitian if any of the following 3 criteria are met: 1) height and weight more than 2 centiles apart; 2) poor, none, or reduced food intake; 3) losses from diarrhoea (>5/day) or vomiting (>3/day). Thus, any of these criteria would lead to dietetic referral using GOSH flowchart, while patients would have to be classified at ‘high’ risk by the other 3 MSTs to be referred to a dietitian.

Data on the variables relating the patient's nutritional status on admission (described in Chapter 7), as well as anthropometric and BC parameter SDS on admission (Chapter 4 and 7), and clinical outcomes (Chapter 8) were used for the analysis of this chapter. Previous chapters and the main methods chapter (Chapter 3) describe the data collection and analysis for these variables.

9.3.3. Data analysis and statistics

The analyses were generally performed first using the 3 MSTs (STAMP, STRONGkids and PYMS) that characterised patients into the three risk categories: 'low', 'medium', 'high' risk. Subsequently, the analysis was performed using the re-calculated binary variables of 'referral/no referral', indicating patients that had been classified as 'high' risk by the tools and who would be then expected to be referred to a dietitian per the tools guidelines of implementation. This new binary category allowed the analysis of the data in terms of risk ratios (RR), but also had the advantage that the GOSH screening flowchart, which only directs patients for dietetic referral or not rather than classifying them into categories of risk, could also be included in the analysis.

The data on malnutrition risk (low, medium or high) assessed by the different MSTs was summarised using descriptive statistics: frequencies and %. Differences between the observed frequencies in medical/surgical and female/male patients was then analysed. Subsequently, the variables associated to the risk of malnutrition on admission using the different tools was tested using Chi-squared and Fisher's exact tests of significance.

Concurrent validity (the comparison of the different MSTs) was assessed using Cohen's kappa to test the agreement between tools in their assessment of the patients into the risk categories, and subsequently in terms of dietetic referral. The diagnostic/criterion validity of the tools was explored by analysing the mean difference in anthropometric (WT, HT) and BC (DXA FM and LM) SDS on admission per categories of risk, and between patients being referred or not by the tools. The RR for having abnormal SDS (<-2 or >2 SDS) for the different parameters if being referred by the MSTs were calculated and summarised in tables with their *CI*. The predictive validity of the tools was finally tested by comparing the risk assessed by the tools to the clinical outcomes: prolonged stay, increased LOS, complications and reduced grip strength. These outcomes have been previously described in Chapter 8. Multivariate prediction models were calculated to adjust for variables such as dietetic referral during hospitalisation, and to compare models that included anthropometric/BC parameters together with the MSTs to test if the tools predicted outcomes better (identified children at risk and not just with malnutrition on admission).

9.4. Malnutrition risk on admission

9.4.1. Quantifying risk of malnutrition using PYMS, STAMP, STRONGkids and GOSH flowchart

The risk of malnutrition on admission, assessed by the 4 tools, is summarised in Table 9.1. STAMP classified a larger percentage of patients as high-risk (35.5%), compared to PYMS (25%) and STRONGkids (18.4%). However, patients enrolled to the study were mostly classified as low-risk using PYMS, and medium-risk using both STRONGkids and STAMP. Regarding differences in the number of patients being referred for dietetic assessment by the tools, GOSH identified the largest number of patients that should be seen by a dietitian during their admission (39.5%), compared to the other three MSTs.

Figure 9.1 shows the differing patterns of categorisation between tools. It is clear that PYMS had a markedly different pattern compared with STRONGkids and STAMP, something that is likely related to the difference in the way the tools assess the current nutritional status of the patients, and the consideration of the patient's underlying diagnosis.

n=152	**PYMS**		**STAMP**		**STRONGkids**		**GOSH**	
	Freq	*%*	*Freq*	*%*	*Freq*	*%*	*Freq*	*%*
low-risk	70	46.1	24	15.8	25	16.4		
medium-risk	44	28.9	74	48.7	99	65.1		
high-risk	38	25.0	54	35.5	28	18.4		
not referred	114	75.0	98	64.5	124	81.6	92	60.5
referred	38	25.0	54	35.5	28	18.4	60	39.5

Table 9.1. Malnutrition risk and dietetic referral on admission by 3 MSTs and GOSH flowchart

The differences between male/female and surgical/medical patients for the different tools are summarised in Tables 9.2 and 9.3. There were no significant differences between the risk categories for male or female patients; not a significant difference in age between the different risk categories of the tools. However, the proportion of patients in the different risk categories was significantly different between surgical and medical admissions using STAMP and STRONGkids. Surgical patients were more often categorised as either medium or high-risk rather than low-risk. This is likely to be mainly the effect of the underlying diagnoses of these patients, something that is assessed by both of these tools but not by PYMS, where surgical patients were still categorised more as high-risk but this marked difference was not observed

(non-significant). However, when assessing the proportions of patients being referred ('high-risk by the MSTs) or not, there was no significant difference between medical and surgical groups of patients assessed using any of the tools.

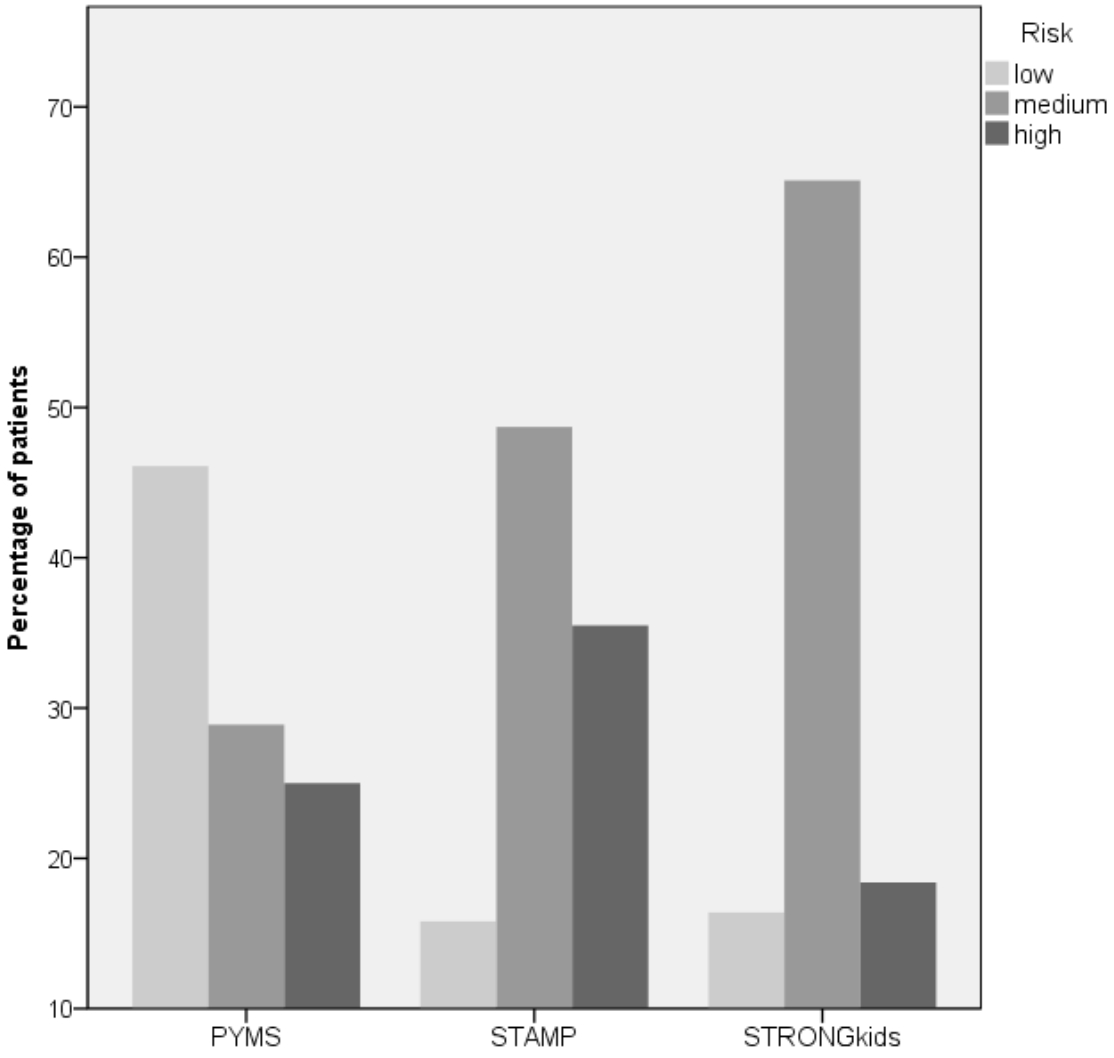


Figure 9.1. Summary graph of malnutrition risk on admission assessed by PYMS, STAMP and STRONGkids.

Graph shows the percentage of patients classified as low, medium and high risk for each MST.

n=152		**Medical**	**Surgical**	*p* [a]	**Sex** (*p* [b])	**Age** (*p* [c])
PYMS	low-risk	55.4	37.2	0.067	0.922	0.853
	medium-risk	25.7	32.1			
	high-risk	18.9	30.8			
STAMP	low-risk	24.3	7.7	0.016*	0.184	0.874
	medium-risk	45.9	51.3			
	high-risk	29.7	41.0			
STRONG kids	low-risk	27.0	6.4	0.001*	0.540	0.976
	medium-risk	52.7	76.9			
	high-risk	20.3	16.7			

Table 9.2. Differences in malnutrition risk on admission between admission groups, male/female and age.

Percentage (%) of medical and surgical patients classified as low, medium and high-risk by the different MSTs. (a) Chi-squared test for differences between medical and surgical groups, (*) significant (p<0.05); (b) Chi-squared test p-value for the differences between male and female, all non-significant; (c) One way ANOVA p-value for differences in mean age between risk groups, all non-significant.

n=152		**Medical**	**Surgical**	*p*	**Sex** (*p*)	**Age** (*p*)
PYMS	not referred	81.1	69.2	0.133	0.852	0.739
	referred	18.9	30.8			
STAMP	not referred	70.3	59.0	0.176	0.397	0.943
	referred	29.7	41.0			
STRONGkids	not referred	79.7	83.3	0.676	0.835	0.849
	referred	20.3	16.7			
GOSH	not referred	56.8	64.1	0.408	0.868	0.696
	referred	43.2	35.9			

Table 9.3. Differences in patient dietetic referral on admission between admission groups, male/female and age.

Percentage (%) of medical and surgical patients that would have been referred to a dietitian. (a) Chi-squared test for differences between medical and surgical groups, all non- significant (p<0.05); (b) Chi-squared test p-value for the differences between male and female, all non-significant; (c) One way ANOVA p-value for differences in mean age between referral groups, all non-significant.

9.4.2. Predictor variables for malnutrition risk on admission

The variables associated with the risk of malnutrition on admission using the different tools was assessed using the collected variables on admission regarding the 4 domains: diet-related, steroid medication, fluid restriction and wheelchair-user. Table 9.4 summarises the observed significance of these tests, showing that diet-related variables were understandably the most associated with risk on admission, particularly dietary restrictions, patients on EN/PN feeding and those who had previously been referred for dietetic advice. It is likely some of these associations are influenced by the underlying diagnoses of the patients, particularly for those patients on EN/PN feeding and who had been seen previously by a dietitian, as these variables could be identifying children with chronic GI conditions who are more at risk of malnutrition; rather than suggesting the dietary advice or the EN/PN prescription is the cause of the higher risk of malnutrition on admission.

n=152	**Steroids**	**EN/PN**	**Restricted diet**	**Intake / appetite problems**	**Dietetic advice**	**Fluid restriction**	**Wheelchair user**
Malnutrition risk [a]							
PYMS	0.837	0.810	0.495	0.198	0.575	0.541	0.736
STAMP	0.425	0.078	0.034	0.093	0.000	0.011	0.090
STRONGkids	0.612	0.003	0.000	0.114	0.000	0.173	0.268
Referral [b]							
PYMS	0.782	0.674	1.000	0.005	0.504	0.052	0.797
STAMP	1.000	0.812	0.243	0.096	0.348	0.276	0.564
STRONGkids	0.771	0.133	0.112	0.039	0.004	0.005	0.057
GOSH	0.723	0.006	0.000	0.067	0.000	0.211	0.740

Table 9.4. Associations between predictor variables and malnutrition risk on admission assessed by different tools.

(a) Analysis on the associations between the predictor variables on admission and the categories of malnutrition risk (low, medium, high), (b) associations between predictor variables and referral/non-referral to a dietitian by the different MSTs and GOSH flowchart. Data analysed using Chi-squared/Fisher's exact tests of significance, Highlighted values show significant results (p<0.05).

9.5. Concurrent validity

The agreement between the tools is summarised in Tables 9.5 and 9.10. The highest overall agreement was found between STRONGkids and STAMP, however, the calculated kappa was only 0.34 indicating a poor agreement in the classification of individual patients according to: 'low', medium' and 'high' risk categories. PYMS showed a poor agreement to both STAMP and STRONGkids with approximately only a 45% overall agreement, and a kappa of approximately 0.2.

The agreement between referral or not by the tools was better, especially between GOSH and STAMP (79% agreement, κ=0.6) and STRONGkids and PYMS (82.9% agreement, κ=0.5). All other associations between the tools were generally poor, with the weakest agreement observed between GOSH and both PYMS and STRONGkids.

n=152	**Agreement** *(%)*	***κ*** [a]	***CI*** [b]		***p*** [c]
STRONG kids * STAMP	61.2	0.34	0.22	0.47	0.000*
STRONG kids * PYMS	46.7	0.23	0.12	0.33	0.000*
STAMP * PYMS	44.1	0.20	0.09	0.30	0.000*

Table 9.5. Agreement between PYMS, STAMP and STRONGkids risk categories on admission

(a) Cohen's kappa (κ) as a measure of agreement between the categories of the MSTs, (b) 95% confidence interval of κ, (c) p-value for significance of κ, (*) all significant (p<0.05).

n=152	**Agreement** *(%)*	***κ*** [a]	***CI*** [b]		***p*** [c]
STRONGkids * PYMS	82.9	0.50	0.34	0.66	0.000*
STAMP * GOSH	78.9	0.55	0.42	0.69	0.000*
STAMP * STRONGkids	73.7	0.36	0.21	0.51	0.000*
STAMP * PYMS	73.7	0.38	0.23	0.54	0.000*
GOSH * PYMS	71.1	0.35	0.20	0.50	0.000*
GOSH * STRONGkids	64.5	0.18	0.04	0.32	0.011*

Table 9.6. Agreement between PYMS, STAMP, STRONGkids and GOSH for patient referral on admission due to the risk of malnutrition.

(a) Cohen's kappa (κ) as a measure of agreement between tools according to patient dietetic referral, (b) 95% confidence interval of κ, (c) p-value for significance of κ, (*) all significant (p<0.05).

9.6. Diagnostic validity: associations to WT, HT, BMI, BC DXA

To assess if the MSTs were able to identify children who were malnourished on admission, the mean SDS for the parameters of WT, HT, DXA LM and DXA FM were compared between the different risk categories of each tool (detail in Appendix 16, Table 1). Figure 9.2 summarises the mean SDS for each parameter by each of the MSTs risk categories. In terms of HT assessment, STAMP and STRONGkids categories were significantly different, so that patients categorised as high-risk had on average lower HT SDS. Furthermore, there was a graded effect, where low-risk categories had the highest mean HT SDS, followed by the medium and then the high-risk patients having the lowest HT SDS. PYMS however, did not show a significant difference in the HT SDS between risk categories, meaning some of the patients with low HT that could possibly benefit from nutritional referral and management, were not being identified by this tool.

For both WT and DXA LM, all MSTs showed significant differences for the parameter's mean SDS between low, medium and high-risk categories. However, the categories deferred more markedly for STAMP and STRONGkids, with low-risk patients showing the highest SDS, followed by the medium-risk, and then high-risk patients having on average the worse (lowest) WT and DXA LM SDS. This pattern was not as discernible for PYMS classification, where particularly low-risk patients had low SDS, particularly for DXA LM, compared to the medium-risk category. This meant at least some of the PYMS-classified low-risk patients would have low HT, WT and LM SDS.

Regarding DXA FM, PYMS and STAMP did not seem to be able to discern patients with differing FM SDS between the risk categories. The mean DXA FM SDS were only significantly different between categories for STRONGkids, where high-risk patients had on average lower FM compared to both the medium-risk and low-risk categories.

The analysis of the binary variables for referral (Table 9.7) corroborate the observed results from the analysis using the categories of risk for PYMS, STAMP and STRONGkids. There was a significant difference between the mean SDS for HT, WT, DXA FM and DXA LM between patients being referred and not referred (low and medium-risk) assessed using STRONGkids; where patients referred had lower mean SDS for the parameters. A similar finding was observed for STAMP, with the exception that the mean DXA FM SDS were not significantly different between referred and not-referred patients. Patients being identified for referral by PYMS only had significantly lower mean SDS for WT and DXA LM (less significant than those of STAMP and STRONGkids); while GOSH referrals were only significantly lower in WT and FM SDS than those not referred.

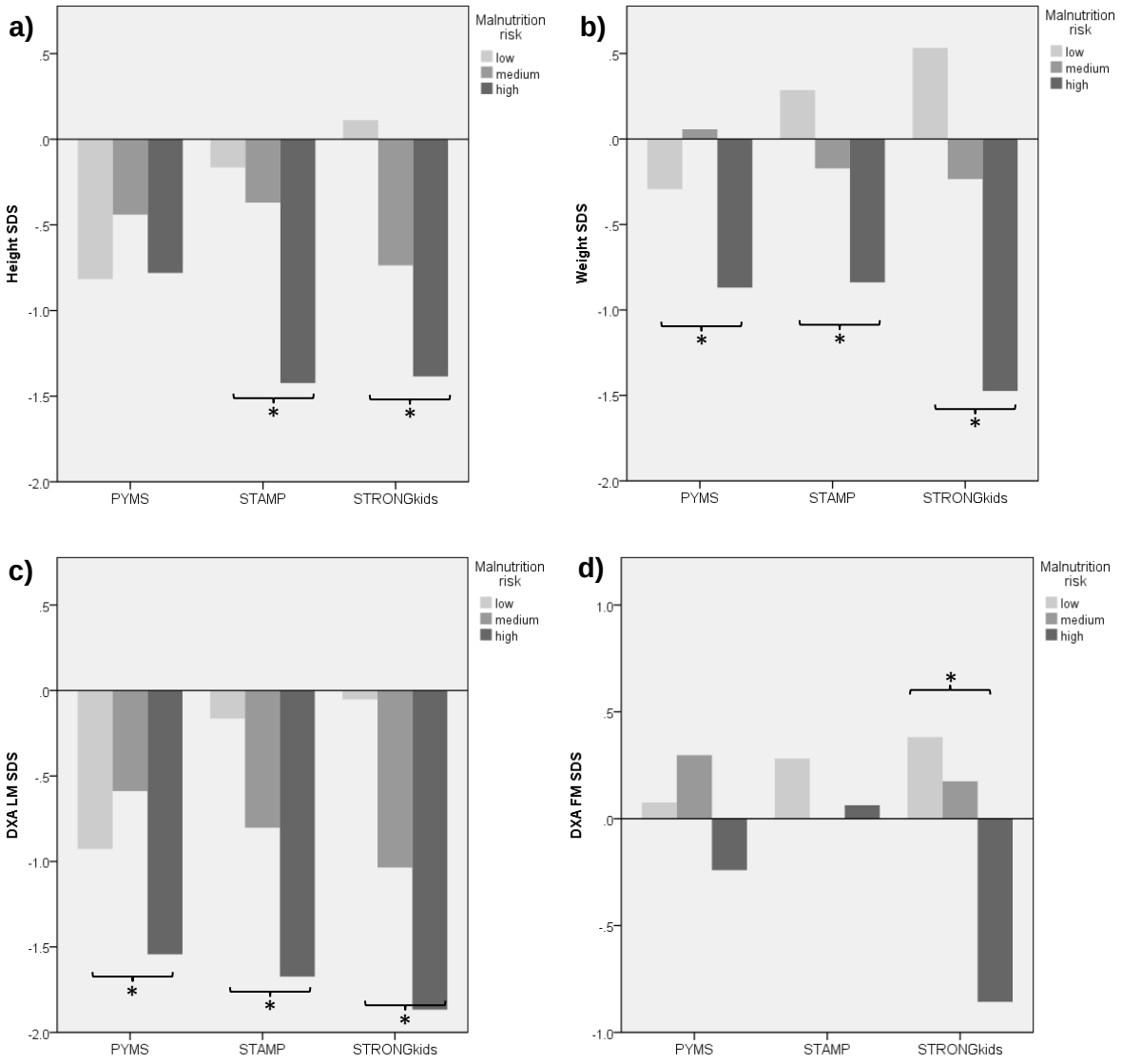


Figure 9.2. Mean SDS of WT, HT DXA LM and DXA FM on admission according to the risk categories for each MST.

Graphs show mean SDS (bar) for (a) HT, (b) WT, (c) DXA LM, (d) and DXA FM for each risk category (low, medium and high) by each of the MSTs. (*) significantly different mean SDS for the parameter between risk categories.

		HT SDS			WT SDS			DXA LM SDS			DXA FM SDS		
		mean	*SD*	*p* [a]	*mean*	*SD*	*p* [a]	*mean*	*SD*	*p* [a]	*mean*	*SD*	*p* [a]
PYMS	not referred	-0.68	1.41	0.731	-0.16	1.54	0.024	-0.79	1.35	0.018	0.16	1.17	0.131
	referred	-0.78	1.82		-0.87	1.98		-1.54	1.76		-0.24	1.43	
STAMP	not referred	-0.32	1.15	0.000	-0.06	1.21	0.006	-0.63	1.21	0.000	0.07	1.02	0.964
	referred	-1.42	1.82		-0.84	2.24		-1.67	1.75		0.06	1.64	
STRONGkids	not referred	-0.55	1.38	0.012	-0.08	1.44	0.000	-0.82	1.37	0.006	0.22	1.15	0.001
	referred	-1.39	1.87		-1.47	2.19		-1.87	1.82		-0.86	1.41	
GOSH	not referred	-0.70	1.50	0.986	-0.60	1.63	0.016	-0.92	1.48	0.665	-0.18	1.07	0.006
	referred	-0.70	1.53		0.07	1.69		-1.04	1.48		0.44	1.39	

Table 9.7. Associations between malnutrition risk and anthropometric/BC SDS on admission.

Table shows mean and SD of the SDS for each parameter (WT, HT, LM, FM) on admission for each of the risk categories. (a) One-way ANOVA testing the differences in mean SDS between risk categories, Highlighted values show significant results (p<0.05).

	HT SDS				WT SDS				DXA LM SDS				DXA FM SDS			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
PYMS	1.5	0.7	3.0	0.318	1.7	0.9	3.3	0.106	2.4	1.2	4.8	0.027	1.9	0.7	5.1	0.308
STAMP	5.1	2.3	11.3	0.000	3.1	1.6	6.1	0.001	4.2	2.0	9.1	0.000	3.8	1.4	10.7	0.012
STRONGkids	2.5	1.2	4.9	0.021	2.6	1.4	4.8	0.008	2.5	1.2	5.2	0.042	2.5	0.9	7.0	0.107
GOSH	1.0	0.5	2.1	1.000	1.0	0.5	2.0	1.000	1.8	0.9	3.6	0.163	2.7	1.0	7.5	0.080

Table 9.8. Risk of abnormal anthropometric and BC SDS in patients classified as high-risk for malnutrition on admission.

(a) RR for abnormal anthropometric/BC SDS on admission between referred and not-referred patients, (b) 95% confidence interval of RR, (C) Fisher's exact test between proportion of patients with abnormal WT, HT, DXA LM and FM SDS between referral groups, Highlighted values show significant results (p<0.05).

The associations between the anthropometric and BC parameters on admission were furthermore tested using the calculated variables for 'abnormally low' (<-2 SDS) WT, HT, DXA LM and FM. Table 9.8 summarises the obtained RR for having a low SDS for the parameters between patients being referred ('high' risk) and those not referred. In general, the risk of having abnormally low SDS for all parameters was higher in the patients being referred than those not-referred. However, this was only significant for STAMP (all parameters) and STRONGkids (all except abnormal FM SDS)

9.7. Predictive validity: associations to clinical outcomes

The associations between the clinical outcomes and the risk of malnutrition assessed by the different MSTs and the GOSH flowchart were analysed by calculating the *RR* for negative outcomes between high-risk (referred) patients and low/medium-risk (not referred) patients. As the summary graphs in Figure 9.3 show (detail on Appendix 16, Table 2), high risk patients classified using STRONGkids, STAMP and PYMS all had significantly increased risk of having a prolonged hospital stay (>9 days) ($p<0.001$). Similarly, high-risk patients had an increased risk for a longer-than-predicted LOS ($p<0.05$), although this was not significant for STAMP ($p=0.073$). The patients referred by the GOSH flowchart however, did not have a significantly increased risk for either a prolonged stay ($p=0.616$) or longer-than-predicted LOS ($p=1.00$).

For the clinical outcome of complications, patients referred by all the MSTs and the GOSH flowchart were at significantly at increased risk compared to non-referred patients ($p=0.000$ PYMS, 0.040 STAMP, 0.021 STRONGkids and 0.026 GOSH). Notably, PYMS was the MST most strongly associated with increased LOS and complications; as well as a decrease in WT during admission as a marker for worsening nutritional status. STAMP and STRONGkids high-risk patients only had a small non-significant increased risk ($p=0.836$ and $p=1.00$ respectively) for this last outcome.

None of the patients referred by the tools had significant increased risk for a decrease in BMI or BIA as parameters of FM and LM respectively. Patients referred by all the tools furthermore showed a non-significant decrease in the risk for decreases in GS as a marker of decreasing muscle function. However, these clinical outcomes had limitations, as discussed in Chapter 8; making it difficult to detect a significant association to the risk from the different MSTs.

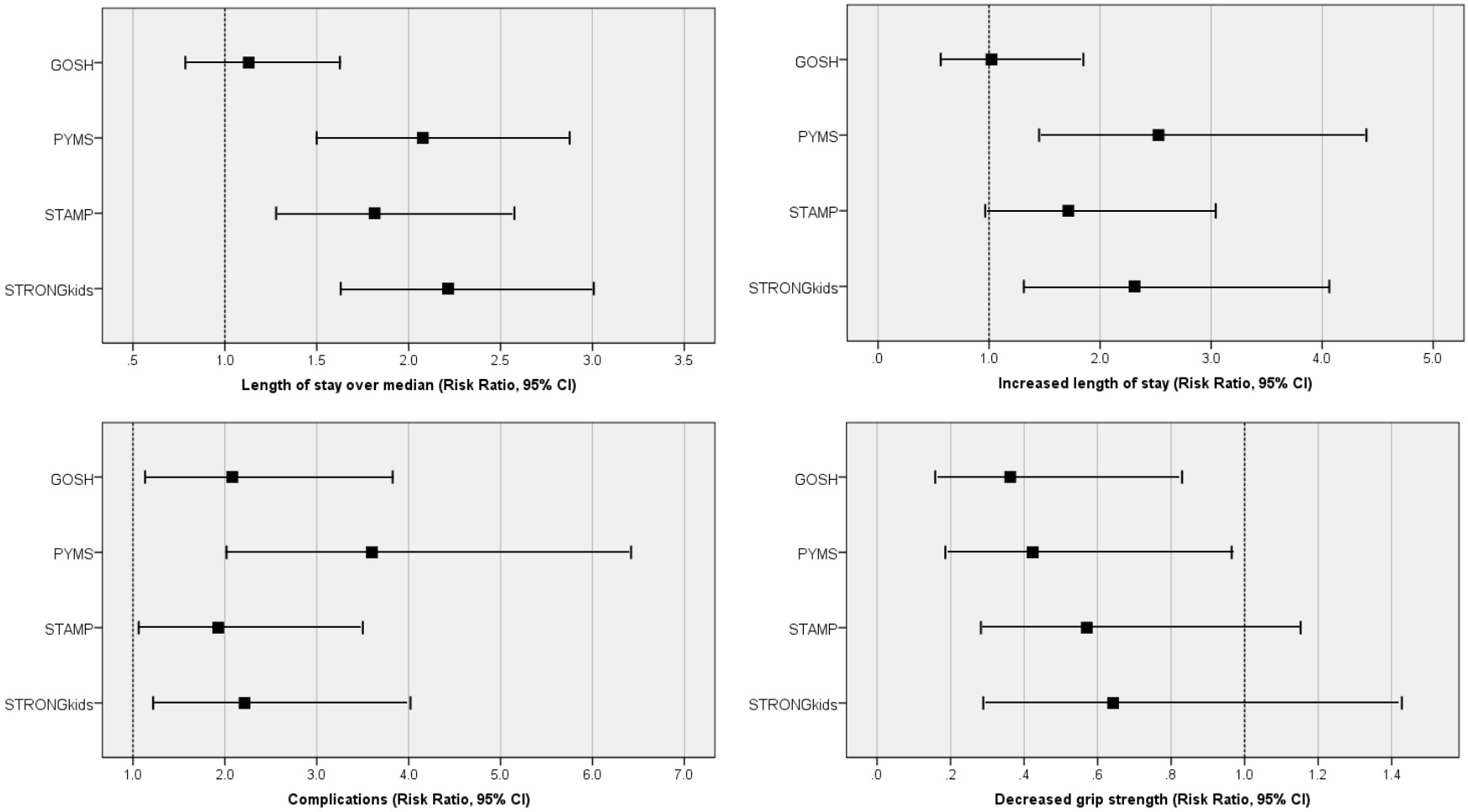
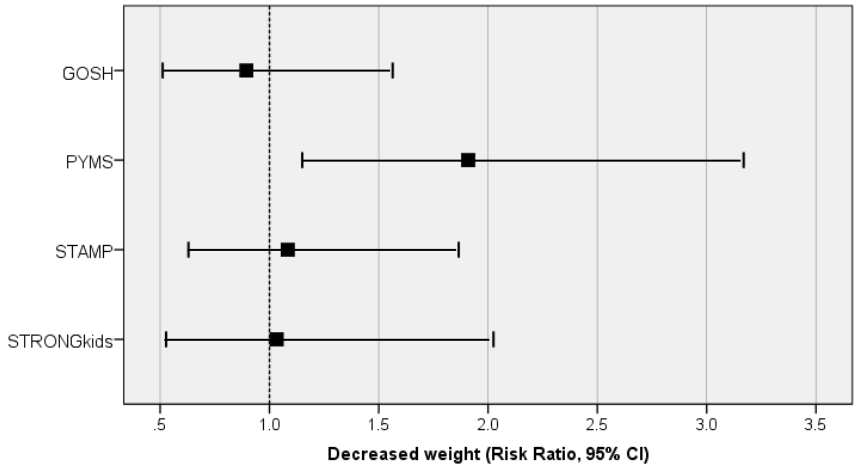
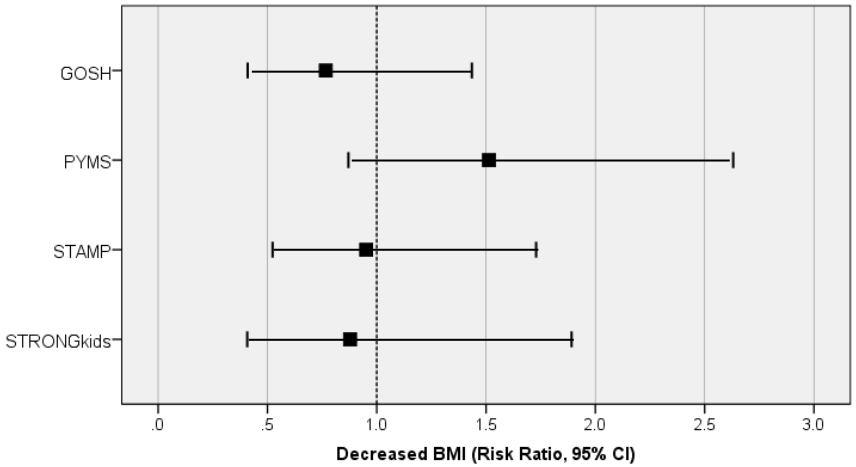


Figure 9.3. Summary of *RR* for worse clinical outcomes between patients categorised as high-risk/referred vs normal/medium-risk.
Graphs show the RR (■) and 95% CI for the RR (I) for each parameter. Dotted line shows a RR=1 (no risk).





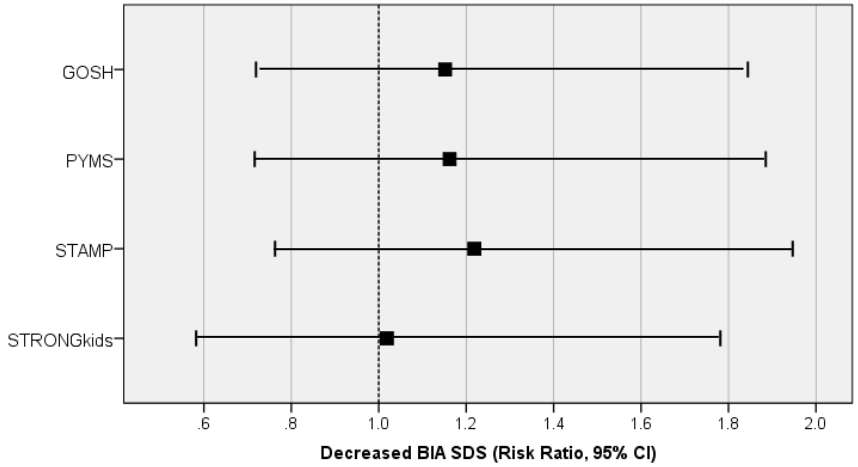


Figure 9.3 (*cont*.) Summary of *RR* for worse clinical outcomes between patients categorised as high-risk/referred vs normal/medium-risk.

9.8. Multivariate regression models: identifying malnutrition risk

Multivariate regression models were constructed to further examine the associations of the MSTs with the clinical outcomes. The outcome of 'increased LOS' was chosen for the analyses, considering the significance found between the variables in the univariate analyses, and the fact that this was also the outcome analysed for the anthropometric and BC parameters in Chapter 8. This would thus allow for the comparison of using BC measurements of LM and FMI, together with the different MSTs and determine the associations of all these tools/parameters to the clinical outcomes.

Table 9.9 summarises the best prediction models for PYMS, STAMP and STRONGkids. Looking at the MSTs as single predictors (referred/not referred) for the increased LOS, PYMS was the tool that best predicted the likelihood on an increased LOS, followed by STRONGkids, and finally STAMP in which case the associations with the outcome were just near-significant. Adjusting the models of PYMS using 'dietetic advice' and STRONGkids using 'complications' resulted in a better prediction, with the new models explaining 19% and 12% of the variance in increased LOS respectively.

To further explore the interplay between the MSTs and the previously explored anthropometric and BC parameters in the previous Chapter, with regards to their associations to clinical outcomes, these variables were analysed in multivariate models with 'increased LOS' as the outcome. The 'best' model from the previous chapter (LM abSDS + FMI abSDS) was combined with the MSTs and other confounding variables (complications, dietetic referral, admission group).

Table 9.10 summarises the best models to predict the likelihood of increased LOS. Model 1 included the parameters of LM abSDS and FMI abSDS, in addition to PYMS (referral/non-referral). This model explained 25% of the variance in the outcome, and correctly classified 87.5% of cases. This suggests that the BC parameters and the screening tools are identifying slightly different groups of children that are likely to have an increased LOS. This model results in an improvement on the use of LM abSDS and FMI abSDS (Model 2); and even more so for the model using PYMS referral as the only predictor for this clinical outcome (Model 3).

n =152		**Predictors**	***B*** [a]	***CI*** [b]		***p*** [c]	**Cox & Snell R^2**	**Nagelkerke R^2**	**% correctly classified cases**
PYMS	Model 1	PYMS (1=refer)	3.6	1.6	8.2	0.002	0.06	0.09	77.0
		Constant	0.2			0.000			
	Model 2	PYMS (1=refer)	3.5	1.3	9.2	0.011	0.13	0.19	76.2
		Dietetic advice (1=yes)	3.5	1.2	10.0	0.018			
		Constant	0.1			0.000			
STRONGkids	Model 1	STRONGkids (1=refer)	3.3	1.4	8.0	0.008	0.04	0.07	77.0
		Constant	0.2			0.000			
	Model 2	STRONGkids (1=refer)	2.7	1.1	6.7	0.031	0.08	0.12	81.6
		Complications (1=yes)	2.9	1.2	6.9	0.015			
		Constant	0.2			0.000			
STAMP	Model 1	STAMP (1=refer)	2.0	0.9	4.4	0.069	0.02	0.03	77.0
		Constant	0.2			0.000			

Table 9.9. Best predictor models for the 3 MSTs on admission to predict the odds of increased LOS.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients ($p<0.05$).

n =118	**Predictors**	***B*** [a]	***CI*** [b]	***p*** [c]	**Nagelkerke R^2**	**% correctly classified cases**
Model 1	PYMS (1=refer)	3.6	1.391 11.543	0.010	0.25	81.4
	LM abSDS (1=yes)	3.6	1.146 11.034	0.028		
	FMI abSDS (1=yes)	6.2	1.533 25.315	0.011		
	Constant	0.1		0.000		
Model 2	LM abSDS (1=yes)	4.4	1.50 13.10	0.007	0.18	82.2
	FMI abSDS (1=yes)	5.8	1.49 22.33	0.011		
	Constant	0.1		0.000		
Model 3	PYMS (1=refer)	3.6	1.6 8.2	0.002	0.09	77.0
	Constant	0.2		0.000		

Table 9.10. Best predictor models to predict the odds of increased LOS.

(a) Coefficients for the predictors in the model; (b) 95% CI of the coefficients; (c) p-value for significance of the coefficients (p<0.05).

9.9. Summary of main findings

- The 3 MSTs identified different percentages of malnutrition risk (high-risk) on admission: 35.5% for STAMP; 25% for PYMS; and 18.4% for STRONGkids. The GOSH flowchart indicated almost 40% of patients should have been referred for dietetic assessment.
- Most of the patients were categorised as low-risk using PYMS, but medium-risk using STAMP and STRONGkids.
- There was a significant difference in the categorisation of risk groups between surgical and medical patients, but not a significant difference in the proportion of patients being referred for dietetic assessment and management (high-risk category).
- The agreement between techniques was generally poor, with the 'best' agreement found between STRONGkids and STAMP (61% overall agreement, κ=0.3).
- Agreement in patient referral was highest between GOSH and STAMP (κ=0.6), and STRONGkids and PYMS (κ=50).
- Associations to the anthropometrical and BC parameters on admission were best for STRONGkids, with significant associations found for WT, HT, DXA LM and FM SDS. Referred patients also had a significant increased risk of having abnormal SDS for all the parameters except DXA FM.
- STAMP had significant associations to HT, WT and DXA LM SDS, and referred patients had a significantly increased risk of having abnormal SDS for all parameters.
- PYMS was only significantly associated with WT and DXA LM SDS, but even in these cases, patients classified as 'low-risk' still had a negative mean SDS for the parameters.
- All three MSTs were significantly associated with clinical outcomes, where high-risk patients had an increased risk for having a prolonged stay, increased LOS and complications. There was also a non-significant tendency for increased risk of weight loss and decreases in BIA SDS during hospitalisation.
- Patients referred by the GOSH flowchart only had a significant increased risk for complications
- Regression models confirmed PYMS was a better predictor for increased LOS in our population, followed by STRONGkids, and finally STAMP.

- Adjusting the model of PYMS with 'Dietetic advice', and STRONGkids with 'Complications' improved the prediction of the clinical outcome (increased LOS)
- Multivariate models using the 'best' model from the previous chapter to predict increased LOS (LM abSDS + FMI abSDS) was tested together with PYMS, STAMP and STRONGkids, and showed a combination of PYMS (referral), abnormal LM and FMI SDS was the strongest predictor model for increased LOS.

9.10. Discussion

Although conceptually, screening for malnutrition in paediatric patients is generally acknowledged to be a valuable tool to identify children at risk of nutritional depletion who might otherwise be missed on admission, the optimal methods and tools to perform this is still unclear (Huysentruyt, Vandenplas, et al. 2016). There have been increasing number of published studies regarding paediatric MSTs (Gerasimidis et al. 2010; Wong et al. 2013; Andrade et al. 2016; White et al. 2014). However, questions still remain unanswered on the value of using screening tools, especially on select populations of patients (Chourdakis et al. 2016).

The results presented in this chapter looked to perform a three-step validation of these three MSTs developed for paediatric populations in European countries. A recent multinational study in European countries was recently published with these same MSTs (Chourdakis et al. 2016). They concluded that the tools performed differently and that a number of children with abnormal anthropometric parameters were not identified by the MSTs. However, the advantage of performing a validation of these MSTs in our study, is that it allowed the opportunity to: 1) compare the risk of malnutrition assessed by the different MSTs to BC measurements obtained with a range of techniques, and most importantly with the clinical reference method of DXA; 2) investigate how the tools perform in a tertiary level hospital with a select group of patients but who are also very heterogeneous in their underlying diagnoses; 3) compare how the MSTs compare to clinical outcomes, particularly LOS; 4) include these MSTs together with the 'best' anthropometric/BC parameters model to establish the best way to predict the clinical outcome.

9.10.1. Malnutrition risk and agreement between tools

The analyses presented in this chapter of the thesis are broadly in agreement with the results from previous studies (Huysentruyt, Vandenplas, et al. 2016; Chourdakis et al. 2016;

Rub et al. 2016), mainly that there is a difference in the proportion of patients classified at high-risk, and thus recommended for dietetic referral, using different screening tools.

Considering the patterns observed between the categories of risk, PYMS had a markedly different pattern compared to both STAMP and STRONGkids. Looking at the differences in the criteria used to assess each domain of the tools, two differences can be identified that might be particularly important for our population: The first is that STAMP and STRONGkids take into account whether the patient has an underlying diagnosis likely to affect their nutrition, while PYMS does not assess this directly. Considering virtually all patients recruited to the study had complex conditions and/or were being admitted for high-risk procedures, this question in both STAMP and STRONGkids was almost always answered 'yes'. Differences between STRONGkids and STAMP however were still likely because STAMP uses two levels of risk for the underlying condition (possible and definite nutritional implications). When patients were not classified as 'definite' or ('yes' for the case of STRONGkids), they still were very likely to have some points added for a diagnosis with 'possible nutritional implications'. This could help explain to a certain extent why STAMP categorised a much larger percentage of patients as high risk.

The second main difference for PYMS compared to the other tools, is the way it assesses the patient's current nutritional status as cut-offs for BMI. Although all three tools use different approaches (STRONGkids uses a subjective assessment, STAMP measurements of HT and WT), for our population specifically I have shown that BMI has important limitations because most patients being admitted to GOSH are short and underweight compared to healthy children, leading to 'normal' BMI calculations that might miss a proportion of children who might benefit from nutritional referral and intervention (Chapters 4, 7 and 8). Conversely, STAMP uses the criteria of weight and height: patients who have a difference in their centiles between WT and HT, or a WT<2nd centile. This last criterion was something that many children in the study fulfilled, and could also help explain the increased categorisation of patients as high-risk using this tool.

All these differences in the assessment criteria in each domain were possibly reflected on the analysis of agreement between tools, which showed a generally poor agreement between all MSTs.

9.10.2. Detecting children with malnutrition on admission: diagnostic validity

Studies looking at the validation of these MSTs have used a range of parameters as the reference method to define nutritional risk, for example, hospital weight loss, dietetic referral, full dietetic assessment, or anthropometric parameters of WT and BMI (Huysentruyt,

Vandenplas, et al. 2016), although recently some evidence has been published using some measurements of BC (SFTs and MUAC) (Chourdakis et al. 2016), However, considering the practical definition for paediatric malnutrition is still a focus of debate, it is unsurprising perhaps that the studies have not used a standardised 'reference diagnostic criteria'. The present study had the advantage of defining 'malnutrition' by a range of different measurements and parameters, all assessed using a standardised method that allows comparisons between them.

The results showed that STRONGkids and STAMP had a good agreement to WT, HT, DXA LM and FM SDS on admission; but PYMS only a significant agreement to two of the parameters (WT and DXA LM). This indicates a number of patients classified as low-risk are still expected to have low SDS for HT and to a certain degree FM. Observations from Chapter 8 suggest that low HT is particularly important in our population as it identifies children with worse clinical outcomes. Thus, there is the potential that these children identified as not having nutritional risk, could have benefited from nutritional assessment and support.

9.10.3. Predicting clinical outcomes: tools for malnutrition risk

Overall, the univariate analysis showed the MSTs were significantly associated to the clinical outcomes, in particular with increased LOS. This last outcome was chosen for additional analysis because it is the most commonly-reported outcome in the available validation studies, albeit measured slightly differently (absolute LOS) (Raslan et al. 2010; Daskalou et al. 2015).

The regression models constructed showed PYMS was the best predictor for increased LOS, followed by STRONGkids. Adjusting for 'complications' and 'dietetic referral', which was surprisingly not significantly associated with any of the binary variables (referral/not) for any of the MSTs improved both models. The advantage of PYMS in predicting clinical outcomes, could be at least in part explained by the inclusion of a question on whether the patient's nutritional status will be affected during their admission, thereby already asking the assessor to predict on the outcome of the patient.

Finally, the advantage of MSTs in predicting nutritional risk was compared to that of other assessment parameters, in this case LM and FMI abSDS as our 'best' model calculated in the previous chapter. The final models indicated that PYMS + LM abSDS + FMI abSDS variables were the best model to predict the likelihood for increased LOS, followed by the model of LM + FMI, and finally PYMS as a single predictor. This suggests that these variables are assessing somewhat complementary aspects and identifying different children. Considering the diagnostic validity of PYMS compared to some of the parameters like HT

and FM was not ideal, inclusion of these BC measurements is likely to improve on the identification of patients with 'malnutrition' defined by abnormal LM and FMI SDS (in this instance) and their associations to the clinical outcome of LOS.

9.10.4. Practical considerations

The results presented in this chapter are in agreement with the current literature that there is not enough evidence yet to advocate the use of one MST over another. In line with previous observations, the MSTs all had different strengths and limitations. Ultimately, it is likely that the choice of tool will depend on the population characteristics (general/specialised hospital, inpatients/outpatients), the aim of implementing it (identifying those with 'malnutrition' and/or predicting clinical outcomes), and the resources available.

Although my results suggest that for our population and to identify those that are at risk of longer LOS specifically, PYMS could be applied on admission and BC measurements performed using DXA (FM and LM), the practicalities of doing this routinely on all patients is unlikely to be feasible. Considering some MSTs include measurements of WT/HT while other do not, the availability of calibrated equipment and other resources to perform these measurements is likely to be an important factor in the choice of tool.

Additionally, although I have reported significant associations, the observational design the study does not allow identifying causality, which is compounded by the fact that the clinical outcomes tested in the study are broad and likely to be affected by un-identified confounders. Until there is evidence that the children identified by these tools indeed have worst outcomes (ideally specific and relevant to their clinical condition), and that intervention can impact on these outcomes; advocating the routine implementation of any tool is unlikely to occur.

9.11. Conclusion

The MSTs assessed in this study differed in prevalence of malnutrition risk identified, and had generally poor agreement between them. STAMP and STRONGkids had more significant associations than PYMS to measurements of WT, HT, DXA LM and FM SDS and abSDS on admission. However, PYMS, and to a certain degree STRONGkids, performed better in identifying those children who are more likely to have worst clinical outcomes, particularly increased LOS. Ultimately, the different MSTs show different strengths and limitations that indicate the choice of tool should be dictated by the particular setting and population being assessed. Future studies into different settings, as well as intervention trials are needed before being able to recommend the implementation of a given tool.

10 Feasibility of implementing BC measurements in clinical practice: perspectives from paediatric dietitians

10.1. Introduction

The previous chapters have address the generic question of whether the use of standardized BC measurements rather than simple weight, can improve the identification of malnutrition, predict clinical outcomes and improve the nutritional management of sick children in a higher-income tertiary paediatric hospital. The results suggest children being admitted to GOSH tend to have an abnormal BC, mainly characterised by low LM and variable amounts of FM. Additionally, BC measurements by DXA, BIA and skinfolds were shown to be valid, practical and acceptable methods that could be used in clinical practice to assess BC. Parameters of BC -LM and FM - also identify children who are likely to stay longer than predicted and have complications during their admission, in our heterogeneous sample of paediatric patients with chronic and complex conditions. This highlights the need for further research into the role that these measurements can have in identifying malnutrition, guiding nutritional management, and potentially improving the clinical outcomes in hospitalised children.

A subsequent research stage to the BodyBasics study was planned to inform the possibility of implementing these measurements as part of routine clinical practice in the future, by means of a feasibility study that would clarify the perceived limitations to the use of BC measurements and their interpretation for guiding nutritional interventions in everyday clinical practice by paediatric dietitians at different centres in the UK and abroad.

10.2. Chapter objectives

The overall aim of this chapter was to investigate how BC measurements could be used for the nutritional management of paediatric patients in practice to: a) Inform future intervention trials researching the benefits of these measurements for improving the nutritional management and clinical outcomes of paediatric patients; and b) Identify barriers and suggest strategies that would facilitate the implementation of these measurements as part of routine clinical practice, if the evidence from intervention studies supported their advantage over simple weight/height.

The specific objectives were:

1. Describe the current practice in the nutritional management of paediatric patients in a range of specialties at tertiary referral centres. [Context]
2. Determine the understanding and perceived role of BC measurements for the nutritional management of patients among paediatric dietitians, and how best to implement them use in practice. [Attitudes and views]
3. Recognise opportunities and barriers for implementing BC measurements as part of the routine nutritional management. [Feasibility]
4. Identify similarities and differences in current practice and feasibility of implementing the BC measurements between similarly specialised referral centres in the United Kingdom (UK) and United States of America (USA). [Generalisability]

10.3. Methods

This last chapter of the thesis investigated the feasibility of the use of BC measurements in clinical practice using a mixed-methods approach. The study had a sequential exploratory design, in two phases:

Phase 1 - Semi-structured interviews and observation were used to explore in detail the views and perceived barriers from paediatric dietitians in specialized centres in the UK and USA. Data analysis from this phase was then used to inform the design of an online closed-question survey that was the instrument for phase 2.

Phase 2 – Online survey questionnaire designed to capture the opinions of greater numbers of paediatric dietitians from a range of settings and conditions in the UK and USA.

Aim 1. Current practice in the nutritional management of paediatric patients

Current dietetic practice was assessed though observation and shadowing of dietitians in their respective centres, while they completed their clinical ward rounds and patient visits. Particular attention was given to collect data on the time and resources available in each paediatric ward, the number of patients and procedures for nutritional assessment and monitoring, with particular interest on the use of anthropometry and BC measurements. This gave context and complement the views and answers obtained from subsequent interviews (Aims 2 & 3). Arrangements were made to spend a couple of hours with each of the dietitians,

previous to their interview, in the range of specialties available in each centre. The observation gathered mostly quantitative data (with subsequent interviews also providing an opportunity to address these topics), and were conducted by (myself) the main researcher who later also conducted the interviews.

Aims 2 & 3. Perceived role, opportunities and barriers for implementing BC measurements in clinical practice by paediatric dietitians

This aim was investigated using semi-structured interviews and an online closed-question survey for paediatric dietitians. The interviews were setup in a tertiary referral centre in the UK (GOSH) and collected some quantitative data (demographics and other data to supplement observation as detailed in Aim 1), but mostly focused on qualitative data. This allowed capturing the attitudes, understanding and practical suggestions on the use of BC measurements in clinical practice in detail. The topics covered in the interview are outlined in Appendix 17 and the interview guide is presented in Appendix 18. The proposed topics and leading questions were developed in consultation with the head of Dietetics team at GOSH to ensure relevant concepts and language was used.

Following the semi-structured interviews, an online survey was designed using the same themes, and constructing the multiple-choice questions based on the responses obtained from the interviews. The survey design allowed the data collection from a much larger sample of dietitians from various regions in the UK with a range of different experiences, to determine the generalisability of the views collected from the interviews and identify common barriers and opportunities for the implementation of these measurements. The constructed survey was piloted with some of the interviewed dietitians to ensure accuracy and appropriate language/understanding of the questions using cognitive interviewing (with both think-aloud and verbal probing techniques). The online survey link was then sent to dietitian members of the British Dietetic Association (BDA) Paediatric group in the UK.

It was contemplated to also send the link to the online survey to paediatric dietitians in the US, and following consultation with members of the Academy of Nutrition and Dietetics (AND), this stage of the research is now on hold awaiting ethical approval in the US before the link can be sent out to the members of AND.

Aim 4. Similarities and differences between referral centres in the UK and USA

Observation and semi-structured interviews were similarly setup as described for Aims 1-3, with dietitians working in 3 tertiary referral centres in Boston, USA: Boston Children's, Massachusetts General Hospital for Children (MGHfC) and Tufts Floating Hospital for Children. This allowed the identification of similarities and differences in practice, suggesting cultural and geographic influences in otherwise similarly specialized centres. The questions in the semi-structured interviews were also piloted with the head of the Dietetics department at MGHfC to ensure the language and concepts are appropriate for the population before conducting them via teleconference or email with interested dietitians.

10.3.1. Subjects and clinical centres

The study involved paediatric dietitians from several centres in the UK and the USA. Specialized paediatric tertiary referral centres were chosen for the semi-structured interviews, as dietitians would be more likely to have ample experience in paediatrics and potentially have a greater knowledge on the use of BC measurements for the management of complex conditions. Similar specialized centres were chosen in both countries: Great Ormond Street Hospital for Children NHS Foundation Trust (GOSH) in London, UK, and Boston Children's, Massachusetts General Hospital for Children (MGHfC) and Tufts Floating Hospital for Children in Boston, USA. The link to the online survey was sent to all members of the Paediatric Group of the BDA, thus enabling targeting dietitians from a range of UK centres with different degrees of specialization and experience for analysing the generalisability of the views collected from the interviews.

10.3.2. Sampling method

Selection of study participants for the semi-structured interviews were approached using stratified purposeful convenience sampling. This sampling method was selected, despite the risk of selection bias, because results were not expected to be a representation of all paediatric dietitians' views at this stage, and also considering the set and limited sampling population available at the specialized centres. The main interest was therefore, to obtain high-quality and rich qualitative data on these highly-specialised dietitian's views that could then also be used to construct the online survey, which would then target most of the population of interest (UK paediatric dietitians) to explore the generalisability of these views within the wider population.

No sample size calculation was performed, as this research was mainly descriptive in nature and there are no previous studies in which to base the estimates. For the interviews,

efforts were made to recruit 1 to 3 members of each specialty dietetics team (one of them being the team's lead dietitian) within each centre. This would allow collecting the views from senior dietitians and more junior members of the team. Alternatively, when centres were organised differently, an effort was made to recruit dietitians form the most diverse range of specialties as possible within each centre. Considering an estimated response rate of 25%, in the case of GOSH this would result in at least 8-10 participants (35 dieticians in total) and 10 for Boston Children's (total of 40 dieticians). In the case of MGHfC, having a small inpatient population, all 3 full-time paediatric dietitians will be targeted for recruitment. An approach similar to the one described above was also followed for dietitians covering paediatric outpatient clinics (Feeding disorders, Obesity & Eating Disorders, Metabolic, Gastroenterology, Epilepsy, Cystic Fibrosis, and Growth clinics), resulting in a total maximum of 10 recruited participants. One more paediatric dietitian was approached to take part in the study from the Frances Stern Nutrition Center at Tufts Floating Hospital for Children, where similarly there is a small inpatient population with only one full-time dietitian covering the paediatric wards. On the other hand, the online survey link was sent to all members of the Paediatric group of the BDA, which at the moment has around 600 members.

Inclusion criteria for the interviews was all dietitians who are specialized in paediatrics and are currently practicing in one or several clinical nutrition specialties in the mentioned referral centres. Dietitians who are exclusively in charge of adult patients or not currently practicing were excluded from the study. For the surveys, the inclusion criteria consisted on just being a member of the BDA Paediatric group, which is expected to cover the majority of registered paediatric dietitians in the UK. Dietitians not currently practicing were excluded from the data analysis.

10.3.3. Recruitment

Dietitians for the semi-structured interviews were identified and recruited in consultation with their respective Dietetics department managers. A possibility of sending a group-wide email from the researchers with details on the study and contact information was pursued, and consultation with each department manager determined the best way to implement this to ensure participation was voluntary but reached all potential participants in the most effective way. The researcher did not have direct access to potential study participant's personal details until they contacted the study team with their interest to be enrolled. Potential study participants had 2 weeks to respond to the email invitation. Reminder emails were sent to heads of department to encourage their team to take part in the study. Dietitians who expressed interest in participating were sent further details on the study (Information sheet –

Appendix 20) and an invitation to arrange a suitable time/date for the interview to take place. A consent form (Appendix 19) was then signed on the day of the interview.

Recruitment for the online survey was arranged through the BDA Paediatric group. A generic link to the online survey was sent to the member in charge of research studies within the group, and then forwarded through mailing-lists to the rest of its members. The researchers did not have direct access to any of the member's personal email addresses. A reminder email encouraging their members to respond was sent a couple of times (weekly). The survey site contained further explanation on the aims of the research study and contact details for the researchers. Implied consent was given by completion and return of the survey questionnaire. The survey link was to be active for approximately 8 weeks based on response rates.

10.3.4. Methods & Data analysis

Interviews to paediatric dietitians

Interviews to collect the dietitian's views for Aims 2-4 were semi-structured, with topics outlined in Appendix 17. It covered 4 main sections/topics: 1) demographics, 2) current practice (context and nutritional assessment), 3) knowledge on BC, and 4) implementation of BC measurements in practice (potential, barriers, and diet prescription).

It was expected that the interview would take 30-45 minutes to complete, with adjustments resulting from consultations with department managers and piloting of questions. Interviews at GOSH were arranged to take place in meeting rooms at the Dietetics department or the Institute of Child Health (where the researcher is based), as available, in one or two sessions. This ensured convenience for the research participants. For interviews to US dietitians, a suitable time/date was arranged to conduct the interview via tele-conference, or alternatively the questions were emailed/setup online. The interviews were administered by myself (PhD student with dietetics background). It was expected that, given the common background and previous research work conducted at GOSH, this would encourage rapport without significantly influencing the participant's responses. The interviews were recorded and later transcribed for content analysis. Data analysis was performed with a thematic analysis approach and summarised using descriptive statistics when possible.

Online survey to paediatric dietitians

A survey questionnaire with closed questions was designed from the interview guide and responses recorded in the interviews. This allowed data collection from a bigger sample covering a range of regions and experiences within the UK, while increasing the chances that the responses were a true reflexion of the participant's attitudes and views and that the responses available in the multiple-choice questions were relevant and covered most possible perspectives.

The survey questions were piloted using cognitive interviewing with dietitians who had completed the semi-structured interview at GOSH, to ensure it was a true reflection of their responses to the interview. It was contemplated to subsequently pilot the survey with a dietitian working at a less-specialized local hospital to ensure it is applicable to different settings and that the concepts/language is appropriate and understandable; however, this was considered unfeasible within the time available once the study started.

The online survey was setup using SurveyMonkey. The link and a short description of the project was sent to the Paediatric group of the BDA to then be forwarded to all its members. The site contained further information on the study and instructions for completing the survey. It was expected it would take no more than 15 minutes to complete.

Data collected from online questionnaires had a unique ID code and was exported to an Excel dataset for data cleaning and merging. Statistical analysis was performed in SPSS software (SPSS Inc. Chicago) using descriptive and inferential tests to summarise the results.

10.3.5. Ethical considerations

Ethical approval was granted by Chair's action from the University College London Research Ethics Committee (Appendix 8).

Recruitment & subject participation

Written consent (Appendix 19) was obtained from the subjects after full and detailed explanation for the interviews, and subjects were able to refuse to participate at any time. For online surveys, implied consent was evident through the completion and return of the questionnaire. An information sheet (Appendix 20) was provided previous to written consent to the interviews, and a modified version was designed and published in the online survey website. Neither the interviews nor the survey were expected to include topics that might be considered sensitive or distressing to the participants. Design and approval of email

correspondence inviting participants to the study in both cases was done in consultation with department managers and the BDA lead research member respectively.

Data protection & confidentiality

All collected data was strictly confidential and identity numbers rather than names were used on data collection sheets and transcribed documents. The researchers did not have access to participant's personal email addresses or information, other than demographics, for the survey. Personal information, including email address, was obtained for interview participants only after they contacted the researchers expressing their interest in participating in the study. Interviews were recorded with the participant's consent for the purpose of transcribing their responses as needed, and was deleted from the recording device once the files were transferred to a secure computer for analysis and storage.

The study data and recordings were held in a locked building and department, on password-controlled computers, each file password-protected. All data collected (including data on computers) was identifiable by a number only and the codes kept separate in a secure location. Data collection and storage procedures at the Childhood Nutrition centre are entirely compatible with the data protection act. This study was covered by the University College London data protection registration, Section 19, Research: Health Research.

10.4. Preliminary results

These next sections will describe the stages of data collection completed to date and some of the preliminary results from the study. Full analysis of the responses, as well as Phase 2 of the study are currently still ongoing and awaiting ethical approval in the USA.

10.4.1. Interviews to paediatric dietitians in specialised centres in the UK

As of May 2016, recruitment and interviews to UK dietitians at GOSH were completed. The results obtained from these interviews were used to construct the online survey, which was then completed by 5 of the interviewed dietitians at GOSH to ensure it reflected their opinions from the interviews.

10.4.2. Pilot survey to paediatric dietitians completing the interviews from the previous stage

The following sections describe the responses obtained from these surveys.

A total of 5 dietitians answered the pilot survey, 3 of the female and 2 males with age ranges of 25-50yr. They had been working in paediatrics from 2.5 up to 15 years, all of them were currently based at GOSH. They looked after a range of patient diagnoses, including BMT, ICU, renal, CF, Metabolic and General Paediatrics in both inpatient and outpatient wards.

Regarding referral procedures, they reported a range of different ways in which they identified patients that need to be seen – from seeing everyone on the ward, to attending rounds, to clinician referral. The most common reasons for referral were low WT, when the patient is on EN/PN feeds, or has a diagnosis with nutritional implications.

10.4.3. Anthropometric measurements

All dietitians reported that anthropometry was performed routinely on all patients, with all selecting WT and HT as the measurements required, and 1 selecting BMI as well. There was only one dietitian who reported other measurements such as HC and even DXA "depending on the disorder". Most of these measurements would be performed by the nursing staff, although 2 of them responded also taking them themselves or by the consultant. Figure 10.1 shows the times at which these anthropometrical measurements would be performed.

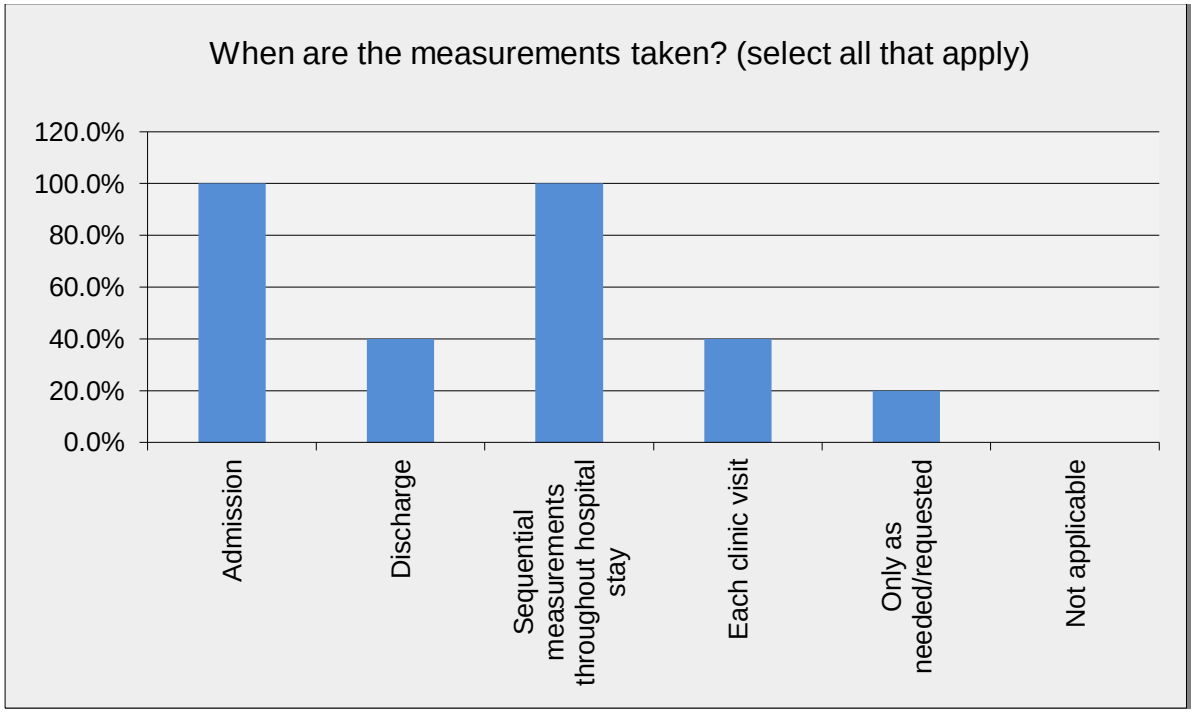


Figure 10.1. Timepoints for anthropometric measurements during hospitalisation

10.4.4. Body composition – definitions & training

Figure 10.2 summarises the definitions of BC selected by the respondents. Notably, most dietitians thought of BC in terms of FM, LM, bone and water, as opposed to the usual fat and lean mass only. They all had knowledge about at least one technique. Figure 10.3 summarises the level of experience per technique. SFTs were the measurements most commonly (although rarely overall) used and where most dietitians had the most knowledge, although not necessarily using them in practice.

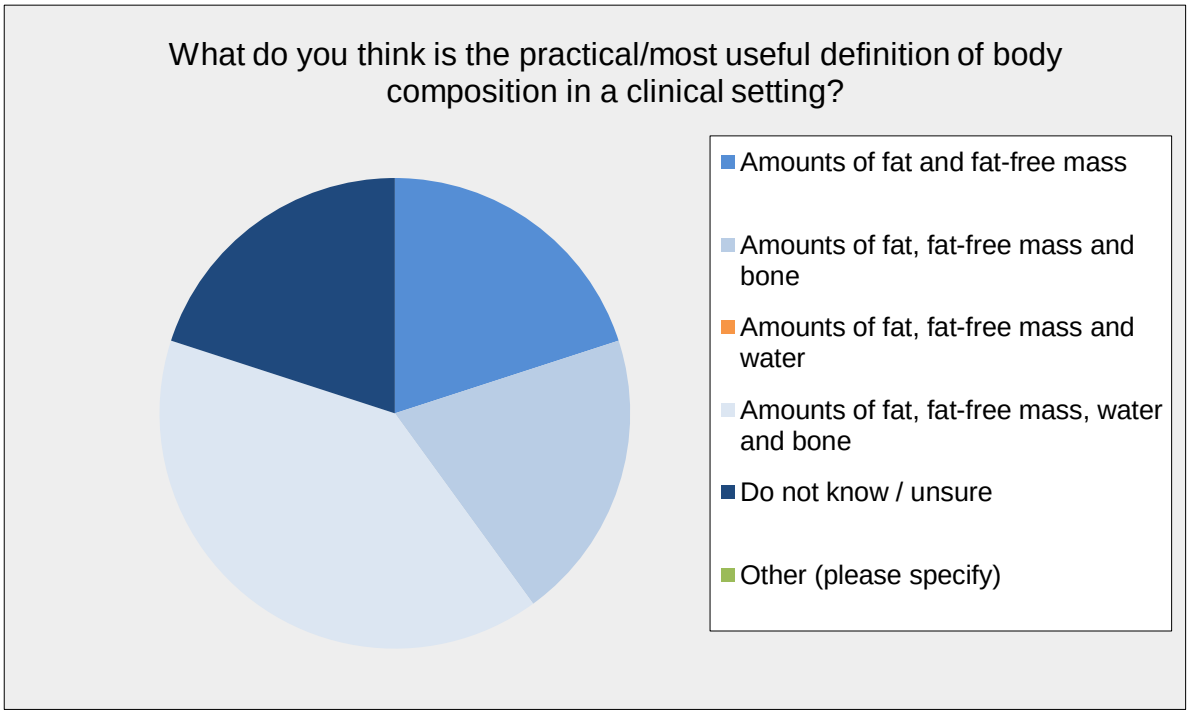


Figure 10.2. Definitions of BC in a clinical setting

Regarding the equipment to measure BC, most dietitians were aware of the common equipment of tape measures and calipers, and knew where the DXA was although most did not use it. BIA was usually thought of as equipment for research or removed from the wards.

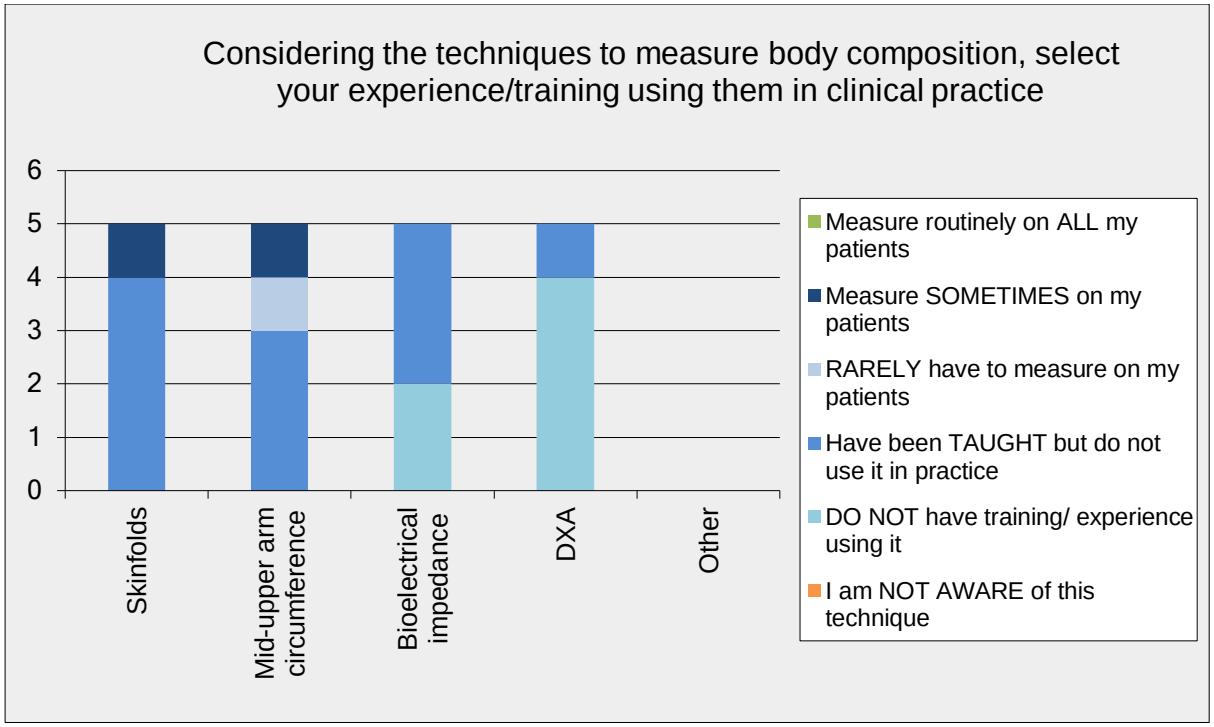


Figure 10.3. Knowledge and training with different BC techniques

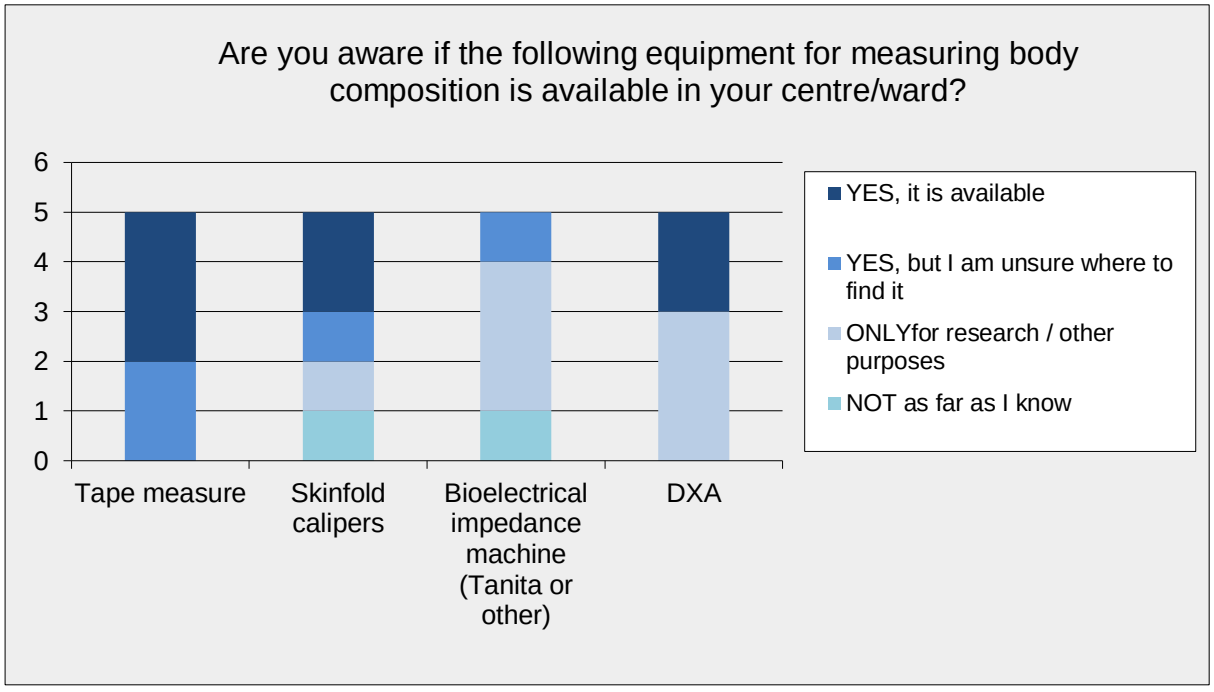


Figure 10.4. Availability of the equipment to measure BC in the wards.

10.4.5. Body composition – scenarios and practice

Regarding what they would do with the BC measurements if they perform them, three said they would take sequential measurements to assess the change in the child, and 2 said they would compare them to reference data for assessment at baseline.

When asked if they thought BC measurements would give them additional information on the patient's nutritional status, 4 out of 5 responded 'yes' and one 'maybe in some cases'. When asked if they would like to have this available for their patients, 3 said yes on everyone, 1 said yes but only in some cases, and 1 was unsure. The explanations provided are shown below in Table 10.1.

Those who are having follow up / ongoing input especially those with chronic conditions requiring dietetic support.
So I can better tailor diet treatment, and can be useful for those who's height is not increasing
With my patients it is very difficult to ascertain whether weight losses or gains are due to fluid shifts, accumulation of fat mass or lean muscle mass - so I would hope having a body composition score would help identify this.
Identifies a baseline and how intervention does/does not change from this

Table 10.1. Responses to the question on whether they would like to have BC scores for their patients

Looking at how they would use the measurements in practice (Figure 10.5), most would use them for: 1) nutritional status assessment at baseline, 2) monitoring nutritional status during hospitalisation, and 3) monitor nutritional prescription. 2 of them would prefer to have the measurements as centiles, while the other 3 as either centiles or SDS.

Regarding when to perform the measurements, most thought of sequential measurements, admission or less so for discharge. With regards to who could perform BC measurements, the consensus was that anyone could so long as they were trained. There did not seem to be a consensus however on whether they thought the current staff was enough (Table 10.2 shows some of the extended responses). Most were also doubtful about finding the time to perform the measurements themselves, and interestingly, when asked about what the preferred techniques would be for their patients, 3 of them answered DXA, 1 BIA and 1 SFTs.

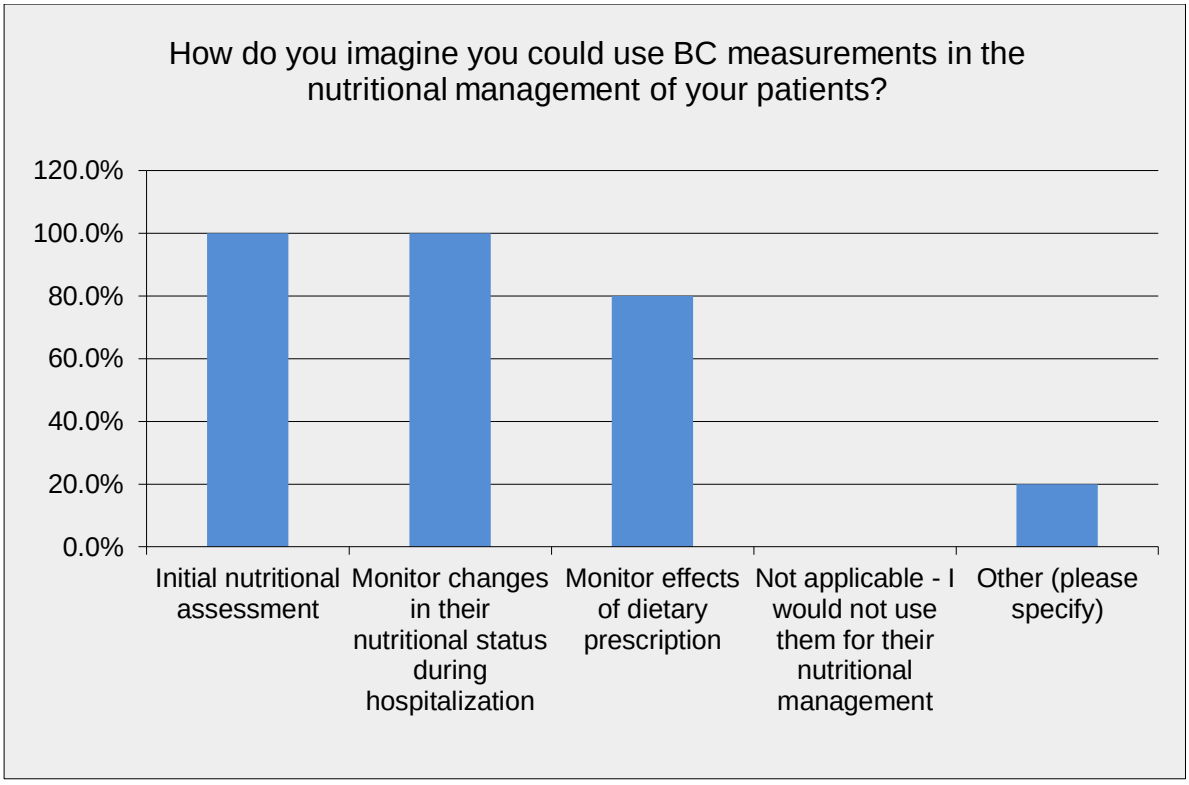


Figure 10.5. Potential use of BC measurements in the nutritional management of patients

Possibly dietitians or nurses. Most importantly is the interpretation which would be dietitian once trained how to interpret z-score or centile.
I assume new staff would be needed depending on how frequently these measurements are going to be used and how long it takes to perform each one. If they were quite quick to do possibly existing staff could do this.
Most staff have a very busy caseload, length of time required to prep patient and take them to scan may be extensive

Table 10.2. Is the current staff enough to perform the measurements of BC or would new staff be needed to cover additional workload?

The dieticians were given a series of scenarios of different BC SDS and asked about what possible dietetic interventions they would start. Table 10.3 and Figure 10.6 below summarise their responses.

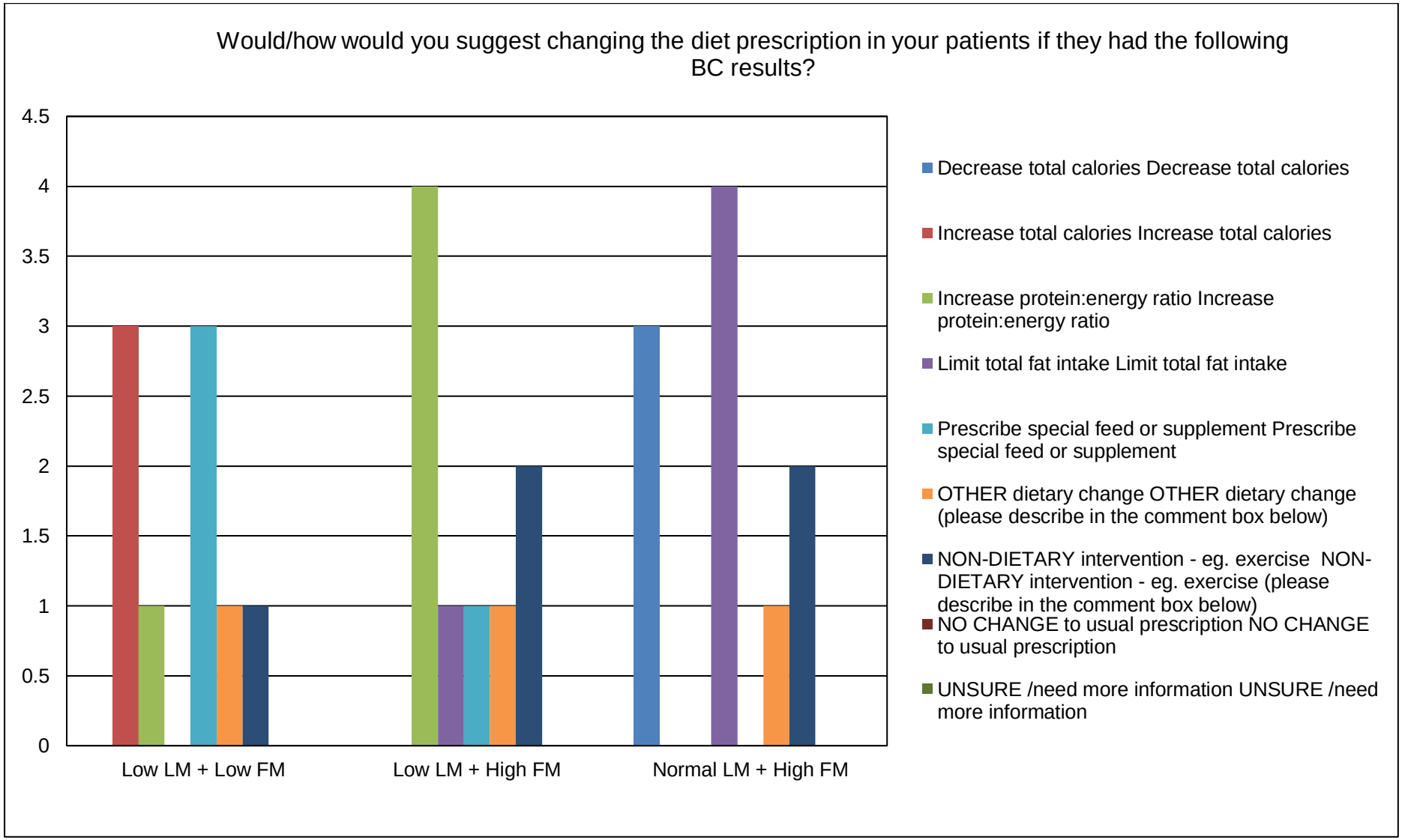


Figure 10.6. scenarios for changes in diet prescription with BC measurements

I think you would also need to know what the patient's weight and BMI centile are at the time and also what previous weight / growth trends have been.
depending their current dietary treatment as often the child may already be on a protein or fat restriction, so intervention based on body composition may include changing the type/source of protein or fat or CHO
Weight bearing exercise for low fat free mass *Cardio for high fat mass*

Table 10.3. Responses to scenarios for changes in diet prescription with BC measurements

10.5. Future work and analysis

Following the pilot survey completion summarised above, the online survey link is now active and awaiting collection of final responses. The interviews to USA dietitians has concluded, and thematic analysis is underway together with interviews from GOSH dietitians to compare practice and points of view between centres and countries with more detail.

11 General Discussion

11.1. Novelty & scope of study

Recent consensus statements have all stressed the need to improve on the diagnosis and treatment of hospital paediatric malnutrition (Cederholm et al. 2015; Becker et al. 2014). However, the 'optimal' way to diagnose malnutrition is still a focus of debate, and recent reviews and working groups (Cederholm & Jensen 2016; Bouma 2017; Beer et al. 2015) have looked at ways to standardise the definitions, both conceptually and in terms of diagnostic parameters. BC measurements – particularly LM – have started to be considered as part of these diagnostic criteria (Cederholm & Jensen 2016). However, there is still the prevailing notion that these measurements are difficult to obtain in clinical practice, and the variety of techniques and handling of outputs, different cut-offs, references, and equations all contribute to this uncertainty over how best to assess it in practice. The available literature on the characterisation of BC in paediatric patients, as well as any associations to clinical outcomes, are also subject to these variety of approaches that make comparisons between studies difficult, and gaps in knowledge difficult to address. Additionally, it has been increasingly recognised that the process of malnutrition screening and nutritional assessment should be linked, to allow a proper identification and management of patients with or at risk of malnutrition (Huysentruyt, De Schepper, et al. 2016).

Thus, the work in this thesis looked to address both the issue of malnutrition screening and diagnosis, proposing the use of BC measurements as parameters that might improve on the current measurements of weight and height, whilst validating three paediatric MSTs. Unlike most evidence so far, it was envisioned to provide a comprehensive view of the issue of malnutrition in a highly specialised tertiary referral centre, rather than small fragmented snapshots. Therefore, it covers methodological issues, through to issues of validity and associations to outcomes, all the way to the feasibility of implementing them into routine practice. This study design has both strengths and limitations (discussed in the next sections), but was intended to provide a starting point for subsequent studies, by providing evidence on how to measure BC and whether it seems it can provide additional information to the standard measurements of weight and height.

11.2. Summary of findings and implications for clinical practice

The results from this thesis have shown that body composition measurements can be practical and acceptable in clinical settings, even in a tertiary level centre. The aim was to provide both researcher and clinicians with evidence, not only on the validity of the techniques, but how these would work and be implemented in practice. Thus, the thesis constantly approaches the aims from a practical standpoint: choosing techniques that are suitable for clinical settings, performing measurements as they would happen in practice rather than controlled research settings and assessing if these are still valid, collecting information on the acceptability of the techniques from the patients, etc. The results show that, by using a standardised method of calculating SDS from the raw values of the techniques rather than using prediction equations that would increase the error of the measurement, BC can be measured in clinical settings either to conduct further studies or if they were to be implemented as part of routine care in the future.

Another practical aspect addressed by the study was how to measure height and perform BIA measurements in patients unable to stand. I have explored a simple adjustment to BIAsup that will allow the measurement of BIA in bedridden patients, and the use of UK BC reference data to calculate the SDS. Regarding height, the analysis shows that estimates using ulna and tibia can often have significant bias, making it difficult to recommend the implementation of certain equations or measurements when they might differ markedly between different settings and patient conditions. However, I was able to test an approach popularly referred to as ‘wisdom of crowds’ whereby the average of many estimates will improve on the accuracy of the aggregate estimate. This approached seemed to be promising with BodyBasics patients, and future research is planned to use this same approach to other measurements that might be biased, such as SFTs. Thus, with further testing, it is expected that these results might provide a more accurate alternative to estimate height and other measurements in these complex patients.

Regarding the use of body composition measurements to identify patients with worse clinical outcomes, the results showed that there does seem to be an advantage and a use of BC measurements, alone or in conjunction with weight and height measurements. The study design however, was not expected to provide unequivocal evidence to directly advocate their use in practice straight away, but rather provide evidence to build up future research. Further studies are needed to show that these measurements can predict not just generic clinical outcomes, but specific outcomes in selected patient groups, and that by identifying these children and intervening it is possible to ultimately change these outcomes and reduce the prevalence of malnutrition.

11.3. Advantages and Limitations

The work in this thesis was planned on the basis of the new reference data for BC in UK children. This reference data (Wells et al. 2012) has allowed me to analyse the outputs from different BC techniques in a standardised way, meaning it is not only possible to compare results between the techniques more easily, but it also allows flexibility in the choice of technique. With this tool, it was now possible to address some of the gaps in the evidence with regards to the assessment of malnutrition in paediatric patients.

Although this approach helped with some of the measurement bias of the techniques, each method and technique has its own limitations, which might be even more relevant in the context of patients with the range of conditions measured in this study. The analysis of the restricted datasets, containing only those measurements performed under adequate conditions and following strict adherence to the measurement protocols, showed no large differences to the analyses with the whole database. However, even if average results do not change for the assessment of the group, this does not exclude the possibility of individual bias in the measurements, and validation for specific disease groups would be beneficial.

It should be considered that, particularly for the methodological aims (Chapters 4-6) validation of techniques and methods could have been limited due to the complex diagnoses of the patients. While these patients are those who are likely to benefit the most (e.g. alternative ways to estimate height in spinal surgery patients), their condition adds another factor of potential error in the analysis. For height estimates, in particular, the results suggest that estimating height using equations form healthy children might not be the best approach in children who are known to have altered growth patterns. The alternative could be to develop more disease-specific references and equations (as with CP patients), but this is almost certainly unfeasible for the large range of diagnoses at GOSH. The study results were able to show what the assessment of these children would currently be with available tools and methods, and provide evidence for the limitations to be considered when using them.

With regards to the sample of patients and the target population, it is recognised that younger children are at high risk for malnutrition. However, considering the reference BC data was only suitable for children 5-18yr, the study was limited to this same age range. The reference data was measured in children over 5yr because of the difficulty of obtaining accurate BC measurements by the different techniques in younger children and infants. It was planned that if there was evidence that the reference proved to be useful in practice, then it could be extended to include children <5yr in the future. The promising results from

this study have provided with some initial evidence in this regard, and thus is something currently under consideration by our research group.

Additionally, although the study looked to research the topic of 'malnutrition' as encompassing both over and under nutrition (abnormal scores rather than low), particularly for fat mass and weight, the study recruited only a limited number of children with overnutrition/obesity and so the results here presented are more relevant for undernutrition. However, because overnutrition and obesity are increasingly recognised as important problems in the paediatric population, more evidence on how they affect clinical outcomes and how they can be assessed using BC measurements is likely to be the focus of future research.

The setting was chosen because GOSH had all the facilities and equipment in place to perform the necessary measurements for the study. Additionally, the close partnership of the hospital with the research institute enabled collaborations between clinicians and researchers for the successful set-up and infrastructure of the project. More importantly, the patient population being admitted to GOSH is quite selective and complex in their clinical diagnoses. Thus, it was considered to be a high-risk population where BC was more likely to be abnormal and in which case BC measurements could potentially be useful, as opposed to a general paediatric hospital where most children might have acute conditions and who's nutritional status is likely to normalise once they are discharged home. However, the specialised nature of the patient population also means that the results from the present study are not necessarily, and unlikely, to be transferable to other less-specialised centres and further research is needed to determine of these measurements are useful in other settings.

The study also had the limitation of not being able to discard any biases in recruitment. Although a log was kept of patients who refused to take part in the study to make sure they were not approached at a later admission, there was no collected information on the total number of eligible patients admitted to the hospital in the recruitment period, and how many of them were able to be targeted for recruitment. Data protection regulations limited the amount of information able to be collected before the patients consented to take part in the study, and so recruitment had to take place by visiting each individual ward every day and asking the clinical staff for information on new admissions. Thus, it is unknown if the study team was not made aware of some potentially suitable admissions and there is the possibility that the recruited patients could have been those with a greater degree of weight loss and nutritional problems.

Additionally, the study was limited by issues of sample size. Calculations for sample size were not possible at the start of the study because of the limited evidence on the associations

of BC measurements to clinical outcomes. The sample was ultimately adequately powered at baseline but underpowered for follow-up, as a large percentage of patients were missed on discharge. This was usually the result of out-of-hour discharges, and was further complicated by the fact that patients were recruited from many wards at the same time and it was difficult to follow-up on their progress more than once a day to check their likely date of discharge. Thus, it is possible that the lack of significant observations to the change in the parameters SDS between admission and discharge could be explained at least in part by the inability to detect a significant change from the number of observations recorded. The results from the study, however, will help with sample size calculations for future studies; and a more targeted recruitment of specific patient groups is also likely to improve recruitment and follow-up and the strength of the obtained results.

The study design in itself could have limitations, as it is unable to demonstrate causality and the observed associations are likely affected by numerous confounding factors. One of these instances are likely to be the clinical outcomes. These generic outcomes were chosen to allow measurement and data collection on all patients recruited to the study regardless of their underlying diagnosis. However, the initial approach of trying to perform sub-group analyses was not feasible considering the wide range and heterogeneity of individual diagnoses. The alternative of adjusting for factors such as steroid use, fluid restriction, diet-related variables and physical activity, did not exclude the possibility of remaining bias. However, even in this heterogenous population and with generic clinical outcomes, finding significant results suggest that there is an effect in at least some of the patient groups and is therefore something that should be investigated further.

Seeing as the study measured many variables and included a large number of statistical tests, there is the potential that some of the significant results were obtained by chance. Although some adjustments to the significance of *p*-values were considered, these results need further corroboration in future studies with more targeted and specific research questions, which can be formulated based on the observations from this study.

Despite these methodological limitations, I have been able to obtain evidence from a wide range of tools and parameters, and help: 1) characterise the extent of malnutrition on a tertiary paediatric setting; 2) identify the possible techniques, their strengths, limitations and alternatives to perform anthropometric and BC measurements that will guide subsequent research and practice; 3) obtain preliminary evidence on the possible advantages that BC measurement can have in the context of paediatric malnutrition that justifies future research in this area; 4) highlight how different techniques and tools perform differently in this selective group of patients, which requires further validation in the future.

11.4. Future study directions

The results and conclusions from his study will guide future research in the advantages of using BC measurements to improve not only the diagnosis, but explore their role for the nutritional management of paediatric patients with complex conditions. Additionally, MSTs should be similarly tested for their ability to impact on patient outcomes, and incorporated into a nutritional care algorithm alongside diagnosis of malnutrition. Only then, can the use of these tools be supported in routine clinical practice.

The identified first step, would be to conduct studies using these standardise methods and techniques in specific patient populations, to determine if there is a significant correlation with relevant and specific clinical outcomes. Ultimately, intervention trials would be the optimal way to determine if the use of these measurement and the various MSTs can be incorporated into the nutritional management and impact the clinical outcomes of these patients. Furthermore, multi-centre studies to research the generalisability of these observations in different patient populations, and extending both the reference data and research into younger children (<5yr) are also much needed research directions.

Indeed, the last results chapter of the thesis described the methodology and some of the preliminary results from a survey setup in the UK and USA to explore the views of paediatric dietitians regarding BC. The short-term use for this collected data will be to inform the design of such trials, as some of the questions focused on what the dietitians in those centres would think about changing in terms of dietetic prescription in response to different BC results. This will have the advantage of getting a wider picture from different centres and cultural backgrounds, that might furthermore lead to collaborations for multi-centre trials in the future.

12 Concluding remarks

The importance of paediatric malnutrition had been recognised for several years, but its diagnosis and management in clinical settings, particularly in developed countries, is still an ongoing problem. Recent consensus suggests that a mayor issue is the lack of evidence in the diagnostic criteria and the best tools to detect malnutrition and malnutrition risk on admission. The work presented in this thesis has looked to address the gaps in knowledge regarding the use of malnutrition screening and body composition measurements in paediatric patients with complex diagnoses. The research here presented has been undertaken with a focus for implementing into routine practice, so that issue of practicality has been a major component throughout the analysis and chapters.

The results from the study suggest BC measurements could be practical and useful in the diagnosis of malnutrition in this selective patient population, in addition to the more simple measurements of weight and height. In addition, the choice of parameter, technique and tools was shown to be an important aspect to consider. Figure 12.1 summarises the main findings from this research.

Future direction from this work will be focusing on improving the evidence for the implementation of these measurements in routine clinical practice. The BodyBasics study was conceived as a starting point for research into specific patient groups and intervention trials, meaning the results from this study will inform the design of the next studies. Data analysis and collection for the feasibility study (Phase 2), is still ongoing and is expected to provide the last piece of evidence needed to plan and advance the research in this area.

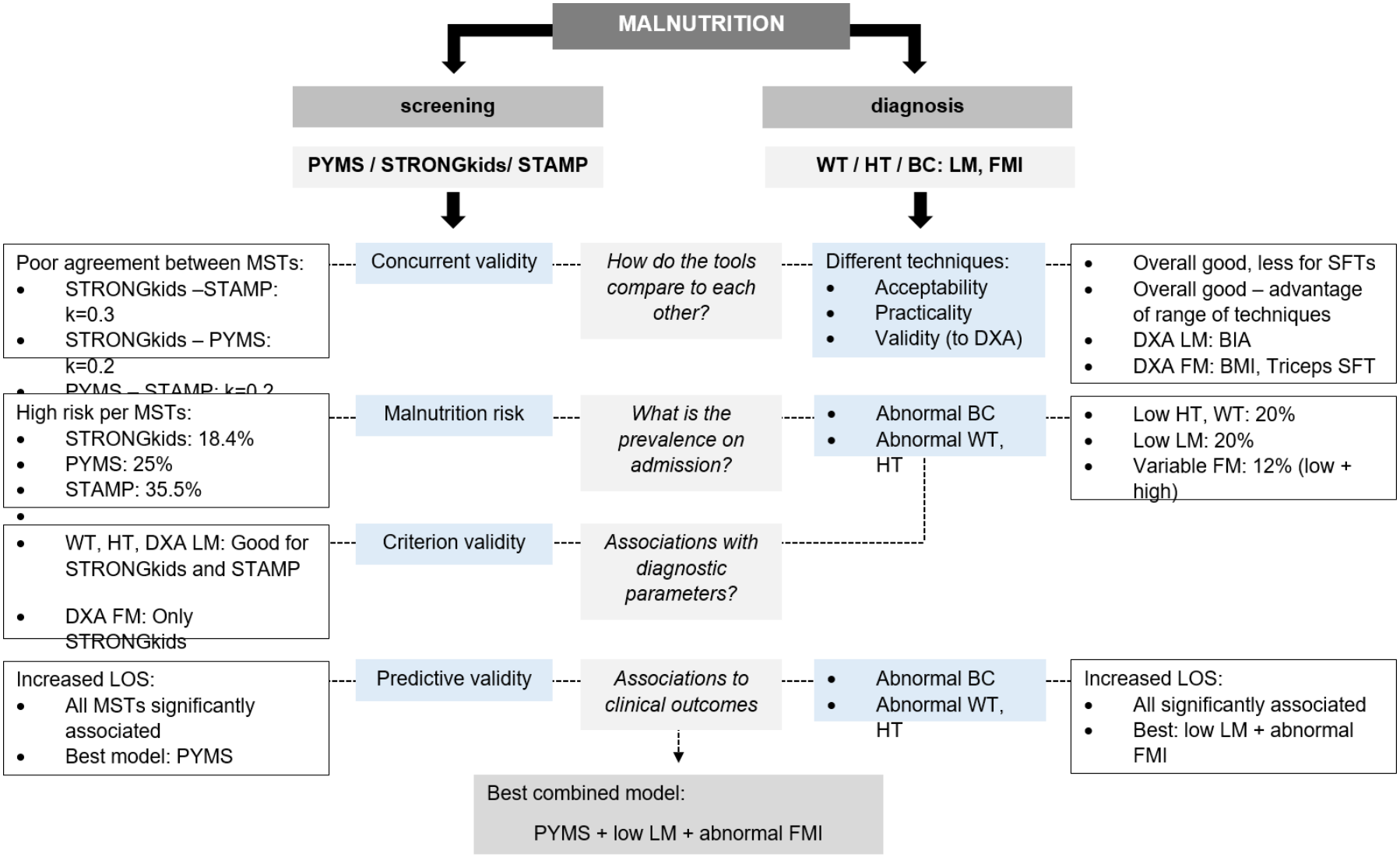


Figure 12.1. Summary diagram of main findings

13 Publications and contributions

13.1. Conference abstracts

NE Lara-Pompa, J Williams, S Macdonald, K Fawbert, J Valente, K Kennedy, V Shaw, JC Wells, S Hill and M Fewtrell. Associating nutritional risk with clinical outcomes in paediatric patients: an appraisal of different tools. Proceedings of The Nutrition Society 2016;75(OCE3):E184

NE Lara-Pompa, J Williams, S Macdonald, K Fawbert, J Valente, K Kennedy, V Shaw, JC Wells, S Hill and M Fewtrell. Ulna and tibia length measurements as alternatives for estimating height in hospitalized children. Proceedings of The Nutrition Society 2016;75(OCE3):E110

NE Lara-Pompa, J Williams, S Macdonald, K Fawbert, J Valente, V Shaw, K Kennedy, JC Wells, S Hill, M Fewtrell. MON-P147: Estimating Height in Paediatric Patients with Cystic Fibrosis: Accuracy of Tibia Length Measurements. *Clinical Nutrition* 2016;35:S207

NE Lara Pompa, J Williams, S Macdonald, K Fawbert, J Valente, K Kennedy, V Shaw, JC Wells, S Hill, M Fewtrell. PTH-225 Paediatric malnutrition screening on admission: a comparison of different tools and their association with body composition and clinical outcomes. *Gut* 2015;64:A509

NE Lara-Pompa, J Williams, S Macdonald, J Valente, JC Wells, S Hill, M Fewtrell. MON-PP254: Measuring Body Composition in Hospitalized Children: Validity, Practicality and Acceptability of Different Methods. *Clinical Nutrition* 2015;34:S221

13.2. Contributions to symposia

- 38th ESPEN Congress on Clinical Nutrition & Metabolism 2016. Copenhagen, Denmark
- World Congress of Pediatric Gastroenterology, Hepatology & Nutrition 2016. Canada
- Nutrition Society Summer Conference 2016. Dublin, Ireland
- 49th ESPGHAN Annual Meeting 2016. Athens, Greece
- 3rd International Conference on Nutrition & Growth 2016. Vienna, Austria
- 30th BSPGHAN Annual Meeting 2016. Bristol, UK.
- 37th ESPEN Congress on Clinical Nutrition & Metabolism 2015. Lisbon, Portugal
- Digestive Disorders Federation Annual meeting 2015. London, UK
- 48th ESPGHAN Annual Meeting 2015. Amsterdam, Netherlands
- 29th BSPGHAN Annual meeting 2015. Stratford-upon-Avon, UK

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15 Appendices

15.1 Information sheets and leaflet

Great Ormond Street Hospital for Children NHS Foundation Trust

Childhood Nutrition Research Centre
UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH

THE BodyBasics STUDY

We are inviting **all children aged 5 years and above** who are going to be admitted to GOSH to take part in this new research study.

This sheet gives some details about the study. You can find more on the Great Ormond Street Hospital (GOSH) website:

http://www.gosh.nhs.uk/research-and-innovation

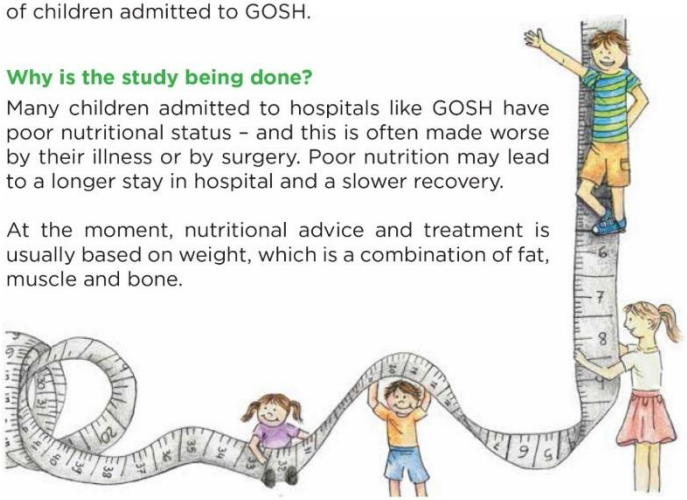
What is the aim of the study?

The aim of this study is to find out whether measurements of body composition (fat and lean mass rather than just weight or height) can help to improve the nutritional care and recovery of children admitted to GOSH.

Why is the study being done?

Many children admitted to hospitals like GOSH have poor nutritional status – and this is often made worse by their illness or by surgery. Poor nutrition may lead to a longer stay in hospital and a slower recovery.

At the moment, nutritional advice and treatment is usually based on weight, which is a combination of fat, muscle and bone.



There is some evidence that **fat and muscle may have different effects on health and on the response to treatment**. We also know that when underweight children are given extra nutrition they sometimes become fatter rather than gaining extra muscle which might be better for their health.

In this project we will test whether measurements of fat and muscle ('body composition measurements') are better than simple measures of weight and height for predicting the length of hospital stay and the child's nutritional status at discharge. This will allow us to decide whether we should use these measurements routinely when children are admitted to hospital.

What will happen to my son/daughter if they take part?

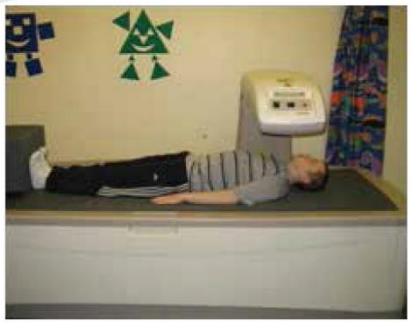
If you and your son/daughter agree to take part in this study, we will answer any questions you may have and then ask you both to sign a consent form. We will do the following:

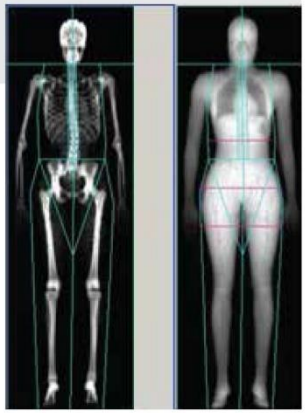
1. Measure your son/daughter's **height** and **weight**, arm and head **circumferences,** and measure **skinfolds** by pressing the fat gently on his/her arm, shoulder and tummy.

(these measurements don't hurt)

2. Measure the amount of **bone, fat and muscle** in the body using a DXA machine. We will ask your son/daughter to lie on a bed with a machine above that will take a picture of the whole skeleton.

We will give your son/daughter a picture of his/her skeleton to keep.





3. Use a technique that athletes use to measure their **body composition** at home. It involves passing a small electrical signal through the body, which is too weak to be felt, and takes only a few seconds.

4. Ask some **questions** about the type of food your son/daughter normally eats and whether (s)he has already received advice from a dietician.

5. With your permission, we will record some details about your child's medical condition from the **medical notes**, including the reason for admission to hospital, previous treatment and drugs taken.

6. After we have completed the measurements, we will ask you and your child to fill in a **short questionnaire** asking how you felt about taking part in the research.

7. We will ask you or your child to keep a **diary** of appetite and what is happening whilst in hospital. You have the choice of whether to do this via an app on a smartphone, tablet or laptop, or paper.

All of these tests together should take around **20 minutes**. Some medical conditions will mean that one or more of the tests cannot be done - and it is important for us to find out how often this happens.

But all children will be able to have some tests and all of the information we get will be useful!

We will **repeat** the measurements and questionnaires (apart from the DXA scan which will only be done once) when your child is discharged from hospital, or after 3 months if (s)he is still a patient.

Who is funding the research study?

The study has funding from the Great Ormond Street Childrens' Charity.

Thank you for reading this leaflet!

If you are **interested** in taking part or would like some more information, please contact us or visit the GOSH website:

EMAIL body.basics@gosh.nhs.uk
TEL. 07864539987
WEBSITE http://www.gosh.nhs.uk/research-and-innovation

Otherwise we will introduce ourselves once you are on the ward.

If you **do not want to take part** and do not want to be contacted by the researchers once admitted, please **text/email** your **child's name** and **consultant's name** and the **date** you expect your child to be admitted to:

EMAIL body.basics@gosh.nhs.uk
TEL/TEXT 07864539987

Outline of study v3 11.02.14

Great Ormond Street Hospital for Children NHS Foundation Trust

Childhood Nutrition Research Centre
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PARENT INFORMATION SHEET

THE BodyBasics STUDY

Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice

Your son/daughter is being invited to take part in a research study. Before you decide whether (s)he should take part or not, it is important to understand why the research is being done and what it will involve.

Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. You can find more general information about research on the Great Ormond Street Hospital (GOSH) website:

http://www.gosh.nhs.uk/research-and-innovation

What is the aim of the study?

The aim of this study is to find out whether measurements of body composition (fat and lean mass rather than just weight or height) can help to improve the nutritional care and recovery of children admitted to GOSH.

Why is the study being done?

We know that many children admitted to hospitals like GOSH have poor nutritional status – and that this is often made worse by their illness or by surgery. Poor nutrition may lead to a longer stay in hospital and a slower recovery. At the moment, nutritional advice and treatment is usually based on weight, which is a combination of fat, lean tissue and bone. There is some evidence that fat and lean tissue may have different effects on health and on the response to treatment. We also know that when underweight children are given extra nutrition they sometimes become fatter rather than gaining extra lean tissue which might be better for their health.

In this project we will test whether measurements of fat and lean tissue ('body composition measurements') are better than simple measures of weight and height for predicting the length of hospital stay and the child's nutritional status at discharge. This will allow us to decide whether we should use these measurements routinely when children are admitted to hospital.

Another aim of our study is to compare the different 'nutrition screening tools' which have been developed to try to predict which children are at most risk of poor nutrition. At the moment, no-one knows whether these screening tools result in better care, or which one is best. We will investigate this in our project to decide which works best for GOSH patients.

Why is my son/daughter being invited to take part?

We are inviting all children aged 5 years and above who are admitted to GOSH to take part in the study.

Does my son/daughter have to take part?

It is up to you and your son/daughter to decide whether or not (s)he takes part. If you do decide to take part you will be given this information sheet to keep. You will be asked to sign a consent form and your son/daughter will be asked to give assent. We will photocopy the consent form for you and keep one for our records. If your son/daughter decides to take part they are still free to withdraw at any time and without giving a reason. A decision to withdraw, or not to take part, will not affect any medical care your son/daughter may be receiving or will receive in the future.

What will happen to my son/daughter if they take part?

If you and your son/daughter agree to take part in this study, we will answer any questions you may have and then ask you both to sign a consent form. We will do the following:

1. Measure your son/daughter's height and weight, arm and head circumferences, and measure skinfolds by pressing the fat gently on his/her arm, shoulder and tummy (these measurements don't hurt).
2. Measure the amount of bone, fat and lean tissue in the body using a DXA machine. We will ask your son/daughter to lie on a bed with a machine above that will take a picture of the whole skeleton – and we will give your son/daughter a picture of his/her skeleton to keep. The DXA scan involves a tiny amount of radiation, which is less than a day's background radiation in the United Kingdom and less than one tenth of the radiation from a flight across the Atlantic.

Parent information sheet v5. 11.02.14

3. Use a technique that athletes use to measure their body composition at home. It involves passing a small electrical signal through the body, which is too weak to be felt, and takes only a few seconds. We will use two different machines to make this measurement. For one machine your child will stand on a platform and hold hand-grips; and for the other (s)he will lie in bed and sticky electrodes will be put on the hands and feet.
4. Measure handgrip strength using a meter that your child will squeeze.
5. Ask some questions about the type of food your son/daughter normally eats and whether (s)he has already received advice from a dietician. We will leave a diary to be completed daily for a week and 2 days per week thereafter until discharged from hospital. We would like you and/or your child to tell us about appetite, fluids and whether (s)he has a fever. You can choose whether to complete this on a smartphone, tablet or laptop by registering with the "Patients Know Best" website and downloading the app, or if you prefer on paper.
6. With your permission, we will record some details about your child's medical condition from the medical notes, including the reason for admission to hospital, previous treatment and drugs taken.
7. After we have completed the measurements, we will ask you and your child to fill in a short questionnaire giving your opinion about

All of these tests together should take a maximum of 20 minutes.
Some medical conditions will mean that one or more of the tests cannot be done - and it is important for us to find out how often this happens - but all children will be able to have some tests and all of the information we get will be useful!

We will repeat the measurements and questionnaires (apart from the DXA scan which will only be done once) when your child is discharged from hospital, or after 3 months if (s)he is still a patient.

What are the possible disadvantages and risks of taking part?

All of the tests are painless and will not harm your son/daughter. The DXA scan involves a tiny amount of radiation, which is less than a day's background radiation in the United Kingdom (to which we are all exposed), and less than one tenth of the radiation from a flight across the Atlantic.

What are the potential benefits of taking part?

Taking part in the study will not have any direct benefit to your son/daughter. We hope that the information we collect from the study will help us decide whether we should measure body composition to assess nutritional status when children are admitted to hospital, and whether these measurements could be used to improve their nutritional management and shorten the time they have to spend in hospital.

Who will have access to the research records?

Only the researchers will have access to the data collected during this study. **The results will be identified by a number only and all information collected will be completely confidential.**

What will happen to the results of the research study?

The results of this research will be published in a medical journal and presented at scientific meetings. We will also send you a summary of the results at the end of the study.

What if something goes wrong?

The research project has been approved by an Independent Research Ethics Committee which believes that it is of minimal risk to your son/daughter. However, any research can carry unforeseen risks and we want you to be informed of your rights in the unlikely event that any harm should occur as a result of taking part in this project.

You have the right to claim damages in a court of law. This would require you to prove fault on the part of the Hospital/Institute.

Who is funding the research study?

The study has funding from the Great Ormond Street Childrens' Charity, and the study sponsor is the UCL Institute of Child Health, London.

Who do I speak to if problems arise?

If you have any complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researchers. If the problems are not resolved, or you wish to comment in any other way, please contact the Patient Advise and Liaison Service (PALS) at GOSH. Tel: 02078297862 or email: pals@gosh.nhs.uk.

Parent information sheet v5. 11.02.14

Who do I speak to if I have any questions about the study?

You can contact one of the researchers- their details are at the end of this leaflet. If you would like to talk to somebody who is not connected to the study you can contact the Patient Advise and Liaison Service (PALS) at GOSH. Tel: 02078297862 or email: pals@gosh.nhs.uk

Details of how to contact the researchers :

Dr Jane Williams
Research Nurse
Institute of Child Health
30 Guilford Street
London WC1N 1EH
Tel: 0207 905 2743
Email: jane.williams@ucl.ac.uk

Nara Elizabeth Lara Pompa
PhD student
Institute of Child Health
30 Guilford Street
London WC1N 1EH
Tel: 0207 905 2806
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Ms Sarah Macdonald
Principal Dietician
Great Ormond Street Hospital for Children
NHS Foundation Trust
Great Ormond Street
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Email: sarah.macdonald@gosh.nhs.uk

STUDY EMAIL body.basics@gosh.nhs.uk
TEL/TEXT 07864539987

Thank-you for reading this information sheet!

Great Ormond Street Hospital for Children NHS Foundation Trust

Childhood Nutrition Research Centre
UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH

PATIENT INFORMATION SHEET
(under 11 years)

THE BodyBasics STUDY

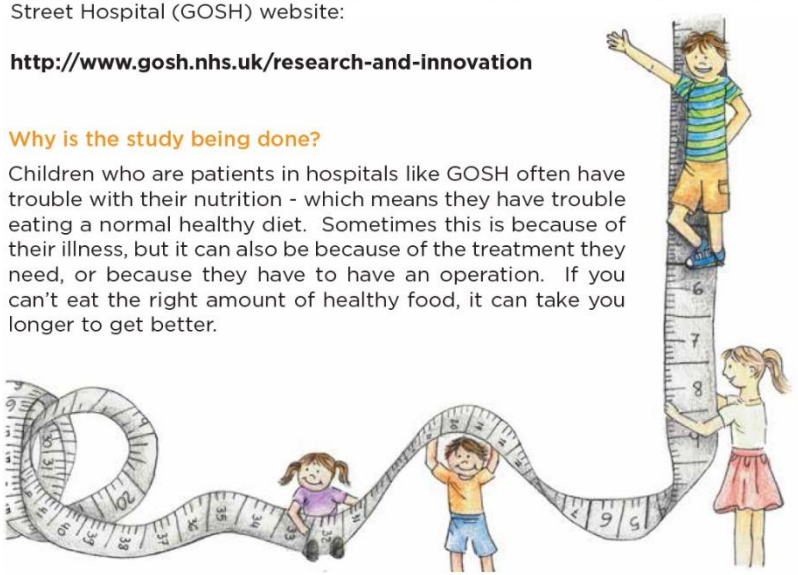
You are being invited to take part in a research study. Take time to decide if you want to **say YES or NO** to this.

Please read this information, or ask someone to read it to you. Don't worry if you don't understand it straight away. Your parents have also been told about this, and you can ask them to help you understand. You can find more general information about research on the Great Ormond Street Hospital (GOSH) website:

http://www.gosh.nhs.uk/research-and-innovation

Why is the study being done?

Children who are patients in hospitals like GOSH often have trouble with their nutrition - which means they have trouble eating a normal healthy diet. Sometimes this is because of their illness, but it can also be because of the treatment they need, or because they have to have an operation. If you can't eat the right amount of healthy food, it can take you longer to get better.



We are trying to find the best way to work out which children need special help with their nutrition while they are in hospital so they get better quicker and can go home sooner. We think that one way of doing this might be to measure the amount of fat and muscle a child has, rather than just the weight or height (which is what we do at the moment).

Why are you asking me to take part in the study?

We are asking you to take part in our study because you are a patient at GOSH and are **at least 5 years old**. We want to study as many children as possible.

Do I have to take part?

No, it is up to you to decide whether or not you want to take part. Even if you decide to take part, you can still leave the study at any time and you don't have to give us a reason.

What do I have to do?

If you agree to take part in the study, we will come and meet you and your parents when you are admitted to GOSH. We will ask you some questions and make some measurements – they are listed below.

None of the measurements are dangerous or hurt

a) We will **weigh** you and measure how **tall** you are.

b) We will measure your **size and shape** using a tape measure.

c) We will ask you to lie on a bed with a camera over the top which takes a **picture of your bones** and measures the amount of fat and muscle in the body. This is called a DXA machine. You need to keep still for a few minutes while it takes a picture. You will get a copy of the picture of your skeleton to take home.

d) We will measure the **fat and muscle** in your body using two machines that sportsmen often use. For one machine you will stand on a platform and hold hand-grips; and for the other you will lie in bed and sticky electrodes will be put on the hands and feet.

e) We will test your **hand strength** by asking you to squeeze a handle as hard as you can.

f) We will ask you and your parents some **questions** about how healthy you are and what you eat.

g) After we have done the measurements, we will **ask you what you thought** about them and whether there were any that you did not like for any reason.

h) We will ask you to keep a **diary** about your appetite and what is happening to you whilst you are in hospital. You can choose to do this on a smartphone/tablet/laptop or on paper.

- Photos of the machines/measurements are shown at the end of the leaflet.
- You will need to **wear loose clothes without any metal** – but you will not have to undress.
- Your parent or guardian will be with you all the time.
- All of these tests together should take about 20 minutes.
- We will do some of the measurements and questionnaires again when you are ready to go home from hospital.

Is there anything dangerous?

None of the measurements are dangerous and none of them hurt. If you don't want to do one of the tests you can tell us.

Who will know about me taking part?

Only the people doing the research will know about you doing the measurements.

Who do I speak to if I have any questions about the study?

You can speak to your parents who also have information about the study. You can also contact one of the researchers- their details are at the end of this leaflet. No one will be told that you have called and you do not have to give your name if you want to ask a question or talk about the tests. If you would like to talk to somebody who is not connected to the study you can contact the Patient Advise and Liaison Service (PALS) at GOSH. Tel: 02078297862 or email: pals@gosh.nhs.uk

Details of how to contact the researchers :

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Research Nurse
Institute of Child Health
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Ms Sarah Macdonald
Principal Dietician
Great Ormond Street Hospital
Great Ormond Street
London WC1N 3JH
Tel: 0207 405 9200 ext 5163
Email: sarah.macdonald@gosh.nhs.uk

STUDY
EMAIL body.basics@gosh.nhs.uk
TEL/TEXT 07864539987

Thank-you for reading this information sheet!

Younger child information sheet v3 11.02.14

Great Ormond Street Hospital for Children NHS Foundation Trust

Childhood Nutrition Research Centre
UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH

PATIENT INFORMATION SHEET
(age 11-15 years)

THE BodyBasics STUDY

Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice

You are being invited to take part in a research study. Before you decide whether to take part or not, it is important to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. You can find more general information about research on the Great Ormond Street Hospital (GOSH) website:

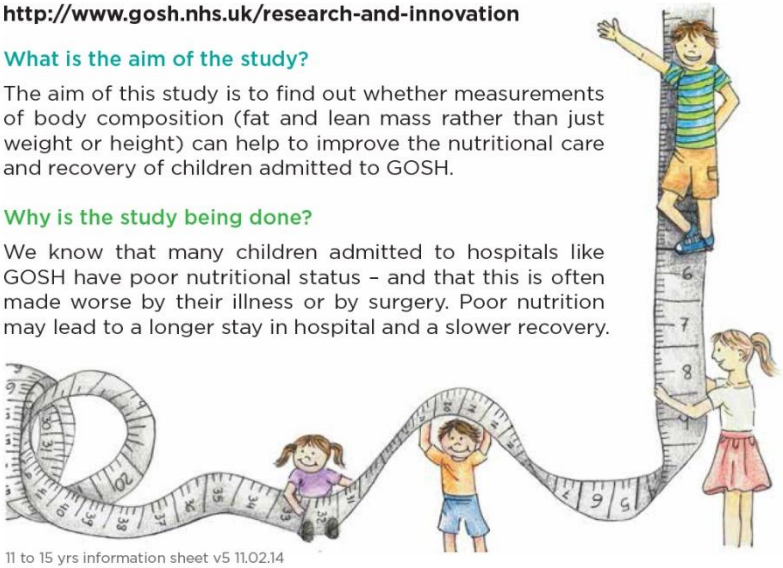
http://www.gosh.nhs.uk/research-and-innovation

What is the aim of the study?

The aim of this study is to find out whether measurements of body composition (fat and lean mass rather than just weight or height) can help to improve the nutritional care and recovery of children admitted to GOSH.

Why is the study being done?

We know that many children admitted to hospitals like GOSH have poor nutritional status – and that this is often made worse by their illness or by surgery. Poor nutrition may lead to a longer stay in hospital and a slower recovery.



At the moment, nutritional advice and treatment is usually based on weight, which is a combination of fat, lean tissue and bone. There is some evidence that fat and lean tissue may have different effects on health and on the response to treatment. We also know that when underweight children are given extra nutrition they sometimes become fatter rather than gaining extra lean tissue which might be better for their health.

In this project we will test whether measurements of fat and lean tissue ('body composition measurements') are better than simple measures of weight and height for predicting the length of hospital stay and the child's nutritional status at discharge. This will allow us to decide whether we should use these measurements routinely when children and young people are admitted to hospital.

Another aim is to compare the different 'nutrition screening tools' which have been developed to try to predict which patients are at most risk of poor nutrition. At the moment, no-one knows whether these screening tools result in better care, or which one is best. We will investigate this in our project to decide which works best for GOSH patients.

Why am I being asked to take part in the study?

All children aged 5 years and above who are admitted to GOSH are being invited to take part in this study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep. Your parent will be asked to sign a consent form and you will be asked to give written assent. We will photocopy the consent form for you and keep one for our records. If you decide to take part you are still free to withdraw at any time and without giving a reason. **A decision to withdraw, or not to take part, will not affect any medical care you may be receiving or will receive in the future**.

What will happen to me if I take part?

If you agree to take part in this study, we will answer any questions you may have and then ask you to sign an assent form. We will do the following:

1. Measure your **height and weight, arm & head circumferences,** and measure **skinfolds** by pressing the fat gently on your arm, shoulder and tummy (these measurements don't hurt).
2. Measure the amount of **bone, fat and lean tissue** in the body using a DXA machine. We will ask you to lie on a bed with a machine above that will take a picture of the whole skeleton – and we will give you a picture of your skeleton to keep. It involves a tiny amount of radiation, which is less than a day's background radiation in the UK, and less than one tenth of the radiation from a flight across the Atlantic.

3. Use a technique that athletes use to measure their **body composition** at home. It involves passing a small electrical signal through the body, which is too weak to be felt, and takes only a few seconds. We will use two different machines to make this measurement. For one machine you will stand on a platform and hold hand-grips; and for the other you will lie in bed and sticky electrodes will be put on the hands and feet.
4. Measure your **hand strength** with a meter that you squeeze.
5. Ask some **questions** about the type of food you normally eat and whether you have already received advice from a dietician. We will also ask you to keep a diary about your appetite and drinks that you have. You can choose to do this on a smartphone, tablet or laptop, or if you prefer, on paper.
6. With your permission, we will record some details about your medical condition from the **medical notes**, including the reason for admission to hospital, previous treatment and drugs taken.
7. After we have completed the measurements, we will ask you to fill in a **short questionnaire** giving your opinion about whether they are acceptable and whether there were any that you did not like for any reason.

All of these tests together should take a **maximum of 20 minutes.**

Some medical conditions will mean that one or more of the tests cannot be done - and it is important for us to find out how often this happens - but everyone will be able to have some tests and all of the information we get will be useful! We will **repeat** the measurements and questionnaires (apart from the DXA scan which will only be done once) when you are discharged from hospital, or after 3 months if you are still a patient.

What are the possible disadvantages and risks of taking part?

All of the tests are painless and will not harm you. The DXA scan involves a tiny amount of radiation, which is less than a day's background radiation in the United Kingdom (to which we are all exposed), and less than one tenth of the radiation from a flight across the Atlantic.

What are the potential benefits of taking part?

Taking part in the study will not have any direct benefit to you. We hope that the information we collect from the study will help us decide whether we should measure body composition to assess nutritional status when children are admitted to hospital, and whether these measurements could be used to improve their nutritional management and shorten the amount of time they have to spend in hospital.

Who will have access to the research records?

Only the researchers will have access to the data collected during this study. **The results will be identified by a number only and all information collected will be completely confidential**

What will happen to the results of the research study?

The results of this research will be published in a medical journal and presented at scientific meetings. We will also send you a summary of the results at the end of the study.

What if something goes wrong?

The research project has been approved by an Independent Research Ethics Committee which believes that it is of minimal risk to you. However, any research can carry unforeseen risks and we want you to be informed of your rights in the unlikely event that any harm should occur as a result of taking part in this project.

You have the right to claim damages in a court of law. This would require you to prove fault on the part of the Hospital/Institute.

Who is funding the research study?

The study has funding from the Great Ormond Street Children's Charity, and the study sponsor is the UCL Institute of Child Health, London.

Who do I speak to if problems arise?

If you have any complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researchers. If the problems are not resolved, or you wish to comment in any other way, please contact the Patient Advise and Liaison Service (PALS) at GOSH. Tel: 02078297862 or email: pals@gosh.nhs.uk.

Who do I speak to if I have any questions about the study?

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11 to 15 yrs information sheet v5 11.02.14

Details of how to contact the researchers :

Dr Jane Williams
Research Nurse
Institute of Child Health
30 Guilford Street
London WC1N 1EH
Tel: 0207 905 2743
Email: jane.williams@ucl.ac.uk

Nara Elizabeth Lara Pompa
PhD student
Institute of Child Health
30 Guilford Street
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Principal Dietician
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Tel: 0207 405 9200 ext 5163
Email: sarah.macdonald@gosh.nhs.uk

STUDY EMAIL body.basics@gosh.nhs.uk
TEL/TEXT 07864539987

Thank-you for reading this information sheet!

Great Ormond Street Hospital for Children NHS Foundation Trust

Childhood Nutrition Research Centre
UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH

PATIENT INFORMATION SHEET
(age 16+ years)

THE BodyBasics STUDY

Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice

You are being invited to take part in a research study. Before you decide whether to take part or not, it is important to understand why the research is being done and what it will involve.

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What is the aim of the study?

The aim of this study is to find out whether measurements of body composition (fat and lean mass rather than just weight or height) can help to improve the nutritional care and recovery of children admitted to GOSH.

Why is the study being done?

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Another aim of our study is to compare the different 'nutrition screening tools' which have been developed to try to predict which patients are at most risk of poor nutrition. At the moment, no-one knows whether these screening tools result in better care, or which one is best. We will investigate this in our project to decide which works best for GOSH patients.

Why am I being asked to take part in the study?

All children aged 5 years and above who are admitted to GOSH are being invited to take part in this study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep. You will be asked to sign a consent form. We will photocopy the consent form for you and keep one for our records. If you decide to take part you are still free to withdraw at any time and without giving a reason.

A decision to withdraw, or not to take part, will not affect any medical care you may be receiving or will receive in the future

What will happen to me if I take part?

If you agree to take part in this study, we will answer any questions you may have and then ask you to sign a consent form. We will do the following:

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Over 16 yrs information sheet v3 11.02.14

Who will have access to the research records?

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What will happen to the results of the research study?

The results of this research will be published in a medical journal and presented at scientific meetings. We will also send you a summary of the results at the end of the study.

What if something goes wrong?

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Tel: 0207 405 9200 ext 5163
Email: sarah.macdonald@gosh.nhs.uk

STUDY EMAIL body.basics@gosh.nhs.uk
TEL/TEXT 07864539987

Thank-you for reading this information sheet!

Over 16 yrs information sheet v3 11.02.14

15.2 Consent Forms

Great Ormond Street NHS Hospital for Children
NHS Foundation Trust

Childhood Nutrition Research Centre
UCL Institute of Child Health

PARENT/GUARDIAN CONSENT FORM

Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice

The BodyBasics Study

Sponsor protocol No: **11NT04** Investigator: **Dr Susan Hill**

Contact details: ☎ :**0207 9200 ext 0114** 💻: **susan.hill@gosh.nhs.uk**

Subject Identification No for this trial: _____

Please **initial box** to indicate agreement:

1	I confirm that I have read and understand the information sheet dated 11.02.14 (version 5) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2	I understand that my child's participation is voluntary and that he/she is free to withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected.	
3	I understand that relevant sections of my child's medical notes and data collected during the study, may be looked at by employees from Regulatory Authorities or from Great Ormond Street Hospital/ Institute of Child Health, where it is relevant to my child's taking part in this research. I give permission for these individuals to have access to my child's records.	
5	I agree to my child taking part in the above study.	
6	I agree to the study team contacting me in the future about further follow-up studies, although I would not be obliged to take part in any future study.	

_____
Name of Subject

_____ _____ _____
Name of Parent/Guardian Date Signature

_____ _____ _____
Name of Person taking consent Date Signature

Only the researchers will have access to the data collected during this study. The results will be identified by a number only and all information collected will be completely confidential.

1 copy for the Parent/guardian, 1 for the R&D section in the Medical Notes, original to be kept in the PI's site file, (version 3, dated11.02.14)

Great Ormond Street NHS Hospital for Children
NHS Foundation Trust

UCL INSTITUTE OF CHILD HEALTH
Childhood Nutrition Research Centre

ASSENT FORM

Title of the Research project:

Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice

The BodyBasics Study

Sponsor Protocol No: **11NT04**

Investigator: **Dr Susan Hill**

Contact details: ☎ : **0207 9200 ext0114** 💻: **susan.hill@gosh.nhs.uk**

Subject Identification No for this trial: _____

Please **initial box** to indicate agreement:

1	I have read and understand the information sheet dated 11.02.14 (version 5) for the above study and have had the chance to ask questions.	
2	I understand that taking part is voluntary and that I can decide not to take part at any time.	
3	I agree to take part in the above study.	

_____ _____ _____
Name of young person Date Signature

_____ _____ _____
Name of Person taking consent (if different from Investigator) Date Signature

Only the researchers will have access to the data collected during this study. The results will be identified by a number only and all information collected will be completely confidential.

1 copy for the Parent/guardian, 1 for the R&D section in the Medical Notes, original to be kept in the PI's site file, (version 3, dated 11.02.14)

Great Ormond Street NHS Hospital for Children
NHS Foundation Trust

Childhood Nutrition Research Centre
UCL Institute of Child Health

PARTICIPANT CONSENT FORM (16 yrs and older)

Title of the Research project:
Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice

The BodyBasics Study

Sponsor Protocol No: **11NT04** Investigator: **Dr Susan Hill**

Contact details: ☎ :**0207 9200 ext 0114** 💻: **susan.hill@gosh.nhs.uk**

Subject Identification No for this trial: _____

Please **initial box** to indicate agreement:

1	I confirm that I have read and understand the information sheet dated 11.02.14 (version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3	I understand that the relevant sections of my medical notes and data collected during the study may be looked at by employees from Regulatory Authorities or from Great Ormond Street Hospital/ Institute of Child Health, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
5	I agree to take part in the above study.	
6	I agree to the study team contacting me in the future about further follow-up studies, although I would not be obliged to take part in any future study.	

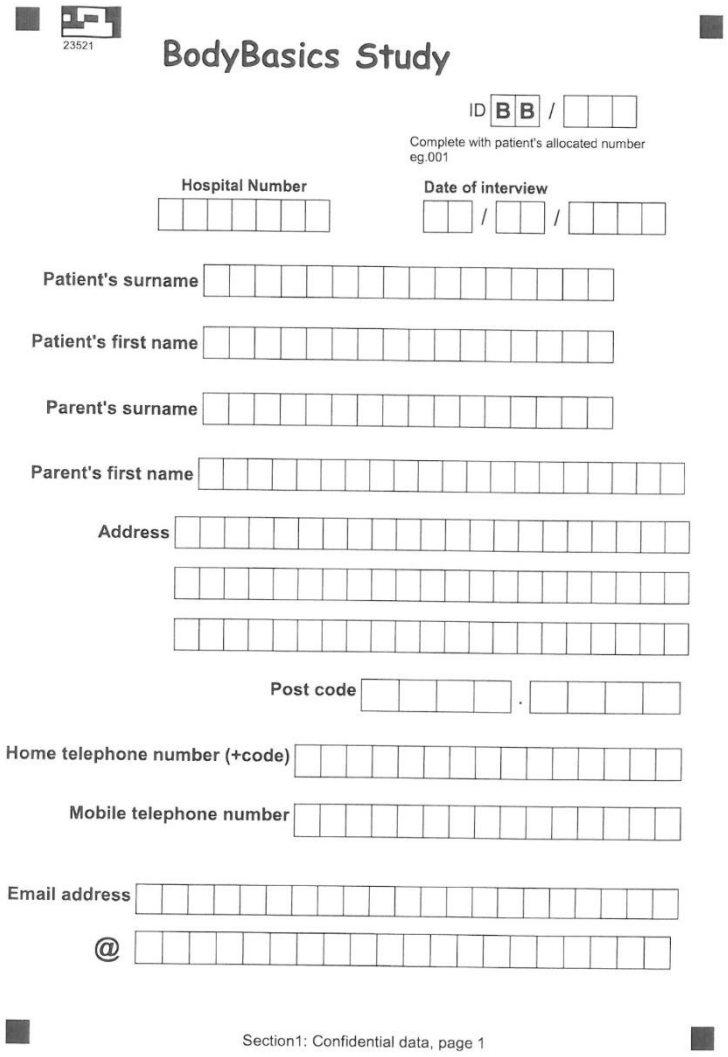
_____ _____ _____
Name of Patient Date Signature

_____ _____ _____
Name of Person taking consent Date Signature

Only the researchers will have access to the data collected during this study. The results will be identified by a number only and all information collected will be completely confidential.

1 copy for the Parent/guardian, 1 for the R&D section in the Medical Notes, original to be kept in the PI's site file, (version 4, dated 11.02.14)

15.3 Admission and Discharge collection forms



23521

BodyBasics Study

ID B B /

Complete with patient's allocated number eg.001

Hospital Number

Date of interview / /

Patient's surname

Patient's first name

Parent's surname

Parent's first name

Address

Post code .

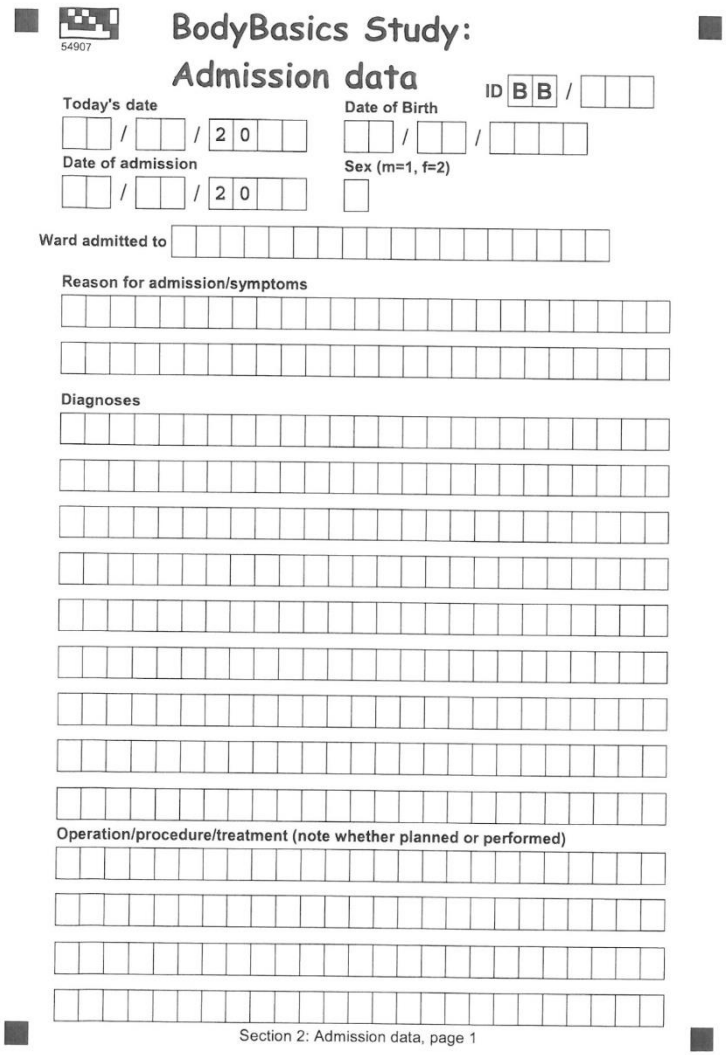
Home telephone number (+code)

Mobile telephone number

Email address

@

Section1: Confidential data, page 1



54907

BodyBasics Study:
Admission data

ID B B /

Today's date / / 2 0

Date of Birth / /

Date of admission / / 2 0

Sex (m=1, f=2)

Ward admitted to

Reason for admission/symptoms

Diagnoses

Operation/procedure/treatment (note whether planned or performed)

Section 2: Admission data, page 1

54907

BodyBasics Study

ID B B /

Oral steroids (do not include inhaled steroids)

In the last 6 months has the patient been prescribed? 1= Yes, 0= No
(If the family do not know or are not sure please refer to patient's notes)

No steroids in the last 6 months

Prescribed low dose steroids in the last 6 months

Prescribed high dose steroids in the last 6 months

Steroid name,dose,frequency and duration

Diet

How does the patient feed? 1= Yes, 0= No, 3= Partly

		Self		Carer
Orally	by		or	
Enterally	by		or	
Parenterally	by		or	

Comments on mode of feeding

54907

BodyBasics Study ID B B /

Does s/he eat the usual family diet?
1=Yes, 0= No

If no, in what way is it different?

What was a typical meal just prior to admission?

54907

BodyBasics Study

ID B B / _ _ _

How long has her/his diet been different from the usual family diet?

Less than 1 week ☐
1 week to 1 month ☐
1 month to 3 months ☐
3 months to 6 months ☐
More than 6 months ☐

Mark X in one box only

What was the patient's appetite like 6 weeks ago? _ _ _ %

Please ask the patient/parent to mark on the scale with 0 as no appetite and 10 for always hungry. Measure the distance from 0 in mm and insert in box above.

What was the patient's appetite like last week? _ _ _ %

Please ask the patient/parent to mark on the scale with 0 as no appetite and 10 for always hungry. Measure the distance from 0 in mm and insert in box above.

Has a dietitian been involved in her/his care? _ _ _

1=Yes <3months
2=Yes 3- 6 months
3=Yes, > 6 months
0= No

What was dietitian's advice?

General healthy eating ☐
Restricted/excluded ☐
Supplemented ☐
Enteral nutrition ☐
Parenteral nutrition ☐

Complete following boxes with details of advice

54907

BodyBasics Study

ID B B / _ _ _

Is the patient fluid restricted? _ _ _ 1= Yes, 0= No

Number of days fluid has been restricted _ _ _

If yes, is this;

Nil by mouth pre surgery _ _ _
Or due to underlying condition _ _ _

1= Yes, 0= No

Comments on condition, fluid and weight

54907

BodyBasics Study

ID B B / ☐☐☐

Physical activity

1= Yes, 0= No

Attending or attended mainstream school ☐☐☐

Wheelchair user taking part in PE or sport ☐☐☐

Wheelchair user NOT taking part in PE or sport ☐☐☐

Ambulatory and taking part in PE or sport ☐☐☐

Ambulatory and NOT taking part in PE or sport ☐☐☐

In the parent's opinion, compared to children of the same age, is their child's activity level?

Much less than peers ☐
Less than peers ☐
Same as peers ☐
More than peers ☐
Much more than peers ☐

Mark X in one box only

54907

BodyBasics Study

Measurements

ID B B / ☐☐☐

Date of measurement ☐☐ / ☐☐ / 2 0 ☐☐

Time of measurements (24hr) ☐☐.☐☐

Who has made the measurements? ☐☐

If any of the following measurements are not completed code the reason in the box as follows; **1. Patient declined, 2. Equipment not available, 3. Failed** and comment in the boxes over the page.

			Reason for non measurement
Height	☐☐☐.☐	☐☐☐.☐	☐
Weight	☐☐☐.☐	☐☐☐.☐	☐
MUAC	☐☐☐.☐	☐☐☐.☐	☐
Head cicumference	☐☐.☐	☐☐.☐	☐
Bicep SFT	☐☐☐.☐	☐☐☐.☐	☐☐☐.☐ ☐
Tricep SFT	☐☐☐.☐	☐☐☐.☐	☐☐☐.☐ ☐
Subscap SFT	☐☐☐.☐	☐☐☐.☐	☐☐☐.☐ ☐
Supra-il SFT	☐☐☐.☐	☐☐☐.☐	☐☐☐.☐ ☐
	FRONT	BACK	
Full ~~Half~~ arm-span	☐☐☐.☐	☐☐☐.☐	☐
Ulna	☐☐☐.☐	☐☐☐.☐	☐
Tibia	☐☐☐.☐	☐☐☐.☐	☐

54907 **BodyBasics Study**

ID B B /

Dominant hand grip strength . . Reason for non measurement

Dominant hand (L or R)? Handgrip setting (4-7)

Dual-energy X-ray absorptiometry

DXA Fat g DXA Lean g DXA BMC kg .

Record here any measurement not done and the reason why. Also note measurements that were not done **at the same time** as that recorded at the top of the previous page. If appropriate record measurements **not taken on the left side**

54907 **BodyBasics Study**

ID B B /

Impedance
Standing (Tanita)

Whole body | Right Leg | Left Leg | Right Arm | Left Arm | Reason for non measurement

Impedance
Lying (Quadscan)

	Test 1 number	Test 2 number
TBW%	.	.
TBW litre	.	.
ECW%	.	.
ECW litre	.	.
ICW%	.	.
ICW litre	.	.
BCM	.	.
Nutrition	.	.
Illness marker	.	.
Impedance 5 kHz		
Impedance 50 kHz		
Impedance 100 kHz		
Impedance 200 kHz		
Resistance 50 kHz		
Reactance 50 kHz	.	.
Phase angle	.	.

54907

BodyBasics Study

ID B B / | | |

Record here any oedema and note whether generalised or affecting limbs and if so, which limbs.

General comments

54907

BodyBasics Study

ID B B / | | |

Predicted length of stay

What is the predicted length of stay in days? | | |

Malnutrition screening tools (complete as if day of admission)

STRONG

1. Is the child in a poor nutritional status judged by subjective clinical assessment (diminished subcutaneous fat &/or muscle mass&/or hollow face? — Score 1 for Yes, 0 for No

2. Is there weight loss during the last weeks-months? — Score 1 for Yes, 0 for No

3. Is one of the following present?
Excessive diarrhoea(5 or more /days &/or vomiting (>3/day)
Reduced food intake during the last few days
Pre-existing nutritional intervention
Inadequate nutritional intake due to pain — Score 1 for Yes, 0 for No

4. Is there an underlying illness with risk for malnutrition (see STRONG list) or expected major surgery? — Score 2 for Yes, 0 for No

Total STRONG score:
4-5 points = High risk
1-3 points = Medium risk
0 points = Low risk

Total STRONG score | | |

GOSH

1. Height and weight > 2 centiles apart? — Score 1 for Yes, 0 for No

2. Food/feed intake poor, none or reduced recently? — Score 1 for Yes, 0 for No

3. Diarrhoea>5/day &/or vomiting >3/day? — Score 1 for Yes, 0 for No

54907

BodyBasics Study

ID B B / ☐☐☐

STAMP

1. Does the child have a diagnosis that has any nutritional implications? (refer to STAMP list)

Score 3 for definite, 2 for possible and 0 for none ☐

2. What is the child's nutritional intake?

No nutritional intake	Score 3	☐
Recently dercreased or poor nutritional intake	Score 2	
No change in eating pattern and good nutritional intake	Score 0	

3. Weight and height plotted on centiles:

>3 centiles apart or weight <2nd centile;	Score 3	☐
≥2 centiles apart;	Score 1	
0 to 1 centile apart (< 2 centiles)	Score 0	

Total STAMP score;
4 or more = high risk
2-3 = medium risk
0-1 = low risk

Total for STAMP ☐

PYMS

1. Is the BMI below the cut-off value in the table (refer to laminated sheet)?

Score 2 for Yes, 0 for No ☐

2. Has the child lost weight recently?

Yes, unintentional weight loss/clothes looser?	Score 1	☐
No	Score 0	

3. Had the child had a reduced intake (including feeds) for at least the past week?

Yes, No intake (or a few sipsof feed only) for at least the last week	Score 2	☐
Yes, Decrease of usual intake for at least the last week	Score 1	
No, usual intake	Score 0	

4. Will the child's nutrition be affected by the recent admission/codition for at least the next week?

Yes, no intake (or a few sips of feed only) for at least the next week	Score 2	☐
Yes, decreased intake &/or increased requirements &/or increased losses for at least the next week	Score 1	
No	Score 0	

Total PYMS score;
2 or more request dietetic review & repeat in 1 week
1 repeat PYMS in 3 days
0 repeat PYMS in 1 week

Total for PYMS ☐

45878

BodyBasics Study: Discharge data

ID B B / ☐☐☐

Complete with allocated number eg. 001

Today's date

☐☐ / ☐☐ / 2 0 ☐☐

Ward discharged from

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Length of hospital stay in days

☐☐☐

Discharged home (1) or another hospital (2)

☐☐☐

Operation/Procedure/Treatment received whilst inpatient

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

45878

Measurements

ID B B / ☐☐☐

Time of measurements (24hr) ☐☐.☐☐

Who is doing the measurements? ☐☐

If any of the following measurements are not completed code the reason in the box as follows; **1. Patient declined, 2. Equipment not available, 3. Failed** and comment in the boxes at the base of the page and over.

		Reason for non measurement
Height	☐☐☐.☐ ☐☐☐.☐	☐
Weight	☐☐☐.☐ ☐☐☐.☐	☐
MUAC	☐☐☐.☐ ☐☐☐.☐	☐
Head cicumference	☐☐.☐ ☐☐.☐	☐
Bicep SFT	☐☐☐.☐ ☐☐☐.☐ ☐☐☐.☐	☐
Tricep SFT	☐☐☐.☐ ☐☐☐.☐ ☐☐☐.☐	☐
Subscap SFT	☐☐☐.☐ ☐☐☐.☐ ☐☐☐.☐	☐
Supra-il SFT	☐☐☐.☐ ☐☐☐.☐ ☐☐☐.☐	☐

Check admission handgrip setting!!!

Dominant handgrip ☐☐.☐ ☐☐.☐ ☐ **Dominant hand L or R?** ☐

Record here any measurement not done and the reason why. Also note measurements that were not done **at the same time** as that recorded at the top of the page.

45878

BodyBasics Study

ID B B / ☐☐☐

Impedance
Standing (Tanita)

Whole body	Right Leg	Left Leg	Right Arm	Left Arm	Reason for non measurement
☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐

Impedance
Lying (Quadscan)

	Test 1 number	Test 2 number	
	☐☐☐	☐☐☐	☐
TBW%	☐☐.☐	☐☐.☐	
TBW litre	☐☐.☐	☐☐.☐	
ECW%	☐☐.☐	☐☐.☐	
ECW litre	☐☐.☐	☐☐.☐	
ICW%	☐☐.☐	☐☐.☐	
ICW litre	☐☐.☐	☐☐.☐	
BCM	☐☐☐.☐	☐☐☐.☐	
Nutrition	☐.☐☐	☐.☐☐	
Illness marker	☐.☐☐☐	☐.☐☐☐	
Impedance 5 kHz	☐☐☐	☐☐☐	
Impedance 50 kHz	☐☐☐	☐☐☐	
Impedance 100 kHz	☐☐☐	☐☐☐	
Impedance 200 kHz	☐☐☐	☐☐☐	
Resistance 50 kHz	☐☐☐	☐☐☐	
Reactance 50 kHz	☐☐☐.☐	☐☐☐.☐	
Phase angle	☐.☐	☐.☐	

45878

BodyBasics Study

ID B B /

Oral steroids (do not include inhaled steroids)

During the hospital stay has the patient had?
1= Yes, 0= No

No steroids

Low dose steroids — No. of days taken

High dose steroids — No. of days taken

Steroid name, dose and duration *(Only complete if unsure of category above)*

Diet

How is the patient fed? 1= Yes, 0= No, 3= Partly

		Self		Carer
Orally	by		or	
Enterally	by		or	
Parenterally	by		or	

Comments on mode of feeding

45878

BodyBasics Study

ID B B /

Is the patient eating their usual diet? 1=Yes, 0=No

In what way does the diet differ from the usual diet?

What is the patient's appetite like today? %

Please ask the patient/parent to mark on the laminated scale scale with 0 as no appetite and 10 for always hungry. Measure the distance from 0 in mm and insert in box above.

Has a dietitian been involved whilst in hospital? 1=Yes 0=No

What was dietitian's advice?

- General healthy eating ☐
- Restricted/excluded ☐
- Supplemented ☐
- Enteral nutrition ☐
- Parenteral nutrition ☐

Complete following boxes with details of advice

45878

BodyBasics Study

ID B B /

Is the patient fluid restricted? 1= Yes, 0= No

Comments on fluid restriction

Record here any oedema and note whether generalised or affecting limbs and if so, which limbs.

Additional Comments

15.4 Appetite scales

Admission Study no. **BB** ☐☐☐ Date _____

What was the patient's appetite like ***6 weeks*** ago? Please ask the patient/parent to mark on scale with 0 as no appetite to 10 for always hungry.

Never hungry — Always hungry

0 **10**

What was the patient's appetite like in the ***last*** **week**? Please ask the patient/parent to mark on scale with 0 as no appetite to 10 for always hungry.

Never hungry — Always hungry

0 **10**

Discharge Study no. **BB** ☐☐☐ Date _____

What is the patient's appetite like **today**? Please ask the patient/parent to mark on scale with 0 as no appetite to 10 for always hungry.

Never hungry — Always hungry

0 **10**

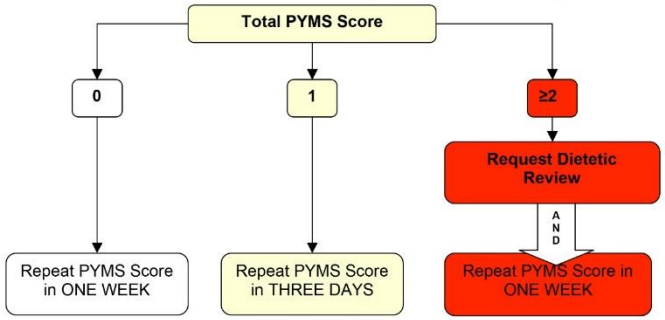
15.5 Malnutrition screening tools

Paediatric Yorkhill Malnutrition Score (PYMS)

Name:		**Hospital No:**	**Date**			
Surname:		**CHI:**	**Nurse Signature**			
DoB:			**Weight**			
Age:		**Sex: F / M**	**Height**			
Ward:		**Consultant:**	**BMI**			
Step 1	**Is the BMI below the cut-off value in the table overleaf?**	NO	**0**			
		YES	**2**			
Step 2	**Has the child lost weight recently?**	NO	**0**			
		YES • Unintentional weight loss • Clothes looser • Poor weight gain (if <2yrs)	**1**			
Step 3	**Has the child had a reduced intake (including feeds) for at least the past week?**	NO Usual intake	**0**			
		YES Decrease of usual intake for at least the past week	**1**			
		YES No intake (or a few sips of feed only) for at least the past week	**2**			
Step 4	**Will the child's nutrition be affected by the recent admission/condition for at least the next week?**	NO	**0**			
		YES For at least the next week • 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 week	**2**			
Step 5	**Calculate total score** (total of steps 1-4)	**Total PYMS Score**				

PYMS must be completed by a registered nurse

PYMS Dietetic Management Pathway



****NB: Regardless of PYMS score if you have any nutritional concerns about this patient please refer to dietitians following initial screening.****

Body Mass Index (BMI) Scoring Guide

(If the BMI calculated is less than that shown for age and gender, answer Yes for Step 1)

Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Boys	15.0	14.5	14.0	13.5	13.5	13.5	13.5	13.5	13.5	14.0	14.0	14.5	15.0	15.5	16.0	16.5	17.0	17.0
Girls	15.0	14.0	13.5	13.5	13.0	13.0	13.0	13.0	13.0	13.5	14.0	14.5	15.0	15.5	16.0	16.5	17.0	17.0

Notes – Comments

	Date: ___/___/_____	Date: ___/___/___	Date: ___/___/___
Nursing Comments (including reason unable to complete PYMS step)			
Health Professional Request made to:	Dietitian □ Dentist □ SALT □ Other □ Specify……	Dietitian □ Dentist □ SALT □ Other □ Specify……	Dietitian □ Dentist □ SALT □ Other □ Specify……
Health Professional Comments			

STAMP screening form

This form can be used to screen a child up to three times – please date, sign and initial the space at the bottom of this sheet every time you do so.

Step 1 – Diagnosis				
Does the child have a diagnosis that has any nutritional implications?	Score	1st screening	2nd screening	3rd screening
Definite nutritional implications	3			
Possible nutritional implications	2			
No nutritional implications	0			
Step 2 – Nutritional intake				
What is the child's nutritional intake?	Score	1st screening	2nd screening	3rd screening
No nutritional intake	3			
Recently decreased or poor nutritional intake	2			
No change in eating patterns and good nutritional intake	0			
Step 3 – W				
t or the centile quick reference tables to determine the child's measurements	Score	1st screening wt: ht:	2nd screening wt: ht:	3rd screening wt: ht:
> 3 centile spaces/≥ 3 columns apart (or weight < 2nd centile)	3			
> 2 centile spaces/= 2 columns apart	1			
0 to 1 centile spaces/columns apart	0			
Step 4 – Overall risk of malnutrition				
Add up the scores from the boxes in steps 1–3 to calculate the overall risk of malnutrition	Score	1st screening	2nd screening	3rd screening
High risk	≥4			
Medium risk	2–3			
Low risk	0–1			

Step 5 – Care plan	
What is the child's overall risk of malnutrition, as calculated in step 4?	Use management guidelines and/or local nutrition policies to develop a care plan for the child
High risk	• Take action • Refer the child to a Dietitian, nutritional support team, or consultant • Monitor as per care plan
Medium risk	• Monitor the child's nutritional intake for 3 days • Repeat the STAMP screening after 3 days • Amend care plan as required
Low risk	• Continue routine clinical care • Repeat the STAMP screening weekly while the child is an in-patient • Amend care plan as required

Please complete after each screening	Date	Signature	Initials
1st screening			
2nd screening			
3rd screening			

Child's name: _____

DOB: _____

Hospital no.: _____

Supported by an educational grant from Abbott Nutrition

Central Manchester University Hospitals NHS Foundation Trust

Diagnosis table

To be used to assign a score for step 1 of STAMP

Definite nutritional implications	Possible nutritional implications	No nutritional implications
▪ Bowel failure, intractable diarrhoea ▪ Burns and major trauma ▪ Crohn's disease ▪ Cystic fibrosis ▪ Dysphagia ▪ Liver disease ▪ Major surgery ▪ Multiple food allergies/intolerances ▪ Oncology on active treatment ▪ Renal disease/failure ▪ Inborn errors of metabolism	▪ Behavioural eating problems ▪ Cardiology ▪ Cerebral palsy ▪ Cleft lip and palate ▪ Coeliac disease ▪ Diabetes ▪ Gastro-oesophageal reflux ▪ Minor surgery ▪ Neuromuscular conditions ▪ Psychiatric disorders ▪ Respiratory syncytial virus (RSV) ▪ Single food allergy/intolerance	▪ Day case surgery ▪ Investigations

- While every effort has been made to include diagnoses that have nutritional implications, this list is not exhaustive
- If you have any queries, please discuss them with a Dietitian

STAMP should be used in association with Trust referral guidelines and policies

Supported by an educational grant from Abbott Nutrition

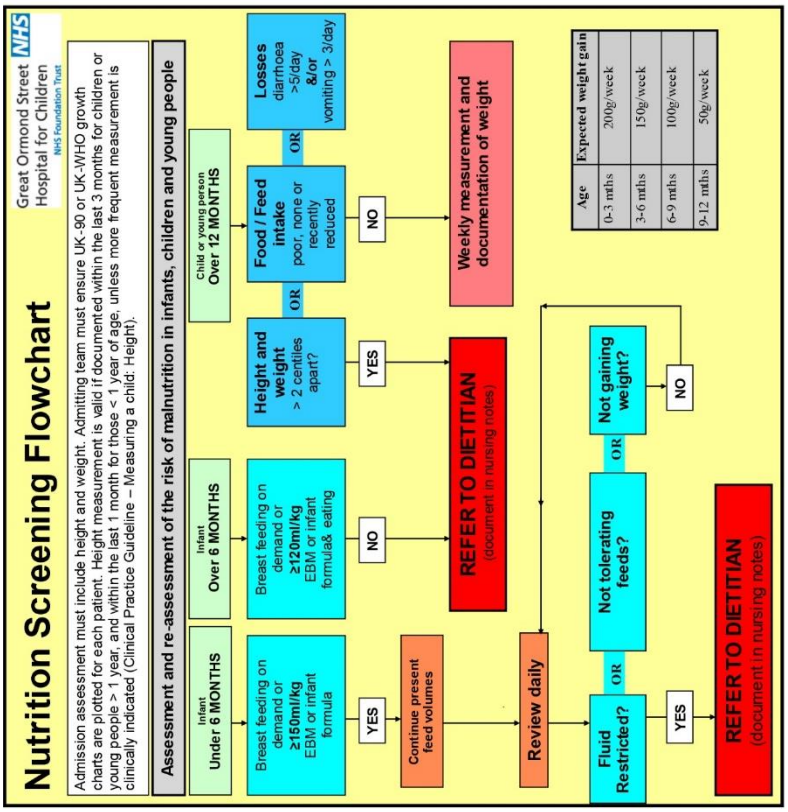
Central Manchester University Hospitals NHS Foundation Trust

List of underlying illnesses with risk for malnutrition

- Anorexia nervosa
- Burns
- Bronchopulmonary dysplasia (maximum age 2 years)
- Coeliac disease
- Cystic fibrosis
- Dysmaturity/prematurity (corrected age 6 months)
- Cardiac disease, chronic
- Infectious disease
- Inflammatory bowel disease
- Cancer
- Liver disease, chronic
- Kidney disease, chronic
- Pancreatitis
- Short bowel syndrome
- Muscle disease
- Metabolic disease
- Trauma
- Mental handicap/retardation
- Expected major surgery
- Not specified (classified by doctor)

STRONGkids: Screening Tool for Risk of Impaired Nutritinal status and Growth

Screening for risk of malnutrition: once a week in children aged 1 month – 18 years	Score → points	
1) Is the patient in a poor nutritional status judged with subjective clinical assessment (diminished subcutaneous fat and/or muscle mass and/or hollow face)?	No	Yes → 1
2) Is there weight loss or no weight gain (infants < 1 year) during the last weeks-months?	No	Yes → 1
3) Is one of the following items present? ▪Excessive diarrhoea (≥5 /day) and/ or vomiting (>3 /day) ▪Reduced food intake during the last few days ▪Pre-existing nutritional intervention ▪Inadequate nutritional intake due to pain	No	Yes → 1
4) Is there an underlying illness with risk for malnutrition (*see list*) or expected major surgery?	No	Yes → 2



STRONG$_{kids}$ screening tool

Risk of malnutrition and need for intervention		
Score	**Risk**	**Intervention and follow-up**
4-5 points	**High risk**	Consult doctor and dietician for full diagnosis and individual nutritional advice and follow-up. Check weight twice a week and evaluate nutritional advice Evaluate the nutritional risk weekly
1-3 points	**Medium risk**	Consider nutritional intervention Check weight twice a week Evaluate the nutritional risk weekly
0 points	**Low risk**	No nutritional intervention necessary. Check weight regularly (according to hospital policy) Evaluate the nutritional risk weekly.

15.6 Patient diaries

STUDY DIARY

THE Body Basics STUDY

Please complete this diary **every day**.

You may fill in the diary yourself or get someone from your family to help you.

If you have any questions you can contact **Sarah**, **Nara** or **Jane**:

EMAIL
body.basics@gosh.nhs.uk

TELEPHONE / TEXT
07864539987

If you are leaving hospital to go home or to another hospital:

Please text/email us or ask a member of staff to tell us you are being discharged so that we can repeat the measurements.

If you are leaving hospital at the week-end:

Please ask a member of staff to weigh you and record the weight here:

.....

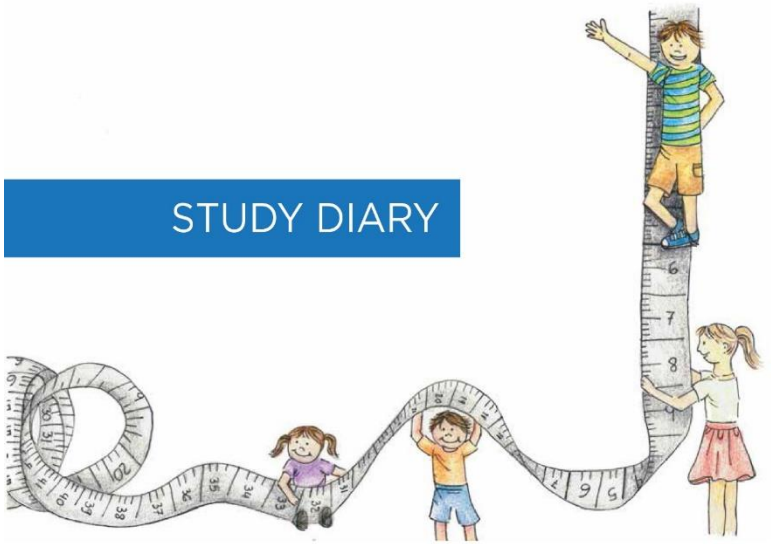
Please leave the booklet on the ward when you leave.

Thank-you for taking part in this study!

STUDY ID .....
DATE OF ADMISSION .....
WARD .....

THE Body Basics STUDY

STUDY DIARY



Version 1, 25/06/2013

INFO

We would like to know a little about your/your child's appetite and health whilst in hospital.

Please answer the questions in **Section 1 once** and the questions in **Section 2 every day for a week**.

If you are in hospital for more than a week, we will bring you another booklet which you only need complete two days a week from week 2 onwards.

If you have any questions or would like some help you can contact **Sarah**, **Nara** or **Jane** who will visit you on the ward. Contact details are on the front page of this booklet.

SECTION 01

When you were admitted we asked you some questions and did some measurements. We would like to know how you felt about having the measurements done.

Please **mark on the line** to show how you feel.

Here are 2 examples:

Mark here if you were **happy** doing the measurement

Mark here if you really **didn't like** doing the measurement

YOU CAN MAKE A MARK ANYWHERE ALONG THE LENGTH OF THE LINE THAT SHOWS HOW YOU FEEL.

ONLY MARK THE LINE FOR MEASUREMENTS THAT YOU HAVE DONE.

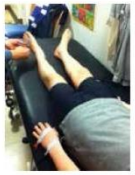
HOW TALL AND HEAVY


MEASURING HEAD AND ARM

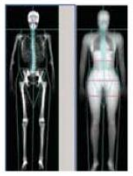

MEASURING FAT

HAND STRENGTH

MEASURING MUSCLE

WHOLE BODY SCAN

SECTION 02

Please complete the questions in this section **every day for a week**.
If you are in hospital for more than a week we will give you another booklet to complete 2 days per week.

DAY 1

(the day after the day you came into hospital)

DATE ...../...../.....

Please mark your answer [X]

And don't forget to **attach a sticker** for the day after you finish!

STICKER of the day

01 Who is answering the questions?

PARENT PATIENT

02 Have you been drinking normally today? YES NO

If not, why not?
Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? YES NO

Vomiting for 3 or more times a day? YES NO

05 How have you had your food today?

By mouth? YES NO

By tube into the stomach? YES NO

By tube into the vein? YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital YES NO

Supplied by your parents/self YES NO

A combination of both YES NO

07 Did you eat your usual amount today? Tick one.

MORE THAN USUAL SAME AS USUAL LESS THAN USUAL

08 What was your appetite like today?

Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

NEVER HUNGRY ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? YES NO

DAY 2

STICKER of the day

Please mark your answer [X]

01 Who is answering the questions?

○ PARENT ····· ○ PATIENT

02 Have you been drinking normally today? ····· YES NO

If not, why not?

Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? ····· YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? ····· YES NO

Vomiting for 3 or more times a day? ····· YES NO

05 How have you had your food today?

By mouth? ····· YES NO

By tube into the stomach? ····· YES NO

By tube into the vein? ····· YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital ····· YES NO

Supplied by your parents/self ····· YES NO

A combination of both ····· YES NO

07 Did you eat your usual amount today? Tick one.

○ MORE THAN USUAL ····· ○ SAME AS USUAL ····· ○ LESS THAN USUAL

08 What was your appetite like today?

Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

NEVER HUNGRY ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? ····· YES NO

DAY 3

STICKER of the day

Please mark your answer [X]

01 Who is answering the questions?

PARENT ○ ○ PATIENT

02 Have you been drinking normally today? YES NO

If not, why not?

Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? YES NO

Vomiting for 3 or more times a day? YES NO

05 How have you had your food today?

By mouth? YES NO

By tube into the stomach? YES NO

By tube into the vein? YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital YES NO

Supplied by your parents/self YES NO

A combination of both YES NO

07 Did you eat your usual amount today? Tick one.

○ MORE THAN USUAL ○ SAME AS USUAL ○ LESS THAN USUAL

08 What was your appetite like today?

Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

0 — 10

NEVER HUNGRY — ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? YES NO

DAY 4

STICKER of the day

Please mark your answer [X]

01 Who is answering the questions?

PARENT ○ ····· ○ PATIENT

02 Have you been drinking normally today? ····· YES NO

If not, why not?
Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? ····· YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? ····· YES NO

Vomiting for 3 or more times a day? ····· YES NO

05 How have you had your food today?

By mouth? ····· YES NO

By tube into the stomach? ····· YES NO

By tube into the vein? ····· YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital ····· YES NO

Supplied by your parents/self ····· YES NO

A combination of both ····· YES NO

07 Did you eat your usual amount today? Tick one.

○ MORE THAN USUAL ····· ○ SAME AS USUAL ····· ○ LESS THAN USUAL

08 What was your appetite like today?

Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

NEVER HUNGRY ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? ····· YES NO

DAY 5

STICKER of the day

Please mark your answer [X]

01 Who is answering the questions?

PARENT ○ ····· ○ PATIENT

02 Have you been drinking normally today? ····· YES NO

If not, why not?

Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? ····· YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? ····· YES NO

Vomiting for 3 or more times a day? ····· YES NO

05 How have you had your food today?

By mouth? ····· YES NO

By tube into the stomach? ····· YES NO

By tube into the vein? ····· YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital ····· YES NO

Supplied by your parents/self ····· YES NO

A combination of both ····· YES NO

07 Did you eat your usual amount today? Tick one.

○ MORE THAN USUAL ····· ○ SAME AS USUAL ····· ○ LESS THAN USUAL

08 What was your appetite like today?

Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

NEVER HUNGRY ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? ····· YES NO

DAY 6

STICKER of the day

Please mark your answer [X]

01 Who is answering the questions?

PARENT ○ ····· ○ PATIENT

02 Have you been drinking normally today? ····· YES NO

If not, why not?
Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? ····· YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? ····· YES NO

Vomiting for 3 or more times a day? ····· YES NO

05 How have you had your food today?

By mouth? ····· YES NO

By tube into the stomach? ····· YES NO

By tube into the vein? ····· YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital ····· YES NO

Supplied by your parents/self ····· YES NO

A combination of both ····· YES NO

07 Did you eat your usual amount today? Tick one.

○ MORE THAN USUAL ····· ○ SAME AS USUAL ····· ○ LESS THAN USUAL

08 What was your appetite like today?

Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

NEVER HUNGRY ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? ····· YES NO

DAY 7

STICKER of the day

Please mark your answer [X]

01 Who is answering the questions?

PARENT ○ ····· ○ PATIENT

02 Have you been drinking normally today? ····· YES NO

If not, why not?
Is it because you are going to have an operation? YES NO

Or is there another reason?
For example, too ill or just had an operation?

.....

.....

03 Have you an intravenous (IV) drip for fluids? ····· YES NO

04 Has there been increased fluid loss (diarrhoea &/or vomiting) today? YES NO

Diarrhoea for 5 or more times a day? ····· YES NO

Vomiting for 3 or more times a day? ····· YES NO

05 How have you had your food today?

By mouth? ····· YES NO

By tube into the stomach? ····· YES NO

By tube into the vein? ····· YES NO

06 If you have had you food by mouth was your food:

Supplied by the hospital ····· YES NO

Supplied by your parents/self ····· YES NO

A combination of both ····· YES NO

07 Did you eat your usual amount today? Tick one.

○ MORE THAN USUAL ····· ○ SAME AS USUAL ····· ○ LESS THAN USUAL

08 What was your appetite like today?

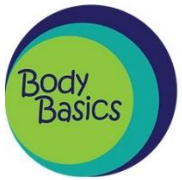
Place a **mark on the line** that shows how hungry you felt on a scale of 0 to 10

NEVER HUNGRY ALWAYS HUNGRY

09 Have you had a fever (high temperature) today? YES NO

10 Have you had surgery today? ····· YES NO

End of patient diary.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MONDAY


TUESDAY

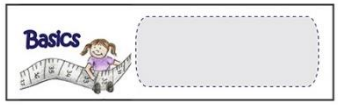

WEDNESDAY


THURSDAY


FRIDAY


SATURDAY


SUNDAY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BODY BASICS

Great Ormond Street Hospital for Children
NHS Foundation Trust

Childhood Nutrition Research Centre
Institute of Child Health

CERTIFICATE OF APPRECIATION

Awarded to

.....

In recognition of your valuable contribution to the BodyBasics study

Signature ..... Date.....

Version 2, 25/06/2013

Body Basics

Great Ormond Street Hospital for Children
NHS Foundation Trust

Childhood Nutrition Research Centre
Institute of Child Health

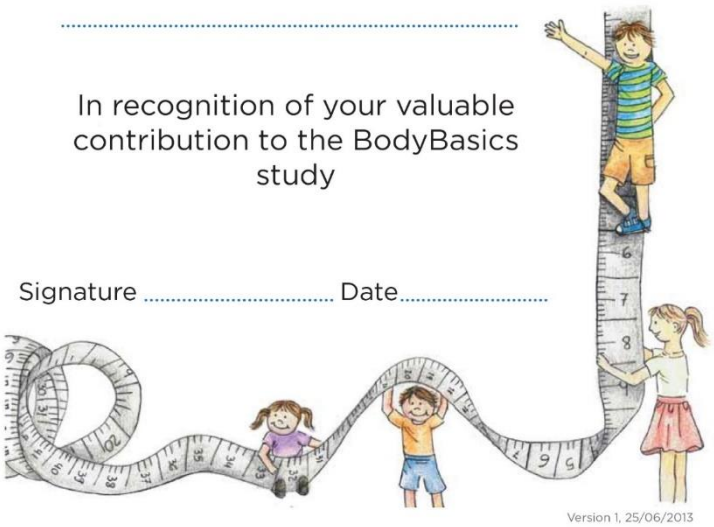
CERTIFICATE OF APPRECIATION

Awarded to

.....

In recognition of your valuable contribution to the BodyBasics study

Signature ..... Date.....



Version 1, 25/06/2013

15.8 Ethical approvals

NHS
Health Research Authority
NRES Committee London - Central
Skipton House
80 London Road
London
SE1 6LH

Telephone: 020 797 22565
Facsimile: 020 797 22592

06 August 2013

Dr Susan M Hill
Consultant Paediatric Gastroenterologist
Great Ormond Street Hospital for Children
Great Ormond Street
London
WC1N 3TH

Dear Dr Hill

Study title:	**Use of body composition measurements in the nutritional management of sick children; translating research into clinical practice.**
REC reference:	**13/LO/1076**
Protocol number:	**V1251**
IRAS project ID:	**127834**

The Research Ethics Committee reviewed the above application at the meeting held on 31 July 2013. Thank you for attending to discuss the application.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Mrs Nischinth Cherodian, NRESCommittee.SECoast-BrightonandSussex@nhs.net.

Ethical opinion

a. The Chair asked Ms Williams to confirm that information was sent out for participants to opt out of the study. Ms Williams said that participants can text or email back that they do not want to take part; once they arrive in hospital they would not be approached. If participants want to take part, one of the care team will contact them.

b. The Chair asked Ms Williams to check with UCL and GOSH how long data should be kept for and informed Ms Williams that data for children is usually 7 years and not 6-12 months as stated in the IRAS form. Ms Williams agreed to check and inform the Committee.

UCL RESEARCH ETHICS COMMITTEE
ACADEMIC SERVICES

UCL

8th July 2016

Professor Mary Fewtrell
Institute of Child Health
UCL

Dear Professor Fewtrell

Notification of Ethical Approval
Re: Ethics Application 6739/001: Use of body consumption measurements in clinical practice. Perspectives of paediatrics dietitians

I am pleased to confirm in my capacity as Chair of the UCL Research Ethics Committee (REC) that I have ethically approved your study until 8th July 2017.

Approval is subject to the following conditions.

1. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form': http://ethics.grad.ucl.ac.uk/responsibilities.php

2. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

3. For non-serious adverse events the Chair or Vice-Chair of the Ethics Committee should again be notified via the Ethics Committee Administrator (ethics@ucl.ac.uk) within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

On completion of the research you must submit a brief report of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

Yours sincerely

Professor John Foreman
Chair of the UCL Research Ethics Committee

Cc: Nara Pompa, Applicant

Academic Services, 1-19 Torrington Place (9th Floor),
University College London
Tel: +44 (0)20 3108 8216
Email: ethics@ucl.ac.uk
http://ethics.grad.ucl.ac.uk/

15.9 Sample size calculations

INITIAL SAMPLE SIZE CALCULATION

Difference to be detected	SD of measurement	Significance	F value	Power	Sample size required per group
0.5	1.27	0.05	8.85	80	102

Adjustment for unbalanced groups:

Sample size required per group	Imbalance ratio *	Group 1	Group 2	Total sample size
102	**4**	64	256	**319**

(*) assuming 20% of patients will be classified as high risk

Power of current recruitment (October 2014)

	high risk *(%)*	high risk *(n)*	no risk *(n)*	total *(n)*	Imbalance ratio
PYMS	28	36	92	128	2.6
STAMP	38	48	80	128	1.7
STRONG	21	27	101	128	3.7

Considering the unbalanced groups:

	Current sample size	Observed imbalance ratio	Group 1	Group 2	Sample size per group if balanced
PYMS	128	2.6	36	92	51
STAMP	128	1.7	48	80	60
STRONG	128	3.7	27	101	43

Power calculation:

	Sample size per group if balanced	Significance	Difference to be detected	SD of measurement *	Power with current sample
PYMS	51	0.05	0.5	1.0	**71**
STAMP	60	0.05	0.5	1.0	**78**
STRONG	43	0.05	0.5	1.0	**64**

(*) observed SD for most measurements of BC: 1.0-1.2

New sample size calculation

Considering unbalanced groups:

	New target total sample size	Observed imbalance ratio	Group 1	Group 2	Calculated sample size required per group
PYMS	**150**	2.6	42	109	60
STAMP	**151**	1.7	56	96	70
STRONG	**150**	3.7	32	119	50

Power calculation:

	Sample size per group if balanced	Significance	Difference to be detected	SD of measurement	Power with current sample
PYMS	60	0.05	0.5	1.0	**78**
STAMP	70	0.05	0.5	1.0	**84**
STRONG	50	0.05	0.5	1.0	**71**

15.10 Audit of ward equipment

Ward	Place kept	HT equipment	Diff on calibration	Place kept	WT equipment	Serial no	Date last calibrated	Diff on calibration	Notes
Safari (S9AB)	HT and WT room	Fixed Seca electronic (Also sitting height-out by 5mm)	Nil	HT and WT room	Marsden integrated (Sit and stand)	42066	Due June 13	Nil	
Safari day care (S9CD)	HT and WT room	Fixed seca electronic	Unable to calibrate due to position of screw		Marsden integrated Marsden sitting	42067 22441	Due June 13	Nil	
Island (S7CD)		Nil		corridor	Seca sitting	43664	Due June 13	Nil	
Island DU (S7CD)	TTT room	Seca fixed electronic (46186)	-0.7		Seca standing	31871	Due June 13	Nil	
Penguin S6D		Harpenden/Holtain 18244	-0.5		Marsden standing Seca sitting	32957 43679	Due June 13	Nil	
Penguin S6C		Holtain stadiometer (+calibration rod) (21982)	Nil		Seca sitting	43680	Due June 13	Nil	
Miffy-TCU S4CD		Nil		Corridor Equip room	Standing Marsden Seca sitting	41678 Nil	Due June 13	Nil	
Peter Pan (S3CD)	Assisted bathroom	Holtain stadiometer (18241)	-0.1	Bathroom	Seca	43669	Due June 13	Nil	
Elephant (6)	TTT room In corridor	Wall mounted-not working Leicester HT measure(portable)	+2mm	TTT room	Seca sitting Standing scales –flat battery		May 2012	Nil	Equipment will move-to room being changed
Lion (6)	Nurses station	Marsden portable	Nil	Corridor	Seca sitting		May 2012	Nil	
Squirrel (5)	TTT room	Holdan stadiometer	-0.5mm	Equip store TTT room	Seca sitting Marsden standing		Both to be calibrated June 2013	Nil -100g at 10kg -225g at 20kg	Charge nurse to be informed
Robin (5)		Leicester HT measure(portable)	Nil	Corridor	Marsden standing Seca sitting		Both to be calibrated June 2013	Nil Nil	

Fox (5)		Share the above measure			Seca sitting X 3	44401 43661 32366	June 13 ? June13	Nil Nil Nil	Standing scales in all rooms-not possible to calibrate
Eagle (7)	TTT room	Seca electronic (not fixed)	47160	nil	In corridor	Marsden standing Marsden standing Marsden sitting Seca sitting	48499 25503 46555 41616	Due May 13	Nil
Bear (6)	TTT room	3 stadiometers Seca electronic (fixed) Seca electronic (not fixed) Portable Seca	47124 47182 48736	-4 mm -1 mm Nil	TTT room Assisted b'room In corridor	Marsden E standing Seca sitting Seca sitting Marsden sitting Marsden standing Marsden standing	46630 18944 43667 46556 41680 43688	All due may 2013	Nil -200g Nil Nil Nil Nil
Koala (5)	In corridor	Seca	48736	Nil	Storage room	Seca sitting Marsden sitting Standing Not calibrated) Marsden	43667 46556 41680	All Due May 13	Nil
Sky (6)	Equipment Room	Holtain stadiometer (+ calibration rod)	45020	-0.45 (ward informed)	Equip room	Seca sitting Marsden standing Hoist scales	43673 nil	Both Due June 13	Nil Nil
Bumblebee (5)	Nurses station	Fixed electronic Seca stadiometer	-	0	Assisted bathroom	Seca sitting	43665	June 13	Nil
Butterfly (4)	Nurses station	Fixed electronic Seca stadiometer		-0.4 (ward informed)		Seca sitting (cream) Marsden sitting Marsden sitting	43663 48856 48855	June 13	Nil Nil Nil
Kingfisher (3)	Weighing room	Holtain stadiometer	43414	+0.1		Seca standing Seca sitting	40028 43666	May 13 June 13	Nil Nil
Badger (Cardiac 5)	TTT room	Fixed Holtain stadiometer	17580	-1mm	Corridor	Seca standing Seca sitting	24500 22753	Both Due May 13	Nil Nil

15.11 Summary of MST validation studies

Author, year	Study design	Subjects	Setting / Country	MST	Malnutrition prevalence	MSTs Applicability	MSTs Concurrent validity	MSTs Criterion validity	MSTs Predictive validity
Mărginean, 2014	Prospective observational study	Two hundred seventy-one children, median age of 5.2 years and median hospital stay of 2.01 days	Tertiary teaching hospital in Romania	STRONGkids	Prevalence of malnutrition and severe malnutrition was 37% and 15% respectively. Higher in smaller age and a longer duration of hospitalization (p=0.0001).			kappa coefficient between STRONGkids and WHO malnutrition (WFH, HFS SDS) was 0.61. When a low serum protein level was used in upgrading STRONGkids risk category, kappa increased significantly to 0.71 (p=0.001).	
Durakbaşa, 2014	Cross-sectional study.	494 paediatric surgical patients (median age 59 months, 75.8% males)	Single paediatric surgery unit of a tertiary referral hospital. Turkey	STRONGkids	13.4% malnutrition, 10.1% acute malnutrition and more commonly in patients aged ≤60 months than aged >60 months (13.4 vs. 6.6%, p=0.012). Chronic malnutrition was identified in 23 (4.6%) of patients. STRONGkids: 35.7% moderate or high risk			8.2% acute malnutrition in low risk patients, 33.3% in high risk (p=0.026). 3.5% chronic malnutrition in patients at low risk and 16.7% in high risk (p=0.057).	
Morais, 2014	Prospective observational multi-centre study	All patients >1 month old, admitted to paediatric or surgical wards. 223 patients were included (53.4% boys). Median age 5.59+/-0.32 years.	Five secondary and tertiary hospitals. Spain	STRONGkids	Moderate/severe acute malnutrition was 10.8%, and 5.8% presented moderate/severe chronic malnutrition.			Agreement between expert and non-expert staff was 94.78% [kappa 0.718 (p< 0.001)]. Moderate/severe AM was significantly higher among children classified at high-risk, both by expert (33.3%, p< 0.001) and non-expert staff (46.7%, p< 0.001). There were no differences regarding CM	Mean LOS was 4.14+/-0.27 days. After adjusting by age, those classified at high-risk by experts had a LOS of 4.79 (3.13-6.46) days longer than those at medium/low risk (p< 0.001).Likewise, when children were classified at high-risk by non-experts the LOS was 5.79 (3.75-7.84) days longer.

Cao, 2014	Prospective observational study	1325 consecutively enrolled hospitalized children	Nanjing Children's Hospital, China	STRONG kids	High, moderate and low nutritional risk were 9.1% (121), 43.3% (574) and 47.6% (630).			Children with high nutritional risk had significantly lower median Z-scores for WFH, WFA, HFA, MUAC and BMI	Higher complication rates, longer stay lengths, greater weight loss and greater hospital expenses were observed in children with high nutritional risk compared to those with moderate or low risk ($p < 0.001$).
Huysentruyt, 2013	Cross-sectional multi-centre study	29 hospitalized children for reproducibility, validity in 368 children between 0.08 and 16.95 y (median 2.2y)	105 hospitalized in a tertiary and 263 in three secondary hospitals, medical and surgical wards. Belgium	STRONGkids	29 (7.9%) and 32 (8.7%) children were chronically (HFA <-2 SD) and acutely (WFH <-2 SD) malnourished	Substantial intra-rater (k ¼ 0.66) and interrater (k ¼ 0.61) reliability. The questionnaire was successfully completed by 97.1% of the patients.		Correlated negatively with WFH SDS (r = –0.23; P < 0.01; odds ratio [OR], 2.47; 95% CI, 1.11–5.49; P < 0.05). Sensitivity and negative predictive value of 71.9% and 94.8% to identify acutely undernourished children.	Did not correlate with weight loss during hospitalization, but correlated with LOS (r = 0.25; OR 1.96; 95% CI, 1.25–3.07; both P < 0.01). sensitivity and NPV to predict a LOS > 4 d were respectively 62.6% and 72%
Spagnuolo, 2013	Prospective observational multi-centre study	144 children 1-18yr (75 males, mean age 6.5 ± 4.5 years), 52 (36%) had an underlying chronic disease. And 1/3 infectious diagnosis	12 hospitals in Campania region, Italy, (including one University hospital), Italy	STRONGkids	STRONGkids: 46 (32%) children were at low risk, 76 (53%) at moderate risk and 22 (15%) at high risk. Higher in <5yr, underlying disease, especially IBD for malnutrition. Twenty-nine (20%) according to BMI (16/144; 11%) and HFA SDS (15/144; 10%)			High risk patients had lower HFA values (−1.07 ± 2.08; p = 0.008) and BMI values (−0.79 ± 2.09; p = 0.0021). Medium plus high risk categories identified malnutrition with a 71% sensitivity (95% CI: 48–89) and 53% specificity (95% CI: 43–63). The positive predictive value was 21% (95% CI: 17–25) and negative predictive value 85% (95% CI: 85–90).	

Hulst, 2010	Prospective observational multi-centre study	424 children median age 3.5 years and median hospital stay 2 days.	44 hospitals: 7 academic and 37 general. Netherlands	STRONGkids	Acute malnutrition 11% (95% CI: 8–15%) and chronic malnutrition 9% (95% CI: 6–12%). Overall prevalence on admission was 19% (95% CI: 15–23%).	98% of the children measured		Children at risk had lower SDS for weight-for-height, a higher prevalence of acute malnutrition compared to those with no nutritional risk.	Longer hospital stay compared to children with no nutritional risk
Marderfeld, 2014	Cross-sectional study	60 children were included in the analysis (38 boys, 63%). Mean age was 7.8+/-4.7y.	Paediatric tertiary hospital. Israel	STAMP	Prevalence of both acute (BMI <-2 SDS) and chronic (height for age <-2) malnutrition was 8%			Good agreement between STAMP applied by nurses and assessment of the dietitian (K = 0.75). Sensitivity, specificity, positive predictive value and negative predictive value were 95.7% (95% CI = 85.75% to 98.83%), 76.9% (95%CI = 49.74% to 91.82%), 93.7 and 83.3 respectively.	
Li, 2014	Prospective observational study	506 children	Paediatric intensive care unit (PICU) of Shanghai Children's Medical Center. China	STAMP	253 children (50.0%) were malnourished, including 225 (44.5%) with undernutrition and 28 (5.5%) with overweight.		*Unclear from abstract*		High risk children had higher incidence of mechanical ventilation, more organ dysfunction, higher incidence of MODS, longer length of PICU stay and length of hospital stay, higher hospital fee, and higher 28day mortality than those at medium risk
Wong, 2013	Cross-sectional study	Sixty-two children (19.4% new admissions, aged 1–18 years (median: 13 years, range 7.8–15.6), 39.4% female and 83.6% Caucasian)	National Spinal Injuries Centre, Stoke Mandeville Hospital, Aylesbury, UK	STAMP	STAMP: The prevalence of undernutrition risk was 58.8%.	Substantial reliability (inter-rater reliability nurse-dietitian: k: 0.752; intra-rater reliability within 24hrs: k: 0.635).	Fair agreement with PYMS (k: 0.314).	STAMP had moderate agreement with dietitian assessment (k: 0.507). STAMP had a sensitivity of 83.3%, specificity of 66.7% and an overall agreement of 76.5%.	

Mccarthy , 2012	Two-phase observational study	122 children were recruited for development phase and a separate cohort of 238 children was recruited for the evaluation phase. 2-17yr medical and surgical wards	Children's division of Central Manchester and Manchester Children's Hospitals University NHS Trust. UK	STAMP	Low percentile weight for age, reported weight loss, discrepancy between weight and height percentile and recently changed appetite were all identified as predictors of nutrition risk.	Nursing staff required minimal training to complete the tool, and it was quick to use and easily interpreted using a simple scoring system.		STAMP demonstrated fair to moderate reliability in identifying nutrition risk compared to the nutrition risk classification determined by a registered dietitian (k = 0.541; 95% confidence interval = 0.461–0.621). Sensitivity and specificity were estimated at 70% (51–84%) and 91% (86–94%), respectively.	
Sikorová, 2012	Cross-sectional study	130 patients (73 boys, 57 girls) aged 2 months to 18 years (average 8 years)	Czech Republic, University Hospital of Ostravaat the Department of Paediatrics	STAMP			Vs Paediatric Nutritional Risk Score. 46.9%. higher proportion of high risk in STAMP		
Lama More, 2012	Descriptive cross-sectional study	250 children (1-18yr).	3rd level children's hospital with both medical and surgical specialities. Spain	STAMP	64 patients (25.6%) under malnutrition risk, 40 malnourished (16%). STAMP: 48.4% under nutritional risk			75% sensitivity and 60.8% specificity identifying patients under risk according to nutritional assessment. It showed 90% sensitivity and 59.5% specificity when identifying malnourished patients.	
Fox, 2012	*Cross-sectional study*	*340 paediatric inpatients, mean age 37+/-49.7 months*	*Royal Children's Hospital. Australia*	*STAMP*	*High risk of malnutrition was identified in 42% (n = 142) of patients, moderate risk in 48% (n = 163) and no risk of malnutrition in 10% (n = 35).*				
Gerasimidis, 2011	Clinical audit. Multi-centre	All patients (1e16 years) admitted over a 4 month period were eligible for screening within 24 h of admission.	3 medical and 1 surgical ward of a tertiary hospital (TPH) and the general paediatric ward (DGH) of a district general hospital. UK	PYMS	9% in DGH vs. 10.5% in TPH were scored as at high risk and 10.4% in DGH vs. 9% in TPH at medium risk of malnutrition. More prevalence in specialist wards	1571 (72.3%) screened with slightly higher rates in the acute wards than in the specialist (75% vs. 70%, p= 0.05).		66 (53%) were assessed by a dietitian of whom 86% were judged to be at true risk of malnutrition	

Author, year	Study design	Subjects	Setting / Country	MSTs	MSTs Applicability	MSTs Concurrent validity	MSTs Criterion validity
Moeeni , 2012	Cross-sectional study	119 children [64 (53%) male] with median age of 3.6 years (range 1–17.2 years; 25% with chronic condition and 45% admitted for surgery	Dr. Shaykh Hospital, a tertiary paediatric teaching hospital located in Mashhad. Iran	STAMP, PYMS and STRONGkids		STRONGkids detected more children with moderate under-nutrition (15⁄21) compared to PYMS (1⁄21) and STAMP (7⁄21; p = 0.0001 and p < 0.05). PYMS was superior in detecting severely under-nourished children (8⁄9) compared to STRONGkids (1⁄9: p = 0.003) but not STAMP (7⁄9: p > 0.05).	WFH SDS correlated with the risk stratification for all three tools (p < 0.001 for each tool). Risk stratification of STRONGkids (but not the other two tools) correlated with HFA SDS (p = 0.04).
Wiskin, 2012	Prospective observational study	46 children with inflammatory bowel disease confirmed by histology	Children attending outpatient clinics and those requiring inpatient stay in regional paediatric gastroenterology service. UK	STAMP, STRONGkids, PYMS, PNRS		Good agreement between STAMP, STRONGkids and PNRS (kappa > 0.6) but there was only modest agreement between PYMS and the other scores (kappa = 0.3)	There was no agreement between the risk tools and the degree of malnutrition based on anthropometric data (kappa < 0.1).
Ling, 2011	Prospective observational study	56 paediatric inpatients - 8 excluded. Surgical and non-surgical, 25/43 with chronic condition	Children's Hospital, Oxford, UK.	STAMP vs STRONGkids		All the patients classified by STRONGkids as high risk were also classified as high risk using STAMP. The additional patients classified as high risk by STAMP were all assessed as being of medium risk by STRONGkids. Both tools identified inpatients under the cardiac and respiratory teams as being high risk for malnutrition.	STAMP scores correlated to anthropometric measures of chronic undernutrition (height-for-age) but not measures of acute undernutrition (BMI). STRONGkids correlated to all anthropometric measures. STAMP and STRONGkids, 57% and 83% of high risk children respectively, received nutritional intervention.
Gerasimidis, 2010	Cross-sectional study	247 children	Tertiary referral hospital and a district general hospital. UK	PYMS vs STAMP SGNA	Moderate agreement to inter-rater reliability to dietitan (k ¼ 0·53). (72·3 %) were successfully screened	PYMS showed similar sensitivity to the STAMP, but a higher positive predictive value. The SGNA had higher specificity than the PYMS but much lower sensitivity.	Nurse-rated PYMS identified 59% of high risk by full dietetic assessment. PYMS showed moderate agreement with the full assessment (k = 0·46). High risk had significantly lower lean mass index than those at moderate or low risk, but no difference in fat.

SGA (Subjective Global Assessment), STAMP (Screening Tool for the Assessment of Malnutrition in Paediatrics), PYMS (Paediatric Yorkhill Malnutrition Score), STRONG (Screening Tool for Risk of Nutritional Status and Growth), SDS (standard deviation score), HT (height), WT (weight), BMI(Body mass Index), WFH (Weight-for-height),HFA (Height-for-age)

15.12. Chapter 4 supplementary results

	n	ICC [a]	Mean difference [b]	CR [c]
Height	109	1.000	-0.04 (-0.08, 0.01)	0.5 cm
WT	113	1.000	0.01 (-0.01, 0.02)	0.2 kg
MUAC	138	0.999	0.03 (0.00, 0.06)	0.3 cm
HC	147	0.999	0.02 (-0.01, 0.04)	0.3 cm
Biceps SFT	104	0.992	0.09 (-0.02, 0.21)	1.4 mm
Triceps SFT	105	0.995	-0.04 (-0.15, 0.07)	1.1 mm
Subscapular SFT	89	0.996	0.07 (-0.02, 0.16)	0.8 mm
Suprailiac SFT	75	0.998	0.02 (-0.12, 0.16)	1.2 mm

Table 1. Reliability of the different anthropometric measurements, using measurements obtained under adequate conditions/technique.

(a) ICC type 3, all values significant (H_0: ICC=0, p<0.001); (b) Mean difference between repeated measurements (95% CI), 1-sample t-test of the mean differences (H_0: MB=0, p<0.05) all non-significant; (c) Repeatability coefficient using the Bland Altman method for repeated measurements.

	n	MB [a]	*p* [b]	LLOA	ULOA	*r* [c]	*p* [d]
BMI	72	0.16	0.003*	-0.81	1.14	0.42	0.000*
Biceps SFT	88	0.33	0.000*	-1.10	1.76	-0.24	0.026*
Triceps SFT	89	0.10	0.212	-1.24	1.45	-0.22	0.037*
Subscapular SFT	78	0.32	0.000*	-1.02	1.66	-0.29	0.011*
Suprailiac SFT	65	0.24	0.002*	-0.90	1.39	-0.32	0.010*
FMI	96	0.12	0.000*	-0.35	0.60	-0.26	0.009*

Table 2. Mean bias, LOA and correlation coefficients for BMI, SFT and FMI SDS compared to DXA fat mass, using measurements obtained under adequate conditions/technique.

(a) Mean bias of the measurements SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

	n	Agreement [a]	*κ* [b]	*p*
BMI	72	92	0.59 (0.30, 0.89)	0.000*
Biceps SFT	88	91	-0.03 (-0.06, 0.0)	0.684
Triceps SFT	89	96	0.49 (0.06, 0.91)	0.000*
Subscapular SFT	78	-	-	
Suprailiac SFT	65	92	-0.02 (-0.04, 0.0)	0.808
FMI	96	96	0.73 (0.49, 0.98)	0.000*

Table 3. Agreement of abnormal scores for BMI, SFTs and FMI compared to DXA fat mass using only accurate measurements.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

	n	MB [a]	*p* [b]	LLOA	ULOA	*r* [c]	*p* [d]
BIA	87	0.01	0.890	-1.10	1.11	-0.32	0.010*
LMI	96	0.25	0.008*	-1.55	2.06	-0.26	0.009*

Table 4. Mean bias, LOA and correlation coefficients for BIA and LMI compared to DXA lean mass, using measurements obtained under adequate conditions/technique.

(a) Mean bias of the measurements SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

	n	Agreement [a]	*κ* [b]	*p*
BIA	87	92	0.65 (0.42, 0.89)	0.000*
LMI	96	86	0.41 (0.15, 0.67)	0.000*

Table 5. Agreement of abnormal scores for BIA and LMI compared to DXA lean mass using only accurate measurements.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

	n	Mean	*SD*	Male			Female			
				n	*Mean*	*SD*	*n*	*Mean*	*SD*	*p* [a]
Age (yr)	152	10.7	3.6	76	10.1	3.9	76	11.4	3.3	0.04*
Height (m)	141	1.4	0.2	72	1.3	0.2	69	1.4	0.2	0.14
LM (kg)	93	25.6	10.1	48	24.8	10.8	45	26.4	9.3	0.45
FM (kg)	93	9.7	8.2	48	7.7	6.4	45	11.9	9.3	0.01*
LMI (kg/m2)	93	13.2	1.6	48	13.5	1.7	45	13.0	1.5	0.16
FMI (kg/m2)	93	4.7	3.0	48	4.0	2.4	45	5.4	3.3	0.02*
Height SDS	111	-0.5	1.4	62	-0.4	1.4	49	-0.6	1.4	0.55
WT SDS	119	-0.5	1.7	58	-0.5	1.8	61	-0.4	1.6	0.73
BMI SDS	84	0.2	1.4	46	0.2	1.4	38	0.3	1.3	0.87
LM SDS	93	-0.8	1.3	48	-0.8	1.4	45	-0.8	1.3	0.81
FM SDS	93	0.1	1.1	48	0.3	1.1	45	-0.2	1.2	0.07**
LMI SDS	88	-0.5	1.1	48	-0.5	1.1	45	-0.5	1.2	0.99
FMI SDS	88	0.2	1.1	48	0.4	1.0	45	-0.03	1.1	0.06

Table 6. Summary of accurate WT, BMI, FM, LM, FMI, LMI values and SDS on admission.
(a) 2-samples t-test comparing the mean values and SDS between male and female, (*) significant p<0.05, (**) significant for non-parametric Mann-Whitney test (p=0.037).

	Correlation coefficient [a]	*p* [b]	% variation [c]
FMI	0.54	0.000	16.0
LMI	0.57	0.000	18.0

Table 7. Correlation of FMI and LMI to height using only accurate measurements.
(a) Pearson's correlation coefficient (r); (b) significance of r (H_0: r=0, p<0.05); (c) % of variation in FMI or LMI due to differences in height.

	n	Gradient [a]	*CI* [b]	
FM				
All patients	93	4.4	3.7	5.0
Boys	48	3.9	2.9	4.8
Girls	45	4.7	3.7	5.6
Medical	58	4.4	3.6	5.2
Surgical	35	4.2	3.1	5.4
LM				
All patients	93	2.4	2.3	2.5
Boys	48	2.5	2.4	2.7
Girls	45	2.4	2.2	2.6
Medical	58	2.4	2.2	2.5
Surgical	35	2.5	2.2	2.7

Table 8. Regression gradients to calculate new indices of FM and LM for all patients, and per sex and admission group, using only accurate measurements.

(a) resulting gradient (corresponding to P) from regressing logHT on logFM and logLM; (b) 95% CI of the regression gradient.

	Correlation coefficient [a]	*p* [b]	% variation [c]
FMI_{new}	0.06	0.573	0.2
LMI_{new}	0.18	0.085	1.6

Table 9. Correlation of new indices of fat and lean mass to height using only accurate measurements.

(a) Pearson's correlation coefficient (r) between HT and the new indices of fat and lean: $FM/HT^{3.8}$ and $LM/HT^{2.4}$; (b) significance of r (H_0: r=0, p<0.05); (c) % of variation in in the new indices attributed to differences in height.

15.13. Chapter 5 supplementary results

	Reasons for unsuccessful measurements [a]		
	Patient refusal	Unavailable equipment *	Failed
BIAst	3	16	39
BIAsup	1	0	41

Table 1. Failed and missing measurements including those not performed with an accurate technique and adequate conditions.

(a) number of failed measurements. The 'failed' category includes those measurements excluded due to inaccurate conditions and/or technique; (*) category refers to cases when the patient was unable to be transferred to the room where the Tanita was setup to perform the BIA_{st} measurements.

n =86	**MB** [a]	***p*** [b]	**LLOA**	**ULOA**	***r*** [c]	***p*** [d]
Raw impedance						
Unadjusted BIA_{sup}	-65.8	0.000	-128.4	-3.2	0.19	0.086
MB-adjusted BIA_{sup}	-0.77	0.823	-63.4	61.8	0.19	0.086
Age-adjusted BIA_{sup}	-4.9	0.142	-64.6	54.8	-0.14	0.204
SDS						
Unadjusted BIA_{sup}	0.61	0.000*	-0.06	1.27	0.54	0.000*
MB-adjusted BIA_{sup}	0.02	0.549	-0.50	0.53	0.13	0.233
Age-adjusted BIA_{sup}	0.03	0.238	-0.48	0.55	-0.06	0.573

Table 2. MB, LOA and correlation coefficients for the different BIA_{sup} impedance adjustments using only measurements obtained under adequate conditions and technique.

(a) Mean bias of SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

	n	Mean	*CI* [a]	
Raw impedance values				
Tanita	94	776	753	798
QuadScan	110	732	708	755
MB-adjusted QuadScan [b]	110	797	774	820
Age-adjusted QuadScan	110	791	770	812
Standard deviation scores				
Tanita	94	-0.75	-0.99	-0.50
QuadScan	107	-0.38	-0.66	-0.10
MB-adjusted QuadScan [b]	107	-0.96	-1.20	-0.71
Age-adjusted QuadScan	107	-0.93	-1.17	-0.69

Table 3. Impedance values and SDS on admission using only accurate measurements of standing Tanita and supine QuadScan.

(a) 95% CI for the mean; (b) QuadScan adjusted by adding the observed MB between measurements (65 impedance).

n =86	**Agreement** [a]	***κ*** [b]	***p*** [c]
Unadjusted BIA_{sup}	93	0.74 (0.54, 0.94)	0.000*
MB-adjusted BIA_{sup}	98	0.91 (0.78, 1.00)	0.000*
Age-adjusted BIA_{sup}	98	0.90 (0.78, 1.00)	0.000*

Table 4. Agreement of abnormal SDS classification using unadjusted and adjusted BIA_{sup} measurements against BIA_{st} measurements obtained only under adequate conditions.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

	Patients with abnormal BIA scores		
	overall	≤ -2SDS	≥ 2SDS
Tanita	11.7	9.1	2.6
QuadScan	19.5	12.6	6.9
MB-adjusted QuadScan	19.5	17.2	2.3
Age-adjusted QuadScan	17.2	16.1	1.1

Table 5. Patients with abnormal BIA scores using Tanita measurements or QuadScan measurements unadjusted and after adjustments using only accurate measurements.

Table shows % patients.

	n	MB [a]	*p* [b]	LLOA	ULOA	*r* [c]	*p* [d]
Unadjusted BIA_{sup}	91	0.60	0.000*	-0.63	1.82	0.17	0.110
MB-adjusted BIA_{sup}	91	0.02	0.769	-1.09	1.12	-0.08	0.458
Age-adjusted BIA_{sup}	91	0.04	0.518	-1.03	1.11	-0.17	0.099
BIA_{st}	87	0.01	0.890	-1.10	1.11	-0.32	0.010*

Table 6. Mean bias, LOA and correlation coefficients for the different BIA measurements SDS compared to DXA lean mass SDS., using measurements obtained under adequate conditions/technique.

(a) Mean bias of the measurements SDS; (b) One-sample t-test of mean bias (H_0: MB=0); (c) Pearson's correlation coefficient; (d) significance of r (H_0: r=0) testing the effect of magnitude of the measurement on the difference observed between techniques; (*) significant (p<0.05).

	n	Agreement [a]	*κ* [b]	*p*
Unadjusted BIA_{sup}	91	89	0.59 (0.37, 0.81)	0.000*
MB-adjusted BIA_{sup}	91	89	0.58 (0.35, 0.81)	0.000*
Age-adjusted BIA_{sup}	91	91	0.64 (0.42, 0.87)	0.000*
BIA_{st}	87	92	0.65 (0.42, 0.89)	0.000*

Table 7. Agreement of abnormal SDS by BIA_{st} and BIA_{sup} with different adjustments compared to DXA lean mass using only measurements obtained with adequate technique.

(a) % of agreement; (b) Cohen's kappa with 95% CI, (*) significant p-value for κ (H_0: κ=0, p<0.05).

15.14. Chapter 7 supplementary results

Admission group	*n*	%	Age		Sex		
			mean [a]	*p* [b]	male [c]	female [c]	*p* [d]
medical	74	48.7	10.1 (3.5)	0.025*	36	38	0.871
surgical	78	51.3	11.4 (3.7)		40	38	

Table 1. Mean age and number of male/female patients per admission group.
(a) Mean age in years (SD) per admission group; (b) Independent samples t-test for difference in age between admission groups (H_0 = no differences in mean age), (*) significant (p<0.05); (c) number of male and female patients per admission group; (d) Fisher's exact test (p<0.05).

	n	SDS [a]	*CI* [b]		*p* [c]
Height	111	-0.49	-0.23	-0.74	0.000**
Weight	119	-0.47	-0.16	-0.77	0.003*
MUAC	139	-0.30	-0.10	-0.49	0.004*
HC	146	-0.63	-0.36	-0.91	0.000**

Table 2. Anthropometric parameter scores on admission using accurate measurements.
(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0: mean SDS=0), (*) significant (p<0.05), (**) significant even after Bonferroni correction for multiple testing (p<0.003).

	abSDS [a]	*CI* [b]		≤ -2SDS [c]	≥ 2SDS [d]
Height	15.3	8.6	22.0	14.4	0.9
Weight	19.3	12.2	26.4	15.1	4.2
MUAC	11.5	6.2	16.8	9.4	2.2
HC	20.5	14.0	27.1	15.8	4.8

Table 3. Abnormal SDS for anthropometric parameters on admission using only accurate measurements.
(a) % of patients with abnormal SDS on admission for each of the parameters; (b) 95% CI for the % of patients with abSDS; (c) % of patients with SDS of -2 or lower; (d) % of patients with SDS of 2 or higher.

	Male		Female		*p* [a]	Medical		Surgical		*p* [a]
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
HT	-0.64	1.5	-0.76	1.5	0.640	-0.57	1.5	-0.85	1.5	0.273
WT	-0.28	1.8	-0.40	1.6	0.668	-0.20	1.5	-0.47	1.9	0.333
MUAC	-0.16	1.0	-0.42	1.3	0.170	-0.27	1.2	-0.30	1.2	0.883
HC	-0.38	1.5	-0.90	1.9	0.059	-0.57	1.5	-0.70	1.8	0.644

Table 4. Mean SDS for anthropometric parameters between groups.

(a) Independent samples t-test comparing the mean SDS between groups, none of the values significant (p<0.05, or corrected p<0.003 for multiple testing).

	Male		Female		*p* [a]	Medical		Surgical		*p* [a]
	mean	*SD*	mean	*SD*		mean	*SD*	mean	*SD*	
Height	-0.42	1.4	-0.57	1.4	0.547	-0.56	1.5	-0.36	1.1	0.438
Weight	-0.52	1.8	-0.42	1.6	0.730	-0.21	1.5	-0.69	1.9	0.118
MUAC	-0.17	1.1	-0.42	1.3	0.220	-0.29	1.2	-0.30	1.2	0.940
HC	-0.36	1.5	-0.91	1.9	0.050	-0.57	1.5	-0.69	1.9	0.670

Table 5. Mean SDS for anthropometric parameters between groups using accurate measurements.

(a) Independent samples t-test comparing the mean SDS between groups, none of the values significant (p<0.05, or corrected p<0.003 for multiple testing).

	n	SDS [a]	*CI* [b]		*p* [c]
Fat mass parameters					
BMI	84	0.24	-0.05	0.53	0.114
Biceps SFT	104	0.40	0.22	0.58	0.000*
Triceps SFT	105	0.12	-0.07	0.30	0.210
Subscapular SFT	89	0.28	0.09	0.47	0.007*+
Suprailiac SFT	76	0.12	-0.08	0.32	0.244
FM DXA	93	0.07	-0.16	0.30	0.564
Lean mass parameters					
BIA_{st}	94	-0.75	-0.99	-0.50	0.000*
BIA_{sup} adjusted	104	-0.94	-1.18	-0.69	0.000*
BIA_{all}	114	-0.87	-1.11	-0.63	0.000*
LM DXA	93	-0.80	-1.06	-0.53	0.000*

Table 6. BC parameters SDS on admission using accurate measurements.

(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS ($H_{0:}$ mean SDS=0), (*) significant (p<0.05, and corrected p<0.003 for multiple testing); (+)p-value for one-sample Wilcox Signed Rank test, significant at p<0.05 but not after corrected p<0.003 for multiple testing.

	abSDS [a]	*CI* [b]		≤ -2SDS [c]	≥ 2SDS [d]
Fat mass parameters					
BMI	10.7	4.1	17.3	2.4	8.3
Biceps SFT	3.8	0.2	7.5	1.0	2.9
Triceps SFT	1.9	0.0	4.5	1.9	0.0
Subscapular SFT	0.0	0.0	0.0	0.0	0.0
Suprailiac SFT	2.6	0.0	6.2	1.3	1.3
FM DXA	7.5	2.2	12.9	4.3	3.2
Lean mass parameters					
BIA_{st}	12.8	6.0	19.5	10.6	2.1
BIA_{sup} adjusted	19.2	11.7	26.8	17.3	1.9
BIA_{all}	17.5	10.6	24.5	15.8	1.8
LM DXA	16.1	8.7	23.6	16.1	0.0

Table 7. Abnormal SDS for BC parameters on admission using accurate measurements.

(a) % of patients with abnormal SDS (abSDS) on admission for each of the parameters; (b) 95% CI for the % of patients with abSDS; (c) % of patients with SDS of -2 or lower; (d) % of patients with SDS of 2 or higher.

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
FM parameters										
BMI	0.25	1.5	0.19	1.3	0.807	0.18	1.3	0.27	1.5	0.686
Biceps SFT	0.56	0.9	0.28	1.0	0.110	0.41	0.9	0.45	1.0	0.791
Triceps SFT	0.16	1.0	0.07	0.9	0.600	0.07	0.9	0.17	1.1	0.593
Subscapular SFT	0.28	0.9	0.36	0.9	0.672	0.27	1.0	0.39	0.8	0.514
Suprailiac SFT	0.23	0.9	0.05	0.8	0.344	0.08	0.9	0.23	0.9	0.429
DXA FM	0.30	1.3	-0.16	1.2	0.024^{+*}	0.01	1.1	0.14	1.3	0.549
FMI	0.38	1.2	0.02	1.1	0.093	0.14	1.1	0.27	1.3	0.553
LM parameters										
BIA_{st}	-0.69	1.2	-0.79	1.3	0.690	-0.76	1.2	-0.72	1.3	0.882
BIA_{sup}	-1.09	1.4	-0.81	1.5	0.274	-0.79	1.5	-1.13	1.4	0.047^{+*}
BIA_{all}	-1.05	1.4	-0.82	1.5	0.362	-0.79	1.4	-1.10	1.4	0.069^{+}
DXA LM	-0.91	1.5	-1.02	1.5	0.704	-0.78	1.3	-1.17	1.6	0.153
LMI	-0.64	1.5	-0.47	1.2	0.499	-0.41	1.1	-0.73	1.6	0.195

Table 8. Differences in SDS for BC parameters according to sex and admission group.

(a) Independent samples t-test comparing the mean SDS between groups; (*) significant ($p<0.05$) but non-significant after correction for multiple testing ($p<0.003$); (+) Tested using independent samples Mann-Whitney U-test due to non-parametric distribution of data.

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	mean	*SD*		mean	*SD*	mean	*SD*	
Fat mass parameters										
BMI	0.22	1.4	0.26	1.3	0.870	0.05	1.2	0.56	1.6	0.093
Biceps SFT	0.49	0.9	0.31	1.1	0.332	0.35	1.0	0.46	1.0	0.566
Triceps SFT	0.12	1.0	0.12	0.9	0.987	0.04	0.9	0.20	1.1	0.386
Subscapular SFT	0.21	0.9	0.34	1.0	0.510	0.17	1.0	0.42	0.8	0.206
Suprailiac SFT	0.19	1.0	0.05	0.8	0.517	0.03	0.9	0.23	0.9	0.333
FM DXA	0.28	1.1	-0.15	1.2	0.037*	-0.07	1.1	0.30	1.2	0.125
FMI	0.40	1.0	-0.03	1.1	0.059	0.02	1.0	0.54	1.2	0.028*
Lean mass parameters										
BIA_{st}	-0.74	1.2	-0.75	1.2	0.954	-0.73	1.1	-0.77	1.3	0.876
BIA_{sup} adjusted	-1.04	1.3	-0.82	1.3	0.381	-0.76	1.3	-1.14	1.3	0.016^{+*}
BIA_{all}	-0.93	1.4	-0.81	1.3	0.618	-0.75	1.3	-1.01	1.3	0.053^{+}
LM DXA	-0.76	1.4	-0.83	1.3	0.807	-0.69	1.2	-0.97	1.5	0.327
LMI	-0.54	1.1	-0.54	1.2	0.996	-0.39	1.1	-0.81	1.3	0.100

Table 9. Differences in SDS for BC parameters per sex and admission group using only accurate measurements.

(a) Independent samples t-test comparing the mean SDS between groups; (*) significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.003); (+) Tested using independent samples Mann-Whitney U-test due to non-parametric distribution of data.

	Male [a]	Female [a]	p [b]	Medical [a]	Surgical [a]	p [b]	Age [c]	*SD*	p [d]
Steroid prescription									
no	59	60		53	66		10.9	3.6	
low	11	8	0.681	11	8	0.113	9.9	3.4	0.455
high	6	8		10	4		10.3	3.8	
High steroids									
no	70	68	0.390	64	74	0.065	10.8	3.6	0.622
yes	6	8		10	4		10.3	3.8	

Table 10. Effect of age, admission group and sex on steroid medication prescription.

(a) number of patients; (b) Chi-squared / Fisher's exact test, all values non-significant (p<0.05, or corrected p<0.003 for multiple testing); (c) mean age (yr); (d) One-way ANOVA testing differences in mean age between groups, all values non-significant.

	Male [a]	Female [a]	*p* [b]	Medical [a]	Surgical [a]	*p* [b]	Age [c]	*SD*	*p* [d]
Fluid restrictions									
no	61	71		66	66		10.7	3.6	
NMB	8	4	0.040+*	6	6	0.390+	11.0	3.9	0.961
limited	7	1		2	6		10.9	4.4	
Restricted fluid									
no	61	71	0.014*	66	66	0.277	10.7	3.6	0.786
yes	15	5		8	12		11.0	4.0	

Table 11. Effect of age, admission group and sex on fluid restriction.

(a) number of patients; (b) Chi-squared / Fisher's exact test, (+) Chi-squared test limited by the number of expected count per cell <5, (*) significant (p<0.05) but non-significant after correction for multiple testing (p<0.003); (c) mean age (yr); (d) One-way ANOVA testing differences in mean age between groups, all values non-significant.

	Male [a]	Female [a]	*p* [b]	Medical [a]	Surgical [a]	*p* [b]	Age [c]	*SD*	*p* [d]
Activity level by parent									
much less	19	17		15	21		11.0	3.5	
less	14	25		18	21		11.3	3.6	
same	26	21	0.282	27	20	0.644	10.3	3.7	0.733
more	10	6		8	8		10.3	3.5	
much more	7	5		5	7		10.9	4.1	
Activity level									
WCh not active	5	3		2	6		11.4	3.7	
WCh active	4	5	0.890+	1	8	0.008+*	11.1	3.2	0.946
walk not active	14	14		10	18		10.7	4.5	
walk active	53	54		61	46		10.7	3.4	
Wheelchair user									
no	67	68	0.500	71	64	0.006*	10.7	3.7	0.555
yes	9	8		3	14		11.2	3.4	

Table 12. Effect of age, admission group and sex on physical activity levels.

WCh=wheelchair, (a) number of patients; (b) Chi-squared / Fisher's exact test, (+) limited by number of expected count per cell, (*) significant (p<0.05) but non-significant after correction for multiple testing (p<0.003); (c) mean age (yr); (d) One-way ANOVA for differences in age between groups.

	Male [a]	Female [a]	*p* [b]	Medical [a]	Surgical [a]	*p* [b]	Age [c]	*SD*	*p* [d]
Feeding categories									
oral self	50	60	0.110[+]	55	55	0.020[+]*	11.1	3.5	0.013*
oral carer	8	5		1	12		9.8	3.5	
oral + EN/PN self	1	1		1	1		15.5	3.5	
oral self + EN/PN carer	12	4		12	4		8.5	3.5	
oral + EN/PN carer	0	3		1	2		13.0	3.6	
EN/PN carer	5	3		4	4		9.4	3.2	
EN / PN feeding regime									
no	58	65	0.350[+]	56	67	0.200[+]	11.0	3.5	0.212
partial	13	8		14	7		9.8	4.1	
full	5	3		4	4		9.4	3.2	
EN / PN feeding									
no	58	65	0.108	56	67	0.081	11.0	3.5	0.082
yes (partial or full)	18	11		18	11		9.7	3.9	

Table 13. Effect of age, sex and admission group on diet-related factors.

(a) number of patients; (b) Chi-squared / Fisher's exact test of significance of the observed frequencies between category groups; (c) mean age (yr); (d) One-way ANOVA testing differences in mean age between groups; (+) chi-squared test limited by the number of expected count per cell <5; (*) significant (p<0.05) but non-significant after correction for multiple testing (p<0.002).

Dietary restrictions									
none	29	39	0.183	27	41	0.095	11.5	3.7	0.014*
minor	16	16		16	16		11.1	3.3	
very restricted	31	21		31	21		9.6	3.5	
Restricted diet									
no	45	55	0.062	43	57	0.038*	11.4	3.5	0.004*
yes (only very restricted)	31	21		31	21		9.6	3.5	
Loss of appetite									
no	56	52	0.199	47	61	0.029*	10.7	3.6	0.518
yes	16	22		24	14		11.2	3.7	
Intake problems									
none	62	65	0.800^{+}	59	68	0.360^{+}	10.8	3.6	0.894
NBM	10	8		10	8		10.5	3.9	
limited by clinical condition	4	3		5	2		10.3	3.6	
Intake / appetite problems									
no	57	52	0.236	46	63	0.009*	10.7	3.6	0.691
yes	19	24		28	15		10.9	3.7	
Prior dietetic advice									
no	28	39	0.051	26	41	0.023*	11.3	3.7	0.124
yes	48	37		48	37		10.3	3.5	

Table 7.13. (*cont.*) Effect of age, sex and admission group on diet-related factors.

	Steroid prescription					Fluid restriction					Wheelchair user				
	No		Yes		*p* [b]	No		Yes		*p* [b]	No		Yes		*p* [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Height	-0.67	1.5	-1.01	1.4	0.421	-0.70	1.5	-0.69	1.7	0.982	-0.57	1.4	-2.63	1.3	0.000*
Weight	-0.37	1.7	0.02	1.3	0.410	-0.40	1.7	0.06	1.8	0.264	-0.16	1.5	-1.74	2.1	0.000*
MUAC	-0.31	1.2	-0.08	1.1	0.476	-0.32	1.2	-0.10	1.2	0.461	-0.26	1.1	-0.48	1.5	0.490
HC	-0.67	1.7	-0.35	1.4	0.511	-0.64	1.6	-0.58	2.1	0.884	-0.47	1.5	-2.13	2.7	0.000*

Table 14. Associations between mean SDS of anthropometric parameters and steroid prescription, fluid restriction and immobility.

(a) mean SDS; (b) Independent samples t-test comparing the mean SDS between groups, (*) significant (p<0.05, and corrected p<0.003 for multiple testing).

	EN / PN feeding					Restricted diet					Intake / appetite problems					Prior dietetic advice				
	No		Yes		*p* [b]	No		Yes		*p* [b]	No		Yes		*p* [b]	No		Yes		*p* [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Height	-0.51	1.4	-1.59	1.8	0.001**	-0.33	1.2	-1.45	1.8	0.000**	-0.82	1.5	-0.42	1.4	0.155	-0.24	1.1	-1.09	1.7	0.001**
Weight	-0.09	1.6	-1.40	1.8	0.000**	0.04	1.4	-1.05	2.0	0.000**	-0.39	1.8	-0.20	1.4	0.547	0.21	1.3	-0.77	1.8	0.000**
MUAC	-0.16	1.1	-0.84	1.3	0.005*	-0.06	1.1	-0.72	1.2	0.001**	-0.30	1.2	-0.26	1.1	0.850	0.16	1.0	-0.64	1.2	0.000**
HC	-0.42	1.5	-1.58	2.0	0.001**	-0.31	1.4	-1.29	2.0	0.001**	-0.77	1.8	-0.31	1.4	0.131	-0.24	1.3	-0.96	1.9	0.009*

Table 15. Associations between mean SDS of anthropometric parameters and diet-related variables on admission.

(a) mean SDS; (b) Independent samples t-test comparing the mean SDS between groups, (*) Significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.003), (**) Significant even after Bonferroni correction for multiple testing.

	Steroid prescription					Fluid restriction					Wheelchair user				
	No		Yes		*p* [b]	No		Yes		*p* [b]	No		Yes		*p* [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Fat mass parameters															
BMI	0.17	1.4	0.73	1.3	0.154	0.16	1.4	0.61	1.5	0.179	0.27	1.3	-0.47	1.9	0.125
Biceps SFT	0.42	1.0	0.49	0.8	0.833	0.40	1.0	0.59	0.8	0.472	0.40	0.9	0.74	0.8	0.282
Triceps SFT	0.12	1.0	0.07	0.6	0.871	0.10	1.0	0.23	0.8	0.622	0.06	0.9	0.81	0.9	0.024*
Subscapular SFT	0.31	0.9	0.47	0.8	0.643	0.28	0.9	0.69	0.9	0.148	0.34	0.9	-0.01	1.2	0.452
Suprailiac SFT	0.16	0.9	0.02	0.9	0.694	0.09	0.9	0.55	0.9	0.105	0.13	0.9	0.41	0.7	0.541
FMDXA	0.03	1.2	0.49	1.3	0.240	-0.05	1.2	0.84	1.1	0.007*	0.08	1.2	-0.11	1.7	0.691
FMI	0.15	1.2	0.61	1.3	0.223	0.07	1.2	0.97	1.1	0.004*	0.19	1.2	0.47	1.9	0.685
Lean mass parameters															
BIA_{st}	-0.72	1.3	-1.01	0.9	0.503	-0.74	1.2	-0.76	1.3	0.960	-0.72	1.2	-3.09	-	0.058
BIA_{sup} adjusted	-0.92	1.5	-1.22	1.5	0.491	-0.95	1.5	-0.96	1.5	0.971	-0.86	1.4	-2.41	1.2	0.003*
BIA_{all}	-0.91	1.4	-1.24	1.5	0.425	-0.94	1.4	-0.92	1.5	0.947	-0.85	1.4	-2.41	1.2	0.003*
LMDXA	-0.97	1.5	-0.96	1.2	0.991	-0.93	1.5	-1.17	1.6	0.548	-0.77	1.3	-4.13	0.9	0.000**
LMI	-0.55	1.4	-0.61	1.3	0.897	-0.48	1.3	-1.08	1.4	0.100	-0.49	1.3	-3.16	1.4	0.001**

Table 16. Associations between mean SDS of body composition parameters and steroid prescription, fluid restriction and immobility.

(a) mean SDS; (b) Independent samples t-test comparing the mean SDS between groups, (*) Significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.003), (**) Significant even after Bonferroni correction for multiple testing.

	EN / PN feeding					Restricted diet					Intake / appetite problems					Prior dietetic advice				
	No		Yes		p [b]	No		Yes		p [b]	No		Yes		p [b]	No		Yes		p [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Fat mass parameters																				
BMI	0.38	1.3	-0.50	1.4	0.004*	0.43	1.2	-0.19	1.6	0.012*	0.24	1.5	0.19	1.2	0.851	0.54	1.3	-0.05	1.5	0.012*
Biceps SFT	0.48	0.9	0.18	1.1	0.194	0.50	0.9	0.27	1.0	0.226	0.43	0.9	0.43	1.0	0.980	0.67	0.9	0.21	0.9	0.008*
Triceps SFT	0.17	1.0	-0.13	1.0	0.190	0.25	0.9	-0.16	1.1	0.029*	0.20	1.0	-0.05	0.8	0.182	0.34	1.0	-0.07	0.9	0.018*
Subscapular SFT	0.41	0.8	-0.17	1.1	0.017*	0.44	0.9	0.03	1.0	0.035*	0.35	0.9	0.27	0.9	0.662	0.65	0.8	0.02	0.9	0.000**
Suprailiac SFT	0.18	0.9	-0.06	0.9	0.340	0.27	0.9	-0.17	0.8	0.031*	0.18	0.9	0.07	0.9	0.585	0.49	0.8	-0.14	0.8	0.001**
FMDXA	0.17	1.2	-0.46	1.3	0.037*	0.27	1.1	-0.36	1.4	0.009*	0.07	1.3	0.06	0.9	0.976	0.36	1.2	-0.20	1.3	0.012*
FMI	0.27	1.2	-0.20	1.1	0.109	0.35	1.1	-0.14	1.4	0.035*	0.23	1.3	0.11	0.9	0.636	0.45	1.1	-0.04	1.2	0.025*
Lean mass parameters																				
BIA_{st}	-0.57	1.1	-1.63	1.5	0.001**	-0.54	1.1	-1.23	1.4	0.009*	-0.76	1.3	-0.70	1.1	0.814	-0.49	1.2	-0.96	1.3	0.054
BIA_{sup} adjusted	-0.74	1.4	-1.94	1.5	0.000**	-0.63	1.3	-1.64	1.6	0.000**	-1.01	1.5	-0.82	1.3	0.492	-0.52	1.4	-1.32	1.5	0.002**
BIA_{all}	-0.74	1.3	-1.89	1.5	0.000**	-0.63	1.3	-1.59	1.5	0.000**	-0.99	1.5	-0.83	1.3	0.563	-0.52	1.3	-1.30	1.4	0.002**
LMDXA	-0.75	1.3	-2.06	1.8	0.000**	-0.74	1.3	-1.48	1.7	0.010*	-1.09	1.6	-0.62	1.2	0.121	-0.71	1.3	-1.21	1.6	0.060
LMI	-0.46	1.3	-1.06	1.6	0.077	-0.54	1.2	-0.59	1.7	0.855	-0.60	1.4	-0.46	1.2	0.620	-0.59	1.2	-0.53	1.5	0.813

Table 17. Associations between mean SDS of body composition parameters and diet-related variables on admission.

(a) mean SDS; (b) Independent samples t-test comparing the mean SDS between groups, (*) Significant ($p<0.05$) but non-significant after Bonferroni correction for multiple testing ($p<0.003$), (**) Significant even after Bonferroni correction for multiple testing

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
HT	-0.51	1.3	-0.49	1.6	0.931	-0.64	1.5	-0.36	1.3	0.403
WT	-0.20	1.8	-0.45	1.6	0.433	-0.18	1.6	-0.48	1.8	0.340
MUAC	-0.15	1.4	-0.64	1.5	0.122	-0.31	1.4	-0.46	1.5	0.646
HC	-0.48	1.3	-0.67	2.1	0.629	-0.65	1.6	-0.50	1.9	0.695

Table 18. Mean SDS for anthropometric parameters between groups.

(a) Independent samples t-test comparing the mean SDS between groups, none of the values significant (p<0.05, or corrected p<0.013 for multiple testing).

	n	**SDS [a]**	***CI* [b]**		***p* [c]**
Height	64	-0.46	-0.81	-0.12	0.010**
Weight	84	-0.15	-0.48	0.19	0.394
MUAC	78	-0.36	-0.67	-0.05	0.024*
HC	77	-0.59	-0.98	-0.21	0.003**

Table 19. Anthropometric parameters scores at discharge using accurate measurements.

(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0=0), (*) significant (p<0.05), (**) significant even after Bonferroni correction for multiple testing (p<0.013).

	abSDS [a]	***CI* [b]**		**≤ -2SDS [c]**	**≥ 2SDS [d]**
Height	15.6	6.7	24.5	14.1	1.6
Weight	14.3	6.8	21.8	8.3	6.0
MUAC	15.4	7.4	23.4	12.8	2.6
HC	22.1	12.8	31.3	19.5	2.6

Table 20. Abnormal SDS for anthropometric parameters at discharge using only accurate measurements.

(a) % of patients with abnormal SDS at discharge for each of the parameters; (b) 95% CI for the % of patients with abSDS; (c) % of patients with SDS of -2 or lower; (d) % pf patients with SDS of 2 or higher.

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	mean	*SD*		mean	*SD*	mean	*SD*	
Height	-0.43	1.3	-0.51	1.5	0.828	-0.64	1.6	-0.20	1.1	0.218
Weight	-0.20	1.6	-0.08	1.5	0.724	-0.20	1.4	-0.03	1.8	0.635
MUAC	-0.08	1.2	-0.64	1.5	0.069	-0.31	1.4	-0.41	1.4	0.759
HC	-0.48	1.3	-0.71	2.1	0.571	-0.65	1.6	-0.53	1.9	0.752

Table 21. Mean SDS for anthropometric parameters between groups using accurate measurements.

(a) Independent samples t-test comparing the mean SDS between groups, none of the values significant (p<0.05, or corrected p<0.013 for multiple testing).

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
FM parameters										
BMI	0.36	1.4	-0.13	1.5	0.145	0.02	1.4	0.25	1.5	0.498
Biceps SFT	0.57	0.9	0.45	1.1	0.675	0.41	0.9	0.66	1.0	0.381
Triceps SFT	0.34	0.9	-0.02	1.2	0.235	0.22	0.9	0.11	1.2	0.736
Subscapular SFT	0.02	0.9	0.77	0.8	0.011*	0.36	0.9	0.36	1.0	0.996
Suprailiac SFT	0.33	0.9	-0.22	0.9	0.102	0.02	0.9	0.17	0.9	0.679
LM parameters										
BIA_{st}	-0.63	1.4	-1.24	1.5	0.187	-1.15	1.5	-0.62	1.5	0.277
BIA_{sup}	-1.06	1.9	-0.79	2.0	0.561	-1.02	1.6	-0.83	2.2	0.684
BIA_{all}	-1.10	1.9	-0.98	1.6	0.780	-1.04	1.5	-1.03	1.9	0.988

Table 22. Mean SDS for BC parameters between groups at discharge.

(a) Independent samples t-test comparing the mean SDS between groups; (*) significant (p<0.05) but non-significant after correction for multiple testing (p<0.006).

	n	SDS [a]	*CI* [b]		*p* [c]
Fat mass parameters					
BMI	58	0.30	-0.03	0.64	0.082
Biceps SFT	42	0.43	0.14	0.72	0.005**
Triceps SFT	45	0.08	-0.23	0.39	0.611
Subscapular SFT	30	0.38	0.06	0.70	0.026*
Suprailiac SFT	25	0.02	-0.35	0.38	0.930
Lean mass parameters					
BIA_{st}	41	-1.00	-1.47	-0.52	0.000**
BIA_{sup} adjusted	55	-1.00	-1.40	-0.59	0.000**
BIA_{all}	61	-1.15	-1.53	-0.77	0.000**

Table 23. BC parameters SDS at discharge using accurate measurements.
(a) Mean SDS; (b) 95% CI for the mean SDS; (c) One-sample t-test of the mean SDS (H_0=0), (*) significant (p<0.05), (**) significant even after Bonferroni correction for multiple testing (p<0.006).

	abSDS [a]	*CI* [b]		≤ -2SDS [c]	≥ 2SDS [d]
Fat mass parameters					
BMI	15.5	6.2	24.8	5.2	10.3
Biceps SFT	0.0	0.0	0.0	0.0	0.0
Triceps SFT	2.2	0.0	6.5	2.2	0.0
Subscapular SFT	0.0	0.0	0.0	0.0	0.0
Suprailiac SFT	0.0	0.0	0.0	0.0	0.0
Lean mass parameters					
BIA_{st}	24.4	11.2	37.5	22.0	2.4
BIA_{sup} adjusted	29.1	17.1	41.1	25.5	3.6
BIA_{all}	29.5	18.1	41.0	27.9	1.6

Table 24. Abnormal SDS for BC parameters at discharge using accurate measurements.
(a) % of patients with abnormal SDS (abSDS) at discharge for each of the parameters; (b) 95% CI for the % of patients with abSDS; (c) % of patients with SDS of -2 or lower; (d) % pf patients with SDS of 2 or higher.

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	mean	*SD*		mean	*SD*	mean	*SD*	
Fat mass parameters										
BMI	0.30	1.2	0.31	1.4	0.982	0.06	1.3	0.69	1.2	0.075
Biceps SFT	0.50	0.9	0.37	1.0	0.657	0.37	1.0	0.50	0.9	0.687
Triceps SFT	0.24	0.9	-0.07	1.2	0.330	0.15	1.0	0.00	1.2	0.633
Subscapular SFT	-0.01	0.8	0.76	0.8	0.014*	0.41	0.9	0.29	1.0	0.758
Suprailiac SFT	0.31	1.0	-0.22	0.9	0.159	0.01	1.0	0.03	0.9	0.950
Lean mass parameters										
BIA_{st}	-0.65	1.5	-1.30	1.6	0.185	-1.18	1.5	-0.62	1.6	0.291
BIA_{sup} adjusted	-1.02	1.4	-0.97	1.7	0.906	-0.85	1.5	-1.18	1.6	0.435
BIA_{all}	-1.14	1.5	-1.16	1.6	0.953	-1.05	1.6	-1.27	1.5	0.587

Table 25. Mean SDS for BC parameters between groups at discharge using only accurate measurements.

(a) Independent samples t-test comparing the mean SDS between groups; (*) significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.006).

	n	Change in SDS [a]	*CI* [b]		*p* [c]
Height	62	0.03	0.00	0.07	0.014* [+]
Weight	63	-0.02	-0.09	0.06	0.680
MUAC	75	-0.05	-0.14	0.03	0.239
HC	75	0.19	0.00	0.38	0.053

Table 26. Change in anthropometric parameters scores between admission and discharge.

(a) Mean difference in the SDS between admission and discharge; (b) 95% CI for the mean change in SDS; (c) One-sample t-test of the mean change in SDS (H_0: mean change=0), (*) significant (p<0.05), (+) One-sample Wilcox Signed Test (H_0: median change=0).

	Frequency [a]	% patients [b]	*CI* [c]	
Height	22	35.5	23.6	47.4
Weight	26	41.3	29.1	53.4
MUAC	41	54.7	43.4	65.9
HC	29	38.7	27.6	49.7

Table 27. Percentage of patients with decreased SDS for anthropometric parameters between admission and discharge using only accurate measurements.

(a) Number and (b) percentage (%) of patients that had a lower standard deviation score at discharge compared to admission for each of the parameters; (c) 95% CI for the % of patients.

	Male		Female		*p* [a]	Medical		Surgical		*p* [a]
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
HT	0.08	0.2	0.11	0.3	0.603	0.03	0.1	0.17	0.3	0.058 [+]
WT	0.02	0.4	-0.03	0.2	0.353	-0.01	0.2	0.01	0.4	0.797
MUAC	0.00	0.5	-0.12	0.3	0.171	0.02	0.3	-0.13	0.5	0.104
HC	0.03	0.7	0.40	0.9	0.056	0.12	0.7	0.29	1.0	0.378

Table 28. Mean change in SDS for anthropometric parameters between groups.

(a) Independent samples t-test comparing the mean change in SDS between groups, none of the values significant (p<0.05, or corrected p<0.013 for multiple testing), (+) Independent samples Mann-Whitney U-test.

	Male		Female		*p* [a]	Medical		Surgical		*p* [a]
	mean	*SD*	mean	*SD*		mean	*SD*	mean	*SD*	
Height	0.05	0.1	0.01	0.2	0.313	0.04	0.1	0.01	0.2	0.445
Weight	0.01	0.4	-0.04	0.2	0.541	0.01	0.2	-0.07	0.5	0.439
MUAC	0.02	0.4	-0.12	0.3	0.115	0.01	0.3	-0.11	0.4	0.211
HC	-0.01	0.7	0.40	0.9	0.145	0.12	0.7	0.26	1.0	0.487

Table 29. Mean change in SDS for anthropometric parameters between groups using accurate measurements.

(a) Independent samples t-test comparing the mean change in SDS between groups, none of the values significant (p<0.05, or corrected p<0.013 for multiple testing).

	n	Change in SDS [a]	*CI* [b]		*p* [c]
Fat mass parameters					
BMI	40	-0.04	-0.18	0.10	0.546
Biceps SFT	38	0.15	-0.07	0.37	0.180
Triceps SFT	42	-0.01	-0.22	0.20	0.901
Subscapular SFT	26	-0.01	-0.22	0.21	0.950
Suprailiac SFT	22	-0.03	-0.27	0.22	0.836
Lean mass parameters					
BIA_{st}	35	-0.14	-0.28	0.00	0.063
BIA_{sup} adjusted	46	-0.08	-0.21	0.05	0.244
BIA_{all}	53	-0.10	-0.22	0.01	0.091

Table 30. BC parameters SDS at discharge using accurate measurements.

(a) Mean difference in SDS between admission and discharge; (b) 95% CI for the mean change in SDS; (c) One-sample t-test of the mean change in SDS (H_0: mean change=0), none significant (p<0.05, or corrected p<0.006 for multiple testing).

	Frequency [a]	% patients [b]	*CI* [c]	
Fat mass parameters				
BMI	19	47.5	32.0	63.0
Biceps SFT	16	42.1	26.4	57.8
Triceps SFT	20	47.6	32.5	62.7
Subscapular SFT	14	53.8	34.7	73.0
Suprailiac SFT	10	45.5	24.6	66.3
Lean mass parameters				
BIA_{st}	21	60.0	43.8	76.2
BIA_{sup} adjusted	25	54.3	40.0	68.7
BIA_{all}	31	58.5	45.2	71.8

Table 31. Percentage of patients with decreased SDS for BC parameters between admission and discharge using only accurate measurements.

(a) Number and (b) percentage (%) of patients that had a lower standard deviation score at discharge compared to admission for each of the parameters; (c) 95% CI for the % of patients.

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
FM parameters										
BMI	-0.09	0.5	-0.16	0.3	0.506	-0.04	0.3	-0.23	0.5	0.084
Biceps SFT	0.11	0.6	0.18	0.7	0.735	0.14	0.6	0.14	0.7	0.997
Triceps SFT	0.04	0.6	0.01	0.7	0.879	0.13	0.6	-0.12	0.7	0.179
Subscapular SFT	-0.07	0.5	-0.03	0.6	0.828	0.09	0.5	-0.48	0.4	0.007*
Suprailiac SFT	0.28	0.5	-0.27	0.6	0.014*	-0.03	0.6	0.08	0.6	0.673
LM parameters										
BIA_{st}	0.01	0.3	-0.22	0.5	0.046*	-0.06	0.3	-0.23	0.6	0.343
BIA_{sup}	0.09	0.8	0.15	1.3	0.797	-0.04	0.6	0.27	1.3	0.220
BIA_{all}	0.09	0.8	-0.03	0.8	0.509	-0.08	0.5	0.13	1.0	0.268

Table 32. Mean change in SDS for BC parameters between groups at discharge.
(a) Independent samples t-test comparing the mean change in SDS between groups; (*) significant (p<0.05) but non-significant after correction for multiple testing (p<0.006).

	Male		Female		p [a]	Medical		Surgical		p [a]
	mean	*SD*	mean	*SD*		mean	*SD*	mean	*SD*	
Fat mass parameters										
BMI	-0.06	0.5	-0.02	0.2	0.766	0.01	0.3	-0.15	0.7	0.432
Biceps SFT	0.12	0.6	0.18	0.7	0.782	0.10	0.7	0.22	0.7	0.608
Triceps SFT	-0.03	0.7	0.00	0.7	0.912	0.08	0.6	-0.13	0.8	0.327
Subscapular SFT	-0.04	0.6	0.03	0.6	0.769	0.15	0.5	-0.44	0.4	0.013*
Suprailiac SFT	0.33	0.4	-0.27	0.6	0.012*	-0.01	0.6	-0.08	0.4	0.815
Lean mass parameters										
BIA_{st}	0.03	0.3	-0.28	0.5	0.036*	-0.04	0.3	-0.36	0.5	0.099[+]
BIA_{sup} adjusted	-0.04	0.5	-0.14	0.5	0.460	0.00	0.4	-0.19	0.5	0.157
BIA_{all}	-0.02	0.4	-0.20	0.5	0.146	-0.02	0.3	-0.21	0.5	0.134

Table 33. Mean change in SDS for BC parameters between groups at discharge using only accurate measurements.
(a) Independent samples t-test comparing the mean change in SDS between groups; (*) significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.006), (+) Independent samples Mann-Whitney U-test

	Male [a]	Female [a]	*p* [b]	Medical [a]	Surgical [a]	*p* [b]	Age [c]	*SD*	*p* [d]
Steroid prescription									
no	46	47		49	44		10.8	3.5	
low	1	1	0.615	1	1	0.540	9.5	4.9	0.380
high	6	3		3	6		9.2	3.8	
High steroids									
no	47	48	0.489	50	45	0.315	10.8	3.5	0.198
yes	6	3		3	6		9.2	3.8	

Table 34. Effect of age, discharge group and sex on steroid medication prescription.
(a) number of patients; (b) Chi-squared / Fisher's exact test, all values non-significant (p<0.05, or corrected p<0.003 for multiple testing); (c) mean age (yr); (d) One-way ANOVA testing differences in mean age between groups, all values non-significant.

	Male [a]	Female [a]	*p* [b]	Medical [a]	Surgical [a]	*p* [b]	Age [c]	*SD*	*p* [d]
Fluid restrictions									
no	39	48		46	41		10.7	3.6	
NBM	6	2	0.039*	5	3	0.020*	9.8	3.3	0.752
limited by diagnosis	6	1		0	7		10.6	3.3	
Restricted fluid									
no	39	48	0.023*	46	41	0.263	10.7	3.6	0.543
yes	12	3		5	10		10.1	3.2	

Table 35. Effect of age, discharge group and sex on fluid restriction.

(a) number of patients; (b) Chi-squared / Fisher's exact test, (*) significant (p<0.05) but non-significant after correction for multiple testing (p<0.003); (c) mean age (yr); (d) One-way ANOVA testing differences in mean age between groups, all values non-significant

.

	Male [a]	Female [a]	*p* [b]	Medical [a]	Surgical [a]	*p* [b]	Age [c]	*SD*	*p* [d]
Feeding categories									
oral self	31	35	0.535	38	28	0.134	11.2	3.4	0.069
oral carer	6	5		2	9		10.3	4.4	
oral self + EN_PN carer	9	4		7	6		8.1	2.8	
oral + EN_PN carer	1	2		2	1		10.7	4.0	
EN_PN carer	8	5		5	8		10.23	3.77	
EN / PN feeding regime									
no	37	40	0.436	40	37	0.600	11.1	3.5	0.034*
partial	10	6		9	7		8.6	3.1	
full	8	5		5	8		10.2	3.8	
EN / PN feeding									
no	37	40	0.276	40	37	0.829	11.1	3.5	0.023*
yes (partial or full)	18	11		14	15		9.3	3.5	
Change in artificial nutrition prescription									
no	50	45	0.662	52	43	0.126	10.6	3.6	0.224
oral to partial EN_PN	3	4		1	6		9.1	3.0	
partial to full EN_PN	1	2		1	2		14.0	4.4	
oral to full EN_PN	1	0		0	1		8.0	-	

Table 36. Effect of age, sex and discharge group on diet-related factors during hospitalisation.

Increased use of EN/PN									
no	50	45	0.755	52	43	0.027*	10.6	3.6	0.823
yes	5	6		2	9		10.4	3.9	
Dietary restrictions									
none	33	38	0.386	37	34	0.216	10.5	3.7	0.245
minor/hospital food	6	2		3	5		11.3	3.5	
for procedure NBM	7	6		9	4		12.3	3.1	
limited by clinical condition	8	5		4	9		9.7	3.1	
Restricted diet									
no	39	40	0.504	40	39	1.00	10.6	3.6	0.584
yes	15	11		13	13		11.0	3.3	
Loss of appetite									
no	25	20	0.653	28	17	0.008*	10.6	3.6	0.590
yes	17	18		11	24		11.0	3.4	
Intake / appetite problems									
no	27	19	0.141	34	12	0.000**	10.5	3.7	0.521
yes	36	46		32	50		11.0	3.6	
Dietary advice during hospitalisation									
no	18	31	0.011*	26	23	0.697	11.7	3.5	0.004*
yes	35	21		27	29		9.7	3.4	

Table 36. *(Cont.)* Effect of age, sex and discharge group on diet-related factors during hospitalisation.

(a) number of patients; (b) Chi-squared / Fisher's exact test of significance of the observed frequencies between category groups; (c) mean age (yr); (d) One-way ANOVA testing differences in mean age between groups; (*) significant ($p<0.05$) but non-significant after correction for multiple testing ($p<0.002$); (**) significant even after correction for multiple testing.

	Steroid prescription					Fluid restriction				
	No		Yes		p [b]	No		Yes		p [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Height	0.08	0.2	0.12	0.1	0.673	0.09	0.2	0.06	0.2	0.678
Weight	-0.02	0.3	0.08	0.5	0.438	-0.01	0.3	-0.01	0.4	0.941
MUAC	-0.07	0.4	0.11	0.4	0.319	-0.04	0.4	-0.15	0.4	0.373
HC	0.25	0.9	-0.14	0.7	0.296	0.26	0.8	0.00	1.1	0.315

Table 37. Associations between the change in SDS of anthropometric parameters, with steroid prescription and fluid restriction at discharge.
(a) mean change in SDS; (b) Independent samples t-test comparing the change in SDS between groups, all non-significant (p<0.05).

	EN / PN feeding					Increased use of EN/PN					Loss of appetite in past week					Dietary advice				
	No		Yes		p [b]	No		Yes		p [b]	No		Yes		p [b]	No		Yes		p [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Height	0.06	0.2	0.13	0.2	0.238	0.08	0.2	0.06	0.1	0.790	0.04	0.1	0.12	0.3	0.239	0.07	0.3	0.09	0.2	0.782
Weight	-0.04	0.3	0.11	0.4	0.061[+]	-0.01	0.3	0.12	0.3	0.186	0.08	0.3	-0.10	0.2	0.009*	-0.08	0.2	0.06	0.4	0.028*
MUAC	-0.07	0.4	-0.03	0.4	0.680	-0.07	0.4	0.03	0.5	0.488	0.03	0.4	-0.18	0.4	0.040*	-0.12	0.3	0.00	0.5	0.225
HC	0.22	0.9	0.26	0.5	0.855	0.25	0.9	0.04	0.4	0.513	0.12	0.6	0.23	1.0	0.573	0.47	0.9	0.03	0.8	0.022*

Table 38. Associations between the change in SDS of anthropometric parameters and diet-related variables at discharge.
(a) mean change in SDS; (b) Independent samples t-test comparing the change in SDS between groups, (*) Significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.003), (+) Independent samples Mann-Whitney U-test.

	Steroid prescription					Fluid restriction				
	No		Yes		*p* [b]	No		Yes		*p* [b]
	mean [a]	*SD*	mean [a]	*SD*		mean [a]	*SD*	mean [a]	*SD*	
Fat mass parameters										
BMI	-0.13	0.4	0.01	0.8	0.451	-0.11	0.4	-0.12	0.5	0.947
Biceps SFT	0.14	0.7	0.17	-	0.966	0.22	0.7	-0.22	0.6	0.090
Triceps SFT	0.04	0.7	-0.52	0.9	0.245	0.02	0.7	0.05	0.7	0.895
Subscapular SFT	-0.05	0.5	-0.05	-	0.996	0.03	0.5	-0.38	0.6	0.096
Suprailiac SFT	-0.01	0.6	0.21	-	0.726	-0.04	0.6	0.23	0.6	0.414
Lean mass parameters										
BIA_{st}	-0.14	0.4	0.20	1.2	0.302	-0.10	0.4	-0.25	0.6	0.466
BIA_{sup} adjusted	0.11	1.1	0.19	0.7	0.850	0.07	1.0	0.34	1.2	0.404
BIA_{all}	0.02	0.8	0.17	0.7	0.626	-0.01	0.7	0.23	1.2	0.323

Table 39. Associations between the change in SDS of BC parameters, with steroid prescription and fluid restriction at discharge.

(a) mean change in SDS; (b) Independent samples t-test comparing the change in SDS between groups, all non-significant (p<0.05).

	EN / PN feeding					Increased use EN/PN					Loss of appetite in past week					Dietary advice				
	No		Yes		p [b]	No		Yes		p [b]	No		Yes		p [b]	No		Yes		p [b]
	mean [a]	*SD*	*mean* [a]	*SD*		*mean* [a]	*SD*	*mean* [a]	*SD*		*mean* [a]	*SD*	*mean* [a]	*SD*		*mean* [a]	*SD*	*mean* [a]	*SD*	
Fat mass parameters																				
BMI	-0.13	0.4	-0.07	0.4	0.615	0.08	0.2	0.06	0.1	0.790	0.09	0.4	-0.27	0.4	0.002**	-0.23	0.4	-0.03	0.4	0.052
Biceps SFT	0.17	0.7	0.14	0.6	0.874	-0.01	0.3	0.12	0.3	0.186	0.12	0.6	0.30	0.8	0.446	0.10	0.7	0.18	0.6	0.679
Triceps SFT	0.03	0.7	0.06	0.7	0.891	-0.07	0.4	0.03	0.5	0.488	-0.01	0.6	-0.05	0.8	0.842	0.09	0.7	-0.04	0.7	0.507
Subscapular SFT	-0.09	0.5	0.18	0.5	0.289	0.25	0.9	0.04	0.4	0.513	0.12	0.5	-0.32	0.6	0.048*	-0.05	0.7	-0.06	0.4	0.951
Suprailiac SFT	-0.02	0.6	0.04	0.7	0.847	0.08	0.2	0.06	0.1	0.790	0.11	0.7	-0.14	0.4	0.376	-0.18	0.6	0.16	0.6	0.149
Lean mass parameters																				
BIA_{st}	-0.11	0.5	-0.15	0.3	0.798	-0.11	0.4	-0.06	0.4	0.741	0.02	0.4	-0.32	0.5	0.028*	-0.30	0.4	0.02	0.4	0.020*
BIA_{sup} adjusted	0.19	1.2	-0.04	0.5	0.443	0.16	0.7	0.17	0.1	0.990	0.14	0.5	0.26	1.5	0.658	0.25	1.6	0.03	0.5	0.410
BIA_{all}	0.07	0.9	-0.06	0.5	0.540	0.01	0.7	0.34	0.5	0.343	0.10	0.4	0.09	1.0	0.982	0.05	1.1	0.02	0.4	0.867

Table 40. Associations between the change in SDS of BC parameters and diet-related variables at discharge.

(a) mean change in SDS; (b) Independent samples t-test comparing the change in SDS between groups, (*) Significant (p<0.05) but non-significant after Bonferroni correction for multiple testing (p<0.003), (**) Significant after Bonferroni correction for multiple testing

15.15. Chapter 8 supplementary results

	Medical		Surgical		p [a]
	median	*range*	*median*	*range*	
Predicted stay	6.0	3-31	9.0	3-76	0.894
Actual stay	5.0	3-39	10.0	3-197	0.091
Difference LOS	0.0	-10-25	0.0	-52,190	0.247

Table 1. Differences in length of stay between medical and surgical admissions.

Length of stay (LOS) in days; (a) Independent samples Mann-Whitney U test comparing the median between medical and surgical admissions (H_0: differences between groups=0, (*) significant ($p<0.05$).

	Prolonged stay				Increased LOS				Complications				Decrease in grip strength			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
Height	2.7	1.3	5.6	0.008*	2.8	1.4	5.5	0.004*	1.2	0.5	2.6	*0.789*	2.6	0.7	9.3	0.154
Weight	2.3	1.2	4.4	0.023*	2.9	1.6	5.4	0.001*	1.1	0.5	2.3	0.808	1.6	0.5	4.5	0.501
DXA LM	2.3	1.1	4.8	0.033*	2.5	1.2	4.9	0.022*	1.8	0.8	3.8	0.156	2.4	0.8	7.0	0.165
DXA FM	1.7	0.6	4.4	0.383	3.1	1.2	8.0	0.031*	1.7	0.6	5.0	0.299	2.0	0.4	11.0	0.638

Table 2. Summary of RR for negative clinical outcomes in patients with abnormal WT, HT, DXA LM and FM SDS on admission.

(a) Ratios (RR) for a prolonged stay, increased LOS, complications or decreased grip strength for those patients with abnormal SDS for HT, WT, DXA LM and DXA FM on admission compared to those with normal SDS, (b) 95% CI of the RR. (c) One sample t-test for the significance of the RR (H_0: RR=1, $p<0.05$). highlighted RR are significant.

	Decrease in weight				Decrease in BMI				Decrease in BIA			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
Height	0.9	0.4	2.2	1.000	0.8	0.2	2.2	0.752	1.5	0.6	3.4	0.415
Weight	2.1	1.0	4.2	0.049*	0.9	0.4	2.2	1.000	0.8	0.3	1.6	0.594
DXA LM	1.4	0.6	3.2	0.427	1.3	0.5	3.7	0.749	1.5	0.6	3.7	0.554
DXA FM	1.5	0.5	4.5	0.519	0.2	0.1	1.7	0.130	1.3	0.3	5.5	1.000

Table 2. *(cont.)* Summary of RR for negative clinical outcomes in patients with abnormal WT, HT, DXA LM and FM SDS on admission.

(a) Ratios (RR) for a prolonged stay, increased LOS, complications or decreased grip strength for those patients with abnormal SDS for HT, WT, DXA LM and DXA FM on admission compared to those with normal SDS, (b) 95% CI of the RR. (c) One sample t-test for the significance of the RR (H_0: RR=1, p<0.05). highlighted RR are significant.

	Prolonged stay					Increased LOS					Complications					Decrease in grip strength				
	No		Yes		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
BMI	0.44	1.3	-0.09	1.5	0.025	0.31	1.3	-0.06	1.5	0.186	0.29	1.4	-0.05	1.3	0.240	0.17	1.5	-0.19	1.4	0.373
DXA LMI	-0.42	1.3	-0.80	1.4	0.138	-0.47	1.4	-0.90	1.3	0.161	-0.42	1.4	-1.19	0.8	0.017	-0.78	1.4	-1.00	1.3	0.583
DXA FMI	0.34	1.1	-0.05	1.3	0.080	0.25	1.1	-0.02	1.5	0.315	0.20	1.2	0.17	1.3	0.900	0.20	1.2	-0.03	1.2	0.504

Table 3. Univariate analysis of the associations between BMI, LMI and FMI SDS on admission with clinical outcomes.

Table shows mean SDS for the parameters on admission. (a) independent samples t-test for the difference in mean SDS between groups (H_0: difference=0), highlighted values show significant (p<0.05) associations.

	Decrease in weight					Decrease in BMI					Decrease in BIA				
	No		Yes		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*
	mean	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*		*mean*	*SD*	*mean*	*SD*	
BMI	0.14	1.3	0.34	1.6	0.483	0.19	1.3	0.41	1.4	0.502	0.44	1.3	0.07	1.5	0.272
DXA LMI	-0.50	1.1	-0.68	1.5	0.522	-0.47	1.1	-0.94	1.4	0.136	-0.47	1.2	-1.06	1.5	0.080
DXA FMI	0.02	1.2	0.35	1.2	0.215	0.13	1.2	0.43	1.1	0.289	0.34	1.1	0.13	1.3	0.469

Table 3. *(Cont.)* Univariate analysis of the associations between BMI, LMI and FMI SDS on admission with clinical outcomes.

	Prolonged stay				Increased LOS				Complications				Decrease in grip strength			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
BMI	0.8	0.4	2.0	0.804	0.9	0.3	2.5	1.000	0.2	0.1	1.5	0.123	0.7	0.2	2.3	0.715
DXA LMI	1.7	0.6	4.9	0.360	1.3	0.4	4.5	0.708	0.9	0.2	3.9	1.000	2.3	0.6	8.3	0.258
DXA FMI	2.0	0.7	6.2	0.326	4.7	1.6	14.1	0.009*	1.0	0.2	4.4	1.000	2.7	0.3	27.8	0.567

Table 4. Summary of RR for negative clinical outcomes in patients with abnormal BMI, LMI and FMI SDS on admission.

(a) Ratios (RR) for a prolonged stay, increased LOS, complications or decreased grip strength for those patients with abnormal SDS for BMI, LMI and FMI on admission compared to those with normal SDS, (b) 95% CI of the RR. (c) One sample t-test for the significance of the RR (H_0: RR=1, p<0.05). highlighted RR are significant.

	Decrease in weight				Decrease in BMI				Decrease in BIA			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
BMI	2.9	1.1	7.6	0.037*	1.5	0.5	4.2	0.524	1.7	0.6	4.6	0.372
DXA LMI	3.5	0.9	13.1	0.067	2.2	0.6	8.5	0.275	2.3	0.7	8.2	0.301
DXA FMI	1.8	0.5	6.6	0.454	0.3	0.1	2.8	0.380	1.0	0.2	4.6	1.000

Table 4. *(Cont.)* Summary of RR for negative clinical outcomes in patients with abnormal BMI, LMI and FMI SDS on admission.

	Prolonged stay					Increased LOS					Complications					Decrease in grip strength				
	No		Yes		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*	*No*		*Yes*		*p*
	Mean	*SD*	*Mean*	*SD*		*Mean*	*SD*	*Mean*	*SD*		*Mean*	*SD*	*Mean*	*SD*		*Mean*	*SD*	*Mean*	*SD*	
Anthropometric parameters																				
HC	-0.36	1.4	-0.99	1.9	0.023	-0.55	1.6	-0.95	1.9	0.223	-0.65	1.8	-0.59	1.2	0.873	-0.30	1.6	-0.58	1.3	0.497
MUAC	-0.08	1.0	-0.54	1.3	0.016	-0.18	1.0	-0.65	1.4	0.037	-0.27	1.2	-0.35	1.2	0.734	-0.12	1.3	-0.65	1.5	0.170
Lean mass parameters																				
BIA_{st}	-0.51	1.2	-1.17	1.3	0.009	-0.58	1.2	-1.43	1.4	0.006	-0.62	1.3	-1.31	1.0	0.013^{+}	-1.01	1.3	-0.96	1.5	0.910
BIA_{sup}	-0.63	1.3	-1.39	1.6	0.003	-0.78	1.3	-1.52	1.8	0.016	-0.83	1.5	-1.41	1.1	0.019^{+}	-0.87	1.4	-1.19	1.5	0.439
BIA_{all}	-0.62	1.3	-1.39	1.5	0.002	-0.77	1.3	-1.51	1.7	0.011	-0.82	1.5	-1.40	1.0	0.016^{+}	-0.92	1.4	-1.20	1.5	0.492
Fat mass parameters																				
Biceps SFT	0.51	0.8	0.31	1.1	0.254	0.48	0.9	0.20	1.3	0.204	0.36	0.9	0.75	1.0	0.077	0.58	1.1	0.24	1.1	0.294
Triceps SFT	0.27	0.8	-0.11	1.1	0.039	0.22	0.9	-0.29	1.2	0.017	0.08	1.0	0.31	0.9	0.322	0.22	0.9	-0.03	1.2	0.429
Subsca-pular SFT	0.43	0.8	0.12	1.0	0.098	0.41	0.8	-0.05	1.1	0.038	0.36	0.9	0.14	1.0	0.388	0.25	1.1	0.15	0.9	0.762
Suprailiac SFT	0.33	0.8	-0.18	1.0	0.009	0.22	0.9	-0.20	0.9	0.092	0.13	0.9	0.24	0.6	0.686	-0.02	1.0	0.12	1.0	0.678

Table 5. Univariate analysis of the associations between other anthropometric and BC SDS on admission with clinical outcomes.

Table shows mean SDS for the parameters on admission. (a) independent samples t-test for the difference in mean SDS between groups (H_0: difference=0), highlighted values show significant ($p<0.05$) associations.

	Prolonged stay				Increased LOS				Complications				Decrease in grip strength			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
HC	2.8	1.0	7.6	0.059*	3.3	1.4	8.2	0.012*	1.3	0.4	3.6	0.746	2.5	0.7	9.0	0.161
MUAC	2.0	0.9	4.4	0.071	1.2	0.5	2.9	0.596	1.0	0.4	2.5	1.000	0.8	0.2	2.9	1.000
BIA_{st}	3.6	1.2	11.2	0.025*	5.9	2.1	16.6	0.002*	2.4	0.8	7.1	0.215	1.0	0.3	3.9	1.000
BIA_{sup}	2.4	1.2	4.7	0.016*	2.3	1.2	4.4	0.020*	1.6	0.8	3.2	0.292	1.5	0.5	5.0	0.714
BIA_{all}	2.8	1.4	5.8	0.004*	2.7	1.4	5.1	0.005*	1.6	0.8	3.3	0.287	1.3	0.4	3.8	0.734
Biceps SFT	6.0	0.7	52.4	0.081	16.5	1.9	140.9	0.005*	6.6	1.2	36.9	0.044*	0.7	0.1	6.7	1.000
Triceps SFT	-	-	-	0.161	-	-	-	0.043*	-	-	-		-	-	-	0.422
Subscapular SFT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Suprailiac SFT	-	-	-	0.133	-	-	-	1.000	-	-	-	1.000	-	-	-	1.000

Table 6. Summary of RR for negative clinical outcomes in patients with other abnormal anthropometric and BC SDS on admission.

(a) Ratios (RR) for a prolonged stay, increased LOS, complications or decreased grip strength for those patients with abnormal SDS for other anthropometric and BC parameters on admission compared to those with normal SDS, (b) 95% CI of the RR. (c) One sample t-test for the significance of the RR (H_0: RR=1, p<0.05). highlighted RR are significant.

15.16. Chapter 9 supplementary results

		Height SDS			Weight SDS			DXA lean mass SDS			DXA fat mass SDS		
		mean	*SD*	*p* [a]	*mean*	*SD*	*p* [a]	*mean*	*SD*	*p* [a]	*mean*	*SD*	*p* [a]
PYMS	low risk	-0.82	1.53		-0.29	1.60		-0.93	1.24		0.08	1.20	
	medium risk	-0.44	1.15	0.433	0.06	1.45	0.043*	-0.59	1.49	0.033*	0.30	1.13	0.225
	high risk	-0.78	1.82		-0.87	1.98		-1.54	1.76		-0.24	1.43	
STAMP	low risk	-0.16	1.10		0.29	1.34		-0.16	0.87		0.28	1.11	
	medium risk	-0.37	1.16	0.000*	-0.17	1.15	0.011*	-0.80	1.28	0.000*	0.00	0.98	0.660
	high risk	-1.42	1.82		-0.84	2.24		-1.67	1.75		0.06	1.64	
STRONG	low risk	0.11	1.00		0.53	1.26		-0.05	0.91		0.38	1.18	
	medium risk	-0.74	1.42	0.002*	-0.23	1.44	0.000*	-1.04	1.41	0.000*	0.18	1.15	0.003*
	high risk	-1.39	1.87		-1.47	2.19		-1.87	1.82		-0.86	1.41	

Table 1. Associations between malnutrition risk and anthropometric/BC scores on admission.

Table shows mean and SD of the SDS for each parameter (weight, height, lean mass, fat mass) on admission for each of the risk categories. (a) One-way ANOVA testing the differences in mean SDS between risk categories, (*) significant (p<0.05).

	Prolonged stay				Increased LOS				Complications				Decrease in grip strength			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
PYMS	2.1	1.5	2.9	0.000	2.5	1.5	4.4	0.003	3.6	2.0	6.4	0.000	0.4	0.2	1.0	0.026
STAMP	1.8	1.3	2.6	0.001	1.7	1.0	3.0	0.073	1.9	1.1	3.5	0.040	0.6	0.3	1.2	0.162
STRONGkids	2.2	1.6	3.0	0.000	2.3	1.3	4.1	0.011	2.2	1.2	4.0	0.021	0.6	0.3	1.4	0.366
GOSH	1.1	0.8	1.6	0.616	1.0	0.6	1.9	1.000	2.1	1.1	3.8	0.026	0.4	0.2	0.8	0.011

Table 2. Associations between malnutrition risk and clinical outcomes.

(a) RR for negative clinical outcomes between referred and not-referred patients, (b) 95% confidence interval of RR, (C) Fisher's exact test between proportion of patients with negative clinical outcomes between referral groups, Highlighted values show significant results (p<0.05).

	Decrease in weight				Decrease in BMI				Decrease in BIA			
	RR	*CI*		*p*	*RR*	*CI*		*p*	*RR*	*CI*		*p*
PYMS	1.9	1.2	3.2	0.023	1.5	0.9	2.6	0.192	1.2	0.7	1.9	0.614
STAMP	1.1	0.6	1.9	0.836	1.0	0.5	1.7	1.000	1.2	0.8	2.0	0.477
STRONGkids	1.0	0.5	2.0	1.000	0.9	0.4	1.9	1.000	1.0	0.6	1.8	1.000
GOSH	0.9	0.5	1.6	0.837	0.8	0.4	1.4	0.463	1.2	0.7	1.8	0.631

Table 2. *(cont.).* Associations between malnutrition risk and clinical outcomes.

(a) RR for negative clinical outcomes between referred and not-referred patients, (b) 95% confidence interval of RR, (C) Fisher's exact test between proportion of patients with negative clinical outcomes between referral groups, Highlighted values show significant results (p<0.05).

15.17. Topics covered in semi-structured interviews

1. DEMOGRAPHICS

- Sex
- Age

2. a. CURRENT PRACTICE context

- Time working/specializing in paediatric dietetics
- Setting of current practice: place/country & general/specialised centre
- Types of patients/specialties currently looking after

2. b. NUTRITIONAL ASSESSMENT procedure (to complement ward observation only)

- Ward setup and capacity: personnel, number of beds
- Time allocated per patient on average for initial assessment & follow up
- Anthropometry – in routine and complex patients
    - What is measured
    - Who makes the measurements
    - When are the measurements taken (admission, discharge, during stay)
    - Purpose of measurements: initial nutritional assessment (growth/malnutrition), monitoring, dietary prescription

3. KNOWLEDGE & EXPERIENCE WITH BC measurements

- Definition → usefulness compared to simple weight
- Techniques for clinical practice
    - Previous experience and training
    - Equipment available in wards (own or shared)

NOTE: "body composition" definition for the context of the interview will be explained, and the possibility of having a fat and lean score as centile or SDS (same as currently done for weight and height) will be explained.

4. a. BC IMPLEMENTATION potential

Assuming in an ideal world, in which we would be able to give a score for <u>every</u> child:

- Would it be useful in your patients
    a) Routine cases
    b) In some – complex cases
- How would you use it
    a) Assess initial nutritional status
    b) Monitor changes
    c) Prescribe diet
- Format for charts preferred
    a) SDS
    b) Centiles

4. b. BC IMPLEMENTATION barriers

Based on previous studies, we know the possible techniques for clinical practice are DXA, BIA or skinfolds. NOTE: give some main points on what the techniques mean in practical terms: time, moving the patient, radiation exposure.

If you were to implement these measurements in practice:

- When? Time → on admission and follow-up
- Who? Personnel → nurse/dietitian & new/existing personnel
- How? Equipment → purchase, maintenance, training

4. c. BC IMPLEMENTATION in practice

- In your patient group, how would you imagine you could use these scores?
- Would you use body composition scores to alter dietetic practice in any way?

4. d. BC IMPLEMENTATION diet prescription scenarios

Consider different scenarios, where the patients all have low or normal weight but markedly different body composition…

- Would you/how would you suggest changing the diet prescription if they had:
    a) Low lean and fat (eg. CF catabolic)
    b) Low lean and normal/high fat (eg. CP immobile)
    c) Normal/low lean and high fat (eg. inflammation or on steroid medication)

- If you consider that changes in diet prescription are unfeasible or ineffective, would you recommend these measurements for monitoring nutritional status rather than diet prescription? Would you rather suggest another intervention (such as physical activity or change in medication)?

- In the patient groups you look after, are there any disease-specific scenarios you would manage markedly differently to the ones discussed? How could body composition measurements be used in this case?

15.18. Interview guide

Study ID: _____ Date: _____ Sex:_____ Age:_____

- Notes for the interviewer are in [ ]
- Further explanations to the question are in ( ) to be used as needed if the participant requires clarification on the question
- Information to be given to the participant to standardize knowledge before continuing to the questions are in *italics*
- Pages 2 and 3 can be completed during a separate session if required

1. How long have you been specializing/working in paediatrics?
2. Where do you currently practice? (place, type of hospital/centre)
3. What specialties or types of patients do you currently look after?

From ward observation - complete during interview as needed

4. How many dietitians cover the wards you look after?
5. How many patients are usually admitted to the wards? What is the maximum capacity?
6. How do you identify patients that need to be seen? (consultant referral, routine screening process, family/patient request)
7. For a routine admission, how much time do you usually allocate to each patient on admission? For follow-up? (minimum/maximum times if this varies too much)
8. Is the previous very different for some specific conditions or diseases? Explain
9. Are anthropometry measurements taken in any of the patients you look after?
   a. Is this for all patients or only for certain groups?
   b. What is measured (height, weight, BMI)?
   c. Who makes the measurements? If other than yourself, do you have access to these measurements in the patient records?
   d. When are the measurements taken (admission, discharge, during stay)?
   e. What are these measurements used for (initial nutritional assessment, monitoring, diet prescription)?

10. What do you understand by "body composition"?
11. Do you know of any techniques to measure body composition? Which ones?
12. Do you have any previous experience or training with any body composition technique? Have you used it in practice?
13. Are you aware of any equipment to measure body composition that might be available in your centre/ward? Do you have access to this equipment?
14. Do you think measurements of body composition could give additional information on the patient's nutritional status compared to weight/height alone? Explain

For the purpose of this interview, we will consider "body composition" to refer to the amounts of fat and fat-free mass. Because we have now measured healthy UK children using a variety of techniques, there is now reference data that allows any patient to potentially be given a standard deviation score or centile, just as it is currently done for weight and height, comparing them to other children of their same age and sex.

Assuming in an ideal world we would be able to measure and give a score to every child:

15. Do you think it would be useful to have body composition scores for your patients (routine patients and complex cases)? Explain
16. If so, how do you imagine you could use them in their nutritional management (initial nutritional assessment, monitor changes, diet prescription)?
17. If body composition scores were to be provided to you, would you prefer them to be as reported as SDS or centiles?

Based on previous studies, we know the possible techniques to measure body composition in clinical practice are DXA, bioelectrical impedance and skinfolds. All of these are relatively quick and practical, although expense of equipment and necessary training vary. DXA is considered the most accurate and it involves a very low level or radiation, equivalent to background radiation - less than a transatlantic flight. This is also the only technique that requires the patient to leave the ward to be measured.

If you were to start implementing these measurements in your practice:

18. When would you suggest they could be done (on admission, follow-up, discharge)?
19. Do you foresee any problems finding the best time to do the measurements? Explain [preconceptions on the time it takes to measure BC]
20. Who do you think would be the best person to do the measurements (nurse, self/dietitian, other)?
21. Do you think the ward has the personnel in place to implement this or would new personnel need to be hired to cover the additional workload? Explain [preconceptions on the difficulty/workload of taking the measurements]
22. What technique would you consider to generally be the best alternative for your ward? Why? [NOTE: give extra information on techniques if unsure]
23. Do you foresee any problems in getting the equipment and giving maintenance to it? Explain

PARTICIPANT CONSENT FORM

Feasibility of implementing body composition measurements in the nutritional management of hospitalised children:

Perspectives of paediatric dietitians

Investigator: **Prof. Mary Fewtrell** Protocol No.:

Contact details: **m.fewtrell@ucl.ac.uk**

Subject study ID:_____

Please **initial box** to indicate agreement

1	I confirm that I have read and understand the ***Information sheet v1 14.04.16*** for the above study. I have had the opportunity to consider the information, ask question and have these answered satisfactorily.	
2	I understand that my participation is voluntary and I can withdraw at any time, without giving any reason.	
3	I understand that relevant data collected during the study may be looked at by employees from Regulatory Authorities or from the Institute of Child Health	
4	I understand that audio recording will be used during the interview, to facilitate writing up my responses and make sure they are recorded accurately and complete. Only the researchers will have access to these recordings and they will be deleted after the completion of the study.	
5	**I agree to taking part in the study**	
6	I agree to the study team contacting me in the future about further follow-up studies, although I will not be obliged to take part in any future study.	

Name of **participant**	Signature	Date
Name of **person taking consent**	Signature	Date

Only the researchers will have access to the data collected during this study. The results will be identified by a number only and all information collected will be completely confidential.

UCL INSTITUTE OF CHILD HEALTH

1 copy for the Participant, original to be kept in the PI's site file.

Version 1, Dated 14.04.16

15.19. Participant consent form

15.20. Information sheet – feasibility study

Childhood Nutrition Research Centre
UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH

UCL INSTITUTE OF CHILD HEALTH

Participant Information Sheet

Feasibility of implementing body composition measurements in the nutritional management of hospitalised children:

Perspectives of paediatric dietitians

You have been invited to take part in a research study. Before you decide whether you should take part or not, it is important to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the aim of the study?

The aim of this study is to explore paediatric dietitian´s opinions, views and possible perceived barriers to the **use of body composition measurements** for the nutritional management of paediatric patients. We will do this through a **semi-structured interview.**

Why is the study being done?

Hospitalized children have a high risk of malnutrition on admission and during their stay. Although weight and height are typically used in the assessment and nutritional management of paediatric patients, these do not distinguish between the proportions of fat and fat-free mass that could potentially be important for the response to treatment and recovery. Preliminary results from our previous study suggested body composition measurements by a range of techniques are acceptable and practical and, with the publication of new reference data on body composition for UK children, it is now possible to give patients a score for their fat and fat-free mass compared to healthy children of the same age and sex.

In this project we want to collect information on the opinions and practical considerations of using these measurements in clinical practice. This will inform possible future intervention studies, where we will explore the use of these measurements for the nutritional management of paediatric patients.

Why am I being invited to take part?

We are inviting all paediatric dietitians at GOSH to take part in the study, because we want to collect the opinions of experienced paediatric dietitians who look after children with complex diagnosis and from a range of specialties.

Participation in this study is completely voluntary.

If you do decide to take part, you will be given this information sheet to keep, and you will be asked to sign a consent form. We will photocopy the consent form for you and keep one for our records. You will still be **free to withdraw at any time and without giving a reason**.

If you agree to take part in this study, we will **arrange a suitable date** to meet you and conduct the interview. During this meeting, and before the interview starts, we will answer any questions you may have and then ask you to sign a consent form if you are still willing to take part in the study. The meeting and interview will take place at a private location (meeting room) either at Great Ormond Street Hospital or the Institute of Child Health.

The interview questions will relate to your **current practice** in the assessment and nutritional management of paediatric patients, especially the use of anthropometry, followed by your **opinion, experiences and suggestions for using body composition measurements**.

The interview should take between **20-30 minutes** to complete, and we can arrange this over one or two sessions depending on your convenience.

With your permission, we would like to **audio record the interview.** The recordings will be used in writing up the interview, to help make sure the write-up is accurate and complete. Only members of the research team shall have access to the recordings and they will be erased from the recorder as soon as it is transferred onto a password-protected computer.

Refusing the recording does not mean you cannot participate in the study.

The risks of participating in this study are minimal. The questions will relate to your professional practice and it is not anticipated that the interview will address any sensitive or distressful subjects. If you do find any questions uncomfortable or hard to answer, we can take a break or stop. If you choose to stop, the interview ca be resumed on another day or you can choose to end your participation in the study.

Taking part in the study will not have any direct benefit and there will be no compensation for your participation, although we hope that the information we collect from the study will help us decide if and what the best way to implement these measurements in practice would be for the purpose of future intervention studies or potentially as part of routine care.

Only the researchers will have access to the data collected during this study. The results will be identified by a number only. All information collected will be kept in password-protected computers in a locked office and deleted after the completion of the study.

What will happen to the results of the research study?

The results of this research will potentially be published in a medical journal and presented at scientific meetings. We will also send you a summary of the results at the end of the study.

Your name will not be used in any written reports or published articles that result from this project and every effort will be made to ensure that descriptions of you as an individual in reports or articles are done in ways that mask your identity.

What if something goes wrong?

The research project has been approved by an Independent Research Ethics Committee which believes that it is of minimal risk. However, any research can carry unforeseen risks and we want you to be informed of your rights in the unlikely event that any harm should occur as a result of taking part in this project. You have the right to claim damages in a court of law. This would require you to prove fault on the part of the Hospital/Institute.

Details of how to **contact the researchers**:

Nara Elizabeth Lara Pompa

PhD student
Childhood Nutrition Research Centre
UCL Institute of Child Health

30 Guilford Street
London WC1N 1EH
Tel. 07742413194
Email n.pompa.11@ucl.ac.uk

Mary Fewtrell

Professor of Paediatric Nutrition
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Thank-you for reading this information sheet