DEVELOPMENT OF SYNTHETIC GROWTH CHARTS FOR ROMANIAN POPULATION

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Abstract

There are no new national growth references for the Romanian population and the current recommendations for short stature evaluation is the use of the Swiss growth charts developed based on a longitudinal study.

The aim of the present paper is to present the new synthetic growth references for Romanian children.

Material and methods. We used local Romanian data from 9 studies with information on height and weight obtained between 1999 and 2016. Based on their plausibility and methodology six studies were selected for generating the National Synthetic Growth References for Romanian Children based on the specific methodology described previously. The selected studies included 8407 subjects measured in schools/kindergartens. Age is reported in years covering a range from 3-18 years. Height and weight were measured at a precision of 0.1 cm and 0.1 kg. All children were measured at normal temperature, in light clothes, without footwear.

Results. We present the charts and tables with the common centiles for height, weight and body mass index for boys and girls.

Conclusion. We suggest synthetic growth references based upon recent growth data from 6 different Romanian regions as new National Growth Charts for Romanian children.

Key words: synthetic growth charts.

INTRODUCTION

The clinical evaluation of height and weight is based on comparisons with specific growth references. Yet, disagreement however exists upon which chart is the right chart to use (1). In many countries, national references for height, weight and body mass index (BMI) are available. Also for Romania several regional

studies have been performed (2, 3), but none of these studies can be considered a national representative sample. As the only available growth chart for the Romanian population has been published more than four decades ago (4, 5), current recommendations from the protocol of growth hormone treatment in short stature in Romania suggest (6) using the Swiss growth charts developed in 1989 by Prader (7) for clinical purposes.

In recent years globally applicable international growth standards and references have been suggested for countries that lack national growth references (8). The idea of such standards goes back to recommendations of a Working Group on infant growth established by the World Health Organization (WHO), and may be justified for infants and very young children who tend to grow similarly under modern affluent conditions. Yet, it appears questionable whether WHO growth standards and references should be used for clinical purposes in Romanian children, particularly as the Romanian population at present undergoes major economic transition that may have major influences also on infant and child growth. It was, thus, considered appropriate to newly develop a national growth chart for Romanian children. Constructing national growth charts is demanding work and most notably, expensive work. It was therefore decided to apply the method of generating synthetic references for the Romanian population.

Synthetic growth references are based on Principal Component Analysis and the Likelihood principle. Based on a global reference combination of longitudinal and cross-sectional modern and historic growth studies with data on height and weight, mean values and a limited number of Principal Components,

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that characterize the variability of growth in this global sample, are known (9). This information is then used to derive estimates of height, weight, BMI and respective centiles from available auxological data of the Romanian population.

MATERIAL AND METHOD

Methods used for generating synthetic growth charts are described in detail elsewhere (9).

In short, the methodology comprises 2 steps:

Step 1:

- Principal Component Analysis was applied to characterize the global variance of the mean values for height, weight and BMI in 196 female and 197 male longitudinal and cross-sectional growth studies from 53 countries published since 1831 (all studies contained information on height, data on height and weight were available in 87 female and 89 male studies).

- Five principal components were able to explain 98.4 % of the between-study variance in mean height, 99.2 % of this variance in mean weight, and 93 % (females) and 94 % (males) of this variance in mean BMI. These components define a growth model that describes the basic human growth pattern from birth to maturity. The component of this growth model can now be used for generating “synthetic” references for height, weight, and BMI of any population of interest that lacks complete annual data of these parameters.

Step 2:

- The Maximum Likelihood Principle is then applied and standard techniques for non-linear optimization are used. This step generates a “synthetic” growth curve that is the most likely curve for the population of interest given the following assumptions:

a) the curve belongs to a population similar to the ones for which the Principal Component Analysis was performed,

b) all differences between the curve and the observed mean heights are errors of these means distributed according to a known standard error of the mean.

- By applying a Bayesian rational, synthetic growth curve find that curve that best compromises between the data available from the population of interest and the global patterns obtained from the Principal Component Analysis.

We used local Romanian data from 9 studies with information on height and weight obtained between 1999 and 2016 (Table 1). Not all of these studies, however, appeared fully plausible. Data from the Childhood Obesity Surveillance Initiative appeared unsuitable because of some uncertainty in respect to the definition of age (10). A “rural” study was excluded because the probands were obtained from general practitioners’ offices without clear selection criteria, and also the numbers appeared limited. We also excluded data from Cluj given the fact that information was available only for height and the fact that it included only subjects from urban areas. Also given the proximity of Targu Mures and Cluj and the fact that the Mures data was more recent, we considered including the former. Six studies (Table 1) remained, and were selected for generating the National Synthetic Growth References for Romanian Children. The 6 studies selected added to 8407 measurements of children 3-18 years of age. This represents approximately 0.22% of the Romanian population below 18 years according to the latest census.

The selected studies included subjects

Table 1. Description of the studies analyzed

No	Location	Number of subjects	Socio-economic status	Ethnicity	Age	Measurement location	Period	Published
	Iasi	556	Not available (NA)	NA	7-13	Schools	2016	no
	Timisoara	2130	NA	NA	3-18	Schools, kindergartens	2011-2012 2013-2014	no
	Mures	1923	NA	NA	6-14	Schools	2013-2014	no
	Bucuresti 1	1108	NA	NA	6-23	Schools	2011	Yes (11)
	Childhood Obesity Surveillance Initiative	4348	NA	NA	8-9	Schools	2013	Yes (10)
	Rural	134	NA	NA	8-15	General practice office (GPO)	2011	abstract only (12)
	Bucuresti 2	1163	NA	NA	3-18	Schools	2015	No
	Cluj	7953	NA	NA	0-18	GPO, schools, kindergartens	1999, 2012-2013	yes (13)
	Petroșani	1527	NA	NA	3-16	Schools, kindergartens	2016	No

measured in schools/kindergartens. Age is reported in years. A 6 years old subject is defined like any subject with the age between 5.5 to 6.49 years. Height and weight were measured by trained medical personnel at a precision of 0.1 cm and 0.1 kg. For every parameter the mean of three measurements was used. All children were measured at normal temperature, in light clothes, without footwear.

The studies provided information from all main regions of the country, recorded in the last five years: Timisoara, Tirgu-Mures, Bucharest (2 cohorts), Petroșani and Iasi. The age range varied between the studies, but overall, covered the full age range from 3 to 18 years. For weight charts, we used the same data sets, excluding one of the Bucharest studies, considered redundant. Height data is showed as means and standard deviations. Weight data was expressed as medians (3 data sets) or means and standard deviations. Based on the number of subjects in each growth study we a priori considered a measurement error of 0.7 (girls) cm and 0.5 (boys) cm for height; 0.7 (girls) kg and 0.5 (boys) kg for weight; and 0.3 kg/m² for BMI.

Original centiles for height and weight were not recorded as this information is provided by the synthetic approach. For generating the synthetic charts, 6 age groups were selected: boys: 4,7,11,13,15, and 18 years; girls: 4,7,9,11,13, and 16 years. These age groups were chosen as they provided information on prepubertal, pubertal and final height. Centiles for weight and BMI were calculated using LMS method (14).

MedCalc v. 12.5 was used for statistical analysis with a level of significance $\alpha=0.05$. Data were tested for normal distribution using the Kolmogorov-Smirnov method. For data comparison, non-parametric tests were used (Wilcoxon).

All the studies taken into consideration were approved by the local ethics committee and written consent was obtained from the parents/legal representatives, which contain information about the possibility of secondary data analysis. Given the fact that for generating the synthetic growth curves we use secondary research, having no contact with and no possibility to identify any of the subjects, a new ethics approval was considered redundant.

RESULTS

1. Height

Tables 2 and 3 show the computed synthetic means and SD scores for height for both sexes. Figure

1 depicts the synthetic growth curves derived for both boys and girls.

When comparing the synthetic references with the existing references currently used in Romania (Swiss, WHO and CDC), there are statistically significant differences between either 2 standards compared ($p<0.0001$).

Romanian boys are in average taller than the Swiss with 0.51 ± 0.84 cm ($p=0.038$), 1.71 ± 0.42 cm than the US ($p<0.0001$) and 1.77 ± 0.57 cm ($p<0.0001$) than the international WHO reference. For girls, the mean differences are 0.35 ± 0.65 cm for the Swiss, 1.03 ± 0.91 cm for the US and 0.81 ± 0.59 cm than the WHO (Fig. 4a).

The maximum difference between the Romanian and the CDC tables for boys is 2.3cm at the age of 12.4 years and the minimum is 0.93cm at the age of 17.6 years. Using the same 2 references for girls, the maximum difference is 2.6cm at the age of 4.6 years and the minimum 0.009cm at the age of 12.1 years.

The maximum difference between the Prader and Romanian growth standards for boys is attained at 14 years (2.5cm), while the minimum is 0.0008cm at 9.9 years. For girls, the corresponding values are 1.39cm maximum (12 years) and respectively 0.003cm minimum (14 years).

The same comparison using the Romanian and WHO standards leads to a maximum difference for boys 2.45cm at 9 years and a minimum of 0.39cm at 2 years of age. For girls the maximum difference is found at 7 years (2.21cm) and the minimum at 12.5years (0.049cm).

2. Weight and BMI

Tables 4-5 show the common centiles for weight analysis and Figure 2 depicts the corresponding curves. While weight centiles are useful, the recent recommendations are for the employment of BMI for weight disturbances definitions, especially after the age of 10 years. In Tables 6 and 7 the common used BMI centiles can be found and Figure 3 shows the corresponding charts.

A comparison between the new Romanian synthetic BMI references and the common used references world-wide (WHO and IOTF) shows there are statistically significant differences between these references ($p<0.0001$).

The maximum differences for boys are 1.17 kg/sqm at age 11.1 years between the Romanian and WHO references and 1.48 kg/sqm (14 years) for the IOTF comparison. The minimum corresponding differences are 0.04 kg/sqm at 5 months (WHO) and

Table 2. Synthetic means and SD for height – boys

Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)
0	50.6	2.0	33	94.9	4.0	66	114.4	4.9	99	130.9	5.7	132	145.3	6.6	165	163.6	8.2	198	175.6	6.8
1	54.2	2.2	34	95.6	4.0	67	114.9	4.9	100	131.3	5.7	133	145.8	6.6	166	164.2	8.3	199	175.7	6.8
2	57.7	2.3	35	96.4	4.1	68	115.5	5.0	101	131.8	5.7	134	146.3	6.7	167	164.8	8.3	200	175.8	6.8
3	61.3	2.4	36	97.1	4.1	69	116.0	5.0	102	132.3	5.8	135	146.8	6.7	168	165.5	8.3	201	176.0	6.7
4	63.6	2.5	37	97.7	4.1	70	116.6	5.0	103	132.7	5.8	136	147.3	6.8	169	165.9	8.3	202	176.1	6.7
5	65.9	2.5	38	98.3	4.2	71	117.1	5.1	104	133.2	5.8	137	147.8	6.8	170	166.4	8.2	203	176.2	6.7
6	68.1	2.5	39	98.9	4.2	72	117.7	5.1	105	133.6	5.8	138	148.3	6.9	171	166.9	8.2	204	176.4	6.6
7	69.6	2.5	40	99.5	4.2	73	118.2	5.1	106	134.1	5.9	139	148.8	6.9	172	167.4	8.2	205	176.4	6.6
8	71.2	2.6	41	100.1	4.3	74	118.7	5.1	107	134.6	5.9	140	149.3	7.0	173	167.9	8.1	206	176.5	6.6
9	72.7	2.6	42	100.7	4.3	75	119.2	5.2	108	135.0	5.9	141	149.8	7.0	174	168.4	8.1	207	176.6	6.6
10	73.9	2.7	43	101.3	4.3	76	119.7	5.2	109	135.4	5.9	142	150.3	7.1	175	168.9	8.0	208	176.6	6.6
11	75.2	2.8	44	101.9	4.4	77	120.2	5.2	110	135.9	5.9	143	150.8	7.1	176	169.4	8.0	209	176.7	6.6
12	76.5	2.8	45	102.5	4.4	78	120.7	5.2	111	136.3	6.0	144	151.2	7.2	177	169.9	8.0	210	176.7	6.6
13	77.5	2.9	46	103.1	4.4	79	121.2	5.2	112	136.7	6.0	145	151.8	7.2	178	170.3	7.9	211	176.8	6.6
14	78.6	3.0	47	103.7	4.5	80	121.7	5.3	113	137.2	6.0	146	152.4	7.3	179	170.8	7.9	212	176.9	6.5
15	79.6	3.0	48	104.3	4.5	81	122.2	5.3	114	137.6	6.0	147	153.0	7.4	180	171.3	7.9	213	176.9	6.5
16	80.7	3.1	49	104.9	4.5	82	122.7	5.3	115	138.0	6.1	148	153.5	7.4	181	171.6	7.8	214	177.0	6.5
17	81.7	3.2	50	105.5	4.5	83	123.2	5.3	116	138.5	6.1	149	154.1	7.5	182	171.9	7.7	215	177.1	6.5
18	82.8	3.2	51	106.0	4.6	84	123.7	5.4	117	138.9	6.1	150	154.7	7.6	183	172.2	7.7	216	177.1	6.5
19	83.7	3.3	52	106.6	4.6	85	124.2	5.4	118	139.3	6.1	151	155.3	7.7	184	172.5	7.6			
20	84.6	3.4	53	107.2	4.6	86	124.7	5.4	119	139.8	6.2	152	155.8	7.7	185	172.8	7.5			
21	85.5	3.4	54	107.7	4.6	87	125.2	5.4	120	140.2	6.2	153	156.4	7.8	186	173.0	7.5			
22	86.4	3.5	55	108.3	4.6	88	125.7	5.5	121	140.6	6.2	154	157.0	7.9	187	173.3	7.4			
23	87.3	3.5	56	108.9	4.7	89	126.1	5.5	122	141.1	6.2	155	157.6	8.0	188	173.6	7.3			
24	88.2	3.6	57	109.4	4.7	90	126.6	5.5	123	141.5	6.3	156	158.1	8.0	189	173.9	7.3			
25	88.9	3.6	58	110.0	4.7	91	127.1	5.5	124	141.9	6.3	157	158.7	8.0	190	174.2	7.2			
26	89.7	3.7	59	110.5	4.7	92	127.6	5.5	125	142.4	6.3	158	159.4	8.1	191	174.5	7.1			
27	90.4	3.7	60	111.1	4.7	93	128.1	5.6	126	142.8	6.4	159	160.0	8.1	192	174.8	7.1			
28	91.2	3.8	61	111.7	4.8	94	128.5	5.6	127	143.2	6.4	160	160.6	8.1	193	174.9	7.0			
29	91.9	3.8	62	112.2	4.8	95	129.0	5.6	128	143.6	6.4	161	161.2	8.1	194	175.0	7.0			
30	92.6	3.9	63	112.7	4.8	96	129.5	5.6	129	144.1	6.5	162	161.8	8.2	195	175.2	7.0			
31	93.4	3.9	64	113.3	4.9	97	130.0	5.7	130	144.5	6.5	163	162.4	8.2	196	175.3	6.9			
32	94.1	3.9	65	113.8	4.9	98	130.4	5.7	131	144.9	6.5	164	163.0	8.2	197	175.4	6.9			

Legend: mo. – months; SD – standard deviation; cm - centimeters.

Figure 1. Synthetic height centiles, Legend - p3 – 3rd percentile, p5 – 5th percentile, p10 – 10th percentile, p25 – 25th percentile, p50 – 50th percentile, p75 – 75th percentile, p90 – 90th percentile, p95 – 95th percentile, p97 – 97th percentile.

Table 3. Synthetic means and SD for height – girls

Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)	Age (mo.)	Mean (cm)	SD (cm)
0	50.3	2.0	33	93.4	3.9	66	113.5	4.9	99	129.7	5.8	132	145.4	7.0	165	159.2	6.3	198	163.4	5.8
1	53.6	2.1	34	94.2	3.9	67	114.1	4.9	100	130.1	5.8	133	145.9	7.0	166	159.5	6.2	199	163.5	5.8
2	56.8	2.2	35	94.9	4.0	68	114.6	4.9	101	130.6	5.8	134	146.4	7.0	167	159.8	6.2	200	163.5	5.8
3	60.0	2.3	36	95.6	4.0	69	115.2	5.0	102	131.0	5.8	135	146.9	7.0	168	160.1	6.2	201	163.6	5.8
4	62.2	2.4	37	96.3	4.0	70	115.7	5.0	103	131.5	5.9	136	147.4	7.0	169	160.3	6.1	202	163.6	5.8
5	64.5	2.4	38	96.9	4.1	71	116.3	5.0	104	131.9	5.9	137	147.9	7.0	170	160.4	6.1	203	163.7	5.8
6	66.7	2.5	39	97.5	4.1	72	116.8	5.0	105	132.4	5.9	138	148.4	7.0	171	160.6	6.1	204	163.7	5.8
7	68.2	2.5	40	98.2	4.2	73	117.4	5.1	106	132.8	5.9	139	148.9	7.1	172	160.8	6.1	205	163.7	5.8
8	69.7	2.6	41	98.8	4.2	74	117.9	5.1	107	133.3	6.0	140	149.5	7.1	173	160.9	6.1	206	163.8	5.8
9	71.1	2.6	42	99.5	4.2	75	118.4	5.1	108	133.7	6.0	141	150.0	7.1	174	161.1	6.1	207	163.8	5.8
10	72.4	2.7	43	100.1	4.3	76	118.9	5.1	109	134.2	6.0	142	150.5	7.1	175	161.3	6.0	208	163.8	5.8
11	73.7	2.7	44	100.7	4.3	77	119.4	5.2	110	134.7	6.1	143	151.0	7.1	176	161.4	6.0	209	163.9	5.8
12	75.0	2.8	45	101.4	4.4	78	119.9	5.2	111	135.1	6.1	144	151.5	7.1	177	161.6	6.0	210	163.9	5.8
13	76.0	2.8	46	102.0	4.4	79	120.5	5.2	112	135.6	6.2	145	151.9	7.1	178	161.7	6.0	211	163.9	5.8
14	77.1	2.9	47	102.6	4.4	80	121.0	5.2	113	136.1	6.2	146	152.3	7.0	179	161.9	6.0	212	164.0	5.8
15	78.1	3.0	48	103.3	4.5	81	121.5	5.3	114	136.6	6.2	147	152.8	7.0	180	162.1	6.0	213	164.0	5.8
16	79.1	3.0	49	103.9	4.5	82	122.0	5.3	115	137.0	6.3	148	153.2	7.0	181	162.2	5.9	214	164.1	5.8
17	80.2	3.1	50	104.4	4.5	83	122.5	5.3	116	137.5	6.3	149	153.6	6.9	182	162.3	5.9	215	164.1	5.8
18	81.2	3.2	51	105.0	4.5	84	123.0	5.3	117	138.0	6.4	150	154.1	6.9	183	162.3	5.9	216	164.1	5.8
19	82.1	3.2	52	105.6	4.6	85	123.5	5.4	118	138.5	6.4	151	154.5	6.9	184	162.4	5.9			
20	83.1	3.3	53	106.2	4.6	86	123.9	5.4	119	138.9	6.5	152	154.9	6.8	185	162.5	5.9			
21	84.0	3.4	54	106.8	4.6	87	124.4	5.4	120	139.4	6.5	153	155.3	6.8	186	162.6	5.9			
22	85.0	3.4	55	107.3	4.6	88	124.8	5.5	121	139.9	6.5	154	155.8	6.8	187	162.7	5.9			
23	85.9	3.5	56	107.9	4.7	89	125.2	5.5	122	140.4	6.6	155	156.2	6.7	188	162.8	5.9			
24	86.8	3.5	57	108.5	4.7	90	125.7	5.5	123	140.9	6.6	156	156.6	6.7	189	162.9	5.9			
25	87.6	3.6	58	109.1	4.7	91	126.1	5.5	124	141.4	6.7	157	156.9	6.6	190	163.0	5.9			
26	88.3	3.6	59	109.7	4.7	92	126.6	5.6	125	141.9	6.7	158	157.2	6.6	191	163.1	5.8			
27	89.0	3.6	60	110.2	4.8	93	127.0	5.6	126	142.4	6.7	159	157.5	6.6	192	163.2	5.8			
28	89.8	3.7	61	110.8	4.8	94	127.4	5.6	127	142.9	6.8	160	157.8	6.5	193	163.2	5.8			
29	90.5	3.7	62	111.3	4.8	95	127.9	5.7	128	143.4	6.8	161	158.1	6.5	194	163.2	5.8			
30	91.2	3.8	63	111.9	4.8	96	128.3	5.7	129	143.9	6.9	162	158.4	6.4	195	163.3	5.8			
31	92.0	3.8	64	112.4	4.9	97	128.8	5.7	130	144.4	6.9	163	158.6	6.4	196	163.3	5.8			
32	92.7	3.8	65	113.0	4.9	98	129.2	5.7	131	144.9	6.9	164	158.9	6.3	197	163.4	5.8			

Legend: mo. – months; SD – standard deviation; cm – centimeters.

Figure 2. Synthetic weight centiles, Legend - p3 – 3rd percentile, p5 – 5th percentile, p10 – 10th percentile, p25 – 25th percentile, p50 – 50th percentile, p75 – 75th percentile, p90 – 90th percentile, p95 – 95th percentile, p97 – 97th percentile.

Table 4. Weight references (kg) for boys

Age (years)	p3	p5	p10	p25	p50	p75	p90	p95	p97
0	2.62	2.72	2.89	3.16	3.47	3.78	4.07	4.25	4.36
0.25	4.85	5.02	5.30	5.76	6.28	6.82	7.32	7.63	7.82
0.5	6.62	6.80	7.10	7.60	8.16	8.74	9.29	9.62	9.83
0.75	7.71	7.91	8.23	8.78	9.41	10.06	10.66	11.04	11.28
1	8.73	8.93	9.25	9.80	10.42	11.07	11.68	12.06	12.30
1.5	10.03	10.24	10.58	11.18	11.89	12.64	13.37	13.84	14.14
2	11.01	11.24	11.63	12.30	13.10	13.95	14.79	15.33	15.68
3	12.64	12.93	13.42	14.28	15.31	16.44	17.56	18.29	18.76
4	14.18	14.52	15.10	16.15	17.44	18.90	20.40	21.41	22.08
5	15.89	16.27	16.93	18.12	19.60	21.30	23.08	24.29	25.09
6	17.65	18.09	18.83	20.18	21.88	23.85	25.94	27.38	28.35
7	19.49	20.00	20.88	22.48	24.55	27.00	29.67	31.55	32.84
8	21.41	22.01	23.05	24.99	27.53	30.65	34.18	36.75	38.55
9	23.57	24.26	25.46	27.72	30.72	34.44	38.70	41.85	44.07
10	25.91	26.73	28.15	30.79	34.27	38.51	43.29	46.73	49.13
11	28.25	29.19	30.83	33.93	38.04	43.14	48.98	53.25	56.26
12	31.04	32.16	34.10	37.79	42.68	48.76	55.71	60.79	64.36
13	34.75	36.10	38.46	42.87	48.66	55.70	63.54	69.12	72.97
14	39.98	41.54	44.21	49.13	55.38	62.70	70.50	75.86	79.45
15	45.75	47.37	50.12	55.09	61.24	68.23	75.45	80.28	83.46
16	51.24	52.75	55.29	59.89	65.57	72.04	78.73	83.23	86.20
17	54.56	55.98	58.38	62.69	68.01	74.02	80.22	84.37	87.12
18	55.76	57.18	59.60	63.93	69.25	75.27	81.45	85.58	88.31

Legend: Kg – kilograms; p3 – 3rd percentile; p5 – 5th percentile; p10 – 10th percentile; p25 – 25th percentile; p50 – 50th percentile; p75 – 75th percentile; p90 – 90th percentile; p95 – 95th percentile; p97 – 97th percentile.

Table 5. Weight references (kg) for girls

Age (years)	p3	p5	p10	p25	p50	p75	p90	p95	p97
0	2.48	2.57	2.72	2.97	3.24	3.51	3.76	3.91	4.00
0.25	4.44	4.60	4.87	5.31	5.81	6.32	6.78	7.07	7.25
0.5	5.94	6.12	6.42	6.92	7.49	8.08	8.63	8.97	9.19
0.75	6.90	7.09	7.41	7.95	8.56	9.21	9.82	10.21	10.45
1	7.74	7.93	8.25	8.80	9.44	10.12	10.76	11.17	11.43
1.5	8.90	9.12	9.49	10.12	10.86	11.63	12.38	12.85	13.15
2	9.90	10.15	10.57	11.28	12.12	13.00	13.84	14.37	14.71
3	11.70	11.99	12.48	13.34	14.37	15.50	16.62	17.35	17.82
4	13.36	13.70	14.28	15.31	16.58	18.01	19.48	20.46	21.11
5	14.90	15.31	16.00	17.26	18.85	20.71	22.69	24.05	24.97
6	16.86	17.31	18.08	19.48	21.27	23.38	25.65	27.24	28.31
7	18.51	19.05	19.99	21.72	23.97	26.68	29.66	31.77	33.23
8	20.43	21.07	22.19	24.30	27.06	30.44	34.24	36.99	38.91
9	22.55	23.31	24.64	27.14	30.42	34.43	38.94	42.19	44.45
10	24.70	25.62	27.23	30.25	34.23	39.13	44.64	48.62	51.39
11	27.31	28.42	30.34	33.97	38.77	44.66	51.26	56.01	59.31
12	30.09	31.44	33.76	38.06	43.56	50.05	56.98	61.75	64.96
13	41.70	42.89	44.92	48.58	53.15	58.39	63.87	67.58	70.05
14	38.99	40.27	42.44	46.39	51.35	57.09	63.12	67.22	69.96
15	41.70	42.89	44.92	48.58	53.15	58.39	63.87	67.58	70.05
16	43.58	44.71	46.64	50.13	54.52	59.60	64.97	68.65	71.11
17	44.35	45.48	47.41	50.92	55.37	60.56	66.11	69.94	72.52
18	44.61	45.75	47.70	51.27	55.78	61.05	66.70	70.60	73.23

Legend: Kg – kilograms; p3 – 3rd percentile; p5 – 5th percentile; p10 – 10th percentile; p25 – 25th percentile; p50 – 50th percentile; p75 – 75th percentile; p90 – 90th percentile; p95 – 95th percentile; p97 – 97th percentile.

Table 6. BMI reference (kg/m²) for boys

Age (years)	p3	p5	p10	p25	p50	p75	p90	p95	p97
0	11.35	11.56	11.91	12.51	13.19	13.92	14.62	15.06	15.34
0.25	14.55	14.81	15.23	15.96	16.80	17.70	18.55	19.10	19.44
0.5	15.10	15.37	15.81	16.58	17.48	18.43	19.35	19.94	20.32
0.75	15.06	15.35	15.82	16.64	17.61	18.65	19.66	20.32	20.74
1	14.91	15.19	15.66	16.47	17.44	18.48	19.51	20.18	20.61
1.5	14.45	14.71	15.16	15.95	16.89	17.92	18.95	19.62	20.06
2	14.13	14.38	14.80	15.53	16.41	17.38	18.35	18.99	19.40
3	14.05	14.27	14.64	15.28	16.06	16.92	17.79	18.36	18.74
4	13.94	14.15	14.48	15.08	15.81	16.61	17.43	17.97	18.32
5	13.76	13.96	14.30	14.90	15.65	16.48	17.35	17.92	18.31
6	13.72	13.93	14.29	14.93	15.73	16.65	17.62	18.28	18.73
7	13.74	13.97	14.36	15.08	15.99	17.06	18.23	19.06	19.62
8	13.97	14.21	14.63	15.39	16.38	17.56	18.88	19.82	20.48
9	14.34	14.59	15.02	15.83	16.88	18.17	19.62	20.68	21.43
10	14.72	15.00	15.46	16.34	17.48	18.90	20.52	21.73	22.60
11	15.17	15.46	15.95	16.88	18.11	19.64	21.41	22.74	23.70
12	15.51	15.82	16.35	17.35	18.67	20.31	22.23	23.66	24.70
13	16.02	16.34	16.90	17.94	19.33	21.07	23.10	24.63	25.74
14	16.47	16.81	17.41	18.52	19.99	21.83	23.97	25.58	26.74
15	17.06	17.41	18.01	19.14	20.60	22.40	24.45	25.95	27.02
16	17.61	17.96	18.57	19.71	21.20	23.01	25.07	26.58	27.64
17	17.99	18.35	18.98	20.14	21.66	23.52	25.62	27.16	28.24
18	18.15	18.53	19.18	20.38	21.95	23.86	26.01	27.57	28.67

Legend: BMI – body mass index; kg/m² – kilograms/square meters; p3 – 3rd percentile; p5 – 5th percentile; p10 – 10th percentile; p25 – 25th percentile; p50 – 50th percentile; p75 – 75th percentile; p90 – 90th percentile; p95 – 95th percentile; p97 – 97th percentile.

Table 7. BMI reference (kg/m²) for girls

Age (years)	p3	p5	p10	p25	p50	p75	p90	p95	p97
0	11.26	11.45	11.77	12.31	12.94	13.60	14.23	14.62	14.87
0.25	13.62	13.87	14.28	14.99	15.81	16.69	17.53	18.06	18.40
0.5	14.44	14.70	15.12	15.85	16.70	17.62	18.51	19.08	19.44
0.75	14.61	14.87	15.30	16.07	16.97	17.96	18.93	19.56	19.97
1	14.56	14.82	15.25	16.00	16.90	17.89	18.86	19.50	19.91
1.5	14.20	14.44	14.85	15.58	16.47	17.46	18.48	19.15	19.60
2	13.92	14.15	14.53	15.22	16.07	17.04	18.05	18.73	19.18
3	13.67	13.88	14.25	14.91	15.73	16.67	17.65	18.33	18.78
4	13.59	13.79	14.14	14.77	15.57	16.49	17.49	18.18	18.65
5	13.39	13.61	13.97	14.64	15.49	16.50	17.61	18.40	18.94
6	13.46	13.67	14.04	14.72	15.59	16.64	17.80	18.64	19.23
7	13.46	13.70	14.11	14.87	15.85	17.06	18.42	19.42	20.12
8	13.69	13.95	14.39	15.21	16.28	17.57	19.02	20.08	20.82
9	13.95	14.23	14.70	15.58	16.73	18.12	19.68	20.82	21.62
10	14.30	14.60	15.12	16.08	17.34	18.88	20.61	21.88	22.77
11	14.72	15.04	15.60	16.65	18.01	19.67	21.55	22.92	23.88
12	15.04	15.41	16.05	17.24	18.81	20.76	22.99	24.64	25.81
13	15.60	15.99	16.65	17.90	19.54	21.58	23.92	25.66	26.89
14	16.32	16.69	17.34	18.55	20.12	22.03	24.19	25.75	26.85
15	16.94	17.30	17.92	19.06	20.52	22.28	24.20	25.58	26.52
16	17.31	17.67	18.29	19.41	20.83	22.50	24.30	25.56	26.41
17	17.51	17.86	18.47	19.57	20.96	22.60	24.35	25.56	26.39
18	17.57	17.92	18.53	19.63	21.00	22.60	24.29	25.45	26.24

Legend: BMI – body mass index; kg/m² – kilograms/square meters; p3 – 3rd percentile; p5 – 5th percentile; p10 – 10th percentile; p25 – 25th percentile; p50 – 50th percentile; p75 – 75th percentile; p90 – 90th percentile; p95 – 95th percentile; p97 – 97th percentile.

Figure 3. Synthetic BMI centiles Legend - p3 – 3rd percentile, p5 – 5th percentile, p10 – 10th percentile, p25 – 25th percentile, p50 – 50th percentile, p75 – 75th percentile, p90 – 90th percentile, p95 – 95th percentile, p97 – 97th percentile.

Figure 4. Height (a) and BMI (b) differences between the synthetic and the common used references.

Legend - Ro - Romanian synthetic reference, CDC - US growth reference, WHO - World Health Organization's growth reference, Prader - Swiss growth reference, IOTF - International Obesity Task Force reference.

0.001 at 2.5 years (IOTF).

For girls these maximum differences are of 0.91 kg/sqm at 2 months (WHO), respectively 1.14 kg/sqm at 12 years (IOTF). The smallest difference was

0.007 kg/sqm at 16.6 years for the WHO and 0.003 kg/sqm at 3.4 years for the IOTF.

On average the new Romanian synthetic references show that boys have a 0.68 ± 0.31 kg/sqm

higher BMI than the WHO and 0.9 ± 0.53 kg/sqm than the IOTF reference population. For girls the same average differences are 0.41 ± 0.32 kg/sqm for the WHO reference and 0.63 ± 0.38 kg/sqm for the IOTF standard (Fig. 4b).

DISCUSSION

From 1997 to 2003, the WHO performed a Multicenter Growth Study collecting data from six countries (United States, Brazil, Ghana, India, Norway, and Oman) on the growth of children from affluent families. The key assumption was that “environmental differences rather than genetic endowments are the principal determinants of disparities in physical growth” (15). These children were exclusively or predominantly breastfed for at least 4-6 months, complementary foods were introduced by 6 months of age, and breastfeeding was continued to at least 12 months of age, and they showed similar growth patterns. Since it was considered not feasible to perform similar longitudinal growth studies in older children, WHO developed a growth reference based on the 1977 USA growth study as an international “normative”, though in fact descriptive, chart from 5 to 19 years of age (16).

Previous clinical experience in Romanian children strongly questions that WHO standards/references are truly suitable for the Romanian population. Particularly in view of current secular trends in height and the marked economic progress in Romania, it appeared desirable to actualize previous National Romanian growth charts.

Recent meta-analyses of historic data (17) summarized currently known empirical data on a century of trends in global adult human height from 1914 to 2014 and reports variation between and within populations of up to 20 cm. This proves the need for up to date growth curves.

The aim of this study was to derive synthetic national growth references for the Romanian population. This approach has been proven cost-effective and in statistical agreement with the classical studies for constructing growth charts and has been used in countries where recent growth charts are not available (Georgia, Kazakhstan) (18) or for specific ethnic sub-populations (19).

There are previous regional studies aiming to provide new growth references (2,3), but there is no recent one with a national representative sample. Limitations of the studies include: all data are from school measurements, which are subject to sampling

error. Medical history was not analyzed, therefore children with conditions which might impair normal growth and development were not excluded. The majority of the studies consisted of children from urban areas. It is worth mentioning that in one sub-study (data from Targu Mures) children in urban areas have higher odds of being short, but not overweight comparing to their rural counterparts (20). Further studies regarding the existing ethnic and maybe regional differences are needed. According to the latest census, 3% of the Romanian population is of Romanes ethnicity (21), almost the same percentage as the Turkish population in Germany (22). In Germany (19) and also in the Netherlands (23, 24), special growth charts are available for ethnic minorities.

In conclusion, we suggest synthetic growth references based upon recent growth data from 6 different Romanian regions as new National Growth Charts for Romanian children.

Conflict of interest

The authors declare that they have no conflict of interest concerning this article.

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