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MULT: A new BMI reference to assess nutritional status of multi-ethnic children and adolescents

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Abstract

Objectives: To develop a new Body Mass Index (BMI) reference (MULT) based on longitudinal data of multi-ethnic populations and to compare it to international BMI references.

Methods: The MULT BMI reference was constructed through the LMS method and the Generalized Additive Models for Location Scale and Shape (GAMLSS), with 81 310 observations of 17 505 subjects aged 0–22 years old, from the United Kingdom, Ethiopia, Peru, India, Vietnam, Brazil, and Portugal. Outlier values were removed based on weight *z*-scores (population level) and based on BMI *z*-scores using the linear mixed effects model (individual level). The MULT *M*, *S* and *L* curves were compared to the ones of the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), International Obesity Task Force (IOTF), and Dutch Growth Study (DUTCH). The MULT BMI percentile cutoffs for overweight and obesity were calculated using the adult BMI values of 25 and 30 kg/m^2 at 17, 18, 19, and 20 years old.

Results: MULT presented the lowest mean BMI values for the ages 102–240 months for boys and 114–220 months for girls. MULT *S* values were similar to the WHO and IOTF for children under 60 months of age and the highest during puberty, while the *L* curve showed to be more symmetric than the other BMI references.

Conclusion: The MULT BMI reference was constructed based on recent data of populations from 10 countries, being a good option to assess the nutritional status of multi-ethnic populations.

1 | INTRODUCTION

Obesity has reached pandemic proportions being responsible for many illnesses worldwide, and it has been recognized as a public health issue, affecting all countries (Bentham et al., 2017). Children with overweight and obesity are more likely to keep these conditions into adulthood as well as to develop noncommunicable diseases, such as diabetes and cardiovascular diseases, at a younger age (Bentham et al., 2017). The BMI-for-age growth chart is the main tool to monitor children and adolescent weight, allowing the detection of underweight, overweight, and obesity conditions (Bentham et al., 2017; De Onis et al., 2007; Ferreira, 2012; Kuczmarski et al., 2002; WHO Multicentre Growth Reference Study Group, 2006). Over the years, several organizations such as the Centers for Disease Control and Prevention (CDC), the International Obesity Task Force (IOTF), and the World Health Organization (WHO) developed BMI references to be used worldwide (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2002; WHO Multicentre Growth Reference Study Group, 2006).

CDC, IOTF, and WHO BMI references are recommended to be used internationally, even though, several countries have found divergences when comparing their national BMI patterns to the ones of these international BMI references, and some countries such as the Netherlands have developed their own BMI growth charts (Ferreira, 2012; Schönbeck et al., 2011). These divergences included the composition of the population, the modeling of the descriptive parameters of the anthropometric index, the age limit, and the cutoff points applied (Cavazzotto et al., 2014; Ferreira, 2012; Iftikhar et al., 2018).

For instance, for children aged 5 years and older, WHO and CDC used data only from the United States population, while the IOTF used data from six countries, presenting a higher ethnic diversity (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2002). Regarding the methodological approach, the Box–Cox power exponential with cubic spline smoothing of curves along with power age transformation, which includes the possibility of modeling a fourth parameter (kurtosis), were applied to the WHO BMI standard/reference (De Onis et al., 2007; WHO Multicentre Growth Reference Study Group, 2006). In the CDC BMI reference, the desired percentiles were estimated from the data, smoothed, and then used to create the LMS parameters while Cole's LMS method (Box–Cox transformation) was applied in the Dutch Growth Study (DUTCH), and in the IOTF BMI reference (Cole et al., 2000; Cole & Lobstein, 2012; Iftikhar et al., 2018; Kuczmarski et al., 2000, 2002; Schönbeck et al., 2011). Although the methodological approach was different in these BMI references, the committee responsible for the WHO reference did not apply the kurtosis fitting, then, WHO final growth charts were generated fitting only the three parameters as applied in the CDC, DUTCH and IOTF BMI references (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2000; Schönbeck et al., 2011; WHO Multicentre Growth Reference Study Group, 2006).

Regarding the age limits and cutoffs, CDC growth charts are presented from 2 to 20 years old, the IOTF growth charts are presented from 2 to 18 years old, the DUTCH growth charts are presented from birth to 21 years old, and WHO are presented from birth to 19 years old (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2000; Kuczmarski et al., 2002; Schönbeck et al., 2011; WHO Multicentre Growth Reference Study Group, 2006). While CDC used *z*-scores and percentiles from the sample to estimate their cutoff points at 20 years of age, the DUTCH and IOTF references applied the BMI values of 17, 25 and 30 kg/m^2 for 18 years old to estimate their percentiles, and WHO used the *z*-score, but also applied the values 25 and 30 kg/m^2 for 19 years old to estimate overweight and obesity percentiles (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2000; Kuczmarski et al., 2002; Schönbeck et al., 2011; WHO Multicentre Growth Reference Study Group, 2006).

Besides the methodological disparities, another disadvantage of the WHO, CDC, IOTF, and DUTCH references is that they are mostly based on cross-sectional data, while longitudinal data would allow the nutritional status assessment over the years, and consider the BMI changes during childhood and adolescence (Ohuma & Altman, 2019). All these distinct methodological approaches generate differences in the nutritional classification and make a diagnosis and comparison of prevalence difficult (Cavazzotto et al., 2014).

Therefore, the aims of this study were to develop new BMI-for-age growth charts and respective percentiles based on recent longitudinal data from multi-ethnic populations (MULT BMI Reference) and compare it to international BMI references/percentiles of CDC, DUTCH, IOTF, and WHO (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2000, 2002; Schönbeck et al., 2011; WHO Multicentre Growth Reference Study Group, 2006).

2 | SUBJECTS AND METHODS

2.1 | Study design and population

Anthropometric and demographic data from multi-ethnic children and adolescents born between 1990 and 2002 were obtained from four longitudinal studies: Millennium Cohort Study (MCS), Young Lives (YL), Adolescent Nutritional Assessment Longitudinal Study (ELANA), and Epidemiological Health Investigation of Teenagers in Porto (EPITeen) (Barnett et al., 2013; Connelly & Platt, 2014; Moreira et al., 2015; Ramos & Barros, 2007).

The MCS started in 2001, recruiting 18 827 children who were born between 2000 and 2002 in the United Kingdom (England, Scotland, Wales, and Northern Ireland) (Connelly & Platt, 2014). This study was conducted by the Centre for Longitudinal Studies at the University of London, (Connelly & Platt, 2014). MCS provides social, economic, demographic and health-related data of the cohort members and their families as well as measures concerning child development, cognitive ability, and educational attainment (Connelly & Platt, 2014). In the MCS, the participants were evaluated at 9 months and at 3, 5, 7, 11, 14, and 17 years of age, and in our analyses, we only included data from the second sweep ($n = 15\,588$) because there was no infant height or BMI data in the baseline (Connelly & Platt, 2014).

The YL started in 2002 following children from four countries: Ethiopia, India (Andhra Pradesh), Peru, and Vietnam (Barnett et al., 2013). YL provides demographic, socio-economic, health, cognitive, physical development, health behaviors, and education participant data (Barnett et al., 2013). YL is composed of two cohorts: a younger cohort with around 8000 children who were born in 2001-2002 and were assessed at 1, 5, 8, 12, and 15 years of age (Barnett et al., 2013). The older cohort comprised about 4000 children who were born in 1994–1995 and assessed at 8, 12, 15, 19, and 22 years of age (Barnett et al., 2013).

The ELANA is a prospective study that was conducted by the State University of Rio de Janeiro (UERJ) between 2010 and 2013 (Moreira et al., 2015). ELANA investigated 1848 adolescents who were born between 1990 and 2000 from four private and two public schools of the metropolitan region of Rio de Janeiro (Brazil) (Moreira et al., 2015). ELANA is composed of two cohorts, a middle and a high school cohort (MS/HS) (Moreira et al., 2015). The adolescents were assessed every year, completing four evaluations in the ELANA MS and three evaluations in the ELANA HS (Moreira et al., 2015).

The EPITeen is a cohort study conducted by the University of Porto Medical School and Institute of Public Health of the University of Porto (ISPUP) that started in 2003/2004 with adolescents aged 13 (Ramos & Barros, 2007). EPITeen is composed of 2942 adolescents who were born in 1990 and attended public and private schools in the city of Porto in Portugal (Ramos & Barros, 2007). The adolescents from the EPITeen were assessed at the ages of 13, 17, 21, 24, and 27 under the cohort evaluation, and anthropometric data at birth and during childhood were retrieved from their child health books (Ramos & Barros, 2007).

Across all the studies, anthropometric measurements were collected by trained professionals that followed a standardized examination protocol to ensure data quality of the measurements (Barnett et al., 2013; Connelly & Platt, 2014; Moreira et al., 2015; Ramos & Barros, 2007). Furthermore, in all the surveys, children under 2 years old were measured in the supine position (length measurement) while children from 2 years old were measured upright (height measurement) (Barnett et al., 2013; Connelly & Platt, 2014; Moreira et al., 2015; Ramos & Barros, 2007).

These datasets provided data from about 32162 and were conducted according to the guidelines laid down in the Declaration of Helsinki (Barnett et al., 2013; Connelly & Platt, 2014; Moreira et al., 2015; Ramos & Barros, 2007). Written informed consent was obtained from all participants and/or their parents or guardians (Barnett et al., 2013; Connelly & Platt, 2014; Moreira et al., 2015; Ramos & Barros, 2007). Data from ELANA was obtained through the authorization of the UERJ and approved by the Ethics Committee of the Institute of Social Medicine of the UERJ (de Moraes et al., 2019; Moreira et al., 2015). Similarly, data from EPITeen was retrieved through the authorization of the ISPUP, and approved by the Ethics Committees of the Hospital S. João and of the ISPUP (Ramos & Barros, 2007). Moreover, data from MCS and YL were obtained through the UK Data Service online platform and approved, respectively, by the UK National Health Service Research Ethics Committee, and by the Central University Research Ethics Committee (Barnett et al., 2013; Boyden, 2018a, 2018b; Cohort and Longitudinal Studies Enhancement Resources, 2019; Connelly & Platt, 2014; Jones & Huttly, 2018; Kelly, 2008; Sanchez et al., 2018; University of London, Institute of Education, & Centre for Longitudinal Studies, 2020a, 2020b; Woldehanna et al., 2018).

2.2 | Data processing and analysis

In order to guarantee data quality, we excluded subjects ($n = 177$) who did not meet our eligibility criteria: ethnicity classification (originally from each study) into one of the five categories (White, Black, Asian Indian, Native Peruvians, and East and Southeast Asians) and/or assessment in all sweeps for the ELANA HS (three sweeps) or in at least four sweeps for the other surveys. Moreover, the following exclusions were performed: missing data

($n = 13\,299$ subjects), measurement errors, in which subjects decreased in height (≥0.5 cm) over the years ($n = 799$ subjects), and implausible values considered as height-for-age *z*-score below −6 standard deviations (SD) or above +6 SD or BMI-for-age *z*-score below −5 SD or above +5 SD ($n = 250$ subjects) (WHO Expert Committee, 1995).

Additionally, in order to have a representative sample of a healthy population, BMI values that had less than 10 observations per age in months ($n = 334$ observations) and outlier weight and BMI values ($n = 10\,399$ observations) were removed from our data pool. The exclusion of outliers on a population level was performed based on the *z*-score for weight. For children under 5 years old, we removed outlier measurements of weight-for-age *z*-scores below −2 SD or above +2 SD based on the WHO reference values, while for children aged 5 years and older, we removed outliers (*z*-scores below −2 SD or above +2 SD) based on the weight of our own sample ($n = 5672$ observations) (WHO Multicentre Growth Reference Study Group, 2006). For removing outliers on an individual level, an equation based on the BMI values for each subject was estimated as a linear mixed effects model using the *nlme* package in R (Pinheiro et al., 2022; R Core Team, 2020). This package fits a linear mixed-effects model in the formulation described in 1982 by Laird and Ware, but allowing for nested random effects (Cole, 1986; Laird & Ware, 1982; Pinheiro et al., 2022). In our analysis, the BMI values were estimated as a function of age and included a random effect in the intercept and in the age coefficient to predict the expected BMI-for-age values. Using *z*-scores, BMI values that were below −2 SD or above +2 SD than the predicted BMI values were excluded to avoid individual outlier effects in our model ($n = 4727$ observations).

The MULT BMI-for-age growth charts were modeled by sex (determined at birth by the presence or absence of a Y chromosome) and from 0 to ≤22 years old. This age group was selected to guarantee the achievement of the final height of the sample, once males can still have some height gain after 18 years old (Cole, 1986; de Oliveira et al., 2023; Kato et al., 1998). MULT BMI reference values were calculated through the RefCurv software, which has a graphical interface written in Python and a statistical engine based on R (Winkler et al., 2020). The RefCurv software uses the Generalized Additive Models for Location Scale and Shape (GAMLSS) package from R and applies the LMS method described by Cole and Green in 1992 (Cole & Green, 1992; Stasinopoulos & Rigby, 2007; Winkler et al., 2020).

The LMS method assumes for positive and independent data that the Box–Cox transformation for each age can be applied to normalize the distribution of the anthropometric values (Cole & Green, 1992). In this study, the method worked by modeling three parameters: the median (*M* curve), the coefficient of variation (*S* curve), and the skewness (*L* curve) of the BMI data as an age function (Cole & Green, 1992). These three parameters applied by the model and adjusted to the BMI data estimated the location, dispersion, and asymmetry for each age (in months) (Cole & Green, 1992). Estimating these parameters for all ages provides an overview of the human growth pattern, which is not limited to unidimensional analysis (Cole & Green, 1992). Furthermore, the LMS method allows adjusting different equations for the median, coefficient of variation, and skewness, which includes parametric and nonparametric functions such as penalized splines (Cole & Green, 1992). This approach affords breadth and flexibility in the model, making it a good technique for modeling BMI data (Cole et al., 2000; Cole & Green, 1992).

In the MULT BMI reference construction, the model class defined by the Box–Cox Cole Green distribution with penalized splines as the smoothing function was chosen for the distribution parameters *L*, and *S* (Cole & Green, 1992; Stasinopoulos & Rigby, 2007; Winkler et al., 2020). On the other hand, for smoothing the parameter *M* (median), B-Spline Basis was applied because it allows the choice of the internal breakpoints (knots) that define the spline, and there was a need to apply the knots considering the peculiarities of human development patterns at each growth stage (Hastie, 1992). Therefore, we applied the knots at 0, 5, and 23 months of age, which are age periods that precede changes in child growth and ways of measuring (Desiraju, 2018; Graber, 2021). At 6 months of age, there is a child growth slowdown: children usually grow around 2.5 cm per month in the first semester of life, while they grow around 1.5 cm in the second semester of life (Desiraju, 2018; Graber, 2021). We chose the second knot at 23 months because at 24 months of age there is another growth slowdown, so children start to grow only around 1 cm per month and they also start to be assessed standing up (height measurement) (Graber, 2021; WHO Multicentre Growth Reference Study Group, 2006).

The degrees of freedom (df) of the *L* and *S* parameter were chosen according to the Bayesian Information Criterion (BIC), to avoid overfitting because each penalized spline has a set of df and depending of the df range selection, it can provide different outcomes (Schwarz, 1978; Winkler et al., 2020). The following df ranges were tested: $L = 0–1$, $M = 3$ (considering the knots 0, 5, and 23) and $S = 0–4$ for boys, and $L = 0–1$, $M = 3$ (considering the knots 0, 5, and 23) and $S = 0–3$ for girls. The df model settings that presented the lowest BIC values were selected (boys: $L = 1$; $M = 3$; $S = 4$/girls: $L = 1$; $M = 3$;

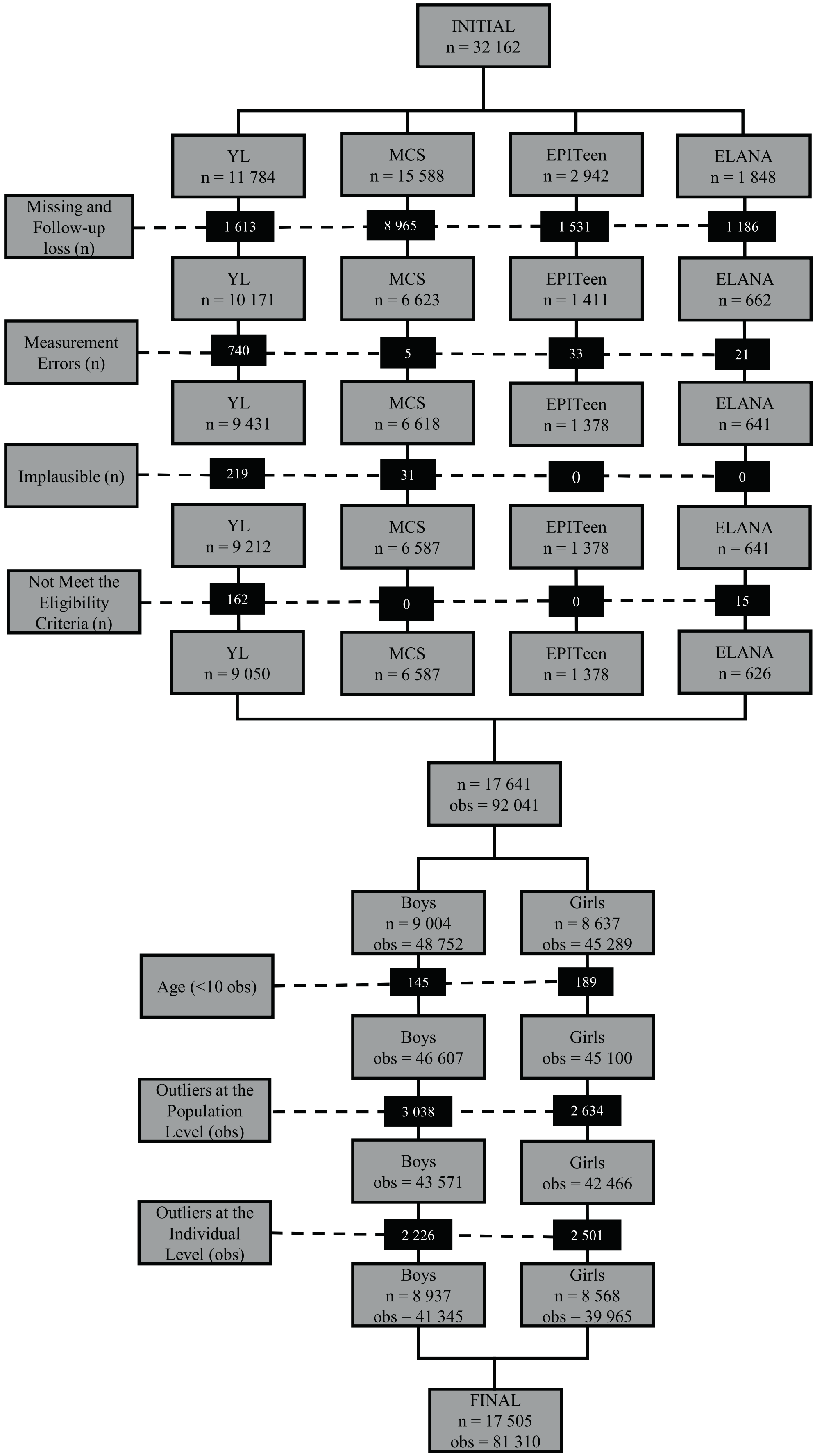

FIGURE 1 Flowchart of the subject and anthropometric data selection. *n*, number of participants. obs, number of BMI values. Measurement Errors: children and adolescents who had decreased their height over the years. Implausible values: height-for-age *z*-score below −6 SD or above +6 SD or BMI-for-age *z*-score below −5 SD or above +5 SD. Outliers at the population level: weight-for-age *z*-score below −2 SD or above +2 SD (based on the WHO reference values for children under 5 years old and based on the weight of our own sample for children from 5 years old and older. Outliers at the individual level: BMI-for-age *z*-score below −2SD or above +2SD (based on the BMI values of the linear mixed effects model).

$S = 3$) (Schwarz, 1978; Winkler et al., 2020). The L, M, S parameters of our final model were fitted through the Rigby and Stasinopoulos algorithm and the BMI mean, median, coefficient of variation, Box–Cox transformation parameter (L curve gross values), and worm plots introduced by Van Buuren and Fredriks were applied to verify the L, M, S curve fittings (Cole & Green, 1992; Rigby & Stasinopoulos, 2004; Stasinopoulos & Rigby, 2007; Van Buuren & Fredriks, 2001; Winkler et al., 2020). This diagnostic approach allows for the assessment of the model assumption, which consists of the age-conditional normality of the transformed BMI, which is a technique widely used in modeling growth references (Van Buuren & Fredriks, 2001).

The MULT BMI reference percentile cutoffs for underweight I, underweight II, underweight III, overweight and obesity were calculated through the BMI values of 18.5, 17, 16, 25 and 30 kg/m^2. Although we presented three cutoff points for underweight in the MULT BMI reference, the value of 17 kg/m^2 (underweight II) was chosen to classify underweight in our growth charts. We decided to apply this value because WHO, IOTF, and DUTCH BMI references also applied it as the underweight cutoff (Cole & Lobstein, 2012; De Onis et al., 2007; Schönbeck et al., 2011). Similarly, the BMI values of 25 and 30 kg/m^2 were applied because they have been recommended by WHO as cutoff points to determine overweight and obesity in adults and they were also applied as cutoff points in the DUTCH, WHO, and IOTF BMI references (Cole & Lobstein, 2012; De Onis et al., 2007; Schönbeck et al., 2011; World Health Organization, 2000). The cutoffs points based on the BMI values of 17, 25, and 30 kg/m^2 were proposed in four different ages, at 17, 18, 19, and 20 years old, generating four percentile options for each nutritional status classification.

The comparison between the CDC, WHO, IOTF, DUTCH, and MULT BMI-for-age growth charts was performed describing the BMI trajectory based on the 50th percentile (M curve), calculating the BMI z-score differences according to the M parameter of our data, and also describing the skewness (L Curve) and the coefficient of variation (S Curve) (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2000; Kuczmarski et al., 2002; Schönbeck et al., 2011; WHO Multicentre Growth Reference Study Group, 2006). Furthermore, the cutoff points for underweight, overweight and obesity of CDC, WHO, IOTF, DUTCH, and MULT BMI references were described (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2000, 2002; Schönbeck et al., 2011; WHO Multicentre Growth Reference Study Group, 2006).

3 | RESULTS

After the exclusion of subjects that did not meet the eligibility criteria or had outlier measurements, 17 505 subjects with 81 310 BMI values (50.85% from boys) were used in the MULT BMI reference construction, as shown in Figure 1. The largest ethnic group of our sample was White (47.4), followed by Asian Indian (14.2%), Black (14.0%), East and Southeast Asians (12.8%), and Native Peruvian (11.7%). The BMI observations and the MULT LMS reference values per sex and age groups are presented in Tables 1 and 2.

The BMI trajectory based on the M curve and the BMI z-score differences between MULT, CDC, WHO, IOTF, and DUTCH BMI references are shown in Figure 2. When compared to the other BMI references, MULT presented lower median BMI values for the ages of 0–12 months for both sexes and for the ages of 102–240 months for boys and 114–220 months for girls. On the other hand, WHO presented the lowest median BMI values for boys from 12 to 78 months and for girls from 12 to 60 months, whereas IOTF presented the lowest median BMI values from 78 to 102 months. Compared to WHO, IOTF and MULT, CDC presented the highest median BMI values for boys from 96 to 240 months and for girls from 96 to 144 months. Regarding the BMI values at 18 years old (216 months), MULT presented the lowest value for boys (20.57 kg/m^2), whereas IOTF presented the lowest value for girls (20.79 kg/m^2). In addition, in the MULT BMI reference, women presented a higher final median BMI (22.07 kg/m^2) than men (21.85 kg/m^2) at 20 years old, as in the IOTF BMI reference at 18 years old.

TABLE 1 Number of observations per age group and sex included in the construction of the LMS parameters of the MULT BMI reference.

Age (year)	Boys (obs)	Girls (obs)
0 to <2	3448	3591
2 to <4	2890	3096
4 to <6	6518	6285
6 to <8	5218	5040
8 to <10	2388	2049
10 to <12	4952	4830
12 to <14	4211	4002
14 to <16	7070	6580
16 to <18	2936	3062
18 to ≤22	1714	1430
Total	41 345	39 965

Abbreviation: obs, number of observations.

TABLE 2 MULT BMI LMS reference values for boys and girls.

	Boys			Girls		
Age (months)	**L**	**M**	**S**	**L**	**M**	**S**
0	0.2289	14.5175	0.0810	0.8244	14.5786	0.0743
1	0.2212	15.5160	0.0808	0.8108	15.3176	0.0745
2	0.2136	16.1522	0.0806	0.7971	15.8073	0.0747
3	0.2059	16.5137	0.0804	0.7834	16.1062	0.0748
4	0.1983	16.6880	0.0802	0.7697	16.2731	0.0750
5	0.1906	16.7629	0.0800	0.7560	16.3667	0.0752
6	0.1829	16.8114	0.0798	0.7423	16.4359	0.0754
7	0.1753	16.8487	0.0796	0.7286	16.4912	0.0756
8	0.1676	16.8756	0.0794	0.7149	16.5337	0.0758
9	0.1599	16.8928	0.0793	0.7013	16.5641	0.0759
10	0.1522	16.9009	0.0791	0.6876	16.5833	0.0761
11	0.1445	16.9007	0.0789	0.6739	16.5923	0.0763
12	0.1368	16.8929	0.0787	0.6602	16.5919	0.0765
13	0.1290	16.8783	0.0786	0.6465	16.5830	0.0767
14	0.1213	16.8575	0.0784	0.6328	16.5664	0.0769
15	0.1135	16.8313	0.0783	0.6192	16.5432	0.0771
18	0.0901	16.7270	0.0778	0.5782	16.4421	0.0776
24	0.0430	16.4682	0.0773	0.4966	16.1781	0.0789
36	−0.0532	16.0265	0.0778	0.3359	15.7470	0.0824
48	−0.1522	15.7191	0.0816	0.1816	15.4828	0.0878
60	−0.2540	15.5371	0.0882	0.0371	15.3709	0.0954
72	−0.3583	15.4717	0.0970	−0.0950	15.3969	0.1053
84	−0.4630	15.5139	0.1074	−0.2128	15.5461	0.1172
96	−0.5650	15.6551	0.1193	−0.3156	15.8039	0.1301
108	−0.6605	15.8864	0.1316	−0.4033	16.1559	0.1427
120	−0.7443	16.1989	0.1429	−0.4751	16.5873	0.1535
132	−0.8103	16.5839	0.1521	−0.5294	17.0838	0.1613
144	−0.8542	17.0324	0.1582	−0.5667	17.6306	0.1653
156	−0.8760	17.5357	0.1609	−0.5913	18.2133	0.1653
168	−0.8780	18.0850	0.1609	−0.6061	18.8173	0.1628
180	−0.8638	18.6714	0.1595	−0.6136	19.4279	0.1591
192	−0.8374	19.2861	0.1578	−0.6163	20.0308	0.1556
204	−0.8009	19.9202	0.1564	−0.6147	20.6112	0.1532
216	−0.7552	20.5650	0.1550	−0.6080	21.1547	0.1520
228	−0.7028	21.2117	0.1530	−0.5978	21.6466	0.1514
240	−0.6470	21.8513	0.1499	−0.5869	22.0724	0.1511

Abbreviations: L, skewness; M, median BMI (50th percentile); S, coefficient of variation.

The *S* and *L* curves of the different BMI references are shown in Figure 3. MULT presented *S* values similar to WHO and IOTF BMI references for children under 60 months of age and the highest *S* values for adolescents (both sexes), especially during puberty onset. In addition, there was a decrease in the *S* values around 192 months for girls, as occurred in IOTF and DUTCH BMI references. Regarding the skewness, the MULT *L* curve showed to be more symmetric than the other BMI references, presenting the closest values to 0, while CDC

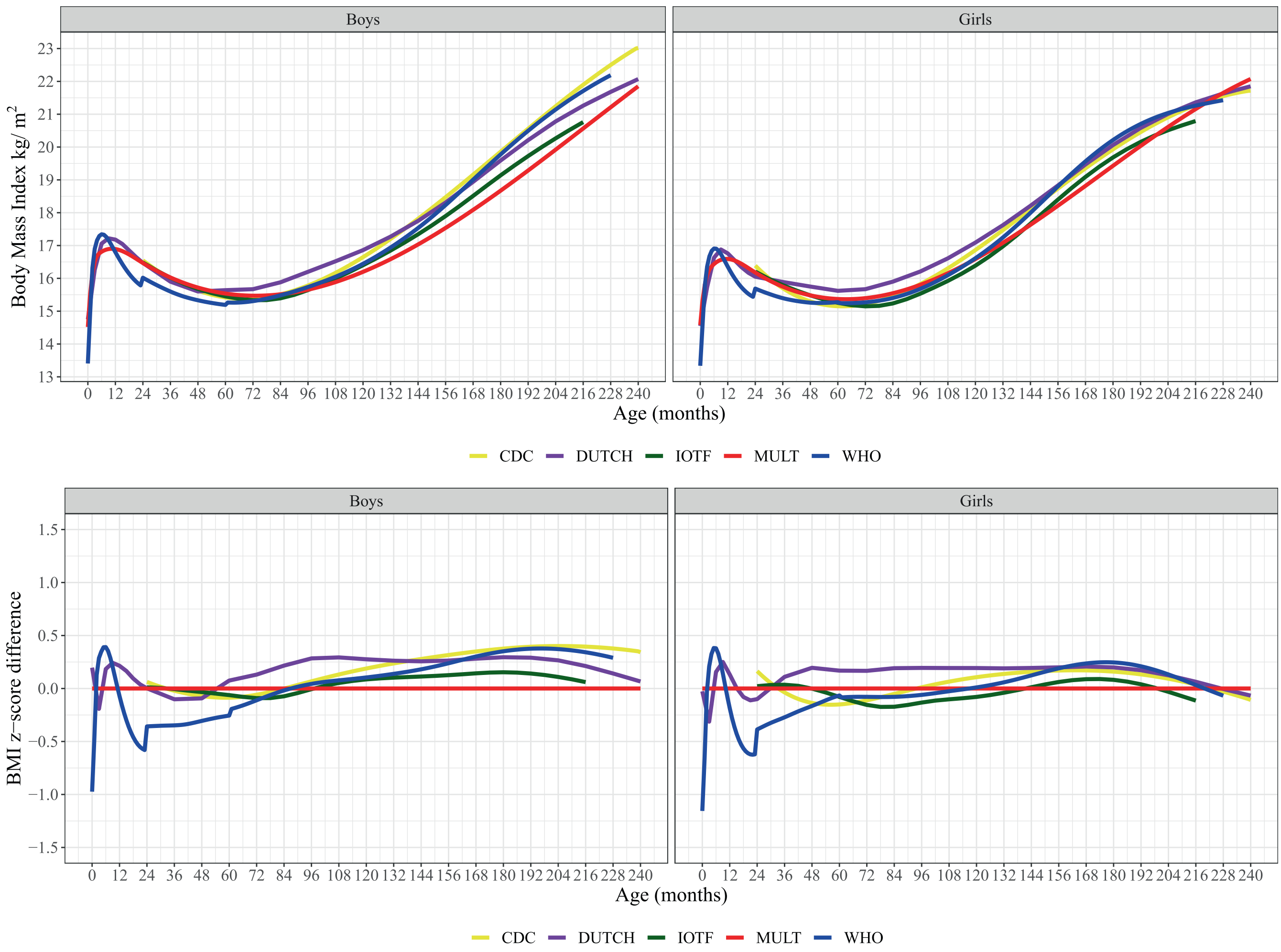

FIGURE 2 Median BMI and *z*-score differences of the five BMI references in boys and in girls.

presented the highest asymmetry presenting values lower than −3.

The BMI percentile cutoff points for underweight, overweight, and obesity of the five BMI references are presented in Table 3. When comparing the percentiles established at 18, 19, and 20 years old, MULT presented values close to WHO at 19 years old, and to IOTF at 18 years old for all the nutritional categories. Although different cutoff points according to the upper age limit (18, 19 or 20 years) were presented, our analysis showed that cutoff points estimated at 19 years of age for boys are the same at 18 years old for girls (underweight = 6th; overweight = 85th; obesity = 98th percentiles). Additionally, there were similarities between the underweight and obesity percentile curves of IOTF and MULT BMI references at 18 years old, as shown in Figure 4. The MULT BMI-for-age charts for boys and girls with the cutoff percentiles proposed at 17, 18, 19, and 20 years old are presented in Figures 5 and 6.

Regarding the model fit, according to the worm plots for boys and girls, there were no deviations from the model's assumptions: each curve passes through the origin of the graphic; the curves had approximately sloped equal to zero, and we did not notice quadratic shapes, which indicates a good fit model, as shown in the Supplementary Information S1 and S2.

4 | DISCUSSION

Growth charts are used to monitor child growth and development (de Oliveira et al., 2022; Ferreira, 2012). They are constructed based on standard or reference populations, which makes them sensitive to assess nutritional status and to detect nutritional risks in children and adolescents (de Oliveira et al., 2022; Ferreira, 2012). Nowadays, there is a lack of BMI references constructed based on multiethnic populations that cover from birth until the end of adolescence, suggesting a need for a new international growth reference (de Oliveira et al., 2022; Ferreira, 2012). Therefore, a new BMI reference constructed based on recent longitudinal data from multi-

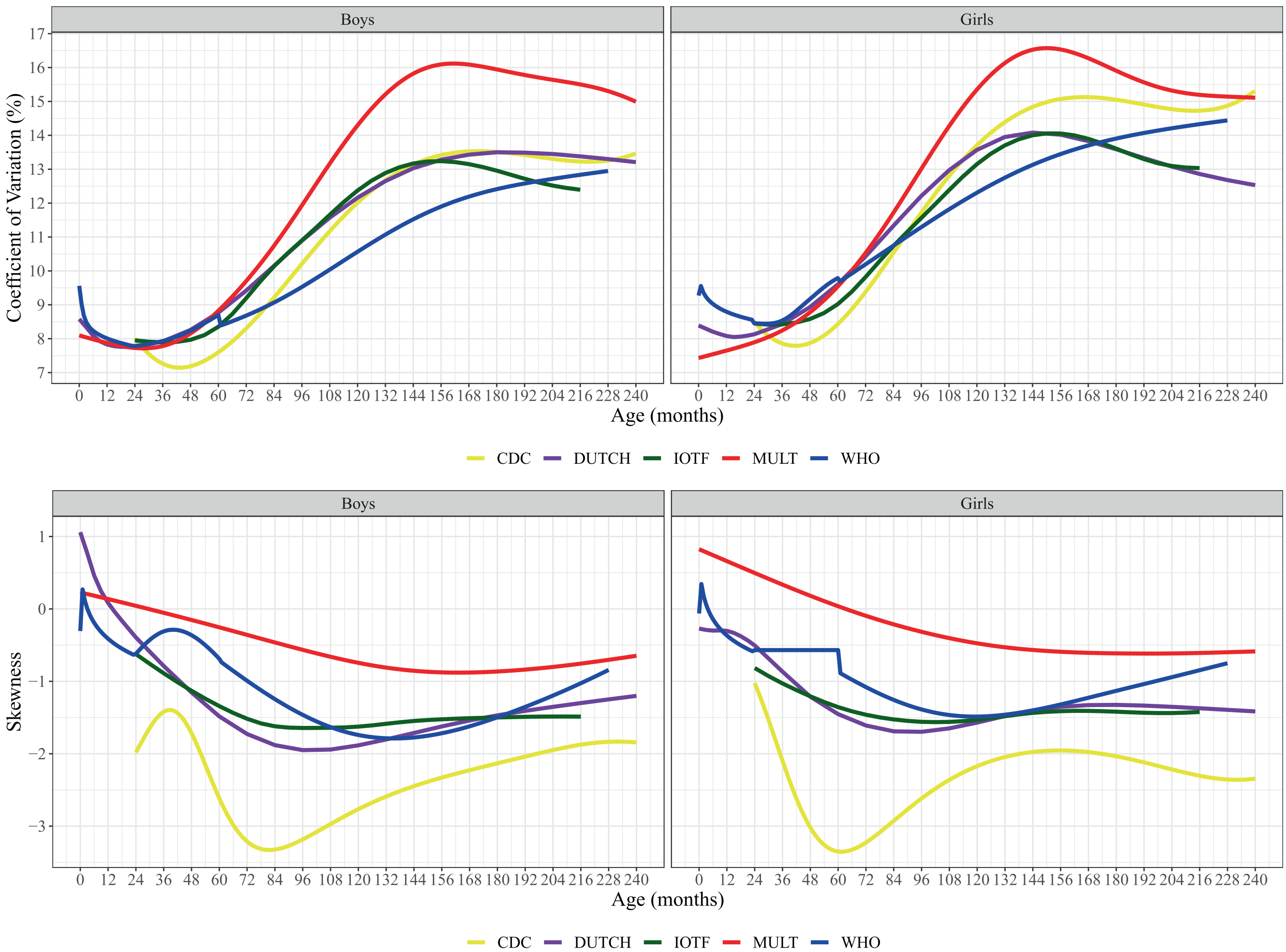

FIGURE 3 *S* and *L* curves of the five BMI references in boys and in girls.

ethnic populations from 10 different countries was presented.

When compared to other international BMI references, the MULT BMI reference showed lower median BMI values for boys and girls for most ages, especially during adolescence. It presented a higher *S* value, while the *L* values were the ones that presented the closest values to 0. These factors indicate a healthy sample, without many people with excessive weight. At the same time, WHO median BMI values were the lowest for children (from 1 to 5 years old) whereas for adolescents it showed higher values, presenting an *M* curve close to the one from CDC. These results suggest that the WHO growth standard for BMI (2006) seems to be accurate to assess nutritional status of children under 5 years old, although there is a concern about its use for children from 5 years world as described in other studies (de Oliveira et al., 2022; Ferreira, 2012).

Some authors point out that WHO growth charts for children under 5 years old were constructed based on multi-ethnic children who were raised in a healthy environment, being exclusively breastfed until at least 3 or 4 months of age, and having a complementary feeding based on legumes, meat, eggs, fruits and vegetables, which allowed these growth charts to be representative of a healthy sample and fit for international use (de Oliveira et al., 2022; Ferreira, 2012).

On the other hand, the use of older data collected from 1963 to 1974 and only from one population (United States) made the WHO 2007 growth charts for school-aged children (from 5 years old) inaccurate for worldwide use (de Oliveira et al., 2022). Asian and African countries such as China, Pakistan, Iran, and Ghana have found greater divergences when comparing their growth patterns to the ones from WHO 2007, and studies conducted in European countries such as Slovakia, Italy, Poland and Portugal indicate the use of the IOTF BMI reference instead of the WHO growth reference for BMI (2007), as it screened overweight and obesity conditions better in their populations (Adom et al., 2020; Iftikhar

TABLE 3 BMI nutritional status classification corresponding to the CDC, WHO, IOTF, DUTCH and MULT BMI references.

		Underweight III	Underweight II	Underweight I	Normal weight	Overweight	Obesity
Boys							
20 years	MULT	Pr < 1.1	Pr < 3.5	Pr < 12.1	Pr ≥ 3.5 & Pr < 80.5	Pr ≥ 80.5 & Pr < 97.2	Pr ≥ 97.2
19 years	MULT	Pr < 2.1	Pr < 5.9	Pr < 17.4	Pr ≥ 5.9 & Pr < 84.5	Pr ≥ 84.5 & Pr < 97.8	Pr ≥ 97.8
	WHO (<5 years)	—	Pr < 3.0	—	Pr ≥ 3.0 & Pr < 97.0	Pr ≥ 97.0 & Pr < 99.9	Pr ≥ 99.9
	WHO (≥5 years)	—	Pr < 3.0	—	Pr ≥3.0 & Pr < 85.0	Pr ≥ 85.0 & Pr < 97.0	Pr ≥ 97.0
18 years	MULT	Pr <3.7	Pr < 9.3	Pr < 23.9	Pr ≥ 9.3 & Pr < 87.9	Pr ≥ 87.9 & Pr < 98.3	Pr ≥ 98.3
	IOTF	Pr <0.5	Pr < 3.0	Pr < 15.5	Pr ≥ 3.0 & Pr < 90.5	Pr ≥ 90.5 & Pr < 98.9	Pr ≥ 98.9
	DUTCH	Pr <0.1	Pr < 2.3		Pr ≥ 2.3 & Pr < 84.0	Pr ≥ 84.0 & Pr < 97.0	Pr ≥ 97.0
17 years	MULT	Pr <10.0	Pr < 14.0	Pr < 39.4	Pr ≥ 14.0 & Pr < 90.8	Pr ≥ 90.8 & Pr < 98.7	Pr ≥ 98.7
17–20 years	CDC	—	—	Pr < 5.0	Pr ≥ 5.0 & Pr < 85.0	Pr ≥ 85.0 & Pr < 95.0	Pr ≥ 95.0
Girls							
20 years	MULT	Pr < 0.1	Pr < 3.1	Pr < 10.9	Pr ≥ 3.1 & Pr < 78.7	Pr ≥ 78.7 & Pr < 96.9	Pr ≥ 96.9
19 years	MULT	Pr < 1.4	Pr < 4.3	Pr < 13.8	Pr ≥ 4.3 & Pr < 81.9	Pr ≥ 81.9 & Pr < 97.5	Pr ≥ 97.5
	WHO (<5 years)	—	Pr < 3.0	—	Pr ≥ 3.0 & Pr < 97.0	Pr ≥ 97.0 & Pr < 99.9	Pr ≥ 99.9
	WHO (≥5 years)	—	Pr < 3.0	—	Pr ≥ 3.0 & Pr < 85.0	Pr ≥ 85.0 & Pr < 97.0	Pr ≥ 97.0
18 years	MULT	Pr < 2.3	Pr < 6.2	Pr <17.9	Pr ≥ 6.2 & Pr < 85.2	Pr ≥ 85.2 & Pr < 98.1	Pr ≥ 98.1
	IOTF	Pr < 0.7	Pr < 3.7	Pr < 16.5	Pr ≥ 3.7 & Pr < 89.3	Pr ≥ 89.3 & Pr < 98.6	Pr ≥ 98.6
	DUTCH	Pr < 0.1	Pr < 2.3		Pr ≥ 2.3 & Pr < 84.0	Pr ≥ 84.0 & Pr < 97.0	Pr ≥ 97.0
17 years	MULT	Pr < 6.1	Pr < 9.1	Pr < 30.0	Pr ≥ 9.1 & Pr < 88.3	Pr ≥ 88.3 & Pr < 98.6	Pr ≥ 98.6
17–20 years	CDC	—	—	Pr < 5.0	Pr ≥ 5.0 & Pr < 85.0	Pr ≥ 85.0 & Pr < 95.0	Pr ≥ 95.0

Note: Pr: Percentile. Underweight III: The cutoff point was calculated using the BMI value of 16 kg/m^2 for IOTF, DUTCH, and MULT BMI growth references. Underweight II: The cutoff point was calculated using the BMI value of 17 kg/m^2 for IOTF, DUTCH, WHO, and MULT BMI growth references. Underweight I: The cutoff point was calculated using the BMI value of 18.5 kg/m^2 for IOTF, CDC, and MULT BMI growth references. Overweight: For WHO, IOTF, DUTCH and MULT BMI growth references the cutoff points were calculated using the BMI value of 25 kg/m^2. Obesity: For WHO, IOTF, DUTCH and MULT BMI growth references the cutoff points were calculated using the BMI value of 30 kg/m^2. 17–20 years: The CDC cutoff points were calculated using the BMI value of 18.5, 25, and 30 kg/m^2 for young adults.

et al., 2018; Ma et al., 2010; Minghelli et al., 2014; Mohammadi et al., 2020; Valerio et al., 2017; Woźniacka et al., 2018).

The concern about the IOTF BMI growth reference is the age limit; there are no growth charts for children under 2 years old, and the upper limit is 18 years old,

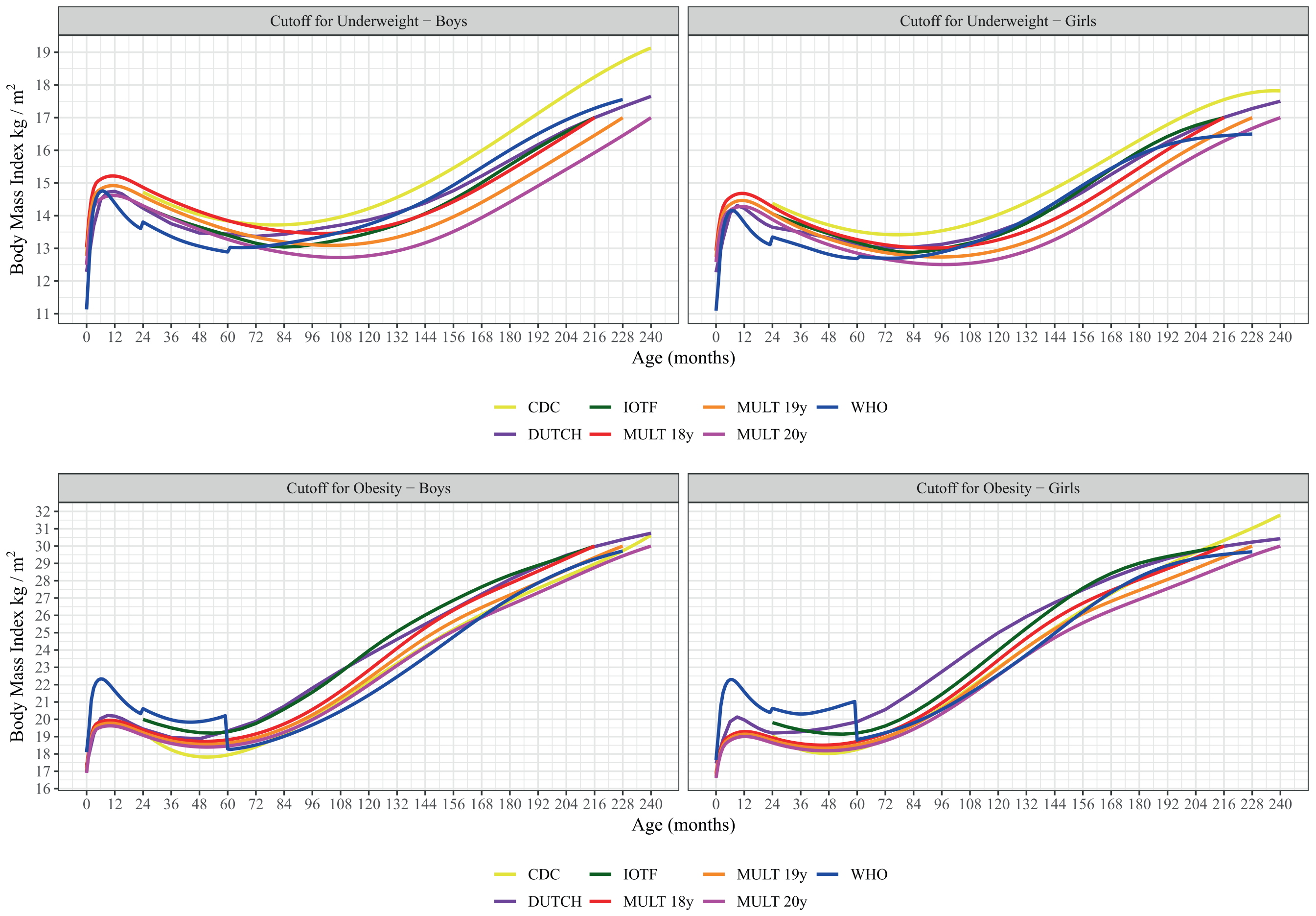

FIGURE 4 BMI cutoffs for underweight and obesity of the five BMI references in boys and in girls.

even though there is some evidence of growth for boys over 18 years old (Cole, 1986; de Oliveira et al., 2023; Kato et al., 1998). This suggests that growth charts should be used until 19 years old, and adult BMI values proposed by the WHO (2000) should start to be used only after that (De Onis et al., 2007; Ferreira, 2012; World Health organization, 2000). Moreover, another study pointed out that cutoffs established before 19 or 20 years can generate greater sex differences (Chinn & Rona, 2002). This is because at 18 years old, the BMI in boys is still increasing, while in girls it is decreasing (Chinn & Rona, 2002).

Another disadvantage of the IOTF reference is the lower *S* values when compared to the MULT BMI reference, especially during the early-middle adolescence, a period of expressive physical changes such as the growth spurt and the development of the sex organs and secondary sexual characteristics (World Health Organization, 2018). The IOTF sample did not have any data from African countries, which was applied in the MULT BMI reference, making the MULT BMI reference the one with the most ethnically diverse sample (Cole et al., 2000). Regarding the applicability of IOTF BMI reference in Africans, a study using the deuterium dilution method to assess nutritional status in school-aged children from Ghana showed that IOTF growth charts did not achieve optimal rates for detecting obesity, presenting high rates of misclassification for the Ghanaians (Adom et al., 2020).

The CDC BMI reference presents some limitations, not only do they use older data from a single country, but they also tried to correct the height of their sample by adding growth patterns of their recent population data, which increased the number of participants with excessive weight (Kuczmarski et al., 2000). This excessive weight is observed in the asymmetric shape of the CDC *L* curve, in its negative values. As shown in a systematic review, CDC usually presented lower performance than IOTF and WHO BMI references in the nutrition status assessment of children and adolescents worldwide (de Oliveira et al., 2022). In addition, studies point out that CDC BMI growth charts overestimated underweight, overweight and obesity in Saudi Arabia, while underestimated overweight in Brazil and obesity in Iran

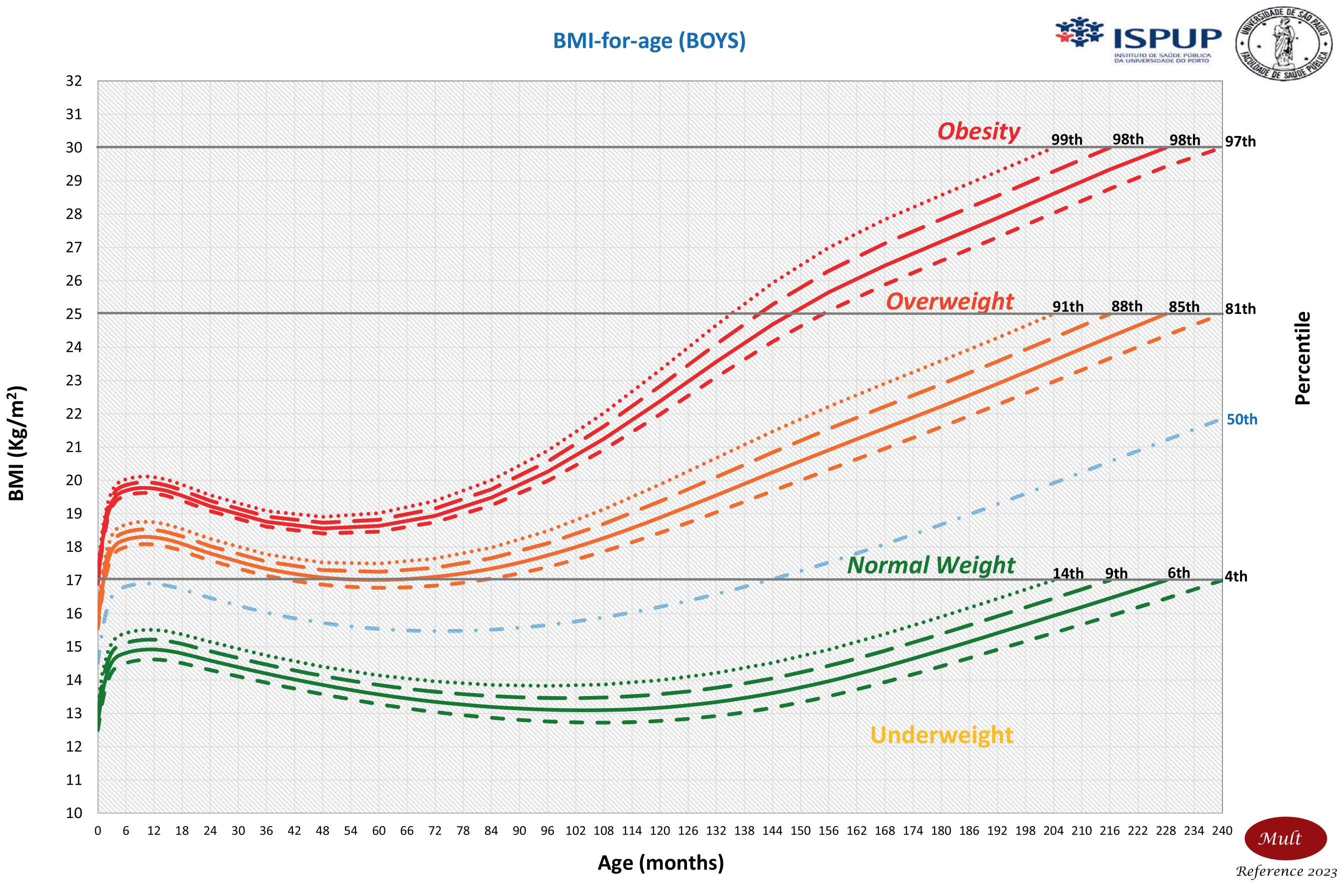

FIGURE 5 BMI-for-age growth chart for boys aged 0–20 years old. Underweight, overweight and obesity percentile cutoffs established at 17, 18, 19, and 20 years old applying the BMI values of 17, 25 and 30 kg/m^2.

(de Oliveira et al., 2022; El Mouzan et al., 2008; Mohammadi et al., 2020; Roman et al., 2015).

Some authors highlight a need for combining data from different populations when estimating growth references, which was applied in the MULT BMI reference (Cole et al., 2000; de Oliveira et al., 2022; WHO Multicentre Growth Reference Study Group, 2006). This BMI reference has an advantage when compared to CDC, WHO, and IOTF BMI references, since MULT constructed a predictive growth model using recent data from multi-ethnic populations from four different continents, which provided among the existent ones, the highest ethnically diverse sample. Furthermore, the MULT BMI reference was constructed based on longitudinal data of subjects born between 1990 and 2002, having age difference no longer than 12 years among them, which did not occur in other BMI references such as the ones from CDC, WHO, and IOTF (Cole et al., 2000; Cole & Lobstein, 2012; De Onis et al., 2007; Kuczmarski et al., 2002). Despite that, the use of longitudinal data allowed the evaluation of the subject's growth trajectory over the years, removing outlier values based on their own BMI values.

The major strengths of this study are the use of standardized longitudinal studies, the large sample size with huge ethnic diversity, the cutoffs established according to the adults' BMI values, and the use of advanced techniques for predicting the MULT BMI reference values and avoiding outlier effects. Moreover, the anthropometric data were collected by trained professionals, instead of coming from self-reported data, which decreases the risk of measurement errors and social desirability bias. The larger sample size with an almost equal distribution of boys and girls, and the exclusions of the outlier measurements were applied to guarantee the data quality and reliability of the model. In addition, Cole's LMS method, GAMLSS, and worm plots were chosen; these are advanced techniques applied in the growth reference constructions and supported by several studies (Iftikhar et al., 2018; Khadilkar & Khadilkar, 2015; Schönbeck et al., 2011). The cutoffs were proposed following the values for overweight and obesity for adults, which provided a smooth transition from the adolescent growth charts to the BMI cutoffs for adults (World Health Organization, 2000).

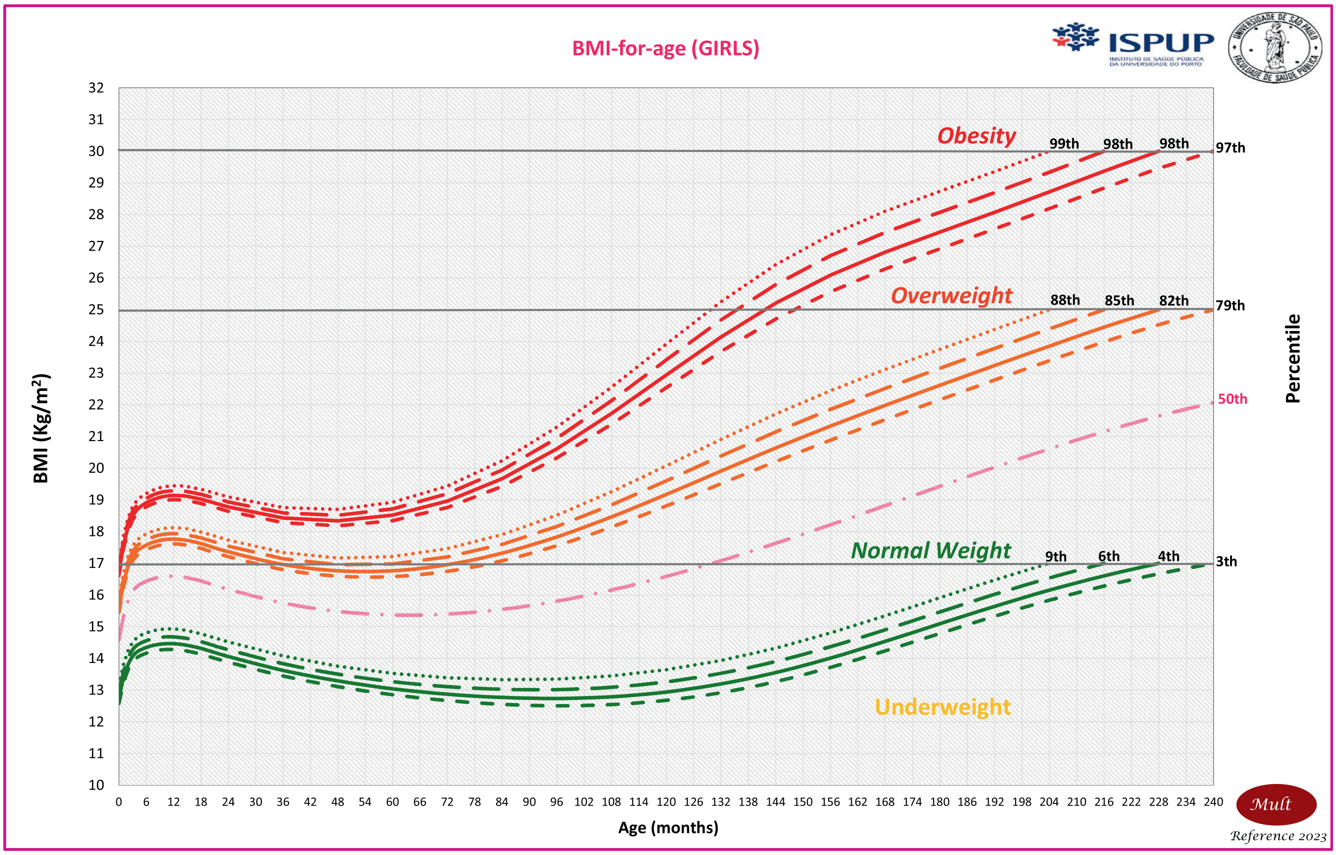

FIGURE 6 BMI-for-age growth chart for girls aged 0–20 years. Underweight, overweight and obesity percentile cutoffs established at 17, 18, 19, and 20 years old applying the BMI values of 17, 25 and 30 kg/m^2.

Nevertheless, there are some limitations, as there was no evaluation of the participant's health status, and some of the samples were not representative of the country, such as those from Brazil and Portugal. However, even though there was no health status evaluation, the exclusion of BMI outlier values in a population and individual levels was applied to guarantee a healthier sample who have not been affected by excessive weight. Although data from some studies are from specific cities rather than national samples, the ethnic patterns are similar. For instance, the EPITeen study is a population-based study from the city of Porto, which is the second largest from Portugal presenting demographic characteristics close to the national data and the city of Rio de Janeiro has more than 15% of immigrants, who came mainly from other states of Brazil (Fundação Ceperj, 2013; Vasconcellos & Bertolucci, 2014; WorldoMeter, 2019).

5 | CONCLUSION

For the first time, a BMI reference based on longitudinal data from multi-ethnic populations that cover all the childhood and adolescence periods (birth to 20 years old) was constructed and presented. The MULT BMI reference presented values close to the WHO BMI reference for children under 5 years old and to the IOTF BMI reference for subjects aged 2 to 18 years old. These findings showed that the MULT BMI reference could be useful to assess the nutritional status of multi-ethnic populations, although there is a need for further studies to verify its accuracy.

AUTHOR CONTRIBUTIONS

Mariane Helen De Oliveira: Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing—Original Draft, Writing—Review & Editing, Visualization, Funding acquisition. **Joana Araújo**: Conceptualization, Methodology, Investigation, Writing—Review & Editing, Supervision, Project administration, Funding acquisition. **Milton Severo**: Methodology, Formal analysis, Investigation, Visualization, Writing—Review & Editing. **Kévin Allan Sales Rodrigues**: Formal analysis, Writing – Review & Editing. **Wolney Lisboa Conde**: Conceptualization, Methodology, Formal analysis, Writing—Review & Editing, Supervision, Project administration.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. The views expressed here are those of the authors. They are not necessarily those of YL, MCS, ELANA, EPITeen studies, or the University of Oxford.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from UK Data Service, ISPUP, and UERJ. Restrictions apply to the availability of these data, which were used under license for this study. MCS and YL data are available from the UK Data Service online platform at URL [https://ukdataservice.ac.uk] and EPITeen and ELANA data are available from the authors with the permission of ISPUP and UERJ, respectively.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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