- 1 Bioelectric impedance vector analysis (BIVA) in hospitalised children; predictors and
- 2 associations with clinical outcomes
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- 11 *Running title*: BIVA in paediatric patients
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14	Abstract

Background: Clinical use of bioelectric impedance is limited by variability in hydration.

16 Analysis of raw bioelectric impedance vectors (BIVA), resistance (R), reactance (Xc)

- 17 and phase angle (PA) may be an alternative for monitoring disease
- 18 progression/treatment. Clinical experience of BIVA in children is limited. We
- 19 investigated predictors of BIVA and their ability to predict clinical outcomes in
- 20 children with complex diagnoses.
- 21 Methods: R, Xc and PA were measured (BODYSTAT Quadscan 4000) on admission in
- 22 108 patients (4.6-16.8 years, mean 10.0). R and Xc were indexed by height (H) and
- 23 BIVA-SDS for age and sex calculated using data from healthy children. Potential
- 24 predictors and clinical outcomes (greater-than-expected length-of-stay (LOS),
- complications) were recorded.
- 26 Results: Mean R/H-SDS was significantly higher (0.99 (SD 1.32)) and PA-SDS lower (-
- 27 1.22 (1.68))) than expected, with a wide range for all parameters. In multivariate
- 28 models, the Strongkids risk category predicted R/H-SDS (adjusted mean for low,
- 29 medium and high risk = 0.49, 1.28, 2.17, p=0.009) and PA-SDS (adjusted mean -0.52, -
- 30 1.53, -2.36, p=0.01). BIVA-SDS were not significantly different in patients with or
- 31 without adverse outcomes.
- 32 Conclusion: These complex patients had abnormal mean BIVA-SDS suggestive of
- **33** reduced hydration and poor cellular health according to conventional interpretation.
- 34 R/H-SDS was higher and PA-SDS lower in those classified as higher malnutrition risk by
- 35 the StrongKids tool. Further investigation in specific patient groups, including those
- 36 with acute fluid shifts and using disease-specific outcomes, may better define the
- 37 clinical role of BIV.

- 39 Abbreviations:
- 40 BIA Bioelectric impedance analysis
- 41 BIVA Vector BIA
- 42 CKD Chronic kidney disease
- 43 FM Fat mass
- 44 FFM Fat-free mass
- 45 EN Enteral nutrition (commercially formulated liquid feed)
- 46 LM- Lean mass
- 47 LOS Length of stay
- 48 PA Phase angle
- 49 PN Parenteral nutrition
- 50 R Resistance
- 51 SDS Standard deviation scores
- 52 Xc Reactance
- 53 Z Impedance
- 54

55 Background

56

57	Body composition measurements can be informative in paediatric patients as fat and
58	lean mass may differentially affect disease progression and response to treatment;
59	they are also important when calculating requirements for dietary/fluid intake and
60	doses for different types of treatment (1). Various methods are available for
61	assessment of body composition, ranging from simple bedside techniques to
62	multicomponent models suitable only in a research setting (1, 2). Bioelectrical
63	impedance analysis (BIA) is increasingly used as it is non-invasive, safe, inexpensive
64	and portable. It measures the resistance of the body to a small electric current, but
65	prediction of body water or fat free mass relies on the assumption that conductivity is
66	proportional to body water and that the hydration of lean tissue can be reliably
67	predicted. These assumptions are not always valid even in healthy children, and are a
68	particular problem in clinical situations where hydration is altered. BIA prediction
69	equations are also population-specific and have poor accuracy in individuals (2).
70	
71	Biolectrical impedance vector analysis (BIVA) as developed by Piccoli is a graphical
72	method that relies on qualitative rather than quantitative analysis of BIA components,

od that relies on qualitative rather than quantitative analysis of BIA components, 12 73 avoiding the need for potentially erroneous assumptions (3). Impedance (Z) is 74 decomposed into its raw values of resistance (R) and reactance (Xc) which are plotted 75 on (R/H-Xc/H) graphs, where data from a population are expected to form an ellipse 76 with one diagonal axis representing variability in hydration, and the orthogonal axis 77 representing variability in body cell mass, a proxy for lean mass (4). Individual data 78 points on this graph can be characterised by a vector, whose angle relative to the x-79 axis is termed 'phase angle'. Phase angle (PA, equal to tan-1(Xc/R)) has been

proposed as a simultaneous marker of cell mass and cellular health, providing an
index of clinical status, and several studies broadly support this hypothesis (5-8). In
one large adult study, fat-free mass (FFM) was the strongest predictor of phase angle
(9). Furthermore, major longitudinal changes in hydration correlate with changes in
the ratio between R/H and Xc/H, for example in adults undergoing hemodialysis (10).
The use of BIVA in paediatric patient groups has been less studied.

86

Vector distribution patterns have been shown to be influenced by sex, race or
ethnicity, BMI and age in both adults and children (11, 12). In particular, we have
shown a clear impact of age in healthy children, with vectors progressively shortening
towards the adult position with increasing age in both males and females (13),
suggesting the need to consider age when interpreting BIVA data.

92

93 The aim of this study was to evaluate the use of BIVA in children admitted to a tertiary

94 children's hospital, using BIVA parameters normalised for age and sex (13).

95 Specifically, we (i) describe the impact of disease on BIVA parameters; (ii) investigate

96 predictors; and (iii) assess whether BIVA parameters on admission predict clinical

97 outcomes. We also explore associations between BIVA parameters and body

98 composition measurements by another method (dual-energy X-ray absorptiometry

99 (DXA)) in order to compare with findings reported in healthy children (12) and to

100 assist with the interpretation of BIVA vectors.

101

102 Methods

103 Study population

104	Children aged \geq 5 years (reflecting the age range of available body composition
105	reference data) were recruited from all wards of a tertiary/quaternary paediatric
106	hospital in London, UK for the BodyBasics study. Inclusion criteria were deliberately
107	broad in order to include an extensive range of diagnoses; all children newly
108	admitted, with expected hospital stay \geq 3days, able to have baseline measurements
109	within 48 hours of admission and before major procedures or treatment were
110	approached. No patient groups were excluded a priori, provided individual children
111	met the inclusion criteria. Ethical approval was obtained from the NRES Committee
112	London-Central. Parents or patients \geq 16 years gave written informed consent and
113	assent was obtained from children <16 years.
111	

115 Data Collection

116 BIA was measured using BODYSTAT Quadscan 4000 at a frequency of 50 khz, as 117 proposed by Piccoli (3). Measurements were recorded with the subject lying supine 118 with no body parts touching one another. Surface electrodes were placed on the left 119 wrist (next to the ulna head and behind the knuckle of the middle finger) and ankle 120 (at the level of the medial and lateral malleoli just below the toes). Two consecutive 121 measurements were taken, and mean R, Xc and PA values calculated. The technical 122 error of measurement (TEM) values (calculated as the square root of the sum of 123 squares of differences between measurements divided by twice the sample size) 124 were: PA 0.024, R 1.0 Ω , Xc 0.28 Ω . 125

Body composition (fat mass (FM) and lean mass (LM)) was measured using DXA(Lunar Prodigy (GE Medical Systems, USA)). Patients wore light indoor clothing and

scans were performed with the patient lying supine. LM was calculated as the sum oflean tissue and bone mineral content.

131	Weight was measured to the nearest 0.01 kg using a standing, sitting or hoist
132	electronic scale (Seca, Germany). Children were asked to remove their shoes and
133	measured in light clothes where possible. Height was measured to the nearest 0.1 cm
134	using a wall-mounted digital display stadiometer (Seca, Germany) or Harpenden wall-
135	mounted stadiometer, or for infectious patients, a portable mechanical stadiometer
136	which was taken into the patient's room. A measuring mat was used where possible if
137	the child was unable to stand. Weight and height measurements were taken in
138	duplicate and the mean value used. BMI was calculated in kg/m^2 .
139	
133	
140	Predictor variables
	<i>Predictor variables</i> Physical activity level, wheelchair use, high-dose steroid treatment in the past 6
140	
140 141	Physical activity level, wheelchair use, high-dose steroid treatment in the past 6
140 141 142	Physical activity level, wheelchair use, high-dose steroid treatment in the past 6 months, the use of parenteral (PN) or enteral (EN) nutrition support at the time of
140 141 142 143	Physical activity level, wheelchair use, high-dose steroid treatment in the past 6 months, the use of parenteral (PN) or enteral (EN) nutrition support at the time of admission, and the main reason for admission (classified as investigation, acute
140 141 142 143 144	Physical activity level, wheelchair use, high-dose steroid treatment in the past 6 months, the use of parenteral (PN) or enteral (EN) nutrition support at the time of admission, and the main reason for admission (classified as investigation, acute medical treatment and surgery) were considered as potential predictors of BIVA-SDS.
140 141 142 143 144 145	Physical activity level, wheelchair use, high-dose steroid treatment in the past 6 months, the use of parenteral (PN) or enteral (EN) nutrition support at the time of admission, and the main reason for admission (classified as investigation, acute medical treatment and surgery) were considered as potential predictors of BIVA-SDS. These variables were selected rather than using disease categories given the complex

- 149 reliance on nutrition support (enteral or parenteral), categorised as none, partial or
- 150 full. Wheelchair use was categorised as 'yes' (regular use) or 'no'. Steroid treatment
- 151 in the past 6 months was designated as 'high' or 'low' dose based on the opinion of

the patient's clinical team and coded 'yes or 'no'. Three malnutrition screening tools
(MSTs) were applied on admission by one of four investigators in the same order: 1)
PYMS (14); 2) STAMP (15); 3) STRONGkids (16). These tools included questions related
to the child's nutritional intake, current nutritional status, increased losses and/or
requirements, and risk associated with the underlying disease. Scores were used to
categorise patients into low-risk (LR), medium-risk (MR) or high-risk (HR) categories,

159 Clinical Outcomes

Data on length of stay (LOS) and complications were collected when the child was
discharged from the hospital or after 3 months if still an inpatient. These outcomes
were chosen because they could be obtained from all patients regardless of their
clinical condition.

164

174

165 The absolute LOS in hospital was expected to be highly variable, so the actual stay 166 was compared to the predicted LOS on admission based on the judgement of the 167 clinical team and standard times for scheduled procedures. LOS was categorised as 168 'increased' versus 'expected'; an 'increased LOS' was defined as LOS longer than 169 predicted and greater than the median of 9 days, to avoid classifying patients as 170 having increased LOS when this was only 1-2 extra days and for administrative 171 reasons unrelated to their clinical condition. 172 173 A patient was considered to have experienced 'complications' during their stay if they

8

had any of the following: 1) transfer to the Intensive Care Unit or to their local

175	hospital rather than discharge home, 2) unplanned increased reliance on artificial
176	nutrition (EN and/or PN), 3) periods of fever or infection treated with antibiotics.
177	
178	Statistics
179	R and Xc were indexed by height to generate R/H (ohm/m), Xc/H (ohm/m) and
180	converted to SDS for age and sex using data from a cohort of 293 healthy children
181	(12). SDS for anthropometric variables and BC were calculated using UK90 reference
182	data (17) and in-house reference data (18), respectively.
183	
184	Statistical analysis was performed using SPSS Statistics 21.0 software (SPSS Inc. USA).
185	One sample t-tests were used to compare the patient SDS with the reference
186	population mean (i.e. a score of 0). For predictor and outcome variables, BIVA-SDS
187	were compared between categories using independent sample T tests, ANOVA or
188	non-parametric equivalent. Relationships between BIVA-SDS and body composition
189	were examined using Pearson's correlation. Linear or logistic regression was used to
190	examine predictors of BIVA parameters and/or clinical outcomes.
191	
192	Results
193	Study Population
194	156 patients were recruited for the BodyBasics study. However, to minimise the
195	contribution of measurement error, and given the need to standardise R and Xc by
196	height, children in whom the height, BIA or weight measurement was considered to

- 197 be suboptimal or compromised, or where the BIVA-SDS was implausible (<-6), were
- 198 excluded from the current analysis. This left 70 subjects for analyses involving R/H-

199 SDS or XC/H-SDS. For analyses involving PA-SDS, which is independent of height, 200 subjects were excluded only if the measurement of BIA was considered to be sub-201 optimal or the BIVA-SDS implausible, leaving 108 subjects. Further details of subject 202 participation and reasons for exclusion are provided in Figure 1. Descriptive data on 203 the main clinical specialty caring for each patient and the main reason for the current 204 admission are shown in Figure 2. Within most specialty categories, patients were very 205 heterogeneous and most had multiple diagnoses, hence this variable was not used in 206 further analyses. However, the main reason for the current admission classified as 207 'investigation', 'acute medical treatment' or 'surgery' was considered as a potential 208 predictor of BIVA parameters and clinical outcomes.

209

210 BIVA-SDS distribution

211 The mean XC/H-SDS of the patients was not significantly different from zero.

212 However, mean R/H-SDS was significantly higher and mean PA-SDS significantly lower

than the population mean. There was a wide range of values for all BIVA-SDS (Table

1). Similarly, there was a wide range of weight, height and body composition SDS;

215 mean weight, BMI and FM were not significantly different from zero, but mean height

and LM-SDS were significantly lower than expected.

217

218 Predictors of BIVA-SDS

219 Age was not significantly correlated with R/H-SDS (r=-0.11), XC/H-SDS (r=0.14) or PA-

220 SDS (r=0.14) on admission. PA-SDS was significantly lower and R/H-SDS significantly

higher in patients classified as high risk by the Strongkids MST. A similar pattern was

seen for the STAMP MST, although the trend for PA-SDS was of borderline

223	significance (p=0.06). R/H-SDS was also higher in children admitted for acute medical
224	treatment or surgery rather than for investigation (p=0.013). There was a trend for
225	higher R/H-SDS and lower PA-SDS in patients receiving high dose steroids or EN/PN.
226	In general linear models including age, reason for admission, Strongkids risk, high
227	dose steroids and EN/PN, the only significant predictor of R/H-SDS and PA-SDS was
228	the Strongkids risk category (adjusted mean R/H-SDS for low, medium and high risk =
229	0.49, 1.28, 2.17, p=0.009 (low versus high p=0.003, medium versus high p=0.02);
230	adjusted mean PA-SDS for low, medium and high risk = -0.52, -1.53, -2.36, p=0.01
231	(low versus high p=0.003, medium versus high p=0.09)).
232	
233	Clinical Outcomes
234	BIVA-SDS on admission were not significantly different in patients who did or did not
235	develop the clinical outcomes of 'increased LOS' or 'complications' (Table 2), although
236	there was a trend towards higher R/H-SDS in those with versus those without
237	complications (mean difference 0.49, 95% CI -0.34 to 1.33) and in those with versus
238	without an increased LOS (mean difference 0.42, 95% CI = -0.26 to -1.11). In logistic
239	regression models including age, reason for admission, Strongkids risk, high dose
240	steroids and EN/PN and either R/H-SDS or PA-SDS, no significant predictors of the
241	clinical outcomes were identified.
242	
243	BIVA-SDS and body composition (Figure 1a,b,c).
244	R/H-SDS was significantly negatively correlated with BMI-SDS (r=-0.54, p<0.001), LM-
245	SDS (r=-0.86, p<0.001) and FM-SDS (r=-0.54, p<0.001).
246	

247	XC/H-SDS was significantly negatively correlated with BMI-SDS (r=-0.29, p=0.02) and
248	FM-SDS (r=-0.46, p<0.001), with a weaker, non-significant negative correlation with
249	LM-SDS (r=-0.24).
250	
251	PA-SDS was significantly positively correlated with BMI-SDS (r=0.22, p=0.02) and LM-
252	SDS (r=0.47, p<0.001). No significant correlation was observed with FM-SDS (r=0.11,
253	p=0.3).
254	
255	Discussion
256	This group of children with a range of complex, generally chronic illnesses had
257	abnormal age- and sex-standardised BIVA measurements, with significantly higher
258	R/H-SDS and lower PA-SDS compared to healthy reference data. Following the
259	conventional interpretation of these measurements, this would suggest these
260	children have lower than expected 'body fluids' and worse 'cellular health'. However
261	there was a wide range of values for each of the BIVA-SDS scores, most likely
262	reflecting the heterogeneity of the group. The same variability was also seen for body
263	composition SDS but the patients had significantly low mean height and LM-SDS
264	compared to healthy reference data, consistent with the interpretation of worse
265	'cellular health' from PA.
266	
267	Despite the finding of abnormal R/H and PA values for age and gender, only the risk
268	category allocated for the Strongkids and STAMP MST and the reason for admission
269	were significant predictors of these variables; patients classified as high risk had
270	significantly higher R/H-SDS and lower PA-SDS, whilst those admitted for acute

medical treatment or surgery also had higher R/H-SDS. There was also a trend
towards higher R/H-SDS and lower PA-SDS in patients receiving high dose steroids or
PN/EN, consistent with a greater severity of illness. However, in multivariable models
the only significant predictor of R/H-SDS and PA-SDS was the Strongkids risk category.

276 A previous study reported significantly higher SD scores for both R/H and Xc/H in 277 children and adolescents with cystic fibrosis compared to healthy subjects (19) using 278 BIVA reference data from healthy Italian children (20), although PA did not differ 279 between the groups. Higher R/H was interpreted as indicating dehydration, whilst the 280 higher Xc/H was suggested to reflect changes in the sodium content in the sweat of 281 the patients, although values were not adjusted for age. Girma et al (21) investigated 282 anthropometric and biochemical correlates of BIVA parameters in Ethiopian children 283 with and without severe acute malnutrition (SAM). All three parameters were lower in children with SAM, and also significantly lower in oedematous than non-284 285 oedematous SAM patients. Whilst R/H and PA were strongly correlated with 286 anthropometric measures, Xc showed stronger correlations with biochemical 287 parameters such as albumin and chloride. Thus the authors suggested that Xc may 288 reflect physiological rather than physical parameters. 289 290 We found no significant difference in BIVA-SDS on admission in patients who did or 291 did not develop complications or those whose LOS was or was not increased.

292 However, there was a trend towards higher R/H-SDS, suggesting lower body fluids

according to the conventional interpretation of this vector, in children who developed

294 complications or who had an increased LOS, although no child was reported to be

295	clinically dehydrated at the time. The lack of significant associations between BIVA
296	and outcomes could reflect the necessary use of generic outcomes combined with
297	the relatively small sample size, and further exploration should include more defined
298	patient groups in order to allow more informative predictors and outcomes to be
299	used. For example, higher SD scores for both R/H and Xc/H were significant predictors
300	of impaired lung function in children with cystic fibrosis, after adjusting for age and
301	sex (11).

302

303	Although we did not <i>a priori</i> exclude any patient groups providing they met the
304	inclusion criteria, our final study population did not include children with chronic
305	kidney disease (CKD) receiving dialysis or those receiving intensive care, thus
306	excluding those most likely to have major acute fluid shifts. It is possible that BIVA is
307	more informative in acutely ill patients than in those with chronic disease, as
308	suggested by previous publications in children. Girma et al. (22) reported lower R, Xc
309	and PA in Ethiopian children with SAM compared to healthy children, as well as
310	correlations between baseline R and patient outcome. Longitudinal changes in these
311	patients were also broadly consistent with Piccoli's model. Bozzetto et al. (23)
312	evaluated relative hydration status in 2-14 year old patients (46 CKD without oedema,
313	21 oedematous nephrotic children with normal renal function, 15 in remission from
314	nephrotic syndrome). A progressive increase of mean vector position was found in
315	patients with CKD stage IV compared to stages II-III and patients in remission.
316	Additionally, progressive vector lengthening was observed in children with severe
317	renal disease, considered to indicate relative dehydration. Azevedo et al (24)
318	reported an association between low Xc/H and R/H in children admitted to a

319	paediatric intensive care unit and multiple organ dysfunction. Both R/H and Xc/H
320	increased significantly between admission and discharge in survivors, while in non-
321	survivors there was a trend for decreased values between admission and the last
322	measurement obtained. Finally, the study by Hauschild et al (11) reported
323	significantly longer vectors, interpreted as a combination of dehydration and reduced
324	cell mass, in children with cystic fibrosis who had reduced lung function, compared to
325	healthy children or those with CF and normal lung function. However, BIVA
326	parameters were not adjusted for age or pubertal status.
327	
328	Our primary aim was to determine whether BIVA parameters were associated with
329	clinical predictors and outcomes. However, we also examined associations between
330	BIVA-SDS and body composition, and found similar patterns to those previously
331	reported in healthy children (14). Thus PA was significantly positively associated with
332	lean mass and BMI, suggesting patients with higher LM and BMI have better 'cellular
333	health', consistent with findings from a large study in healthy adults which reported
334	that the strongest predictors of PA were age, height and FFM (9). The correlation
335	between LM and PA was stronger in our cohort than reported in healthy children,
336	perhaps due to the greater range of both LM and PA in this group. R/H was negatively
337	correlated with LM, FM and BMI, with the strongest correlation for LM. According to
338	conventional interpretation this suggests that greater tissue masses, particularly LM,

are associated with higher 'body fluids', although it is not clear whether this

340 interpretation refers to intra- or extracellular fluid, or indeed a combination. Xc/H was

also significantly negatively correlated with FM and BMI, with a stronger correlation

342 for FM than for BMI. Thus those with higher measured tissue mass, especially FM,

343	have a lower value for a marker commonly interpreted as indicating 'body cell mass',
344	which is clearly difficult to explain. Similar but stronger correlations were reported in
345	our analyses in healthy children (13), suggesting that the conventional interpretation
346	of R and Xc in younger age-groups may be more complicated than originally thought.
347	It could be argued for example that Xc, which relates to the opposition to current flow
348	through membranes, might also be an indicator of 'cellular health'. It is also possible
349	that the interpretation of BIVA parameters should depend on underlying clinical
350	characteristics, in particular whether there are disturbances of hydration.

352 An alternative explanation for the observed associations between BIVA parameters 353 and body composition is that they reflect residual effects of body shape that are not 354 removed by indexing the vector measurements for height. Specific BIVA has been 355 proposed as a potential solution to this problem, since R and Xc are indexed by a 356 correction factor derived from arm, calf and waist circumferences divided by height. 357 To date, this method has been used in adults and the elderly (25, 26), and studies are 358 needed in healthy children, particularly to establish whether the same correction 359 factor is appropriate. We were unable to use specific BIVA in our population as we did 360 not have the necessary circumference measurements; indeed, waist circumference 361 measurements may be difficult to obtain in children who may have organomegaly, 362 ascites or recent surgery. Another potential method for further adjusting vectors 363 would be to consider relative body proportions, for example limb length in relation to 364 height. Theoretically, measurements of leg length could be obtained from DXA scans. 365 However our previous attempts to do this in paediatric patients have been hampered

366 by difficulties in standardising measurements, especially in those in whom optimal

367 positioning is not possible because of their underlying condition.

368

369	BIVA was originally proposed by Piccoli as a qualitative method using raw BIA data to
370	avoid the need for assumptions in converting measurements to body composition.
371	However, the strong dependence of BIVA parameters on age makes the use of this
372	simple graphical approach problematic in children and we therefore converted
373	measurements to SDS for age and sex. Whilst this differs subtly from Piccoli's method,
374	it retains the important advantage of avoiding the use of assumptions or prediction
375	equations to convert BIVA into body composition, and in that respect still has
376	advantages over conventional BIA.
377	
378	The strengths of this study include the use of SDS account for the effects of age and
379	sex on vector components, allowing the investigation of the impact of other clinical
380	factors. Furthermore we studied a fairly large group of children with complex clinical
381	conditions. We avoided a significant impact of measurement error by excluding
382	children in whom the measurement of BIA was considered to be compromised in any
383	way and, for Xc/H and R/H-SDS, also when the height or weight measurement was
384	compromised. However, the heterogeneity of our population also represents a
385	weakness, because it precluded the use of specific indicators of clinical condition or
386	outcome. We also did not assess pubertal status, which has been shown to influence
387	BIVA parameters (27), although we adjusted for age and sex which will to some extent
388	address effects of puberty on body size.

389

390	In conclusion, this group of children with complex clinical conditions had abnormal
391	mean BIVA-SDS suggestive of reduced 'body fluids' and poorer 'cell health' according
392	to conventional interpretation. These measures were related to MST risk according to
393	the StrongKids and STAMP tools, and to the reason for admission, but were not
394	apparently influenced by other factors considered as clinical predictors and were not
395	significantly related to clinical outcomes; possibly reflecting the necessary use of
396	generic predictors and outcomes in this heterogeneous population. Children with
397	adverse outcomes showed a trend towards higher R/H-SDS on admission, suggesting
398	lower 'body fluids'. Further investigation in specific patient groups, including those
399	with acute fluid shifts and using disease-specific outcomes, may help to better define
400	the clinical role of BIVA.
401 402	
403	Acknowledgements
404	We thank all the children and parents who participated in the study.
405	

406 Conflict of interest statement

407 Professor Wells has received two BIA machines gratis from Bodystat, used in previous

- 408 research. Bodystat had no role or influence over the research reported here. The
- 409 other authors declare no conflicts of interest.

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529 Figure legend

- 530 Figure 1. Subject flow through the study
- 531 Figure 2. Distribution of subjects by main clinical specialty. (a) n=70 subjects included
- 532 for analysis of R/H-SDS and Xc-SDS; (b) n=108 subjects included for analysis of PA-SDS
- 533 Figure 3. Scatterplots of a) BMI SDS, b) lean mass SDS and c) fat mass SDS against
- 534 BIVSDS

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Table 1. Descriptive data and baseline BIVA-SDS

n=70 unless stated		Number	%
Boys		38	54
Wheelchair use		9	13
Artificial ^a feeding	No	56	80
	Partial	9	13
	Full	4	6
Activity Level cf healthy children of the same age ^b			
	Much less	16	23
	Less	16	23
	Same	24	34
	More	7	10
	Much more	5	7
Receiving high dose steroids		10	14

	Mean (SD)	95% Cl ^c	Range
Age (years)	9.97 (3.44)		4.6 to 16.8
Weight SDS	-0.29 (1.38)	-0.56 to 0.10	-5.02 to 2.75
Height SDS	-0.52 (1.31)	-0.83 to -0.21	-4.62 to 2.17
BMISDS	0.11 (1.20)	-0.17 to 0.40	-3.21 to 2.61
FMSDS (n=61)	0.054 (1.09)	-0.22 to 0.33	-3.02 to 2.07
LMSDS (n=61)	-0.92 (1.26)	-1.24 to -0.60	-4.79 to 1.61
XC/H-SDS	-0.05 (1.37)	-0.38 to 0.27	-3.98 to 2.84
R/H-SDS	0.99* (1.32)	0.68 to 1.31	-2.16 to 4.20
PASDS (n=108)	-1.22* (1.68)	-1.54 to -0.90	-5.95 to 5.05

Values are n(%) or mean (SD) ^a parenteral or enteral nutrition; data missing for 1 subject ^b Data missing for 2 subjects

^c 95% confidence intervals for mean

*p<0.001; one-sample t-test vs 0.

Table 2. BIVA-SDS according to different categories of predictor and outcome variables.Valuesare mean (SD)

	PASDS	XCSDS	R/H-SDS
Predictors <i>Main reason for admission</i> Investigation (35, 26 ^ª) Medical treatment (35, 32) Surgery (39, 12)	-0.97 (2.07) -1.34 (1.45) -1.34 (1.49)	-0.55 (1.53) 0.26 (1.26) 0.19 (1.02)	0.47 (0.95) 1.36 (1.44) 1.15 (1.40)**
Activity level Much less (n=25, 16) Less (n=25, 16) Same (n=34, 24) More (n=12, 7) Much (more n=7, 5)	-1.01 (1.45) -1.22 (2.0) -1.39 (1.73) -1.18 (1.31) -1.36 (2.25)	0.42 (1.00) -0.31 (1.53) -0.34 (1.50) 0.14 (1.31) -0.09 (1.37)	1.48 (1.39) 0.78 (1.13) 0.87 (1.13) 0.61 (2.0) 1.16 (1.76)
<i>Receiving EN/PN</i> No (n=85, 56) Partial (n=14, 9) Full (n=6, 4)	-1.19 (1.80) -1.29 (1.27) -1.49 (0.86)	-0.09 (1.40) 0.01 (1.09) -0.15 (1.09)	0.93 (1.38) 1.21 (1.04) 1.26 (1.2)
<i>High dose steroids</i> No (n= 95, 61) Yes (n= 10, 8)	-1.18 (1.75) -1.62 (1.04)	-0.10 (1.41) 0.07 (0.99)	0.92 (1.34) 1.49 (1.07)
<i>Wheelchair use</i> No (n=90, 60) Yes (n= 13, 9)	-1.25 (1.77) -1.07 (1.12)	-0.11 (1.37) 0.11 (1.42)	0.99 (1.34) 0.90 (1.15)
MSTs^b PYMS Low (n=55, 39) Medium (n=33, 15) High (n=20, 16)	-1.06 (1.39) -1.19 (1.96) -1.71 (1.90)	-0.01 (1.20) -0.15 (1.0) -0.06 (2.01)	0.85 (1.22) -0.06 (2.01) 1.23 (1.67)
<i>STAMP</i> Low (n=22, 11) Medium (n=55, 38) High (n=31, 21)	-0.57 (1.91) -1.21 (1.26) -1.71 (1.90)*	-0.71 (1.52) 0.09 (1.04) 0.03 (1.74)	0.13 (1.04) 0.97 (1.25) 1.49 (1.37)**
StronaKids			

StrongKids

Low (n=21, 11) -0.28 (1.90) -0.65 (1.66) -0.06 (1.04)

Medium, (n=70, 43) High (n=17, 16)	-1.34 (1.43) -1.88 (1.97)**	. ,	0.95 (1.08) 1.84 (1.56)***
Outcomes Complications No (n= 84, 57) Yes (n= 21, 12)	-1.21 (1.79) -1.26 (1.25)	-0.14 (1.45) 0.22 (0.78)	0.9 (1.30) 1.39 (1.40)
<i>Increased LOS</i> No (n=72, 47) Yes (n= 33, 22)	-1.13 (1.72) -1.44 (1.65)	-0.15 (1.38) 0.08 (1.35)	0.85 (1.18) 1.27 (1.58)

^a First number = n for PASDS, second number = n for R/H-SDS and XC/H-SDS ^bMalnutrition screening tools *p=0.06, **p<0.05, ***p<0.005 ANOVA



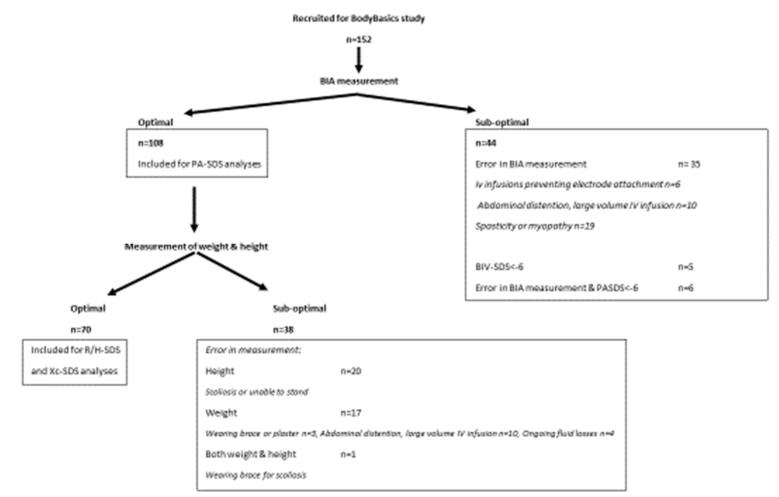
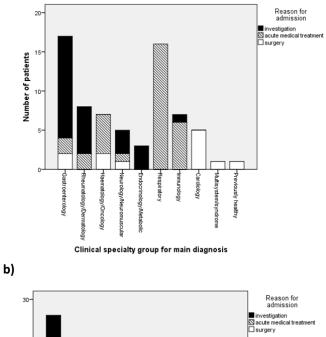
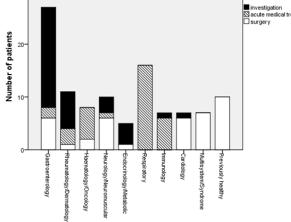


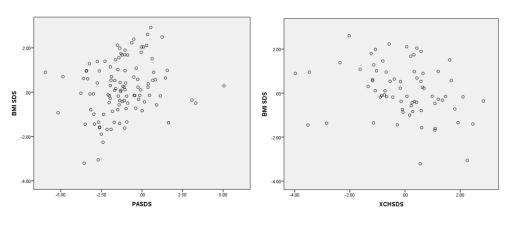
Figure 2



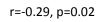


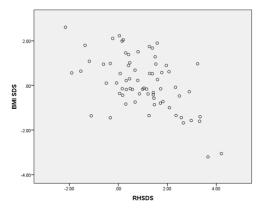
Clinical specialty group for main diagnosis

Figure 3a.



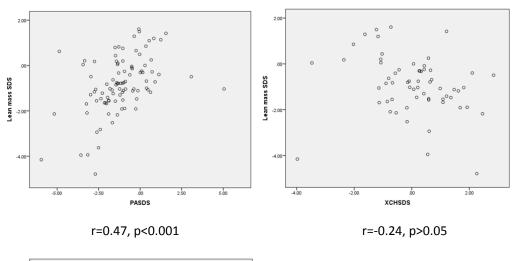
r=0.22, p=0.02

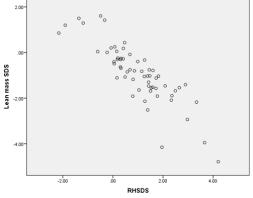




r=-0.54, p<0.001

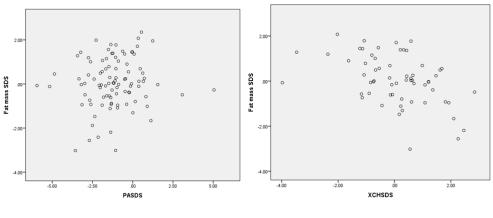
Figure 3b.



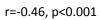


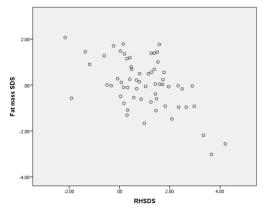
r=-0.86, p<0.001











r=-0.54, p<0.001