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Evaluating growth references used in Switzerland: a comparative analysis in Zurich schoolchildren

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Summary

INTRODUCTION: The Swiss Society of Paediatrics currently recommends the growth references of the World Health Organization (WHO), while the Paediatric Endocrinology Centre Zurich (PEZZ) has proposed alternative growth references. Specialists and researchers also use International Obesity Task Force (IOTF) references to define overweight and obesity. We investigated the fit of anthropometric measurements from schoolchildren in the canton of Zurich to these three growth references and assessed the prevalence of overweight, obesity and short stature across the three references.

METHODS: We analysed data from 3755 children aged 6–17 years in the cross-sectional LuftiBus in the School (LUIS) study, collected in the period 2013–2016 in the canton of Zurich. We calculated z-scores of height, weight and body mass index (BMI) based on WHO, PEZZ and IOTF references. We compared the mean and distribution of z-scores to the expected standard normal distribution using the Anderson-Darling test. We classified overweight, obesity and severe obesity based on cutoff values given by the three references. We defined short stature as <3rd percentile of height for age.

RESULTS: The mean z-scores in LUIS were 0.56 for height, 0.28 for weight and 0.06 for BMI based on WHO references; 0.15 for height, 0.06 for weight and -0.01 for BMI based on PEZZ references; and 0.19 for BMI based on IOTF references. The Anderson-Darling test showed that children in LUIS fit worse to WHO and IOTF than to PEZZ references. The WHO classified fewer children as overweight than PEZZ and IOTF references (WHO: 8%; PEZZ: 15%; IOTF: 13%) but more children as obese or severely obese (6%; 4%; 3%). The WHO defined fewer chil-

dren as being of short stature than PEZZ references (1% vs 3%).

CONCLUSIONS: Our findings suggest that anthropometric data of schoolchildren in Zurich (LUIS) differ notably from WHO and IOTF references potentially leading to misclassification of overweight, obesity and short stature. Thus it would be timely to develop new nationally representative growth references for Switzerland.

Introduction

Growth references and their corresponding percentile curves are used by general practitioners and specialist paediatricians (a) to detect abnormal growth patterns that could be related to underlying physical diseases or developmental disorders, (b) to identify short stature or overgrowth, and (c) to determine whether a child fulfils criteria for overweight or obesity based on body mass index (BMI) percentiles. Early identification of atypical growth patterns and developmental deviations is crucial for prompt intervention and management of chronic conditions or developmental delays. For example, short stature can indicate endocrinological, genetic or chronic systemic diseases. Correct detection of obesity in children is important because childhood obesity is a known predictor of ill health in

ABBREVIATIONS

BMI: body mass index

IOTF: International Obesity Task Force

LUIS: LuftiBus in the School

PEZZ: Paediatric Endocrinology Centre Zurich

Swiss-SEP:

Swiss neighbourhood index of socioeconomic position

WHO: World Health Organization

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adulthood and is associated with cardiovascular disease, type 2 diabetes and cancer [1, 2].

In 2011, the Swiss Society of Paediatrics (SSP) replaced the growth curves from the Zurich Longitudinal Studies [3] by the WHO curves. For this purpose, several WHO datasets were merged and reanalysed [4]. The growth references for schoolchildren and adolescents aged 5 to 19 years were derived from data of white and African American children collected in the US between 1963 and 1974 [5–8]. The new growth curves remained a topic of debate. Humans grow taller now than they did several decades ago, and growth varies across ethnicities and regions of the world [9, 10]. Thus, the WHO growth references reflect a different population from the one that lives in Switzerland today and the representativeness of the references has been questioned [11, 12]. In 2019, the Paediatric Endocrinology Centre Zurich (PEZZ), an endocrinology group practice, proposed alternative growth references for Swiss children. These references were based on data from paediatric primary care practices, school medical services, the federal statistical office and the Swiss military medical service, primarily representing central and eastern regions of Switzerland [13]. A third growth reference that is being used in Switzerland was published by the International Obesity Task Force (IOTF) based on data collected between 1963 and 1993 from children in Brazil, Hong Kong, the Netherlands, Singapore, the UK and the USA [14]. In Switzerland, the IOTF references are mainly used by paediatric endocrinologists or researchers to assess overweight and obesity in children.

Given this diversity of growth references used in parallel in Switzerland, we reused data from a large population-based study of schoolchildren from the canton of Zurich, the "LuftiBus in the School" (LUIS) study, to compare the fit of anthropometric data of these children to WHO, PEZZ and IOTF growth references. We examined the fit for the entire study population and for subgroups defined by sex, age, origin of parents, socioeconomic status and degree of urbanisation. We also investigated how prevalence estimates of overweight, obesity and short stature would vary depending on the growth references used to classify the data.

Materials and methods

Study design and population

The "LuftiBus in the School" (LUIS) study was a cross-sectional study of lung health in schoolchildren aged 6–17 years conducted from 2013 to 2016 in the canton of Zurich (ClinicalTrials.gov NCT03659838, described in detail elsewhere [15]). All 490 schools in the canton of Zurich were invited to participate and 37 schools accepted. Participating schools were visited by a bus – the LuftiBus – equipped with spirometers and scales to measure lung function and anthropometric parameters. The study was approved by the ethics committee of the canton of Zurich (KEK-ZH-Nr: 2014-0491) and informed consent, including information on reuse of anonymised data for research purposes, was obtained prior to participation.

Height, weight and body mass index

At the start of the study, LuftiBus technicians received training on measuring height and weight according to WHO recommendations [16]. For anthropometric measurements, children removed their shoes and wore light clothing. LuftiBus technicians used a calibrated stadiometer to record body height to the closest centimetre and a calibrated scale to record body weight to the nearest 100 grams. We calculated age- and sex-dependent z-scores for height, weight and BMI based on WHO [4], PEZZ [13] and IOTF [14] growth references using Cole's Lambda-Mu-Sigma (LMS) method [17] (see appendix). We adapted a method by Daymont et al. [18] to detect possible outliers resulting from recording or transcription errors by the LUIS study team: We recentred height, weight and BMI zscores around the median z-score at each age year to account for the possibility that the whole study sample might differ from the reference population. We then excluded children with a recentred z-score <-4 or >4 as recommended [16, 19].

We used cutoff values for BMI z-scores published by the WHO, PEZZ and IOTF growth references to classify children into normal weight, overweight, obesity and severe obesity (appendix table S1). We defined short stature as <3rd percentile, normal height as between the 3rd and 97th percentiles, and tall stature as >97th percentile for all references [20].

Potential explanatory factors for growth

We obtained socioeconomic information (origin of parents, education of parents, home address) from parent-completed questionnaires. We grouped parental countries of origin into five categories: Switzerland (both parents born in Switzerland), Switzerland one parent (one parent born in Switzerland, other parent born outside of Switzerland), Northern/Western Europe (both parents born in northern or western Europe), Southern/Eastern Europe (both parents born in southern or eastern Europe), Other/Mixed (parents born in Africa, America, Asia, or Oceania or parents with mixed origin excluding Swiss parents). We defined these geographical regions based on the United Nations standard country or area codes for statistical use, M49 [21]. We classified education of parents into three categories based on the highest education level achieved by one of the parents: primary education (compulsory schooling only; ≤9 years), secondary education (vocational training; 10-13 years) and tertiary education (higher vocational training, college or university degree; ≥14 years). We used the Swiss neighbourhood index of socioeconomic position (Swiss-SEP) as an area-based measure of socioeconomic status [22]. The Swiss-SEP ranges from 0 to 100 where a higher value reflects a higher socioeconomic position of that neighbourhood. We assigned the nearest Swiss-SEP value to the geographical coordinates of the children's home address. When the home address was missing (n = 405, 11%), we assigned the median Swiss-SEP value of children attending the same school. We classified Swiss-SEP into five categories based on the quintiles published by Panczak et al. [22]. We classified degree of urbanisation into three categories based on the location of the school and according to the classification of the Federal Statistical Office [23]: large urban (cities ≥50,000 inhabitants and popula-

tion density $\geq 1500/\text{km}^2$), small urban (towns and suburbs ≥ 5000 inhabitants and population density $\geq 300/\text{km}^2$) and rural (outside of large and small urban regions).

Statistical analyses

We assessed the fit of children in LUIS to the three growth references by calculating means and standard deviations for height, weight and BMI z-scores. In a perfectly fitting sample, the z-scores would be standard normally distributed (mean 0, SD 1). We classified mean z-scores deviating >0.5 from the reference population as strong deviations, 0.25-0.5 as moderate deviations, 0.05-0.25 as weak deviations and 0-0.05 as no noticeable deviations [10]. We used the Anderson-Darling test to assess the fit of z-score distributions to the expected standard normal distribution, as it allows for comparing two distributions. The test quantifies goodness of fit using the A2 statistic, where lower values indicate a better fit. The p-value represents the probability of the null hypothesis that the z-score distribution is drawn from a standard normal distribution. The Kolmogorov-Smirnov test produced similar results (available upon request).

We assessed the fit to growth references in the entire population and within strata defined by factors selected a priori based on a literature review and expert opinion: sex, age, origin of parents, Swiss-SEP and degree of urbanisation. For this, we estimated mean z-scores by age and their pointwise 95% confidence interval (CI) using penalised cubic (3rd degree) B-spline regression over age for girls and boys separately to assess the fit of the growth references graphically across age [24]. We also employed penalised cubic B-spline regression to compare mean height, weight, and BMI of children in LUIS with the 50th percentiles of WHO, PEZZ and IOTF growth references across age. We compared the fit to growth references across potential explanatory factors again by computing the Anderson-Darling A². Furthermore, we used univariable linear regression models to determine the association between potential explanatory factors and z-scores of height, weight and BMI. We chose to report regression results exclusively for z-scores based on PEZZ references because these provided the best correction for age and sex, and the results were consistent with those obtained from other references. We included variables jointly in multivariable models based on significance in univariable models (p <0.05) and measures of model fit.

We calculated the prevalence of BMI and height categories and their 95% CI based on the different references. We used Cohen's Kappa to quantify agreement between growth references. We interpreted Cohen's Kappa 0.41–0.60 as moderate, 0.61–0.80 as substantial and 0.81–1.00 as almost perfect agreement according to Landis and Koch [25]. We repeated prevalence estimates of BMI and height categories in strata defined by sex, age, origin of parents, Swiss-SEP and degree of urbanisation.

We used the statistical software R Studio version 2023.3.1 [26] with the R version 4.2.0 [27] for all analyses.

Results

Study population

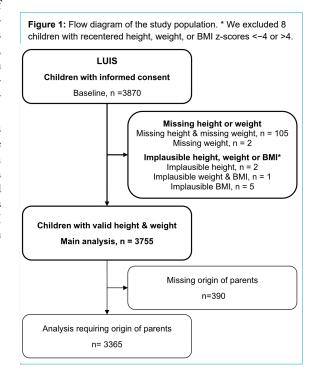
Of 3870 eligible children from the LUIS study, we excluded 107 children with missing height or weight measurements, and a further 8 children with height, weight or BMI z-scores of <-4 or >4 (figure 1), leaving 3755 children (50% girls) in our analysis. For analyses requiring the origin of the parents, we further excluded 390 (10%) children with unknown origin of parents.

The median age was 13 years (IQR 10–14, table 1 and appendix table S2). Most children had parents originally from Switzerland (both parents: 51%, one parent: 16%). The median Swiss-SEP was 69 (IQR 61–76), and half of the children were in the highest Swiss-SEP quintile category. Boys and girls had similar median height and weight.

Fit of children in LUIS to WHO, PEZZ and IOTF references

Children in LUIS deviated strongly in height (mean z-score: 0.56), moderately in weight (0.28) but only weakly in BMI (0.06) from WHO references according to the criteria of Natale et al. [10] (table 2). Mean height (0.15) and weight (0.06) deviated weakly, while BMI (-0.01) did not deviate noticeably from PEZZ references. Mean BMI (0.19) deviated weakly from IOTF references.

According to the Anderson-Darling test, body height of children in LUIS fit better to PEZZ references (A^2 : 48.1) than to WHO references (A^2 : 578.1) (table 2 and figure 2). The distribution of height measurements in LUIS deviated significantly from both reference populations (test for standard normal distribution of z-scores, p <0.001). Body weight in LUIS fit better to PEZZ (A^2 : 10.0) than to WHO references (A^2 : 123.8), but neither of the z-scores followed the standard normal distribution (p <0.001). BMI in LUIS fit better to PEZZ (A^2 : 0.8) than to WHO (A^2 : 24.3) and



IOTF references (A^2 : 64.1). Only the PEZZ BMI z-scores agreed with the standard normal distribution (p = 0.474).

Factors influencing fit of growth references

A better fit to PEZZ compared to WHO references was also apparent from penalised cubic B-spline regression, with mean height and weight z-scores based on PEZZ references closer to the expected zero value for most ages in

both boys and girls (figure 3 and appendix figure S1). Only among girls aged 17 years, for height, and 10–11 years, for weight, were the WHO mean z-scores closer to zero than z-scores derived from PEZZ references, although 95% CIs of mean z-scores from WHO and PEZZ references overlapped. Height z-scores were closer to zero among older children (>10 years) than among younger children (<8 years) for both WHO and PEZZ references. Mean BMI z-

Table 1: Characteristics of participants of the LuftiBus in the School (LUIS) study.

			Girls, n (%)	Boys, n (%)	Total, n (%)
			1872 (50%)	1883 (50%)	3755 (100%)
Age in years	Median (IQR)		12.8 (10.1–14.2)	12.7 (9.9–14.3)	12.8 (10.0–14.3)
	Groups, n (%)	6–8	333 (18%)	345 (18%)	678 (18%)
		9–11	441 (24%)	440 (23%)	881 (23%)
		12–14	838 (45%)	825 (44%)	1663 (44%)
		15–17	260 (14%)	273 (14%)	533 (14%)
Origin of parents, n (%)	Switzerland (both parents)		965 (52%)	968 (51%)	1933 (51%)
	Switzerland (one parent)		279 (15%)	305 (16%)	584 (16%)
	Northern/Western Europe (b	oth parents)	103 (6%)	100 (5%)	203 (5%)
	Southern/Eastern Europe (b	oth parents)	199 (11%)	183 (10%)	382 (10%)
	Other/Mixed		142 (8%)	121 (6%)	263 (7%)
	Missing		184 (10%)	206 (11%)	390 (10%)
Education of parents, n (%)	Primary education		54 (3%)	51 (3%)	105 (3%)
	Secondary education		475 (25%)	473 (25%)	948 (25%)
	Tertiary education		714 (38%)	679 (36%)	1393 (37%)
	Missing		629 (34%)	680 (36%)	1309 (35%)
Swiss-SEP 2.0*	Median (IQR)		69 (61–76)	69 (62–77)	69 (61–76)
	Groups, n (%)	1: 0–49	70 (4%)	68 (4%)	138 (4%)
		2: 50–56	232 (12%)	227 (12%)	459 (12%)
		3: 57–61	221 (12%)	210 (11%)	431 (11%)
		4: 62–69	405 (22%)	436 (23%)	841 (22%)
		5: 70–100	944 (50%)	942 (50%)	1886 (50%)
Urbanisation, n (%)	Rural		128 (7%)	119 (6%)	247 (7%)
	Small urban: towns, suburbs	i	807 (43%)	828 (44%)	1635 (44%)
	Large urban: cities		937 (50%)	936 (50%)	1873 (50%)
Height in cm	Median (IQR)		156 (141–164)	156 (141–170)	156 (141–166)
Weight in kg	Median (IQR)		45 (33–56)	44 (33–58)	45 (33–57)

IQR: interquartile range.

Table 2:

Mean height, weight and BMI z-scores of 3755 participants of the LuftiBus in the School (LUIS) study based on the WHO, PEZZ and IOTF references; and the fit of the z-scores to a standard normal distribution.

			World Health Organiza tion (WHO)	Paediatric Endocrinol- ogy Centre Zurich (PEZZ)	International Obesity Task Force (IOTF)
Height z-score	Mean (95% CI)		0.56 (0.53-0.59)	0.15 (0.12–0.19)	NA
Standard deviation	Standard deviation		1.00	1.03	NA
	Anderson-Darling test*	A ²	578.1	48.1	NA
		p-value	<0.001	<0.001	NA
Weight z-score Mean (95% CI)			0.28 (0.25–0.31)	0.06 (0.03-0.09)	NA
	Standard deviation		1.01	0.98	NA
	Anderson-Darling test*	A ²	123.8	10.0	NA
		p-value	<0.001	<0.001	NA
Body mass index	Mean (95% CI)	•	0.06 (0.03–0.10)	-0.01 (-0.04-0.02)	0.19 (0.16-0.23)
z-score	Standard deviation		1.14	1.01	1.05
	Anderson-Darling test*	A ²	24.3	0.8	64.1
		p-value	<0.001	0.474	<0.001

CI: confidence interval; NA: not applicable.

^{*} Swiss-SEP: Swiss socioeconomic position version 2.0, census data for period 2012–2015. The five groups are based on quintiles published by Panczak et al. [22]. A higher score corresponds to a higher socioeconomic position.

^{*} Anderson-Darling test to assess goodness of fit of the observed z-score distribution based on the WHO, PEZZ and IOTF growth references to a standard normal distribution, A²: test statistic (lower value indicates better fit).

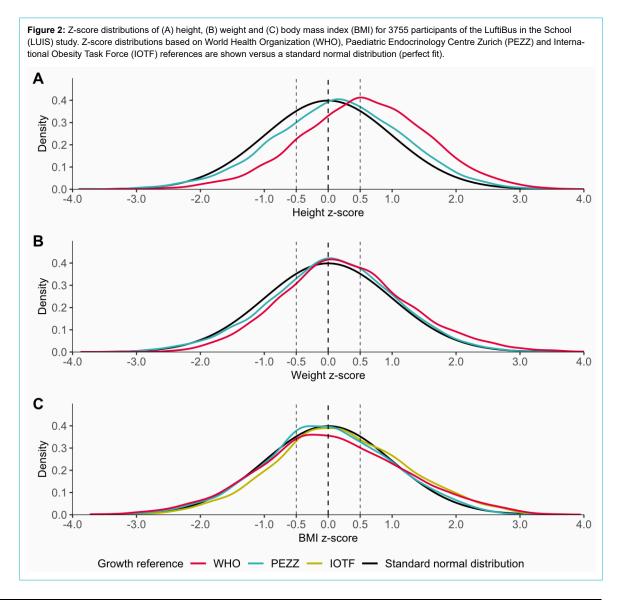
scores deviated only weakly from zero in both boys and girls for all three references. IOTF BMI z-scores were further away from zero than the WHO and PEZZ ones in older children (>12 years). The 95% CIs of locally estimated mean z-scores widened at younger and older ages due to fewer observations and boundary effects of the B-spline regression. The absolute differences between mean height, weight and BMI of children in LUIS and the 50th percentiles of PEZZ, WHO and IOTF references, as estimated by penalised cubic B-spline regression, closely mirrored the age-specific z-scores (appendix figure S2). For instance, 6-year-old girls in LUIS were, on average, 4 cm taller than the 50th percentile of PEZZ references and 6 cm taller than the 50th percentile of WHO references.

Height and weight of children in LUIS fit PEZZ references better than WHO references across all strata of sex, age, origin of parents and Swiss-SEP, and in most categories of urbanisation (appendix table S3). BMI fit best to PEZZ references in girls and boys and in most categories of age, origin of parents, Swiss-SEP and degree of urbanisation.

Univariable and multivariable linear regression confirmed that height, weight and BMI z-scores of children in LUIS based on PEZZ references differ by age, origin of parents, Swiss-SEP and degree of urbanisation (appendix tables S4, S5 and S6). Height z-scores tended to decrease with age and increase with Swiss-SEP. Height z-scores were larger in children with parents born in Northern/Western Europe and Southern/Eastern Europe compared to children with parents born in Switzerland. Height z-scores were larger in children living in urban regions compared to rural regions. Weight and BMI z-scores tended to decrease with Swiss-SEP. Weight and BMI z-scores were higher in children with parents from Southern/Eastern Europe and Mixed/Other origin compared to children with parents from Switzerland. Weight and BMI z-scores were higher in children living in an urban region compared to a rural region. The linear regression did not show any differences in height, weight or BMI z-scores by sex.

Prevalence of overweight, obesity and short stature differ by growth reference

Cohen's Kappa showed substantial – but not perfect – agreement between the different growth references for BMI categories (appendix table S1). The prevalence of normal weight in LUIS children was comparable between WHO and IOTF (85%), but slightly lower for PEZZ references (81%, figure 4). The WHO classified fewer children as overweight (8%) compared to PEZZ (15%) and

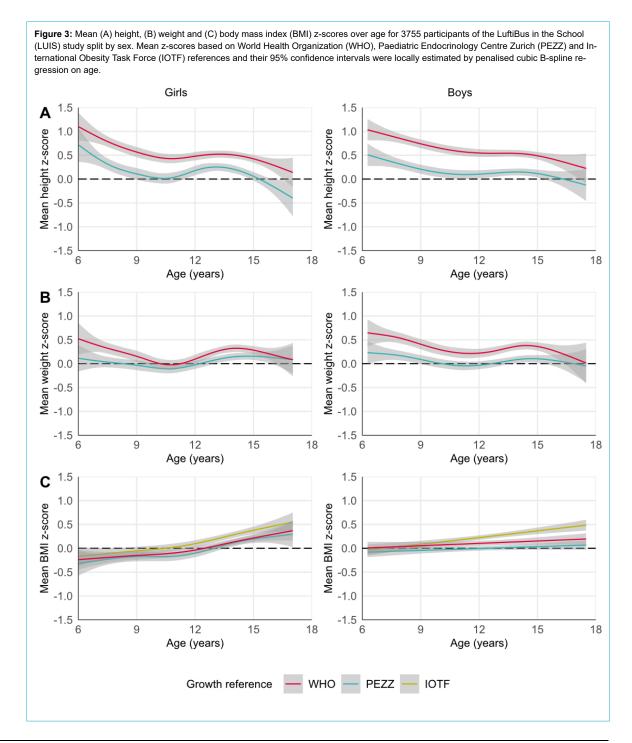


IOTF (13%) references. In contrast, the WHO classified more children as obese (5%) and severely obese (2%) compared to IOTF (obese 3%, severely obese: 0.3%), and more children as severely obese compared to PEZZ references (0.6%).

The prevalence of overweight and obesity varied across the origin of parents, Swiss-SEP and degree of urbanisation, but showed little variation between age groups or between boys and girls (appendix figure S3). We observed the following patterns regardless of the growth reference used: Overweight, obesity and severe obesity appeared to be more prevalent in children with parents of Southern/ Eastern Europe or Other/Mixed origin compared to those of Swiss origin. Additionally, we observed a higher prevalence of overweight, obesity and severe obesity in the

two lowest Swiss-SEP categories compared to the highest Swiss-SEP category. Overweight was more prevalent in large and small urban areas compared to rural areas. Classification into BMI categories by the three growth references had a substantial agreement across all factors (table available upon request).

The height categories differed between WHO and PEZZ references, which was reflected by only moderate agreement according to Cohen's Kappa (figure 4 and appendix table S1). The WHO estimated fewer children as being of short stature (1%) compared to PEZZ references (3%) but estimated more children as being of tall stature (9% vs 4%). The height categories did not differ across sex, age group, origin of parents, Swiss-SEP or degree of urbanisation (appendix figure S3).



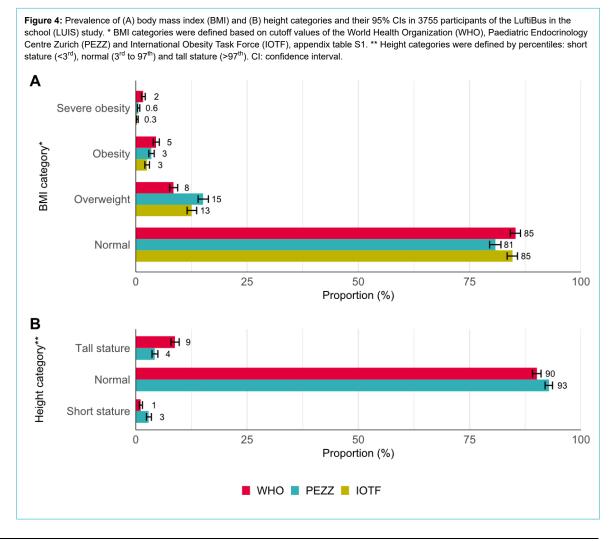
Discussion

Comparing anthropometric data from LuftiBus in the School (LUIS), a population-based study of schoolchildren from the canton of Zurich, to three currently used growth references in Switzerland, this study found a poor fit to World Health Organization (WHO) and International Obesity Task Force (IOTF) growth references, while fit to Paediatric Endocrinology Centre Zurich (PEZZ) references, developed recently in the same region, Zurich and Lucerne, was better overall and within population strata. Children in LUIS were taller compared to the WHO reference population, particularly at younger ages. Children living in urban environments and those whose parents came from Northern or Western Europe were taller compared to children from rural regions and with Swiss parents. Children from urban regions, lower Swiss neighbourhood index of socioeconomic position (Swiss-SEP) index, and whose parents came from Southern or Eastern Europe had a higher BMI. Prevalence estimates of overweight, obese or short stature in LUIS differed depending on the growth references that were used to classify children.

Comparison with other studies

The anthropometric data of children from the Zurich region (LUIS) differed from the WHO growth references as previously reported for this region [13]. The same has been reported in Germany [28], Austria [29] and France [30].

Improved socioeconomic and nutritional circumstances over the last century have contributed to a general increase in adult human stature across the world [9, 31], and this has been accompanied by a decrease in the age of onset of puberty [32]. Since the WHO growth references for schoolchildren and adolescents used data collected between 1963 and 1974 [7], both a secular increase in adult height and an earlier onset of puberty could explain why the children in our study (2013-2016) were taller [9, 33]. Height is strongly determined by genetic background with twin studies suggesting up to 80% heritability of body stature [34]. Adult men and women of Central and Latin American or Asian origin tend to be shorter compared to North Europeans, Central Europeans or North Americans, with a gap of up to 20 cm between the tallest and shortest populations [9]. The US studies, from which WHO references were derived, consisted of children with white (73-85%) and African-American (15-27%) ethnicity [5, 6]. In our study, 80% of the children were of European origin and 20% of mixed or unknown origin. Such differences in ethnic mix can also influence the fit of growth references. Our multivariable regression models confirmed parental origin, areabased socioeconomic status and urbanisation as significant predictors of height, weight and BMI although the models explained little of the overall variability between study participants since the adjusted R² for the regression model was 1.3% for height, 4.4% for weight and 5.5% for BMI.



Children in LUIS were slightly taller than the population from which the PEZZ growth references were derived. LUIS included a higher proportion of children with a Swiss origin and a lower proportion of children with an Other/ Mixed background than the PEZZ population (appendix table S2). However, this does not appear to explain the observed differences, as height z-scores were similar between Swiss children and those of Other/Mixed origin. However, the slightly higher socioeconomic status of children in LUIS compared to the PEZZ reference population might have contributed to the small height difference [35].

We found a clear difference in prevalence estimates of obesity, including severe obesity, depending on whether we used WHO (6%), PEZZ (4%) or IOTF (3%) references to classify children. This has also been reported for IOTF and US Centers for Disease Control and Prevention (CDC) references [36]. Prevalences of obesity, including severe obesity (3%) and overweight (13%) in LUIS, using IOTF references, were almost identical to reports of Gesundheitsförderung Schweiz: 4% obesity, including severe obesity, and 13% overweight in schoolchildren (6–16 years) in the city of Zurich for the years 2014/15 [37], which were also calculated with IOTF references. Similar to other Swiss studies [38, 39], we found that children living in lower Swiss-SEP locations, in urban areas and those whose parents originated from Southern or Eastern Europe had a higher prevalence of overweight and obesity.

Strengths and limitations

Our study is limited by its regional scope, potential selection bias related to the socioeconomic status of the study population, the lack of information on pubertal stage and its initial design. We cannot extrapolate our results to all Swiss children because LUIS only includes children from the canton of Zurich, in German-speaking Switzerland. More people have a migration background in Zurich (46%) than in Switzerland as a whole (40%) [40]. Half of the study participants lived in a location in the highest Swiss-SEP quintile. Although the Swiss-SEP in LUIS (median 69, IQR 61–76) was only slightly higher than for all households in Zurich with one or more children (median 66, IQR 58–73) [15], this might differ from other regions and could have led to overestimation of height and underestimation of BMI in our study resulting in poorer fit for height references and better fit for BMI references. The primary objective of the LUIS study was to investigate lung function rather than body growth. Consequently, we did not have information on Tanner pubertal stage and could not account for puberty-related changes in growth in our analysis.

The study benefits from the population-based approach, the standardised anthropometric measurements and the incorporation of information on the origin of parents and socioeconomic status.

Implications

This study shows that growth patterns of schoolchildren in the region of Zurich do not fit well with currently used WHO references. Similarly, the BMI of Zurich schoolchildren, particularly adolescents, does not fit well with IOTF references. Poorly fitting growth references may lead to misclassification of overweight, obesity or short

stature. Such misclassification can result in uncertainties in clinical decision-making including delayed treatments and unnecessary referrals [41, 42]. Additionally, it may lead to inaccurate prevalence estimates of obesity on the population level. The PEZZ growth references fit better with anthropometric measurements of Zurich schoolchildren and might reduce misclassification of obesity or short stature in this Zurich paediatric population. Nevertheless, it remains crucial for paediatricians to consider not only single measurements and cutoff values, but to rely primarily on longitudinal trajectories of height and weight and to take into account parental height, Tanner stage, bone age and medical history when determining abnormal growth [43].

Hence, new growth references representing children living in Switzerland are needed. Ideally, new Swiss growth references should be derived from nationally representative, longitudinally collected data that includes all regions of Switzerland [44]. Longitudinally collected data from primary care, hospitals (SwissPedHealth, https://sphn.ch/network/projects/project-page_nds_swisspedhealth/) and school medical services would be available and useful.

In conclusion, the WHO growth references currently used in Switzerland may lead to misclassification of overweight, obesity and short stature. Consequently, the development of new, representative national growth references is warranted.

Availability of data and material

Researchers can obtain datasets for analysis if a detailed concept sheet is presented for the planned analyses and approved by the principal investigators (Alexander Moeller, Philipp Latzin and Claudia Kuehni).

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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Appendix

1 Calculation of z-scores

We calculated age and sex dependent z-scores for body height, body weight, and BMI based on WHO [1], PEZZ [2], and IOTF [3] growth references. We used cubic interpolation of the published LMS-values to determine the exact LMS-values for each age in days, as described by Vidmar, Cole and Pan [4]. We used a formula from Cole and Green [5] to calculate z-scores (z) with our measurement (x) and the L(λ), M(μ), and S(σ) values, see formula (1):

$$z = \frac{\left(\frac{x}{\mu}\right)^{\lambda} - 1}{\lambda \sigma} \tag{1}$$

We used a correction method described by the WHO to correctly compute z-scores >3 and <-3 [6], see formulas (2), (3), (4), (5) and (6):

$$z^* = \begin{cases} z & if & |z| \le 3\\ 3 + \left(\frac{x - SD3pos}{SD23pos}\right) & if & z > 3\\ -3 + \left(\frac{x - SD3neg}{SD23neg}\right) & if & z < -3 \end{cases}$$
 (2)

where

$$SD3pos = \mu(1 + \lambda * \sigma * 3)^{\frac{1}{\lambda}}$$
 (3)

$$SD3neg = \mu (1 + \lambda * \sigma * (-3))^{\frac{1}{\lambda}}$$
 (4)

$$SD23pos = \mu(1 + \lambda * \sigma * 3)^{\frac{1}{\lambda}} - \mu(1 + \lambda * \sigma * 2)^{\frac{1}{\lambda}}$$
 (5)

$$SD23neg = \mu (1 + \lambda * \sigma * (-2))^{\frac{1}{\lambda}} - \mu (1 + \lambda * \sigma * (-3))^{\frac{1}{\lambda}}$$
 (6)

We adapted a method from Daymont et al. [7] to detect possible outliers resulting from recording or transcription errors by the LUIS study team: We recentered height, weight, and BMI z-scores around the median z-score at each age year to account for the possibility that the whole study sample could be different from the reference population. We excluded children with a recentered z-score of <-4 or >4 [8, 9]. We used the recentered z-scores only for data cleaning.

2 Supplementary figures and tables

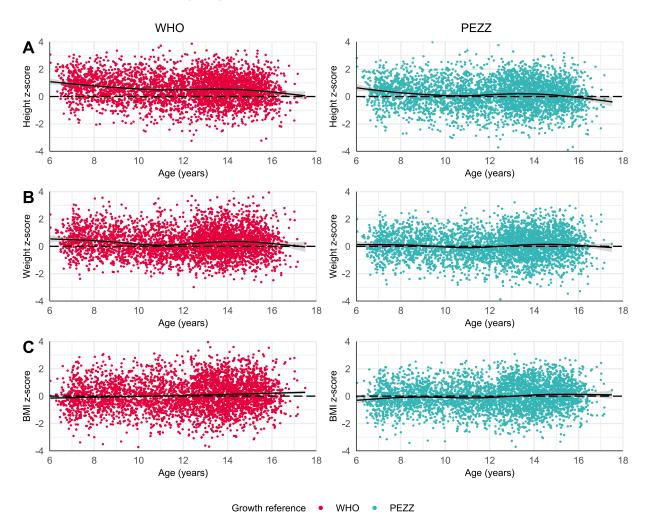


Figure S1. Scatterplot of **A)** height, **B)** weight, and **C)** BMI z-scores by age for 3755 children of the <u>LuftiBus in the School (LUIS)</u> study based on WHO and PEZZ references. Mean z-scores and their 95% confidence intervals were locally estimated with penalized cubic B-Spline regression.

BMI: Body mass index; PEZZ: Paediatric Endocrinology Centre Zurich; WHO: World Health Organization.

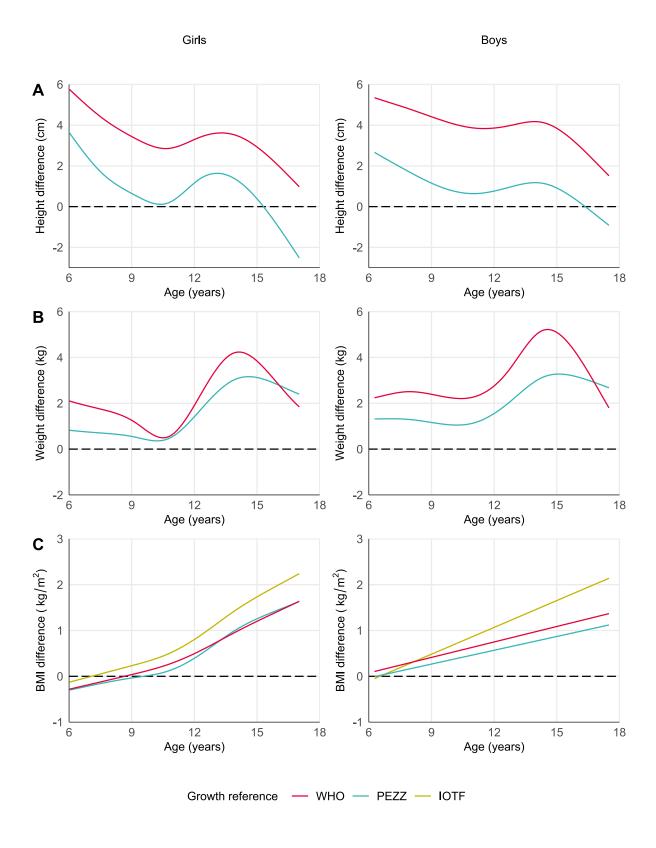


Figure S2. Difference between mean **A)** height, **B)** weight, and **C)** BMI of 3755 participants of the <u>LuftiBus in the school (LUIS) study</u> and the corresponding 50th percentile of WHO, PEZZ, and IOTF references over age. Mean height, weight, and BMI were locally estimated by penalized cubic B-spline regression on age. Positive differences indicate that estimated means of LUIS children were higher than the 50th percentile of the growth reference.

BMI: Body Mass Index; PEZZ: Paediatric Endocrinology Centre Zurich; WHO: World Health Organization; IOTF: International Obesity Task Force.

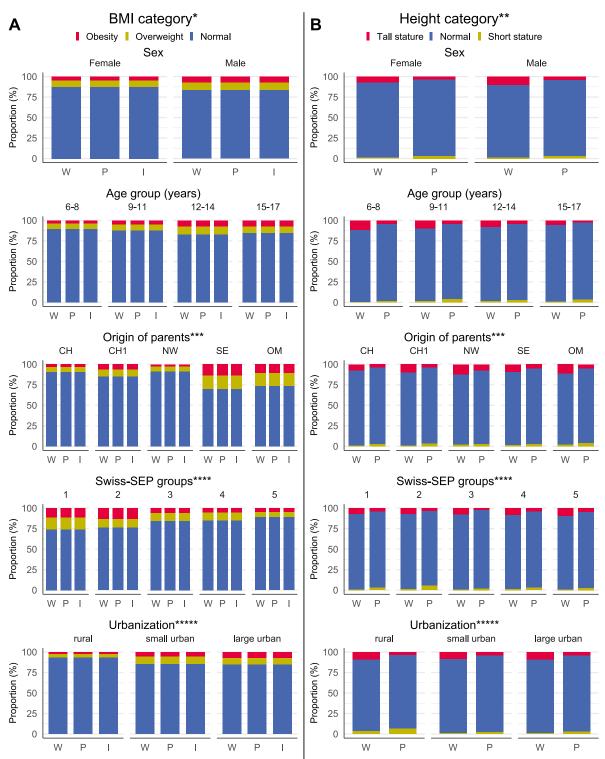


Figure S3. Prevalence of the **A)** BMI and **B)** height categories for 3755 children of the <u>LuftiBus in the school</u> (<u>LUIS</u>) study by sex, age, origin of parents, Swiss-SEP, and urbanization.

* BMI categories were defined based on cutoff values of the WHO, of PEZZ, and IOTF, see supplementary Table S1. For readability we plotted obesity (obesity + severe obesity), overweight, and normal weight.

**** Swiss-SEP: Swiss socioeconomic position version 2.0, census data from 2012 - 2015. The 5 groups are based on quintiles published by Panczak et al. [10]. A higher score relates to a higher socioeconomic position. ***** Urbanization: rural: rural areas; small urban: towns and suburbs; large urban: cities.

BMI: Body Mass Index; P: PEZZ, Paediatric Endocrinology Centre Zurich; W: WHO, World Health Organization; I: IOTF, International Obesity Task Force.

^{**} Height categories were defined by percentiles: short stature (<3rd), normal (3rd to 97th), and tall stature (>97th).

*** Origin of parents: CH: both parents from Switzerland; CH1: one parent from Switzerland; NW: both parents from Northern/Western Europe; SE: both parents from Southern/Eastern Europe; OM: Other/Mixed, parents from other or not from the same regions. For the origin of parents, we included n = 3365 children.

Table S1. Cutoff values for the BMI and height categories based on WHO, PEZZ, and IOTF growth references. Number of children and proportions in BMI and height categories in 3755 children of the <u>LuftiBus in the school</u> (LUIS) study.

	WHO	PEZZ	IOTF
BMI category			
Severe obesity			
cutoff, percentile	BMI > 99.5	Girls: BMI > 99.3 Boys: BMI > 98.8	Girls: BMI > 99.8 Boys: BMI > 99.8
n	62	22	11
% (95% CI)	1.7 (1.3, 2.1)	0.6 (0.4, 0.9)	0.3 (0.2, 0.5)
Obesity			
cutoff, percentile	97 < BMI ≤ 99.5	Girls: 96.8 < BMI ≤ 99.3 Boys: 95.5 < BMI ≤ 98.8	Girls: 98.6 < BMI ≤ 99.8 Boys: 98.9 < BMI ≤ 99.8
n	171	131	94
% (95% CI)	4.6 (3.9, 5.3)	3.5 (2.9, 4.1)	2.5 (2.0, 3.1)
Overweight			
cutoff, percentile	90 < BMI ≤ 97	Girls: 82.9 < BMI ≤ 96.8 Boys: 78.9 < BMI ≤ 99.5	Girls: 89.3 < BMI ≤ 98.6 Boys: 90.5 < BMI ≤ 98.9
n % (05% OL)	318	568	472
% (95% CI)	8.5 (7.6, 9.4)	15.1 (14.0, 16.3)	12.6 (11.5, 13.7)
Normal weight	D141 . 00	011 5111 100 0	011 5141 100 0
cutoff, percentile	BMI ≤ 90 3204	Girls: BMI ≤ 82.9 Boys: BMI ≤ 78.9 3034	Girls: BMI ≤ 89.3 Boys: BMI ≤ 90.5 3178
% (95% CI)	85.3 (84.1, 86.4)	80.8 (79.5, 82.0)	84.6 (83.4, 85.8)
Cohen's Kappa (95% CI)*	ref	0.74 (0.71, 0.76)	0.73 (0.71, 0.76)
eight category			
Tall stature			
cutoff, percentile	Height > 97	Height > 97	NA NA
• •	330	160	NA NA
n % (95% CI)	8.8 (7.9, 9.8)	4.3 (3.7, 5.0)	NA NA
Normal	0.0 (7.9, 9.0)	4.3 (3.7, 5.0)	IVA
	2 < Unight < 07	2 < Haight < 07	NA NA
cutoff, percentile	3 ≤ Height ≤ 97	3 ≤ Height ≤ 97	
n % (05% CI)	3372	3486	NA NA
% (95% CI)	90.1 (89.1, 91.0)	92.8 (91.9, 93.6)	NA NA
Short stature	Hoight > 0	Hoight > 0	ALA
cutoff, percentile	Height ≥ 3	Height ≥ 3	NA NA
n % (05% OL)	41	109	NA NA
% (95% CI)	1.1 (0.8, 1.5)	2.9 (2.4, 3.5)	NA NA
Cohen's Kappa (95% CI)*	ref	0.60 (0.56, 0.65)	NA

^{*} Cohen's Kappa to quantify agreement of BMI and height categories between WHO compared to PEZZ or compared to IOTF growth references. We interpreted Cohen's Kappa between 0.61-0.80 as substantial and 0.41-0.60 as moderate agreement, according to Landis and Koch [11]

according to Landis and Koch [11].

BMI: Body mass index; IOTF: International Obesity Task Force; NA: not applicable; PEZZ: Paediatric Endocrinology Centre Zurich; ref: reference; WHO: World Health Organization.

Table S2: Characteristics of children of the <u>LuftiBus in the School (LUIS)</u> study compared to the population of the PEZZ growth references.

	LUIS Children N = 3755	PEZZ N = 30,141
Sex , n (%)		,
Girls	1872 (50)	16,540 (55)
Boys	1883 (50)	13,601 (45)
Age (years)		
groups, n (%)		
6-7	409 (11)	2166 (18)**
8-9	533 (14)	1327 (11)
10-11	617 (16)	3528 (29)
12-13	1,076 (29)	1710 (14)
14-15	1,019 (27)	1983 (16)
16-17	101 (3)	1514 (12)
Origin of parents*, n (%)		
CH	1,933 (51)	9510 (32)
CH (one parent)	584 (16)	3674 (12)
DE, FR, AUT, SCAND, BENELUX	184 (5)	1265 (4)
IT, ES, PT	81 (2)	1176 (4)
BALKAN	257 (7)	2008 (7)
Turkey	18 (<1)	433 (1)
Other/Mixed/Missing	698 (19)	12,075 (40)
Swiss-SEP 2.0***		
Observed quartiles		
1	<61.4	<58.8
2	61.4 – 69.5	58.8 - 64.9
3	69.5 – 76.5	64.9 - 72.3
4	>76.5	>72.3

^{*} Origin of parents: CH (both parents): both parents from Switzerland; CH (one parent): one parent from Switzerland; DE, FR, AUT, SCAND, BENELUX: both parents from Germany, France, Austria, Denmark, Norway, Finland, Sweden, Island, Belgium, the Netherlands, or Luxembourg; IT, ES, PT: both parents from Italy, Spain, or Portugal; BALKAN: both parents from Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Kosovo, Montenegro, North Macedonia, Romania, Serbia, or Slovenia; Turkey: both parents from Turkey; Other/Mixed/Missing: parents from other or not from the same regions, or missing origin of parents.

** The population of the PEZZ growth references also included 14,784 children below 6 years and 3129 children above 18 years, hence the number of schoolchildren between 6-18 years was 12,228. The percentages for the age groups are calculated based on the 12,228 schoolchildren.

PEZZ: Paediatric Endocrinology Centre Zurich

^{***} Swiss-SEP: Swiss socioeconomic position version 2.0 published by Panczak et al. [10], census data from 2012 - 2015. Reported are the quartiles of Swiss-SEP values observed in the LUIS data and observed in the population of the PEZZ growth references [2]. For example, the highest 25% of Swiss-SEP values were >76.5 in LUIS, while the highest 25% of Swiss-SEP values were >72.3 in the population of the PEZZ growth references.

Table S3: Mean height, weight, and BMI z-scores based on WHO, PEZZ, and IOTF growth references by sex, age, origin of parents, Swiss-SEP, and urbanization; and the fit of z-scores to a standard normal distribution.

				WHO			PEZZ			IOTF	
					n Darling*			on Darling*			n Darling*
		n	mean (sd)	A^2	p-value	mean (sd)	A^2	p-value	mean (sd)	A^2	p-value
					Sex						
Girls	Height z-score	1872	0.52 (0.98)	250.1	<0.001	0.15 (1.02)	23.0	<0.001	NA	NA	NA
	Weight z-score	1872	0.21 (0.97)	37.6	<0.001	0.05 (0.99)	4.2	0.007	NA	NA	NA
	BMI z-score	1872	0.02 (1.10)	5.3	0.002	-0.02 (1.04)	1.0	0.356	0.15 (1.05)	21.6	<0.001
Boys	Height z-score	1883	0.60 (1.02)	333.7	<0.001	0.16 (1.03)	25.8	<0.001	NA	NA	NA
	Weight z-score	1883	0.35 (1.05)	97.7	<0.001	0.07 (0.98)	6.7	<0.001	NA	NA	NA
	BMI z-score	1883	0.10 (1.17)	23.1	<0.001	0.00 (0.97)	1.0	0.358	0.23 (1.04)	45.0	<0.001
					Age						
6-8	Height z-score	678	0.82 (0.92)	232.1	<0.001	0.32 (0.95)	37.6	<0.001	NA	NA	NA
	Weight z-score	678	0.44 (0.95)	61.7	<0.001	0.12 (0.89)	8.2	<0.001	NA	NA	NA
	BMI z-score	678	-0.04 (1.06)	2.3	0.063	-0.11 (0.94)	5.5	0.002	0.01 (0.97)	1.0	0.368
9-11	Height z-score	881	0.51 (1.04)	106.8	<0.001	0.06 (1.07)	2.4	0.054	NA	NA	NA
	Weight z-score	881	0.12 (0.94)	6.7	< 0.001	-0.08 (0.95)	3.6	0.014	NA	NA	NA
	BMI z-score	881	-0.05 (1.11)	5.0	0.003	-0.13 (0.97)	8.4	<0.001	0.03 (0.98)	1.5	0.182
12-14	Height z-score	1663	0.53 (1.01)	236.2	<0.001	0.19 (1.03)	31.8	<0.001	NA	NA	NA
	Weight z-score	1663	0.31 (1.05)	67.8	<0.001	0.10 (1.02)	10.8	<0.001	NA	NA	NA
	BMI z-score	1663	0.13 (1.19)	28.5	<0.001	0.05 (1.05)	4.7	0.004	0.29 (1.09)	66.7	<0.001
15-17	Height z-score	533	0.39 (0.95)	41.4	<0.001	0.00 (1.01)	0.43	0.820	NA	NA	NA
	Weight z-score	533	0.24 (1.03)	13.7	<0.001	0.09 (1.01)	3.6	0.014	NA	NA	NA
	BMI z-score	533	0.18 (1.10)	8.8	<0.001	0.12 (0.99)	4.2	0.007	0.40 (1.04)	39.6	<0.001
				Orig	in of paren	its**					
Switzerland	Height z-score	1933	0.52 (0.98)	256.2	< 0.001	0.11 (1.00)	11.9	<0.001	NA	NA	NA
(both parents)	Weight z-score	1933	0.14 (0.94)	18.9	<0.001	-0.07 (0.93)	8.0	<0.001	NA	NA	NA
	BMI z-score	1933	-0.10 (1.06)	11.7	<0.001	-0.15 (0.95)	23.9	<0.001	0.04 (0.97)	2.9	0.033
Switzerland	Height z-score	584	0.61 (1.02)	111.9	< 0.001	0.19 (1.04)	13.9	<0.001	NA	NA	NA
(one parent)	Weight z-score	584	0.28 (1.04)	19.8	< 0.001	0.04 (1.02)	1.1	0.298	NA	NA	NA
	BMI z-score	584	0.01 (1.16)	4.7	0.004	-0.06 (1.03)	1.5	0.166	0.13 (1.06)	5.3	0.002
Northern/	Height z-score	203	0.77 (1.06)	58.6	<0.001	0.34 (1.10)	12.5	<0.001	NA	NA	NA
Western Europe	Weight z-score	203	0.27 (0.92)	7.1	<0.001	0.03 (0.90)	0.8	0.447	NA	NA	NA
	BMI z-score	203	-0.12 (1.03)	2.4	0.058	-0.17 (0.91)	4.1	0.007	-0.01 (0.94)	0.8	0.453
Southern/	Height z-score	382	0.65 (0.98)	80.4	<0.001	0.27 (1.00)	14.2	<0.001	NA	NA	NA
Eastern Europe	Weight z-score	382	0.71 (1.08)	87.1	<0.001	0.48 (1.00)	46.9	<0.001	NA	NA	NA
	BMI z-score	382	0.59 (1.18)	67.6	<0.001	0.45 (1.02)	42.9	<0.001	0.70 (1.08)	91.9	<0.001
Other/ Mixed	Height z-score	263	0.53 (1.14)	37.8	<0.001	0.15 (1.16)	5.1	0.002	NA	NA	NA
	Weight z-score	263	0.50 (1.06)	29.8	<0.001	0.28 (1.02)	12.1	<0.001	NA	NA	NA
	BMI z-score	263	0.39 (1.23)	23.7	<0.001	0.28 (1.07)	12.4	<0.001	0.50 (1.12)	34.6	<0.001
				Swiss	S-SEP grou	ps***					
1: 0 - 49	Height z-score	138	0.49 (0.98)	17.3	<0.001	0.12 (1.00)	1.6	0.151	NA	NA	NA
	Weight z-score	138	0.55 (1.04)	19.2	<0.001	0.35 (0.98)	9.0	<0.001	NA	NA	NA
	BMI z-score	138	0.49 (1.15)	16.7	<0.001	0.37 (1.00)	10.2	<0.001	0.63 (1.05)	26.6	<0.001
2: 40 - 56	Height z-score	459	0.41 (1.03)	38.1	< 0.001	0.03 (1.05)	1.1	0.292	NA	NA	NA
	Weight z-score	459	0.43 (1.15)	36.9	< 0.001	0.21 (1.11)	12.6	<0.001	NA	NA	NA
	BMI z-score	459	0.35 (1.29)	37.7	<0.001	0.24 (1.14)	18.8	<0.001	0.49 (1.19)	58.1	<0.001
3: 57 - 62	Height z-score	431	0.55 (0.92)	67.1	<0.001	0.15 (0.95)	5.8	<0.001	NA	NA	NA
	Weight z-score	431	0.32 (0.99)	19.8	<0.001	0.11 (0.96)	3.3	0.016	NA	NA	NA
	BMI z-score	431	0.13 (1.15)	5.3	0.002	0.05 (1.01)	1.0	0.394	0.25 (1.05)	13.4	<0.001
4: 62 - 69	Height z-score	841	0.52 (1.03)	108.2	<0.001	0.12 (1.06)	6.7	0.001	NA	NA	NA
	Weight z-score	841	0.23 (1.03)	18.1	<0.001	0.01 (1.00)	0.5	0.828	NA	NA	NA
	BMI z-score	841	0.03 (1.16)	5.5	0.002	-0.04 (1.03)	1.0	0.366	0.17 (1.06)	12.0	<0.001
5: 70 - 100	Height z-score	1886	0.62 (1.00)	359.3	<0.001	0.21 (1.02)	41.7	<0.001	NA	NA	NA
	Weight z-score	1886	0.24 (0.96)	47.3	<0.001	0.02 (0.94)	3.6	0.014	NA	NA	NA
	BMI z-score	1886	-0.03 (1.07)	5.3	0.002	-0.10 (0.94)	11.5	<0.001	0.09 (0.97)	7.1	<0.001
				Url	oanization*	***					
			0.20 (4.06)	19.7	<0.001	-0.05 (1.08)	0.9	0.425	NA	NA	NA
Rural	Height z-score	247	0.39 (1.06)			0.00 (0.00)	12.5	< 0.001	NA	NA	NA
Rural	Height z-score Weight z-score	247 247	-0.09 (0.97)	2.4	0.056	-0.32 (0.99)	12.5	<u> </u>	IVA	7 47 1	
Rural					0.056 <0.001	-0.41 (1.00)	20.5	<0.001	-0.25 (1.02)	8.6	<0.001
	Weight z-score	247 247 1635	-0.09 (0.97) -0.38 (1.13) 0.54 (0.99)	2.4		-0.41 (1.00) 0.16 (1.02)	20.5 21.1				<0.001 NA
	Weight z-score BMI z-score	247 247	-0.09 (0.97) -0.38 (1.13)	2.4 18.1	<0.001	-0.41 (1.00)	20.5	<0.001	-0.25 (1.02)	8.6	
Rural Small urban	Weight z-score BMI z-score Height z-score	247 247 1635	-0.09 (0.97) -0.38 (1.13) 0.54 (0.99)	2.4 18.1 230.6	<0.001 <0.001	-0.41 (1.00) 0.16 (1.02)	20.5 21.1	<0.001 <0.001	-0.25 (1.02) NA	8.6 <i>NA</i>	NA
	Weight z-score BMI z-score Height z-score Weight z-score	247 247 1635 1635	-0.09 (0.97) -0.38 (1.13) 0.54 (0.99) 0.26 (1.02)	2.4 18.1 230.6 43.9	<0.001 <0.001 <0.001	-0.41 (1.00) 0.16 (1.02) 0.05 (0.99)	20.5 21.1 2.8	<0.001 <0.001 0.036	-0.25 (1.02) NA NA	8.6 NA NA	NA NA
Small urban	Weight z-score BMI z-score Height z-score Weight z-score BMI z-score	247 247 1635 1635 1635	-0.09 (0.97) -0.38 (1.13) 0.54 (0.99) 0.26 (1.02) 0.06 (1.13)	2.4 18.1 230.6 43.9 10.5	<0.001 <0.001 <0.001 <0.001	-0.41 (1.00) 0.16 (1.02) 0.05 (0.99) -0.01 (1.00)	20.5 21.1 2.8 0.3	<0.001 <0.001 0.036 0.901	-0.25 (1.02) <i>NA</i> <i>NA</i> 0.21 (1.04)	8.6 NA NA 33.7	<i>NA NA</i> <0.001

^{*} Anderson-Darling test to assess goodness of fit of the observed z-score distribution based on the WHO, PEZZ, or IOTF growth references to a standard normal distribution, A²: test statistic for goodness of fit, Color coding: green: best fit in respective group. ** For the origin of parents, we included n = 3365 children.

BMI: Body mass index; IOTF: International Obesity Task Force; NA: not applicable; PEZZ: Paediatric Endocrinology Centre Zurich; sd: standard deviation; WHO: World Health Organization.

^{***} Swiss-SEP: Swiss socioeconomic position version 2.0, census data from 2012 - 2015. The 5 groups are based on quintiles published by Panczak et al. [10]. A higher Swiss-SEP relates to a higher socioeconomic position.

^{*****} Urbanization: rural: rural areas; small urban: towns and suburbs; large urban: cities.

Table S4: Linear regression of height z-scores based on PEZZ references on age, sex, origin of parents, Swiss-SEP, and urbanization.

			Height z-s	core				
	Univa	ariable mode			Multivariable model			
	β-coefficient (95% CI)	std. error	p-value	adj. R ²	β-coefficient (95% CI)	std. error	p-value	adj. R ²
Age				0.005				
(1 year increase)	-0.03 (-0.04, -0.01)	0.01	<0.001	0.005	-0.03 (-0.05, -0.02)	0.008	<0.001	
Sex								
Girls	ref	ref	ref	0	NA	NA	NA	
Boys	0.01 (-0.06, 0.07)	0.03	0.815		NA	NA	NA	
Origin of parents*								
Switzerland (both parents)	ref	ref	ref		ref	ref	ref	
Switzerland (one parent)	0.08 (-0.01, 0.18)	0.05	0.086	0.000	0.06 (-0.03, 0.16)	0.05	0.188	
Northern/Western Europe	0.23 (0.08, 0.38)	0.08	0.003	0.003	0.19 (0.04, 0.33)	0.08	0.015	0.013
Southern/Eastern Europe	0.16 (0.04, 0.27)	0.06	0.006		0.22 (0.10, 0.34)	0.06	<0.001	
Other/Mixed	0.04 (-0.10, 0.17)	0.07	0.585		0.08 (-0.06, 0.21)	0.07	0.263	
Swiss-SEP**				0.000				
(per increment of 20)	0.10 (0.04, 0.16)	0.04	<0.001	0.003	0.06 (-0.02, 0.14)	0.04	0.125	_
Urbanization***			•		, , , , , , , , , , , , , , , , , , ,		•	
Rural	ref	ref	ref	0.000	ref	ref	ref	
Small urban	0.21 (0.07, 0.35)	0.07	0.003	0.002	0.27 (0.12, 0.42)	0.08	<0.001	
Large urban	0.23 (0.09, 0.37)	0.07	0.001		0.20 (0.05, 0.35)	0.08	0.010	

^{*} Origin of parents: For the univariable model on origin of parents and for the multivariable model we included n = 3365 children. ** Swiss-SEP: Swiss socioeconomic position version 2.0, census data from 2012-2015. A higher score relates to a higher

socioeconomic position.

*** Urbanization: rural: rural areas; small urban: towns and suburbs; large urban: cities.

adj: adjusted; NA: not applicable, not included in multivariable model based on results of univariable model. PEZZ: Paediatric Endocrinology Centre Zurich; ref: reference.

Table S5: Linear regression of weight z-scores based on PEZZ references on age, sex, origin of parents, Swiss-SEP, and urbanization.

		1	Neight z-s	score				
	Univa	ariable mode			Multivariable model			
	β-coefficient (95% CI)	std. error	p-value	adj. R ²	β-coefficient (95% CI)	std. error	p-value	adj. R ²
Age				0				
(1 year increase)	0.01 (-0.00, 0.02)	0.01	0.221	U	NA	NA	NA	
Sex								
Female	ref	ref	ref	0	NA	NA	NA	
Male	0.01 (-0.05, 0.07)	0.03	0.732		NA	NA	NA	1
Origin of parents*								
Switzerland (both parents)	ref	ref	ref		ref	ref	ref	
Switzerland (one parent)	0.12 (0.03, 0.21)	0.05	0.013	0.004	0.10 (0.01, 0.19)	0.05	0.034	
Northern/Western Europe	0.10 (-0.03, 0.24)	0.07	0.141	0.034	0.10 (-0.04, 0.24)	0.07	0.167	0.044
Southern/Eastern Europe	0.55 (0.45, 0.66)	0.05	<0.001		0.49 (0.38, 0.60)	0.06	<0.001	
Other/Mixed	0.36 (0.23, 0.48)	0.06	<0.001		0.30 (0.17, 0.43)	0.06	<0.001	
Swiss-SEP**				0.004				
(per increment of 20)	-0.12 (-0.18, -0.007)	0.03	< 0.001	0.004	-0.08 (-0.15, -0.01)	0.04	0.019	
Urbanization***								
Rural	ref	ref	ref	0.010	ref	ref	ref	
Small urban	0.37 (0.24, 0.50)	0.07	<0.001	0.012	0.39 (0.25, 0.53)	0.07	<0.001	
Large urban	0.45 (0.32, 0.58)	0.07	<0.001		0.42 (0.27, 0.56)	0.07	<0.001	

^{*} Origin of parents: For the univariable model on origin of parents and for the multivariable model we included n = 3365 children. ** Swiss-SEP: Swiss socioeconomic position version 2.0, census data from 2012 - 2015. A higher score relates to a higher

^{***} Urbanization: rural: rural areas; small urban: towns and suburbs; large urban: cities.
adj: adjusted; NA: not applicable, not included in multivariable model based on results of univariable model. PEZZ: Paediatric Endocrinology Centre Zurich; ref: reference.

Table S6: Linear regression of BMI z-scores based on PEZZ references on age, sex, origin of parents, Swiss-SEP, and urbanization.

			BMI z-sc	ore				
	Univ	ariable mode		Multivariable model				
	β-coefficient (95% CI)	std. error	p-value	adj. R ²	β-coefficient (95% CI)	std. error	p-value	adj. R ²
Age				0.009				
(1 year increase)	0.04 (0.02, 0.05)	0.01	<0.001	0.009	0.01 (-0.01, 0.02)	0.01	0.342	
Sex								
Female	ref	ref	ref	0	NA	NA	NA	
Male	0.01 (-0.05, 0.08)	0.03	0.702		NA	NA	NA	
Origin of parents*								
Switzerland	ref	ref	ref		ref	ref	ref	
(both parents)								
Switzerland (one parent)	0.09 (0.00, 0.18)	0.05	0.046	0.040	0.07 (-0.02, 0.17)	0.05	0.106	
Northern/Western Europe	-0.02 (-0.16, 0.12)	0.07	0.805	0.043	-0.00 (-0.15, 0.14)	0.07	0.945	0.057
Southern/Eastern Europe	0.61 (0.50, 0.72)	0.05	<0.001		0.49 (0.38, 0.61)	0.06	<0.001	
Other/Mixed	0.43 (0.31, 0.56)	0.06	<0.001		0.34 (0.22, 0.47)	0.07	<0.001	
Swiss-SEP**				0.004				
(per increment of 20)	-0.22 (-0.28, -0.16)	0.03	<0.001	0.004	-0.16 (-0.24, -0.09)	0.04	<0.001	
Urbanization***	, , ,	•	•		, , , , , , , , , , , , , , , , , , ,	•	•	
Rural	ref	ref	ref	0.010	ref	ref	ref	
Small urban	0.40 (0.27, 0.53)	0.07	<0.001	0.012	0.43 (0.29, 0.58)	0.07	<0.001	
Large urban	0.45 (0.32, 0.59)	0.07	<0.001		0.46 (0.31, 0.60)	0.07	<0.001	

^{*} Origin of parents: For the univariable model on origin of parents and for the multivariable model we included n = 3365 children. ** Swiss-SEP: Swiss socioeconomic position version 2.0, census data from 2012 - 2015. A higher score relates to a higher

^{***} Urbanization: rural: rural areas; small urban: towns and suburbs; large urban: cities.
adj: adjusted; BMI: body mass index; NA: not applicable, not included in multivariable model based on results of univariable model. PEZZ: Paediatric Endocrinology Centre Zurich; ref: reference.

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