



Applied nutritional investigation

Associations of bioelectrical impedance and anthropometric variables among populations and within the full spectrum of malnutrition



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ABSTRACT

Objectives: The aim of this study was to evaluate body composition variability assessed by bioimpedance in relation to nutritional status assessed by anthropometry in children and adolescents living in countries characterized by contrasting nutritional conditions.

Methods: The sample was comprised of 8614 children (4245 males; 4369 females), aged 3 to 19 years, from Nepal (477 children), Uganda (488 children and adolescents), UK (297 children and adolescents) and US (7352 children and adolescents). Height-for-age (HAZ) and body mass index-for-age (BAZ) z-scores were calculated according to WHO growth references. Specific bioelectrical impedance vector analysis (BIVA) was used to evaluate body composition variability. In each population sample, the relationship of HAZ and BAZ with bioelectrical outcomes was analysed by confidence ellipses and cubic spline regression, controlling for sex and age.

Results: The participants from Uganda and Nepal were more affected by undernutrition, and those from the US and UK by obesity. In all groups, phase angle and specific vector length were weakly associated with HAZ, with null or opposite relationships in the different samples, whereas they were positively associated with BAZ. The stronger association was between vector length, indicative of the relative content of fat mass, and BAZ in the UK and US samples. Confidence ellipses showed that the relationships are more strongly related to phase angle in Nepalese and Ugandan samples.

Conclusions: Bioelectrical values were more strongly associated with BAZ than HAZ values in all population samples. Variability was more related to markers of muscle mass in Ugandan and Nepalese samples and to indicators of fat mass in UK and US samples. Specific BIVA can give information on the variability of body composition in malnourished individuals.

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Introduction

Malnutrition affects millions of children and adolescents, with a global increase in the prevalence of overweight and obesity while undernutrition is still widespread in low-income countries [1,2] and is common in pediatric patients [3,4]. Both extremes of

malnutrition are associated with an increased risk of diseases, especially of noncommunicable diseases such as cardiovascular diseases, certain cancers, and diabetes, and with higher risk of death [5].

Usually, malnutrition is assessed on the basis of anthropometric measurements of height and weight, and the derived body mass index (BMI: $\text{weight}/\text{height}^2$, kg/m^2) [6]. The widespread epidemiological use of anthropometry is due to the method being relatively easy to apply, non-invasive and inexpensive, and reflecting the full

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spectrum of nutritional status [6]. By convention, individual measurements of children and adolescents are standardized in relation to sex and age as z-scores, and the resulting indices (height-for-age, HAZ; weight-for-height, WHZ; BMI-for-age, BAZ) allow assessment of chronic or acute undernutrition (categorized as stunting, indicated by low HAZ, or wasting, low WHZ), or overweight and obesity (high BAZ) [6]. Stunting is a complex multifactorial condition that typically commences in utero and worsens in infancy and leads to linear growth failure, which is difficult to recover from. Conversely, wasting is due to a low weight in relation to height and indicates recent and severe weight loss associated with infections and/or insufficient food intake, but treatment is possible [6].

Although informative, anthropometry does not differentiate body composition variability associated with height or weight variability. Both fat and fat-free mass (FM and FFM) are causally and independently related to health status, particularly to the efficiency of immune function [7], and with mortality risk [4,8,9]. Hence, body composition analysis can be insightful for the understanding of malnutrition, and for planning more targeted clinical and public health interventions to prevent or treat it.

The relationship between anthropometric indices of malnutrition and body composition has not yet been extensively studied, although research in the field has intensified during recent decades [10–22]. Such studies may contribute to define the physiological correlates of growth deviations and are potentially helpful to delineate the risk of non-communicable diseases. Indeed, different expressions of malnutrition can be differently associated with body composition changes and different populations may have evolved different biological responses to the same expression of malnutrition. According to a focused review [10] and more recent research [11], severe wasting is associated with major deficits in both FFM and FM. The association of stunting with body composition is less evident and heterogeneous across samples, showing both lower and higher FM levels [10].

Among the existing methods for the assessment of body composition, bioelectrical impedance analysis (BIA) is the most appropriate for epidemiological purposes given its non-invasiveness, low cost and feasibility, which as with anthropometry allows measurements to be obtained even in remote and difficult settings. The use of the conventional approach, predicting fat-free mass using calibrated regression equations, has limitations as samples of children can vary in terms of age and health condition compared to those used to derive the models. This is particularly relevant to the analysis of nutritional status, as undernourished children can be characterized by edema, thus violating the assumption of constancy in FFM hydration and hindering the conversion of raw bioelectrical data into body composition values [23]. The use of alternative approaches, directly analyzing bioelectrical values without prior assumptions on bioelectrical relationships or physical status, is more advisable.

Among such procedures, phase angle (PhA) and *specific* bioelectrical impedance vector analysis (*specific*BIVA; [24]), that analyses phase angle along with impedance vector length, represent suitable options. Phase angle is a recognized indicator of body cell mass, muscle mass in particular, and the quality of cell membranes [25,26], that has shown a good association with dilution techniques in the evaluation of intracellular/extracellular water (ICW/ECW) [27]. In adult and pediatric populations, there is evidence of its association with nutritional status [12]. *Specific* BIVA applies a correction factor based on anthropometry to bioelectrical measurements, in order to reduce the effect of body size and thus disentangling variability in size from that of body composition. It has been validated in US adults [24], showing accuracy in evaluating

FM%, and being associated with skeletal muscle index. It has also demonstrated good agreement with reference methods (DXA, 4-component model) in different populations, in both sexes and various age groups, including children and adolescents [28,29].

The aim of this study is to analyze the relationship of body composition assessed by bioimpedance with nutritional status assessed by anthropometry in children and adolescents. In order to increase the variability of the panorama analyzed, the within-sample relationships were studied in groups living in countries characterized by contrasting environmental, cultural, general welfare, and nutritional status, over the full spectrum of malnutrition.

Methods

Samples and variables

The whole sample examined in this study is part of the BIA International Dataset project [30] and is composed of 8614 children (4245 males; 4369 females) aged 3–19 years, from four countries characterised by different environmental and socio-economic conditions: Nepal, Uganda, United Kingdom, United States (Supplementary Table 1).

Nepal is a federal parliamentary republic in South Asia. According to Central Intelligence Agency [31], it is a low-income country with an estimated real GDP per capita of \$4,000 in 2022. Population density is relatively low, with most people living in rural areas; only 21.9% of the population is urbanised. The median age in Nepal is 27.6 years, and life expectancy at birth is 73 years. The Nepalese (NEP) sample is composed of 477 children (245 males; 232 females) aged 5–6 years, participants in a longitudinal birth cohort from the rural lowland Terai area (Province 2) started in 2012 and followed up in 2018, where the original cohort was selected on the basis of the following inclusion criteria: 1) the mother planned to live in the region under study for the next 12 months, 2) the child was a singleton baby, and 3) the baby was measured within 72 hours of birth. The study was approved by the Nepal Health Research Council (N. 13/2018), and written informed consent was provided by parents.

Uganda is a presidential republic in East Central Africa. It is a low-income country with an estimated real GDP per capita of \$2,300 in 2022 [31]. The population density is relatively high compared to other African countries, but only 26.8% of the population is urbanised. The median age is 15.7 years and life expectancy at birth is 69.3 years. The Ugandan (UGA) sample is composed of 488 children and adolescents (224 males; 264 females) aged 3–16 years. It represents a subsample of a survey carried on in different primary schools belonging to rural or poor contexts near or inside Kampala [32]. All children that were present at school during the data collection period were included in the analysis, excepted for those with absent or unreliable information on their age. The data survey was approved by the Uganda AIDS Support Organization (TASO) independent ethics committee (TASOREC/020/18-UGREC-009) and written informed consent for the analysis was provided by the schools, since head teachers are identified as the legal guardians of the children.

The United Kingdom (UK) is a parliamentary constitutional monarchy in Western Europe. It stands as a high-income country with an estimated real GDP per capita of \$47,600 in 2022 [31]. The population is predominantly urban (84.6%), concentrated largely in and around London. The median age is 40.8 years, with a life expectancy at birth of 82.2 years. The UK sample is composed of 297 children and adolescents (128 males; 169 females) aged 5 to 18 years. The sample derives from a previously analyzed database, that includes children and adolescents of European ancestry who

were either healthy or receiving treatment for obesity but with other pathological conditions excluded [28]. The studies were approved by the Ethical Committee of UCL Institute of Child Health and Great Ormond Street Hospital (N. 11345/001), and written informed consent was obtained from participants aged 18 years, while assent was obtained from those aged <18 years along with written informed consent from their parents.

The United States (US) is a constitutional federal republic in North America. It is a high-income country with an estimated real GDP per capita of \$64,600 in 2022 [31]. The majority of the population (83.3%) lives in urban areas. The median age is 38.9 years and life expectancy at birth is 80.9 years. The US sample derives from the National Health and Nutrition Examination Survey (NHANES) years 1999 to 2004, that is the most recent NHANES survey including bioimpedance data and is composed of 7352 children and adolescents (3772 males; 3580 females) aged 8–19 years. Case selection was based on the availability of measurements and of quality of data, as defined by NHANES. The survey was approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board, and written informed consent was obtained for each participant or their tutor.

Height (cm) and weight (kg) were taken by trained technicians following standard international criteria using different anthropometric equipment: Tanita scale (Tanita Corp, Japan); Toledo digital scale (Mettler-Toledo Inc, Columbus, USA); Seca mechanical scale (Seca GMBH, Hamburg, Germany); ShorrBoard stadiometer (MD, USA); Seca mechanical or electronic stadiometer (Seca GMBH, Hamburg, Germany).

Bioelectrical measurements of resistance and reactance were taken at 50 kHz using the following devices (Bodystat 500 Touch, Bodystat Ltd, UK, in the Nepalese sample; Quadscan 4000 instrumentation, Bodystat, UK, in the UK sample; BIA - Vitality Analyzer, IPGDx, LLC, Littleton, US, in the Ugandan sample; HYDRA ECF/ICF Bio-Impedance Spectrum Analyzer, Model 4200; Xitron Technologies, Inc., San Diego, CA, USA, in the US sample).

Body mass index (BMI) was calculated as weight (in kg) divided by the square of height (in m). Anthropometric indices of nutritional status (HAZ: height-for-age Z-scores; BAZ: body mass index-for-age Z-scores) were calculated according to WHO criteria [6] and to WHO Child Growth Standards or references [33,34]. Malnutrition was defined as an index <−2 or >2 SD: stunting (HAZ <−2), wasting (BAZ <−2), and obesity (BAZ >2). Specific BIVA was applied for the body composition assessment. This approach is based on the analysis of bioelectrical vectors, defined by resistance and reactance standardized for body size (height and cross-sectional areas) or by their derived measurements: vector length ($Z_{sp} = (R_{sp}^2 + X_{csp}^2)^{0.5}$) and phase angle ($PhA = \arctan X_c/R \cdot 180/\pi$). A detailed description of the whole procedure (standardization of values and interpretation) can be found elsewhere (e.g., [24]; www.specificBIVA.com). The projection of bioelectrical vectors on the Cartesian plane allows the analysis of body composition: vector length is positively related to %FM, and phase angle to ICW/ECW ratio, body cell mass, and skeletal muscle index [24]. This study used confidence ellipses, which graphically represent the distribution of bioelectrical vectors and allow the statistical analysis between groups.

Statistical analysis

Descriptive statistics of anthropometric and bioelectrical variables were calculated for each sex, population group, and age class separately.

The association between anthropometric indices of nutritional status and body composition was analyzed by multiple nonlinear

regression, controlling for the effect of sex and age. The absence of correlation values near 1 among explanatory variables and the large sample of children and adolescents allowed us to exclude the effects of collinearity.

Due to the curvilinear association between variables, regression analysis was performed using cubic splines, that is a kind of mathematical curve usable to interpolate complex relationships in data, with a normally distributed response variable [35]. Because different samples may not show the same relationship, the space of spline coefficients is of infinite dimension; hence, spline coefficients cannot be constrained to estimate the differential effects of specific factors, such as, in our case, different countries. Consequently, splines have been estimated separately for each country, although using the same model for each sample, as follows:

$$Y = \alpha + L(\text{sex}, \text{age}) + S(Z_{sp}, \text{PhA}),$$

where Y is the response (HAZ or BAZ), L is the usual linear term (with the corresponding linear coefficient) which can derive from a categorical variable, such as sex, or a quantitative one, such as age, and S represents the cubic spline term, which is the nonlinear function of the corresponding quantitative variable, Z_{sp} or PhA , composed by spline coefficients. Although splines cannot be conveniently written in an analytical form, they can be interpreted by looking at the overall estimated functions, showing the direction and the strength of the association between the non-linear predictor and the response variable, along with 95% confidence intervals (shadow areas in the graphs). The peculiarities of each sample can be perceived considering the difference in scale, slope and shape of the relative splines.

In this study, the uncertainty around splines and regression coefficients was based on normality assumption of residuals, confirmed by evaluating Quantile-Quantile plots of the theoretical normal quantiles against the empirical quantiles of residuals. The significance of the relationship was assessed using usual F test.

Within each population, in the subsample of children aged 5 to 10 years (in detail: NEP, 5–6 years; UGA, 5–10 years; UK, 5–10; US, 8–10 years) confidence ellipses for groups with different nutritional status (based on HAZ and BAZ) were projected on the RXc plane and groups with divergent nutritional status, specified by HAZ or BAZ limits as described above, were compared by means of Hotelling's T^2 test.

Following consensus on the approach based on Bayesian statistics [36], we used p-values lower than 0.005 for the significance level. Statistical analyses were performed using the free software R with the MASS library (<http://www.R-project.org>) and specific BIVA software (www.specificbiva.com).

Results

The population samples showed contrasting anthropometric, nutritional and bioelectrical characteristics (Supplementary Table 1, Fig. 1). HAZ and BAZ values were higher in the UK and US samples with respect to the Ugandan and, especially, the Nepalese samples. Undernutrition was frequent among Nepalese children (stunting: 31.4%; wasting: 20.0%) and, to a lower degree, in the Ugandan sample (stunting: 12.2%; wasting: 5.9%) but was almost absent in the US sample (stunting: 1.9%; wasting: 1.2%), and totally absent in the UK sample. Conversely, obesity was frequent in the UK and US children and adolescents (UK: 31.5%; US: 20.7%) but absent in the Ugandan and Nepalese samples. Bioelectrical values varied similarly. In fact, Z_{sp} (indicative of %FM) was lower in the Nepalese and Ugandan samples (both sexes and all age groups) than in UK and US samples (Supplementary Table 1). PhA (indicative of ICW/ECW and a proxy of skeletal muscle mass) was higher

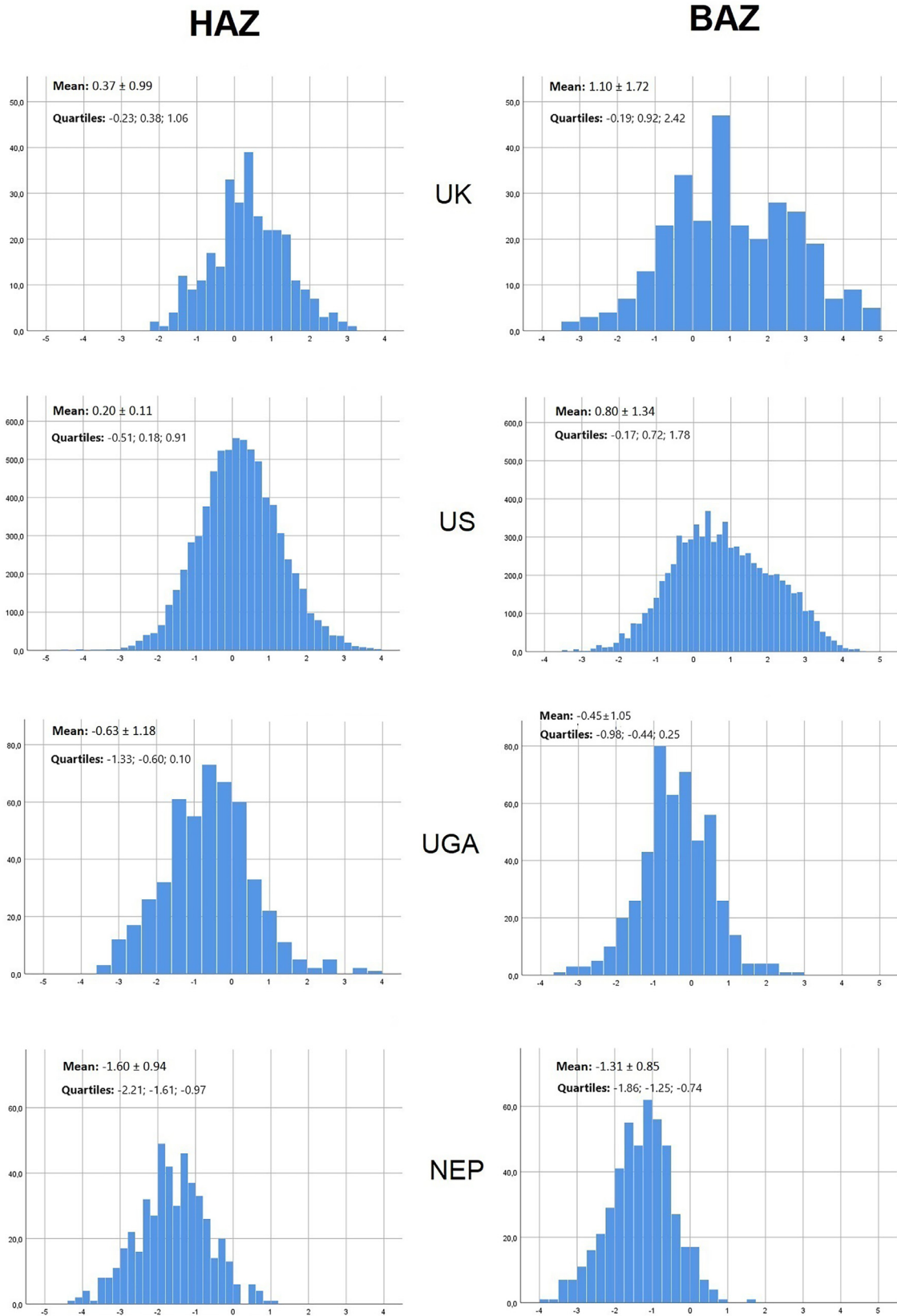


Fig. 1. Histograms showing the distribution of HAZ and BAZ values in the sexes and population groups. HAZ: height-for-age z scores; BAZ: BMI-for-age z scores. NEP: Nepal; UGA: Uganda; UK: United Kingdom; US: United States.

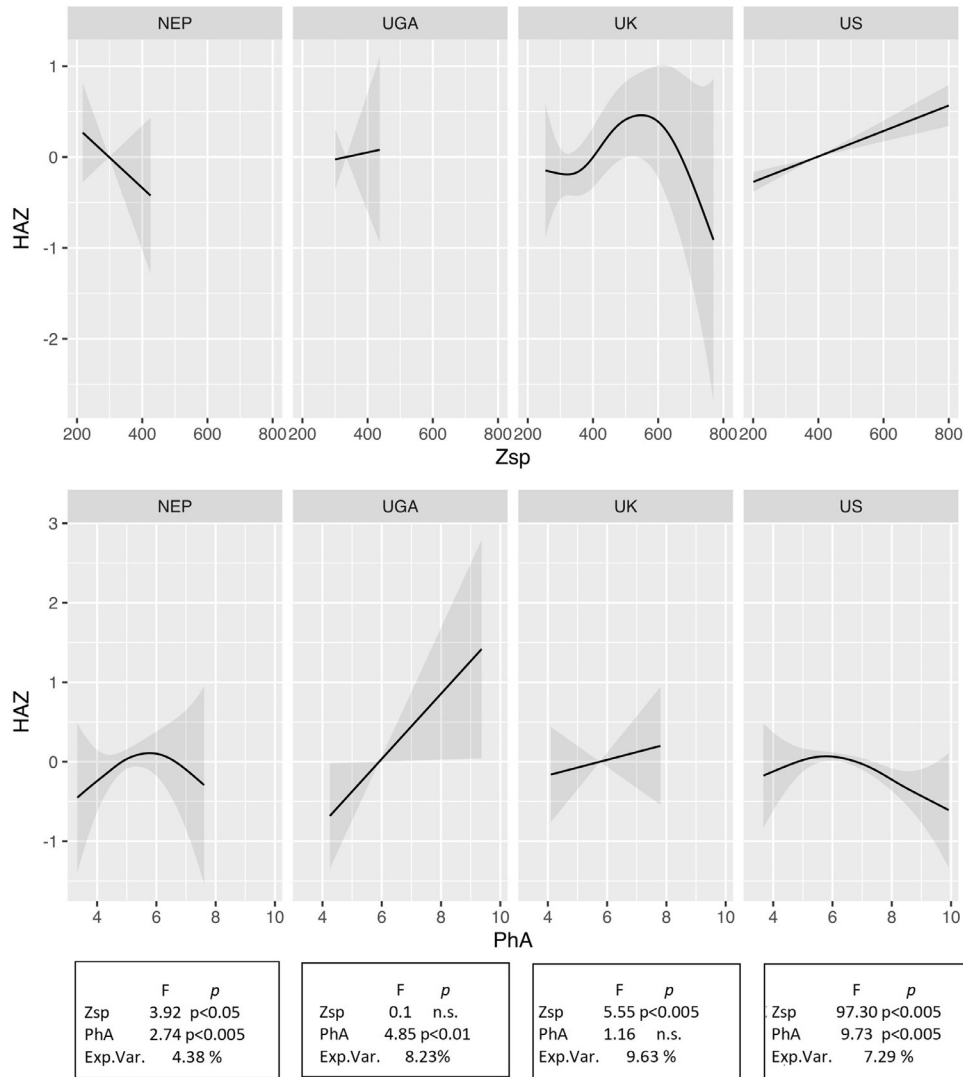


Fig. 2. Results of cubic splines regression results between HAZ values and bioelectrical predictors.

Filled areas show the 95% C.I. about the regression mean estimated with the corresponding spline. HAZ: height-for-age z scores; Zsp: specific vector length; PhA phase angle; NEP: Nepal; UGA: Uganda; UK: United Kingdom; US: United States.

in the Ugandan, especially among females, and US samples, and lower in the Nepalese and UK samples (Supplementary Table 1).

Regression analysis residuals were normally distributed, thus showing the appropriateness of the statistical model.

Bioelectrical values were more strongly associated with BAZ than HAZ values in all population samples, controlling for the effect of sex and age (Figs. 2-5). In particular, HAZ was not clearly associated with bioelectrical variables, with null or weak relationships, or opposite relationships in the different samples, and with a low proportion of variance explained, ranging between 4.4% (Nepal) and 9.6% (UK) (Fig. 2). Zsp was positively related to HAZ in the US and tendentially in the UK samples, unrelated or negatively related in the Ugandan and Nepalese samples (Fig. 2). PhA was positively related to HAZ in the Ugandan and, tendentially, in the Nepalese samples, unrelated or negatively related in the UK and in the US samples (Fig. 2). In the sub-sample of children aged 5-10 years, confidence ellipses (Fig. 3) summarize the above relationships, highlighting a similarity between Nepalese and Ugandan children, where better nutritional status was associated with higher phase angle, and with reduced or steady vector lengths, whereas in the

UK and US samples increasing HAZ scores were associated with longer vectors and with lower or unchanged phase angle values.

The relationship between body composition and nutritional status was clearer in the case of BAZ, with a higher proportion of variance explained, particularly in the US and UK samples (82.7% and 70.9%, respectively) with respect to the Nepalese and Ugandan samples (14.6% and 12.4%, respectively) (Fig. 4). Zsp and PhA were always positively associated with BAZ (Fig. 4). Confidence ellipses representing the group of children 5-10 years old showed that the above relationships are more strongly related to phase angle in Nepalese and Ugandan samples, but to vector length in the UK and US samples (Fig. 5).

Discussion

The population samples analyzed in this research were characterized by contrasting nutritional status, with the UK and US children and adolescents more affected by overweight and obesity, and the Ugandan and Nepalese ones by undernutrition. The relationship between nutritional status and body composition varied

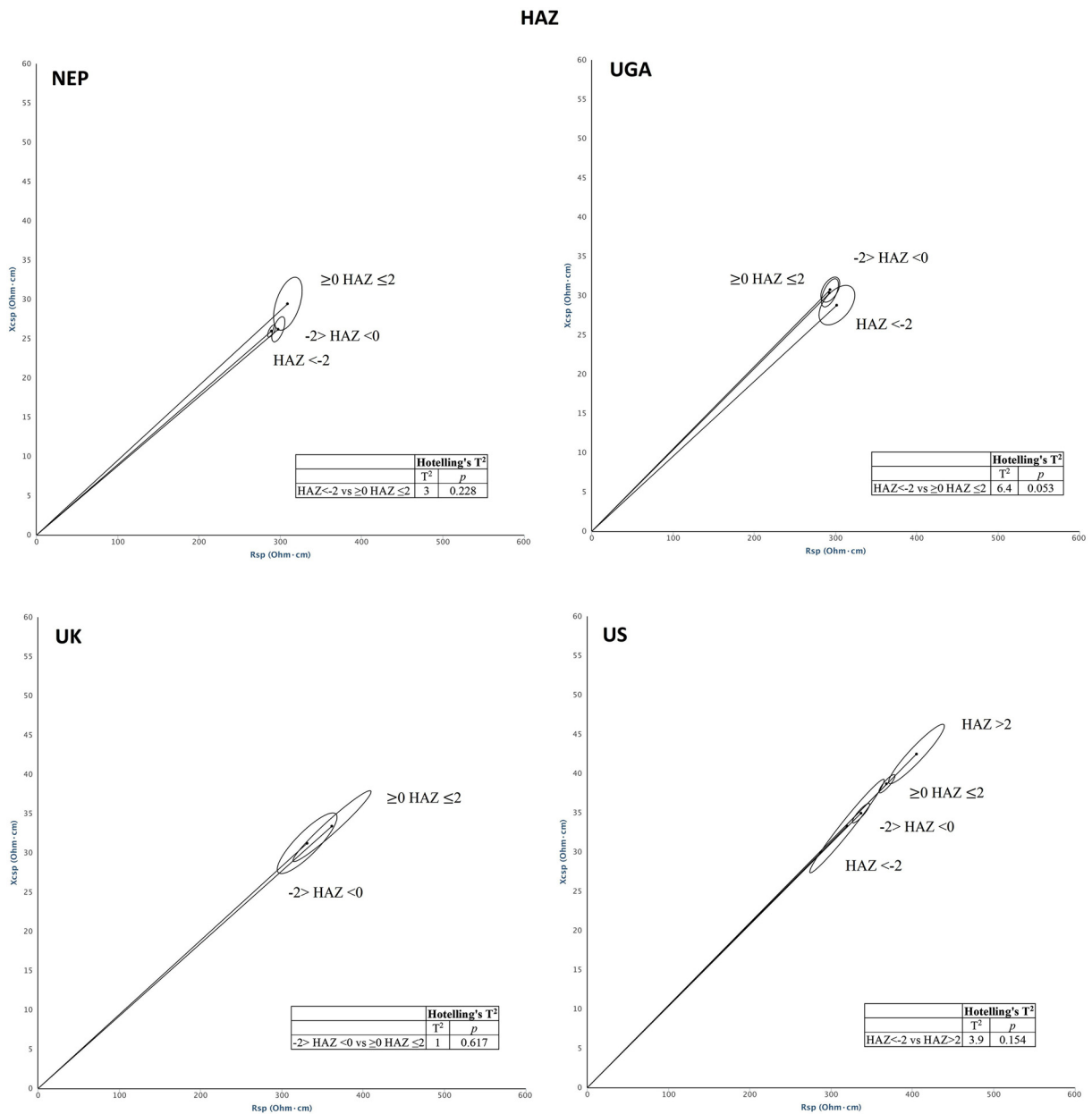


Fig. 3. Specific confidence ellipses in groups of different nutritional status according to HAZ. HAZ: height-for-age z scores; Rsp: specific resistance; Xcsp: specific reactance; NEP: Nepal; UGA: Uganda; UK: United Kingdom; US: United States.

according to the anthropometric indicator and the prevalent form of malnutrition in the population. Regression models showed that, in all population samples, HAZ was poorly associated with body composition differences, as indicated by the low levels of variance explained and the few significant associations with bioelectrical values.

Similar results have been observed in previous research [10]. Stunting typically originates early in life, before birth and is largely irreversible as height is more difficult to recover than weight [37]. As a consequence, different nutritional and lifestyle conditions during children's growth can lead to variable expressions of weight and body composition (e.g. continued thinness or high fatness), whereas height does not change similarly. Such long-term relative stability of HAZ allows the use of stunting as a robust indicator of undernutrition at the population level. However, at the individual

level, a low HAZ does not necessarily imply poor child well-being, even though some common determinants can be shared [38]. This may explain why the associations of HAZ with body composition were weak, as already observed by other authors [11,15,18], and also the inconsistent results of the literature [10,12], with some studies showing higher phase angles in stunted children [16] and others the opposite pattern ([39]; present study).

Keeping in mind the low explained variance of the observed relationships and hence the importance of factors not included in the model - such as household and mother's characteristics, diet, infectious diseases - some significant tendencies can be perceived. HAZ was positively related to Zsp in the US and UK samples (characterized by higher values of HAZ), but unrelated or negatively related in the Ugandan and Nepalese ones, whereas it was negatively related or unrelated to PhA in the US and UK samples, but

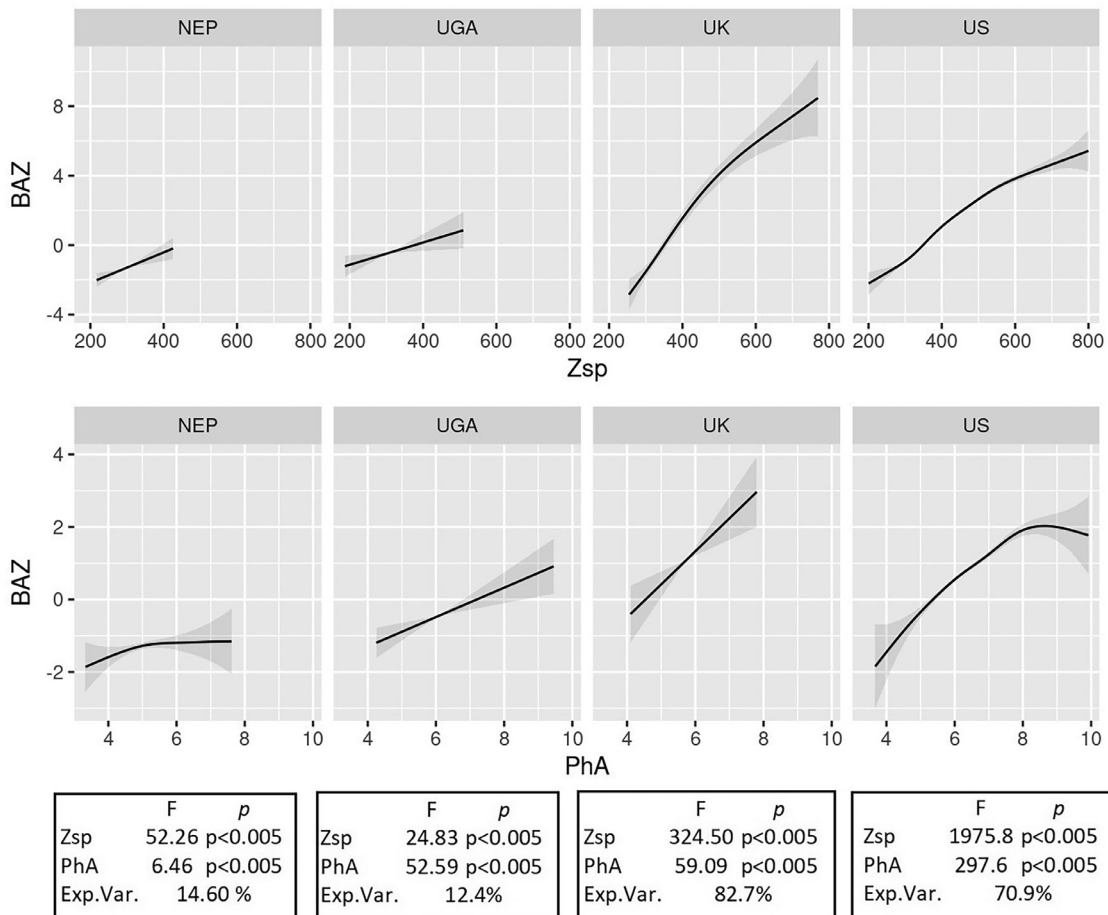


Fig. 4. Results of cubic splines regression results between BAZ values and bioelectrical predictors.

Filled areas show the 95% C.I. about the regression mean estimated with the corresponding spline. BAZ: BMI-for-age z scores; Zsp: specific vector length; PhA phase angle; NEP: Nepal; UGA: Uganda; UK: United Kingdom; US: United States.

positively related in the Ugandan and Nepalese ones. This suggests that both extremes of stature variability, highlighted by different population samples, are characterized by relatively higher body fat (as indicated by Zsp), and lower ICW/ECW ratio or body cell mass and cell membrane quality (as contextually suggested by PhA). Body fat preservation at the detriment of fat-free tissue has been already observed among other samples of undernourished children [17,40], similar to the 'thin-fat phenotype' described in South Asian neonates and children [13,14,41,42], and could be viewed as an ultimate survival strategy [17,43], likely modulated by proximate factors, such as alimentary habits and physical activity levels. On the other side, in higher income countries, such as the US and UK, diet is broadly characterized by highly caloric foods, that, along with common sedentary habits, induce fat accumulation, but also allow skeletal development [44].

BIA parameters explained a greater proportion of variance in BAZ, particularly in the US and UK samples, that is among populations mainly affected by overweight and obesity, where bioelectrical variability almost completely explains weight variability. A clear and predictable increase of Zsp, indicating %FM increase, appears particularly evident with increasing BAZ, especially in the UK and US samples, along with an increase of phase angle. Considering that a correlation of PhA with fat-free mass has been described previously in adults [24,45], this highlights that obesity, as defined by BMI, incorporates higher levels of both FM and FFM, consistent with other pediatric studies [46,47].

The positive relation between BAZ and phase angle, similarly observed in other studies [12], in this research was particularly clear in the analysis of Ugandan (5–10 years old) and Nepalese children (5–6 years old), where differences between confidence ellipses were more related to PhA than vector length. This observation is consistent with the greater variability in FFM than in FM among undernourished children, already discussed in relation to stunting and observed among wasted Cambodian [17] or Chinese [19] children, and among relatively thin (BMI below 50th percentile) US children and adolescents [20].

Among the strengths of this study, it is the first to analyze body composition assessed by BIA in relation to the full spectrum of malnutrition assessed by anthropometry in large samples of children and adolescents from four different continents, including remote and difficult settings. This allowed us to attribute associations with bioelectrical outcomes directly to undernutrition on one side and obesity on the other, independent of environmental or genetic factors.

The main limitation of the research is related to the lack of a wider representation of body composition variability in human populations and of international bioelectrical references that would allow the contextual interpretation of body composition in all population groups. Indeed, this is one of the objectives of the BIA International data project [30]. Another limit is related to the lack of results from dilution techniques that would have been useful to disentangle the variability of PhA in terms of ICW or ECW

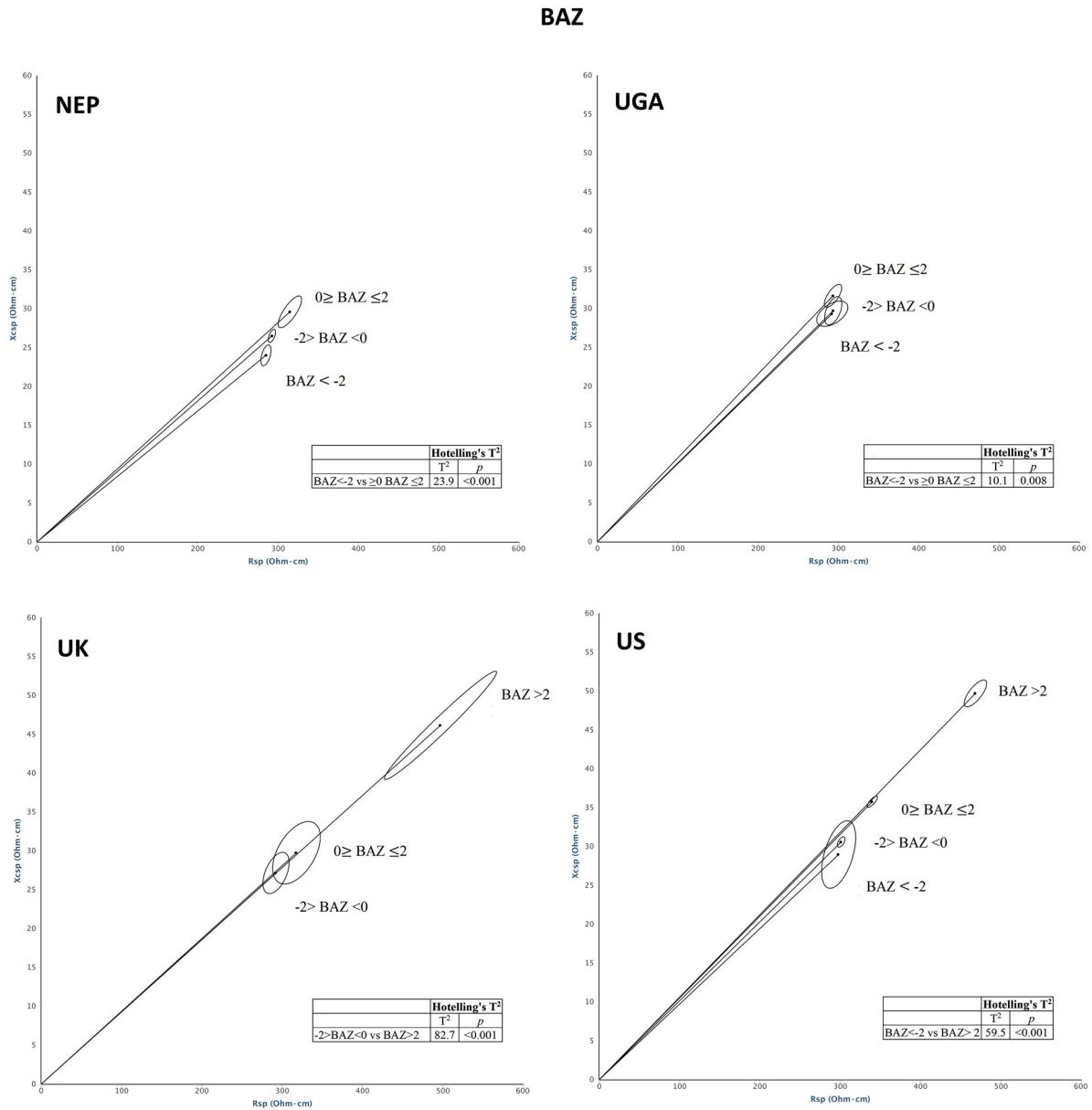


Fig. 5. Specific confidence ellipses in groups of different nutritional status according to BAZ. BAZ: BMI-for-age z scores; Rsp: specific resistance; Xcsp: specific reactance; NEP: Nepal; UGA: Uganda; UK: United Kingdom; US: United States.

variation. Also, the use of different bioimpedance devices hampers the direct comparison of bioelectrical values among samples. However, this limit should cancel out in the comparison of within-sample bioelectrical-anthropometric relationships carried out in this study. The potential effect of imprecision on age [48] among undernourished children was negligible, as in the Nepalese sample age was known to the day and in the Ugandan sample it has proven to be irrelevant [32].

Conclusions

This research generated novel findings on the relationship between anthropometric indicators of malnutrition and body composition variability.

The relationship between nutritional status (defined on the basis of anthropometry) and body composition (defined on the

basis of BIVA) varied according to the anthropometric indicator and the population cluster, as the samples from Uganda and Nepal were more characterized by undernutrition, and those in the US and UK more affected by obesity. In all populations, HAZ was weakly associated with BIVA variation, whereas BAZ showed a positive relation with bioelectrical indicators of fat and muscle mass, and particularly in the case of %FM (as highlighted by US and UK samples). Indicators of fat mass tended to vary less than markers of muscle mass among undernourished children (as highlighted by Ugandan and Nepalese samples), whereas they varied more than muscle mass among children with overweight or obesity (as highlighted by UK and US samples). From a methodological point of view, specific BIVA was shown to be a suitable method to be used in association with anthropometric indices in order to evaluate body composition in malnourished children. For this purpose,

reference values representing multipopulational bioelectrical variability would be helpful.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Elisabetta Marini: Writing – review & editing, Writing – original draft, Supervision, Formal analysis, Data curation, Conceptualization. **Silvia Stagi:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation. **Stefano Cabras:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation. **Ornella Comandini:** Writing – review & editing, Investigation. **Jude Thaddeus Ssen-samba:** Writing – review & editing, Investigation. **Mary Fewtrell:** Writing – review & editing, Investigation. **Laura Busert-Sebela:** Writing – review & editing, Investigation. **Naomi M. Saville:** Writing – review & editing, Investigation. **Carrie P. Earthman:** Writing – review & editing, Investigation. **Analiza M. Silva:** Writing – review & editing, Methodology, Conceptualization. **Jonathan C.K. Wells:** Writing – review & editing, Methodology, Conceptualization.

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Supplementary materials

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