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ORIGINAL ARTICLE

Blood pressure reference values for European non-overweight school children: The IDEFICS study

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OBJECTIVES: To provide oscillometric blood pressure (BP) reference values in European non-overweight school children.
DESIGN: Cross-sectional analysis from the IDEFICS study (www.ideficsstudy.eu) database.
METHODS: Standardised BP and anthropometric measures were obtained from children aged 2 to 10.9 years, participating in the 2007–2008 and 2009–2010 IDEFICS surveys. Age- and height-specific systolic and diastolic pressure percentiles were calculated by GAMLSS, separately for boys and girls, in both the entire population ($n = 16\,937$) and the non-overweight children only ($n = 13\,547$). The robustness of the models was tested by sensitivity analyses carried out in both population samples.
RESULTS: Percentiles of BP distribution in non-overweight children were provided by age and height strata, separately for boys and girls. Diastolic BP norms were slightly higher in girls than in boys for similar age and height, while systolic BP values tended to be higher in boys starting from age 5 years. Sensitivity analysis, comparing BP distributions obtained in all children with those of non-overweight children, showed that the inclusion of overweight/obese individuals shifted the references values upward, in particular systolic BP in girls at the extreme percentiles.
CONCLUSIONS: The present analysis provides updated and timely information about reference values for BP in children aged 2 to <11 years that may be useful for monitoring and planning population strategies for disease prevention.

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INTRODUCTION

Measuring blood pressure (BP) during physical examination in paediatric clinical practice was quite unusual until a few years ago. As a result, BP distributions for children have only been published recently. In particular, this gap has been filled by the publication of the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents[1] by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (NHBPEP), who provided systolic (SBP) and diastolic (DBP) pressure percentiles stratified by sex and height from a large US representative population aged 1–17 years.

BP in children is determined by both height and, as for adults,[2] weight; however, in the paediatric age group, the portion attributable to height may be physiological, whereas that contributed by excess weight may not be. Indeed the NHBPEP percentiles were stratified by height, but also included overweight and obese children.[1] Accordingly, the increased prevalence of paediatric hypertension previously reported[3] could be explained partly by the increased prevalence of overweight and obesity in children.[4] However, the inclusion of overweight individuals in the normative BP values might lead to values as high as those that are used to define higher-than-normal BP in adults (for example, $>120/80$ mm Hg),[2] being considered as 'normal BP' for a child. For these reasons, Rosner *et al.*[5] first calculated normative BP values in non-overweight children only and, for this purpose, re-analysed the NHBPEP data;[1] thus, reference BP values in childhood and adolescence are available for the US population in both the entire population[1] and non-overweight individuals.[5]

In Europe, normative BP values are available from several population samples[6–9] in which overweight and obese children were included; BP norms for non-overweight children and adolescents are available from European studies only referring to single countries, namely Germany[10] and Poland.[11]

The present study aims to provide age-, height-, and sex-stratified SBP and DBP reference values in non-overweight European children, 2.0–10.9 years old, participating in the IDEFICS study. Further, the study compared these normative values with those obtained from the entire sample of children participating in the study by including overweight and obese children in the analysis.

PARTICIPANTS AND METHODS

The IDEFICS study (Identification and prevention of Dietary- and lifestyle-induced health EFfects In Children and infantS) is an epidemiological multicentre European project, funded by the European Commission within the Sixth Framework Program, that aimed to identify nutritional and lifestyle-associated aetiological factors linked to childhood obesity and related morbidities. A cohort of 16 228 children aged 2–9 years (51% of the eligible sample), recruited from eight European countries (Germany, Hungary, Italy, Cyprus, Spain, Estonia, Sweden and Belgium), was examined at baseline between September 2007 and May 2008, according to a standardised protocol.[12] A follow-up survey was carried out from September 2009 to May 2010, during which an additional 2517 children, who did not

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participate in the baseline survey, were included (newcomers). Parents, or legal guardians, provided written informed consent to participate in the full programme or in a selected set of examination modules. For each survey centre, the approval of the local ethics committee was obtained.

The overall sample (Figure 1) included 16 937 children (baseline survey plus newcomers at the follow-up survey) aged 2.0–10.9 years after the exclusion of 1808 participants (boys = 50.8%; age = 5.2 ± 1.9 years; body mass index (BMI) = 16.3 ± 2.3 kg m^{-2}, mean (*M*) ± s.d.) for whom BP data were missing, who were on average slightly younger than those included. For the purposes of the present analysis, the subgroup of non-overweight children ($n = 13\,547$) was selected for the main analysis.

Physical examination

Children underwent physical examination in a quiet and warm room, according to a standardised procedure with validated intra- and inter-observer reliability for all the measurements.[13,14] Body weight was measured, with participants fasting and wearing underwear, using a prototype of the TANITA BC 420 SMA digital scale (TANITA Europe GmbH, Sindelfingen, Germany) specifically adapted for children. Height was measured by a stadiometer (seca 225, seca, Birmingham, UK), with children standing with feet slightly apart and back touching the vertical board and with head in a Frankfort plane. As for the weight measurement, the children were wearing underwear only, with all hair ornaments removed and all braids undone. For the purpose of the present analysis, sex-specific height percentiles were calculated for each 1-year age step.

BMI was calculated as weight in kilograms divided by the square of the height in meters. Participants were classified as normal weight, overweight or obese according to the standard criteria adopted by the International Childhood Obesity Task Force, recently updated by Cole and Lobstein.[15] The present analysis was carried out in both the entire population and non-overweight children only.

BP was measured with an automated oscillometric device (Welch Allyn 4200B-E2, Welch Allyn Inc., Skaneateles Falls, NY, USA),[16] according to a standardised procedure. Briefly, the right arm was commonly used, unless it was injured. For the choice of the appropriate cuff size, arm circumference measurement was taken; the length of the upper arm was determined by measuring (with a SECA 200 band) the distance between the acromion and the olecranon along the lateral side of the upper arm with the participant standing upright, with the elbow flexed to 90° with the palm facing superiorly. The midpoint was marked on the lateral side of the arm. With the arm relaxed and the elbow extended with the palm facing the observer, the tape was placed around the arm without compressing the tissues, perpendicularly to the long axis of the arm at the marked midpoint, and the circumference recorded to the nearest 0.1 cm. The cuff length for BP measurement was chosen according to the arm circumference and positioned with the bottom edge ~2 cm above the cubital fossa.[1]

Children were asked to sit for at least 5 min before measurement, with pre-school children seated preferably on their parent's lap. Older children were asked to sit in a chair supporting the back and feet with legs uncrossed. A pillow was used, if necessary, to support the arm while the measurement was taken. Two recordings were taken, with a 2-min interval between each, plus a further measurement in case of a >5% difference in BP between the first two readings. The average of the two (or three) measurements was used for statistical analysis.

Databases included automated plausibility checks. All numerical variables were entered twice, independently. Inconsistencies identified by additional plausibility checks were rectified by the study centres.

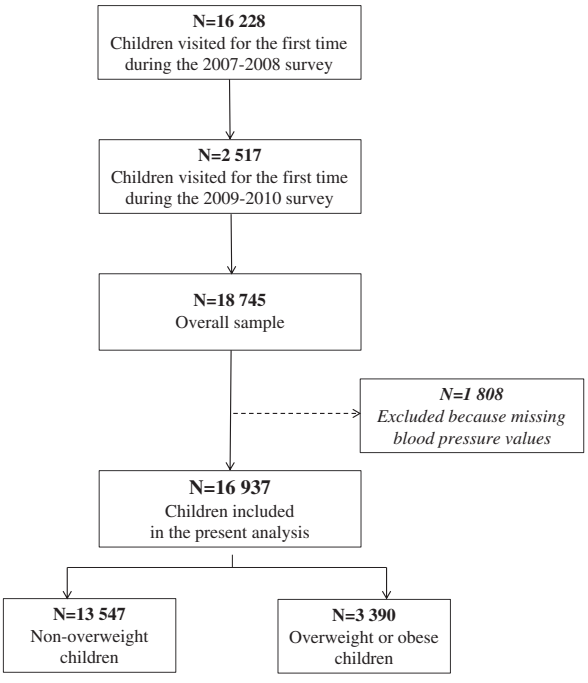

Figure 1. Composition of the sample under investigation.

BP percentile calculation

To calculate percentile curves for the whole study sample and non-overweight children, we used the General Additive Model for Location Scale and Shape (GAMLSS) that was developed by Rigby and Stasinopoulos.[16] This method is an extension of the LMS method to model the distribution of SBP and DBP depending on multiple covariates while accounting for dispersion, skewness,and particularly the kurtosis of this distribution.[17,18]

We calculated percentile curves of SBP and DBP as a function of the covariates age and height stratified by sex using the GAMLSS method as extension of the LMS method. The LMS method models three parameters: the skewness (*L*) accounts for the deviation from a normal distribution using a Box–Cox transformation, the median (*M*) of the outcome variable is modelled depending on one explanatory variable, and the coefficient of variation (*S*) accounts for the variation of data points around the mean and adjusts for non-uniform dispersion. The GAMLSS method is able to particularly model the kurtosis using other distributions and to include more than one covariate. We used the GAMLSS package (version 4.1–0) of the statistical software R (version 3.0.1).[19] Different distributions, that is, Box–Cox power exponential, Box–Cox Cole and Green, and Box–Cox t (BCT) distribution, were fitted to the observed distributions of SBP as well as DBP. Moreover, the influence of age and height on parameters of the considered distributions were modelled as a constant, as a linear function or as a cubic spline of the covariates. Worm plots were used as a diagnostic tool to assess whether adjustment for kurtosis was required.[20] Goodness of fit was assessed by the Bayesian Information Criterion and by Q–Q plots to select the final model including the fitted distribution of SBP and DBP and the influence of covariates on distribution parameters. Finally, age- and height-dependent curves for the 1st, 3rd, 10th, 25th, 50th, 75th, 90th, 97th and 99th percentiles were calculated based on the model that showed the best goodness of fit,[18,19] separately for boys and girls.

With regard to the complete sample, the final models for both SBP and DBP in boys and girls were based on a BCT distribution. With regard to SBP, in both samples $\log(\mu)$ for boys and μ for girls were modelled as a linear function of age and height, and $\log(\sigma)$, ν and $\log(\tau)$ as constant for both sexes with one exception: in non-overweight girls ν was linearly dependent on age. With regard to DPB, in both samples μ was modelled as a linear function of age and height for girls and non-overweight boys, but in the overall sample of boys $\log(\mu)$ was modelled as a linear function of age and height. In all DBP models the parameters $\log(\sigma)$, ν and $\log(\tau)$ were considered as constant.

BP percentiles (for SBP and DBP) of the resulting curves in both non-overweight children only and the entire population were reported stratified by 1-year age steps from 2.0 to 10.9 years and by seven age-specific height percentiles (3rd, 10th, 25th, 50th, 75th, 90th and 97th).

For sensitivity analyses, we compared the 1st, 10th, 25th, 50th, 75th, 90th and 99th percentile curves based on the whole study sample with the percentile curves based on non-overweight children for both SBP and DBP.

RESULTS

Table 1 shows the characteristics of the population under investigation, either as a whole (panel A) or restricted to non-overweight children (panel B). The sample was equally composed of boys and girls (girls = 49.6% and 48.8% in the entire population and in non-overweight children, respectively). The prevalence of overweight/obesity was 21% for girls and 19% for boys. However,

Table 1. Characteristics of participants: (a) entire population; (b) non-overweight children only

Age (years)	*Girls*										*Boys*									
	2–< 3	*3–< 4*	*4–< 5*	*5–< 6*	*6–< 7*	*7–< 8*	*8–< 9*	*9–< 10*	*10–< 11*	*All*	*2–< 3*	*3–< 4*	*4–< 5*	*5–< 6*	*6–< 7*	*7–< 8*	*8–< 9*	*9–< 10*	*10–< 11*	*ALL*
(a)																				
N	200	960	1196	1002	1398	1945	1287	299	112	8399	224	1016	1290	1121	1390	1854	1239	286	118	8538
Height (cm)	93 (3)	100 (4)	106 (5)	114 (5)	120 (5)	126 (5)	131 (5)	137 (7)	143 (6)	119 (13)	94 (4)	101 (5)	108 (5)	114 (5)	121 (5)	128 (5)	132 (6)	138 (6)	142 (6)	119 (13)
BMI (kg m^{-2})	16.1 (1.6)	15.9 (1.5)	15.8 (1.9)	15.9 (2.1)	16.3 (2.5)	16.8 (2.8)	17.3 (3.1)	18.1 (3.5)	18.0 (3.7)	16.5 (2.6)	16.3 (1.4)	15.9 (1.5)	15.9 (1.8)	16.0 (2.0)	16.4 (2.7)	16.9 (2.8)	17.3 (3.1)	17.9 (3.3)	18.2 (3.2)	16.5 (2.6)
Ow/Ob (%)	14.5	12.0	16.0	20.0	23.0	24.0	28.0	29.0	23.0	21.0	10.0	9.0	13.0	16.0	22.0	25.0	23.0	28.0	36.0	19.0
SBP (mm Hg)	94 (7)	96 (8)	98 (8)	99 (8)	101 (9)	103 (9)	105 (9)	106 (8)	111 (9)	101 (9)	94 (7)	96 (8)	97 (8)	99 (8)	102 (8)	104 (9)	105 (9)	107 (9)	108 (8)	101 (9)
DBP (mm Hg)	63 (6)	63 (6)	63 (6)	63 (6)	64 (6)	65 (6)	65 (6)	65 (6)	67 (6)	64 (6)	61 (6)	62 (6)	61 (6)	62 (6)	63 (6)	64 (6)	64 (6)	65 (6)	66 (7)	63 (7)
(b)																				
N	177	845	1007	810	1075	1471	926	211	87	6609	201	926	1129	948	1088	1390	958	207	91	6938
Height (cm)	92 (3)	100 (4)	106 (4)	113 (5)	120 (5)	126 (5)	131 (5)	136 (7)	142 (6)	117 (12)	94 (4)	101 (4)	108 (4)	114 (5)	121 (5)	127 (5)	131 (5)	138 (7)	140 (6)	118 (12)
BMI (kg m^{-2})	15.7 (1.0)	15.5 (1.0)	15.2 (1.1)	15.1 (1.1)	15.2 (1.2)	15.5 (1.3)	15.7 (1.5)	16.2 (1.5)	16.4 (1.9)	15.4 (1.3)	16.0 (1.1)	15.6 (1.1)	15.4 (1.1)	15.3 (1.1)	15.3 (1.2)	15.6 (1.2)	15.9 (1.4)	16.2 (1.5)	16.8 (1.7)	15.6 (1.2)
SBP (mm Hg)	94 (7)	96 (8)	97 (8)	98 (8)	100 (8)	102 (8)	103 (8)	104 (7)	109 (8)	100 (9)	94 (7)	96 (8)	97 (8)	99 (8)	100 (8)	102 (8)	104 (8)	106 (9)	107 (7)	100 (8)
DBP (mm Hg)	62 (6)	63 (6)	62 (6)	63 (6)	63 (6)	64 (6)	64 (6)	64 (5)	67 (6)	63 (6)	61 (6)	62 (6)	61 (6)	62 (6)	63 (6)	63 (6)	64 (6)	65 (6)	65 (7)	62 (6)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; Ow/Ob, overweight/obesity; SBP, systolic blood pressure. Data are shown as mean (s.d.).

differences in prevalence were observed across age categories, with overweight and obesity being less common among kindergarten children in comparison with older participants (Table 1).

Table 2 shows the age- and height-stratified SBP distribution in non-overweight children participating in the IDEFICS study; in particular, the 1st, 3rd, 10th, 25th, 50th, 75th, 90th, 97th and 99th SBP percentiles are shown separately for boys and girls. Similarly, Table 3 shows the same DBP percentiles in non-overweight children by age and height.

BP showed a significant positive age and height trend. It seems as though this trend is more pronounced for height (Supplementary Figures A and B) in the age range under investigation. SBP percentiles tended to be higher in girls than in boys up to the age of 5 years; subsequently the trend was reversed, with higher BP values in boys than in girls; as depicted in Table 2, the older the child, the greater the difference between sexes. DBP, in contrast, showed a different pattern (Table 3), being higher in girls than in boys at any age under investigation.

The corresponding age- and height-specific SBP and DBP percentiles from the population as a whole are provided, separately for boys and girls, in Supplementary Tables A and B.

In Figure 2, BP percentiles (1st, 3rd, 10th, 25th, 50th, 75th, 90th, 97th and 99th) are depicted in non-overweight girls (left) and boys (right); in particular, SBP (top panels) and DBP (bottom panels) at median height were obtained from age 2 to 10.9 years. The plots show, in both girls and boys, a steeper increase of SBP than DBP; further, as expected, a trend to higher DBP values in girls than in boys was observed in the age range under investigation.

Figure 3 shows the same data as in Figure 2, but referring to the entire population, thus also including overweight and obese children: in this case, differences between sexes, in particular higher DBP values at the same age and height, were even more apparent. Further, in this sample, 12.7% and 9.0% of children showed SBP and DBP values, respectively, above the 97th percentile calculated in non-overweight children.

Finally, sensitivity analyses were carried out (Figure 4) at 1st, 10th, 25th, 50th, 75th, 90th and 99th SBP (top panels) and DBP (bottom panels) in girls (left) and boys (right) in order to compare the plots between the whole sample and non-overweight children only. There was an apparently more pronounced positive age trend of SBP values in girls than in boys at the extreme percentiles of the distribution when overweight and obese children were included in the analysis. Sensitivity analysis did not show differences in DBP plots between the entire sample and overweight/obese children only, for both boys and girls.

DISCUSSION

The present study provides normative age- and height-specific SBP and DBP values drawn from a large sample of European girls and boys in the age range 2.0–10.9 years participating in the IDEFICS study. BP percentiles were calculated in non-overweight children and in the entire population and then sensitivity analyses were carried out to test the robustness of our models.

The study shows that, among non-overweight children, SBP is higher in girls than in boys up to the age of 5 years, a trend that is reversed in older children, while DBP distribution is shifted to the right in girls, in comparison with boys, at any age and percentile of height. Differences in BP between boys and girls (with higher values in the latter) have been previously documented in the age range 2–11 years, both in the general population[21–24] and in selected samples of non-overweight children adopting the GAMLSS method.[5,10]

The study also provides a comparison between BP norms obtained in a large sample of school children either including or excluding overweight or obese participants. It is apparent from this analysis that differences between sexes appear to be more

Table 2. Percentiles of systolic BP (mm Hg) in non-overweight children calculated with GAMLSS

Age (years)	*Ht (cm)*	*Percentiles for girls*									*Age (years)*	*Ht (cm)*	*Percentiles for boys*								
		1	*3*	*10*	*25*	*50*	*75*	*90*	*97*	*99*			*1*	*3*	*10*	*25*	*50*	*75*	*90*	*97*	*99*
2– < 3 (*n* = 200)	85	76.1	78.6	82.1	86.0	90.7	96.0	101.5	108.0	113.7	2– < 3 (*n* = 224)	85	74.5	77.7	81.9	86.0	90.6	95.6	100.5	106.0	110.8
	87	76.6	79.1	82.7	86.6	91.3	96.6	102.2	108.7	114.4		88	75.2	78.4	82.6	86.8	91.5	96.5	101.4	107.0	111.8
	89	77.1	79.6	83.2	87.1	91.9	97.3	102.9	109.4	115.2		91	75.9	79.2	83.4	87.6	92.3	97.4	102.4	108.0	112.9
	92	77.8	80.4	84.0	88.0	92.8	98.2	103.9	110.5	116.3		93	76.3	79.6	83.9	88.1	92.9	98.0	103.0	108.7	113.6
	94	78.3	80.9	84.6	88.5	93.4	98.8	104.5	111.2	117.0		96	77.0	80.4	84.7	88.9	93.8	98.9	103.9	109.7	114.6
	97	79.1	81.7	85.4	89.4	94.2	99.8	105.5	112.2	118.1		98	77.5	80.9	85.2	89.5	94.3	99.5	104.6	110.3	115.3
	100	79.8	82.4	86.2	90.2	95.1	100.7	106.5	113.3	119.2		101	78.2	81.6	85.9	90.3	95.2	100.4	105.5	111.3	116.3
3– < 4 (*n* = 960)	92	77.3	80.0	83.7	87.7	92.5	97.9	103.4	109.7	115.2	3– < 4 (*n* = 1016)	92	76.0	79.3	83.6	87.8	92.5	97.6	102.6	108.2	113.1
	95	78.0	80.7	84.5	88.5	93.4	98.8	104.4	110.8	116.3		95	76.7	80.0	84.3	88.6	93.4	98.5	103.5	109.2	114.1
	97	78.5	81.2	85.0	89.1	94.0	99.4	105.0	111.5	117.0		98	77.4	80.8	85.1	89.4	94.2	99.4	104.5	110.2	115.2
	100	79.3	82.0	85.8	89.9	94.9	100.4	106.0	112.5	118.1		101	78.1	81.5	85.8	90.2	95.1	100.3	105.4	111.2	116.2
	102	79.8	82.5	86.4	90.5	95.4	101.0	106.7	113.2	118.8		103	78.6	82.0	86.4	90.7	95.6	100.9	106.0	111.9	116.9
	105	80.5	83.3	87.2	91.3	96.3	101.9	107.7	114.3	119.9		106	79.3	82.7	87.1	91.5	96.5	101.7	107.0	112.9	117.9
	108	81.3	84.1	88.0	92.2	97.2	102.9	108.7	115.3	121.1		109	80.0	83.4	87.9	92.3	97.3	102.6	107.9	113.9	119.0
4– < 5 (*n* = 1196)	98	78.2	81.0	84.9	89.1	94.0	99.4	104.9	111.1	116.3	4– < 5 (*n* = 1290)	99	77.6	80.9	85.2	89.5	94.4	99.6	104.7	110.4	115.4
	101	79.0	81.8	85.7	89.9	94.9	100.4	105.9	112.1	117.4		102	78.3	81.7	86.0	90.4	95.3	100.4	105.6	111.4	116.4
	104	79.7	82.6	86.5	90.7	95.8	101.3	106.9	113.2	118.5		105	79.0	82.4	86.8	91.2	96.1	101.3	106.6	112.4	117.5
	107	80.5	83.3	87.3	91.6	96.6	102.2	107.9	114.2	119.6		108	79.7	83.1	87.5	92.0	96.9	102.2	107.5	113.4	118.5
	110	81.2	84.1	88.1	92.4	97.5	103.2	108.9	115.3	120.7		111	80.4	83.8	88.3	92.8	97.8	103.1	108.4	114.4	119.5
	113	81.9	84.9	88.9	93.3	98.4	104.1	109.9	116.3	121.8		114	81.1	84.6	89.1	93.6	98.6	104.0	109.4	115.4	120.6
	116	82.7	85.6	89.7	94.1	99.3	105.0	110.8	117.4	122.9		117	81.8	85.3	89.8	94.4	99.5	104.9	110.3	116.4	121.6
5– < 6 (*n* = 1002)	104	79.2	82.1	86.2	90.4	95.5	101.0	106.4	112.4	117.5	5– < 6 (*n* = 1121)	105	78.9	82.3	86.7	91.1	96.0	101.2	106.4	112.3	117.4
	108	80.2	83.1	87.2	91.6	96.7	102.2	107.7	113.8	119.0		108	79.6	83.0	87.5	91.9	96.8	102.1	107.4	113.3	118.4
	111	80.9	83.9	88.0	92.4	97.6	103.1	108.7	114.9	120.0		111	80.3	83.7	88.2	92.7	97.7	103.0	108.3	114.3	119.4
	114	81.6	84.7	88.8	93.2	98.4	104.1	109.7	115.9	121.1		115	81.2	84.7	89.2	93.7	98.8	104.2	109.6	115.6	120.8
	117	82.4	85.4	89.6	94.1	99.3	105.0	110.7	117.0	122.2		118	81.9	85.4	90.0	94.5	99.7	105.1	110.5	116.6	121.8
	120	83.1	86.2	90.4	94.9	100.2	106.0	111.7	118.0	123.3		121	82.6	86.2	90.8	95.4	100.5	106.0	111.5	117.6	122.9
	123	83.8	87.0	91.2	95.8	101.1	106.9	112.7	119.1	124.4		125	83.5	87.1	91.8	96.4	101.7	107.2	112.7	118.9	124.3
6– < 7 (*n* = 1398)	110	80.1	83.2	87.4	91.8	97.0	102.5	107.9	113.8	118.7	6– < 7 (*n* = 1390)	111	80.2	83.7	88.1	92.6	97.6	102.9	108.2	114.2	119.3
	113	80.8	83.9	88.2	92.7	97.9	103.4	108.9	114.9	119.8		115	81.1	84.6	89.2	93.7	98.7	104.1	109.5	115.5	120.7
	117	81.8	85.0	89.3	93.8	99.1	104.7	110.2	116.3	121.2		118	81.8	85.4	89.9	94.5	99.6	105.0	110.4	116.5	121.7
	120	82.5	85.7	90.1	94.6	99.9	105.6	111.2	117.3	122.3		121	82.5	86.1	90.7	95.3	100.4	105.9	111.3	117.5	122.8
	123	83.3	86.5	90.9	95.5	100.8	106.6	112.2	118.4	123.4		125	83.5	87.1	91.7	96.3	101.6	107.1	112.6	118.8	124.1
	127	84.2	87.5	91.9	96.6	102.0	107.8	113.5	119.7	124.9		128	84.2	87.8	92.5	97.1	102.4	108.0	113.5	119.8	125.2
	130	85.0	88.3	92.7	97.4	102.9	108.8	114.5	120.8	126.0		132	85.1	88.7	93.5	98.2	103.5	109.2	114.8	121.1	126.6
7– < 8 (*n* = 1945)	115	80.7	84.0	88.4	92.9	98.2	103.7	109.1	114.9	119.6	7– < 8 (*n* = 1854)	117	81.5	85.0	89.6	94.1	99.2	104.6	110.0	116.0	121.3
	119	81.7	85.0	89.4	94.1	99.4	105.0	110.4	116.3	121.0		120	82.2	85.8	90.3	94.9	100.0	105.5	110.9	117.0	122.3
	123	82.6	86.0	90.5	95.2	100.5	106.2	111.7	117.7	122.5		124	83.1	86.7	91.4	96.0	101.2	106.7	112.2	118.4	123.7
	126	83.4	86.7	91.3	96.0	101.4	107.2	112.7	118.7	123.6		127	83.8	87.5	92.1	96.8	102.0	107.6	113.1	119.3	124.7
	130	84.3	87.8	92.4	97.1	102.6	108.4	114.0	120.1	125.0		131	84.8	88.4	93.1	97.8	103.2	108.8	114.4	120.7	126.1
	133	85.1	88.5	93.2	98.0	103.5	109.4	115.0	121.1	126.1		134	85.5	89.1	93.9	98.6	104.0	109.7	115.3	121.7	127.1
	137	86.1	89.5	94.2	99.1	104.7	110.6	116.3	122.5	127.5		138	86.4	90.1	94.9	99.7	105.1	110.9	116.6	123.0	128.5
8– < 9 (*n* = 1287)	120	81.3	84.7	89.3	94.0	99.4	105.0	110.3	116.0	120.5	8– < 9 (*n* = 1239)	122	82.6	86.2	90.8	95.3	100.5	106.0	111.4	117.6	122.9
	124	82.3	85.7	90.4	95.2	100.6	106.2	111.6	117.3	121.9		126	83.5	87.1	91.8	96.4	101.6	107.2	112.7	118.9	124.2
	128	83.2	86.8	91.5	96.3	101.8	107.5	112.9	118.7	123.4		129	84.2	87.9	92.5	97.2	102.5	108.1	113.6	119.9	125.3
	132	84.2	87.8	92.5	97.4	102.9	108.7	114.2	120.1	124.8		133	85.2	88.8	93.6	98.3	103.6	109.3	114.9	121.2	126.7
	136	85.2	88.8	93.6	98.5	104.1	110.0	115.6	121.5	126.2		137	86.1	89.8	94.6	99.4	104.7	110.5	116.1	122.5	128.0
	139	85.9	89.5	94.4	99.4	105.0	110.9	116.5	122.5	127.3		140	86.8	90.5	95.4	100.2	105.6	111.4	117.1	123.5	129.1
	143	86.9	90.5	95.5	100.5	106.2	112.2	117.8	123.9	128.8		144	87.7	91.5	96.4	101.2	106.7	112.5	118.3	124.9	130.5
9– < 10 (*n* = 299)	125	81.9	85.5	90.3	95.1	100.6	106.2	111.5	117.0	121.4	9– < 10 (*n* = 286)	127	83.7	87.3	92.0	96.6	101.8	107.4	112.9	119.1	124.5
	130	83.1	86.7	91.6	96.5	102.1	107.8	113.1	118.8	123.2		131	84.6	88.3	93.0	97.7	103.0	108.6	114.2	120.4	125.9
	134	84.0	87.7	92.7	97.7	103.2	109.0	114.4	120.1	124.6		134	85.3	89.0	93.7	98.5	103.8	109.5	115.1	121.4	126.9
	138	85.0	88.7	93.7	98.8	104.4	110.3	115.7	121.5	126.1		138	86.2	90.0	94.8	99.5	104.9	110.7	116.3	122.8	128.3
	142	85.9	89.8	94.8	99.9	105.6	111.5	117.1	122.9	127.5		142	87.2	90.9	95.8	100.6	106.1	111.9	117.6	124.1	129.7
	145	86.7	90.5	95.6	100.7	106.5	112.4	118.0	123.9	128.6		146	88.1	91.9	96.8	101.7	107.2	113.0	118.9	125.4	131.0
	149	87.6	91.5	96.7	101.9	107.7	113.7	119.4	125.3	130.0		150	89.0	92.9	97.8	102.8	108.3	114.2	120.1	126.7	132.4
10 < 11 (*n* = 112)	130	82.4	86.2	91.2	96.2	101.8	107.4	112.7	118.1	122.4	10– < 11 (*n* = 118)	132	84.8	88.4	93.1	97.8	103.1	108.8	114.4	120.7	126.1
	135	83.6	87.5	92.6	97.6	103.3	109.0	114.3	119.8	124.2		135	85.5	89.1	93.9	98.6	104.0	109.7	115.3	121.7	127.1
	140	84.8	88.7	93.9	99.0	104.7	110.5	116.0	121.5	125.9		139	86.4	90.1	94.9	99.7	105.1	110.9	116.6	123.0	128.5
	144	85.7	89.7	94.9	100.2	105.9	111.8	117.3	122.9	127.4		143	87.3	91.1	95.9	100.8	106.2	112.0	117.8	124.3	129.9
	148	86.7	90.7	96.0	101.3	107.1	113.0	118.6	124.3	128.8		148	88.5	92.3	97.2	102.1	107.7	113.5	119.4	125.9	131.6
	152	87.6	91.7	97.1	102.4	108.3	114.3	119.9	125.7	130.2		152	89.4	93.3	98.2	103.2	108.8	114.7	120.6	127.3	133.0
	156	88.6	92.7	98.1	103.5	109.5	115.5	121.2	127.0	131.6		155	90.1	94.0	99.0	104.0	109.6	115.6	121.6	128.3	134.0

Abbreviations: BP, blood pressure; GAMLSS, General Additive Model for Location Scale and Shape;[17] Ht, height. Height values were expressed in cm and corresponded to the 1st, 3rd, 10th, 25th, 50th, 75th, 90th, 97th and 99th age- and sex-specific percentiles.

pronounced in the population including overweight and obese children at an older age and at the extremes of the distribution. Previous studies have consistently shown that sex differences are more pronounced during pre-puberty[21–24] that usually occurs in girls earlier than in boys. The BP sexual dimorphism we observed in the population as a whole is a well-documented phenomenon in adults.[25] Our findings could be explained by the earlier occurrence of biological changes leading to sexual maturation in

Table 3. Percentiles of diastolic BP (mm Hg) in non-overweight children calculated with GAMLSS

Age (years)	*Ht (cm)*	*Percentiles for girls*									*Age (years)*	*Ht (cm)*	*Percentiles for boys*								
		1	*3*	*10*	*25*	*50*	*75*	*90*	*97*	*99*			*1*	*3*	*10*	*25*	*50*	*75*	*90*	*97*	*99*
2– < 3 (*n* = 200)	85	46.9	49.7	53.3	56.8	60.8	64.8	68.8	73.1	76.7	2– < 3 (*n* = 224)	85	46.0	48.6	52.1	55.5	59.4	63.5	67.5	71.9	75.6
	87	47.1	49.9	53.5	57.0	61.0	65.0	69.0	73.3	77.0		88	46.2	48.8	52.3	55.7	59.6	63.8	67.8	72.2	75.9
	89	47.2	50.0	53.6	57.2	61.1	65.2	69.2	73.6	77.2		91	46.4	49.0	52.5	56.0	59.9	64.0	68.0	72.5	76.2
	92	47.4	50.3	53.9	57.4	61.4	65.5	69.5	73.9	77.5		93	46.5	49.2	52.6	56.1	60.0	64.2	68.2	72.7	76.4
	94	47.6	50.4	54.0	57.6	61.6	65.7	69.7	74.1	77.8		96	46.7	49.4	52.8	56.3	60.3	64.4	68.5	73.0	76.7
	97	47.8	50.6	54.3	57.9	61.9	66.0	70.0	74.4	78.1		98	46.8	49.5	53.0	56.5	60.4	64.6	68.7	73.1	76.9
	100	48.0	50.8	54.5	58.1	62.1	66.3	70.3	74.8	78.5		101	47.0	49.7	53.2	56.7	60.7	64.8	68.9	73.4	77.2
3– < 4 (*n* = 960)	92	47.3	50.1	53.8	57.3	61.3	65.4	69.4	73.7	77.4	3– < 4 (*n* = 1016)	92	46.5	49.1	52.6	56.1	60.0	64.1	68.2	72.6	76.4
	95	47.5	50.4	54.0	57.6	61.5	65.7	69.7	74.0	77.7		95	46.7	49.3	52.8	56.3	60.2	64.4	68.4	72.9	76.7
	97	47.7	50.5	54.2	57.7	61.7	65.9	69.9	74.3	77.9		98	46.8	49.5	53.0	56.5	60.5	64.6	68.7	73.2	77.0
	100	47.9	50.7	54.4	58.0	62.0	66.2	70.2	74.6	78.3		101	47.0	49.7	53.2	56.7	60.7	64.9	69.0	73.5	77.3
	102	48.0	50.9	54.6	58.2	62.2	66.3	70.4	74.8	78.5		103	47.1	49.8	53.4	56.9	60.9	65.1	69.2	73.7	77.5
	105	48.2	51.1	54.8	58.4	62.4	66.6	70.7	75.1	78.9		106	47.3	50.0	53.6	57.1	61.1	65.3	69.4	74.0	77.8
	108	48.4	51.3	55.0	58.7	62.7	66.9	71.0	75.5	79.2		109	47.5	50.2	53.8	57.3	61.4	65.6	69.7	74.3	78.1
4– < 5 (*n* = 1196)	98	47.6	50.5	54.1	57.7	61.7	65.8	69.8	74.2	77.9	4– < 5 (*n* = 1290)	99	46.9	49.6	53.1	56.6	60.6	64.8	68.9	73.4	77.1
	101	47.8	50.7	54.3	57.9	61.9	66.1	70.1	74.5	78.2		102	47.1	49.8	53.3	56.9	60.8	65.0	69.1	73.6	77.4
	104	48.1	50.9	54.6	58.2	62.2	66.4	70.4	74.9	78.6		105	47.3	50.0	53.6	57.1	61.1	65.3	69.4	73.9	77.7
	107	48.3	51.1	54.8	58.5	62.5	66.7	70.7	75.2	78.9		108	47.5	50.2	53.8	57.3	61.3	65.5	69.7	74.2	78.0
	110	48.5	51.4	55.1	58.7	62.8	67.0	71.1	75.5	79.3		111	47.7	50.4	54.0	57.5	61.6	65.8	69.9	74.5	78.3
	113	48.7	51.6	55.3	59.0	63.0	67.3	71.4	75.8	79.6		114	47.9	50.6	54.2	57.8	61.8	66.1	70.2	74.8	78.6
	116	48.9	51.8	55.5	59.2	63.3	67.6	71.7	76.2	79.9		117	48.0	50.8	54.4	58.0	62.0	66.3	70.5	75.1	78.9
5– < 6 (*n* = 1002)	104	47.9	50.8	54.5	58.1	62.1	66.2	70.3	74.7	78.4	5– < 6 (*n* = 1121)	105	47.3	50.1	53.6	57.1	61.1	65.3	69.5	74.0	77.8
	108	48.2	51.1	54.8	58.4	62.4	66.6	70.7	75.1	78.8		108	47.5	50.3	53.8	57.4	61.4	65.6	69.7	74.3	78.1
	111	48.4	51.3	55.0	58.7	62.7	66.9	71.0	75.5	79.2		111	47.7	50.4	54.0	57.6	61.6	65.9	70.0	74.6	78.4
	114	48.6	51.5	55.3	58.9	63.0	67.2	71.3	75.8	79.5		115	48.0	50.7	54.3	57.9	61.9	66.2	70.4	74.9	78.8
	117	48.9	51.8	55.5	59.2	63.3	67.5	71.6	76.1	79.9		118	48.1	50.9	54.5	58.1	62.2	66.4	70.6	75.2	79.1
	120	49.1	52.0	55.7	59.4	63.5	67.8	71.9	76.4	80.2		121	48.3	51.1	54.7	58.3	62.4	66.7	70.9	75.5	79.4
	123	49.3	52.2	56.0	59.7	63.8	68.1	72.2	76.8	80.6		125	48.6	51.3	55.0	58.6	62.7	67.0	71.3	75.9	79.8
6– < 7 (n = 1398)	110	48.3	51.1	54.8	58.4	62.5	66.7	70.7	75.2	78.9	6– < 7 (*n* = 1390)	111	47.8	50.5	54.1	57.6	61.7	65.9	70.1	74.6	78.5
	113	48.5	51.4	55.1	58.7	62.7	67.0	71.0	75.5	79.2		115	48.0	50.7	54.3	57.9	62.0	66.2	70.4	75.0	78.9
	117	48.8	51.7	55.4	59.0	63.1	67.3	71.5	75.9	79.7		118	48.2	50.9	54.5	58.1	62.2	66.5	70.7	75.3	79.2
	120	49.0	51.9	55.6	59.3	63.4	67.6	71.8	76.3	80.0		121	48.4	51.1	54.7	58.4	62.4	66.7	71.0	75.6	79.5
	123	49.2	52.1	55.9	59.5	63.7	67.9	72.1	76.6	80.4		125	48.6	51.4	55.0	58.7	62.8	67.1	71.3	76.0	79.9
	127	49.5	52.4	56.2	59.9	64.0	68.3	72.5	77.0	80.8		128	48.8	51.6	55.2	58.9	63.0	67.3	71.6	76.3	80.2
	130	49.7	52.6	56.4	60.1	64.3	68.6	72.8	77.4	81.2		132	49.0	51.8	55.5	59.2	63.3	67.7	71.9	76.6	80.6
7– < 8 (*n* = 1945)	115	48.5	51.4	55.1	58.7	62.8	67.0	71.1	75.6	79.3	7– < 8 (*n* = 1854)	117	48.2	50.9	54.5	58.1	62.2	66.5	70.6	75.3	79.1
	119	48.8	51.7	55.4	59.1	63.2	67.4	71.5	76.0	79.8		120	48.3	51.1	54.7	58.3	62.4	66.7	70.9	75.5	79.4
	123	49.1	52.0	55.7	59.4	63.5	67.8	71.9	76.4	80.2		124	48.6	51.4	55.0	58.6	62.7	67.1	71.3	75.9	79.8
	126	49.3	52.2	56.0	59.7	63.8	68.1	72.2	76.8	80.6		127	48.8	51.6	55.2	58.9	63.0	67.3	71.5	76.2	80.1
	130	49.6	52.5	56.3	60.0	64.2	68.5	72.6	77.2	81.0		131	49.0	51.8	55.5	59.1	63.3	67.6	71.9	76.6	80.5
	133	49.8	52.7	56.5	60.3	64.4	68.7	72.9	77.5	81.4		134	49.2	52.0	55.7	59.4	63.5	67.9	72.2	76.9	80.8
	137	50.0	53.0	56.8	60.6	64.8	69.1	73.4	78.0	81.8		138	49.4	52.3	56.0	59.7	63.8	68.2	72.5	77.3	81.2
8– < 9 (*n* = 1287)	120	48.7	51.6	55.4	59.0	63.1	67.3	71.4	75.9	79.7	8– < 9 (*n* = 1239)	122	48.5	51.3	54.9	58.5	62.6	66.9	71.2	75.8	79.7
	124	49.0	51.9	55.7	59.4	63.5	67.7	71.9	76.4	80.1		126	48.7	51.5	55.2	58.8	62.9	67.3	71.5	76.2	80.1
	128	49.3	52.2	56.0	59.7	63.8	68.1	72.3	76.8	80.6		129	48.9	51.7	55.4	59.0	63.2	67.5	71.8	76.5	80.4
	132	49.6	52.5	56.3	60.0	64.2	68.5	72.7	77.2	81.1		133	49.2	52.0	55.7	59.3	63.5	67.9	72.1	76.9	80.8
	136	49.9	52.8	56.6	60.4	64.6	68.9	73.1	77.7	81.5		137	49.4	52.2	55.9	59.6	63.8	68.2	72.5	77.2	81.2
	139	50.1	53.1	56.9	60.6	64.8	69.2	73.4	78.0	81.9		140	49.6	52.4	56.1	59.9	64.0	68.5	72.8	77.5	81.5
	143	50.4	53.4	57.2	61.0	65.2	69.6	73.8	78.5	82.3		144	49.8	52.7	56.4	60.2	64.4	68.8	73.1	77.9	81.9
9– < 10 (*n* = 299)	125	49.0	51.9	55.6	59.3	63.4	67.7	71.8	76.3	80.1	9– < 10 (*n* = 286)	127	48.8	51.6	55.3	58.9	63.1	67.4	71.7	76.3	80.3
	130	49.3	52.3	56.0	59.7	63.9	68.2	72.3	76.9	80.7		131	49.1	51.9	55.6	59.2	63.4	67.8	72.0	76.7	80.7
	134	49.6	52.6	56.4	60.1	64.2	68.5	72.7	77.3	81.1		134	49.3	52.1	55.8	59.5	63.6	68.0	72.3	77.0	81.0
	138	49.9	52.9	56.7	60.4	64.6	68.9	73.1	77.7	81.6		138	49.5	52.4	56.1	59.8	63.9	68.3	72.6	77.4	81.4
	142	50.2	53.2	57.0	60.8	65.0	69.3	73.5	78.2	82.0		142	49.8	52.6	56.3	60.1	64.3	68.7	73.0	77.8	81.8
	145	50.4	53.4	57.2	61.0	65.2	69.6	73.9	78.5	82.4		146	50.0	52.9	56.6	60.3	64.6	69.0	73.4	78.2	82.2
	149	50.7	53.7	57.6	61.4	65.6	70.0	74.3	78.9	82.8		150	50.3	53.1	56.9	60.6	64.9	69.4	73.7	78.5	82.6
10 < 11 (*n* = 112)	130	49.2	52.2	55.9	59.6	63.7	68.0	72.1	76.7	80.5	10– < 11 (*n* = 118)	132	49.2	52.0	55.7	59.4	63.5	67.9	72.2	76.9	80.8
	135	49.6	52.5	56.3	60.0	64.2	68.5	72.7	77.2	81.1		135	49.4	52.2	55.9	59.6	63.8	68.1	72.4	77.2	81.1
	140	49.9	52.9	56.7	60.5	64.6	69.0	73.2	77.8	81.6		139	49.6	52.5	56.2	59.9	64.1	68.5	72.8	77.5	81.5
	144	50.2	53.2	57.0	60.8	65.0	69.4	73.6	78.2	82.1		143	49.9	52.7	56.4	60.2	64.4	68.8	73.2	77.9	81.9
	148	50.5	53.5	57.4	61.1	65.4	69.8	74.0	78.7	82.5		148	50.2	53.0	56.8	60.5	64.8	69.2	73.6	78.4	82.4
	152	50.8	53.8	57.7	61.5	65.7	70.1	74.4	79.1	83.0		152	50.4	53.3	57.1	60.8	65.1	69.6	74.0	78.8	82.8
	156	51.1	54.1	58.0	61.8	66.1	70.5	74.8	79.5	83.5		155	50.6	53.5	57.3	61.1	65.3	69.8	74.2	79.1	83.1

Abbreviations: BP, blood pressure; GAMLSS, General Additive Model for Location Scale and Shape;[17] Ht, height. Height values were expressed in cm and corresponded to the 1st, 3td, 10th, 25th, 50th, 75th, 90th, 97th and 99th age- and sex-specific percentiles.

girls. Alternatively, the overall higher prevalence of overweight and obesity observed in girls in the IDEFICS sample might be responsible.

The sensitivity analysis also provided insight regarding the possibility that determining reference BP values in children including overweight and obese individuals may be subject to bias.[5] Body weight and height are the most important determinants of BP in children, as BP increases linearly with both anthropometric factors. In fact, differences exist between the two factors in their association with BP: while changes in BP associated

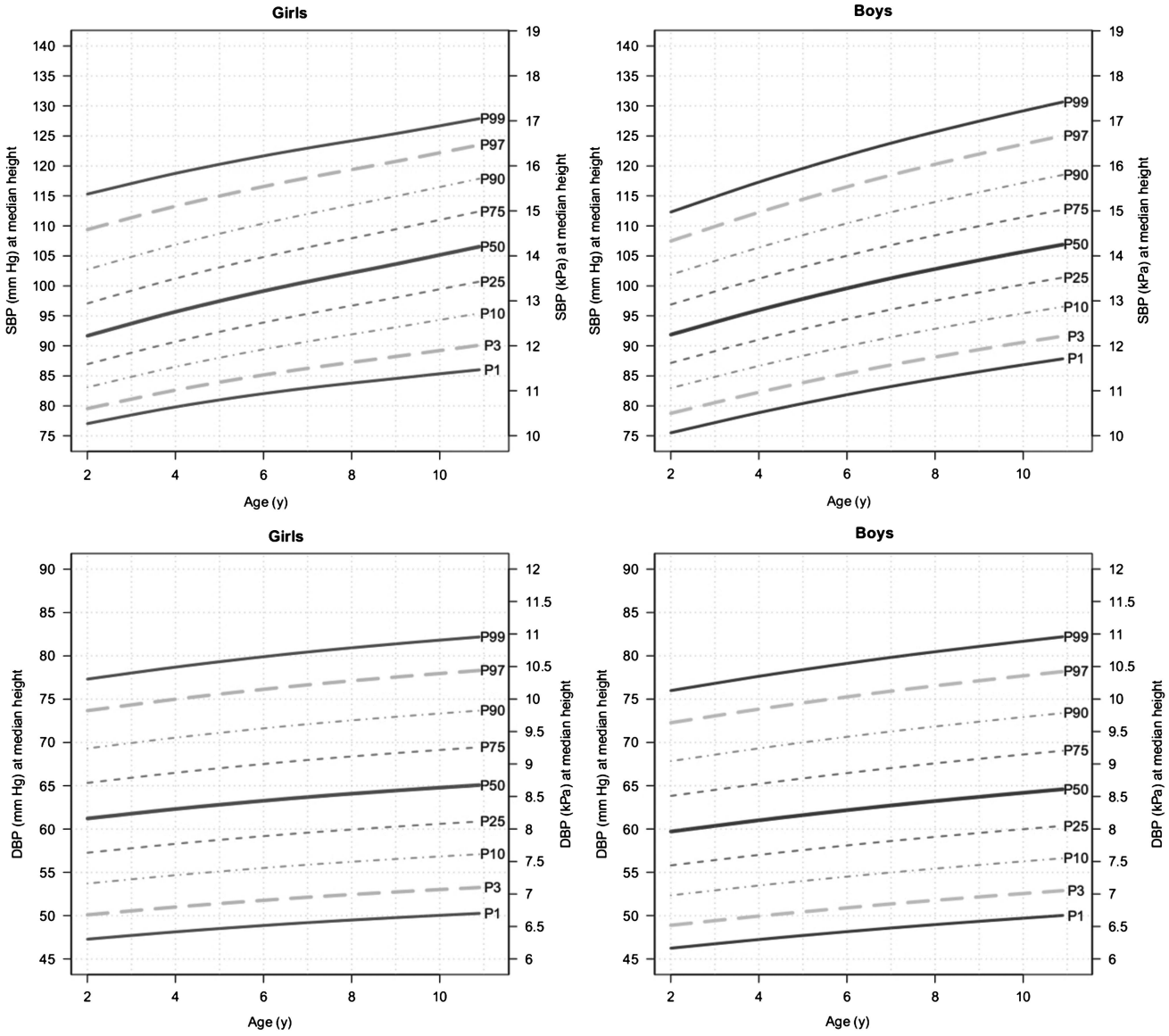

Figure 2. Systolic (top panels) and diastolic (bottom panels) blood pressure percentiles at median height by age in non-overweight girls (left, $n=6609$) and boys (right, $n=6938$) participating in the IDEFICS study. DBP, diastolic blood pressure; SBP, systolic blood pressure. Non-overweight children included thin and normal weight children according to Cole and Lobstein.[15]

with changes in height may be considered the consequence of a physiological process, the relationship between body weight and BP is, at least in part, a physiopathological deviation from normality.[5,10,21,26,27] Indeed, adult prehypertension, that is, SBP $\geqslant 120$ and/or DBP $\geqslant 80$ mm Hg, was documented in our sample in 0.8% and 2.1% overweight/obese children, respectively, in the age groups 2–6 and 6–11 years. Only $\leqslant 0.4\%$ non-overweight participants had an SBP of at least 120 mm Hg. In practice, calculating the BP norms for a general population would keep children within the norms although they would be included in an 'at-risk' category if they were adults.[28]

It should be clearly stated that the present paediatric reference BP values do not provide criteria to diagnose hypertension in children. In the IDEFICS study, BP measurements were taken on a single occasion, thus making it difficult to classify hypertension because of the known intrinsic variability of BP, well documented in the paediatric population,[29] which in this case could lead to a possible overestimation of BP values. In the NHBPEP report,[1] the criteria used to define hypertension were provided, but, in that study, BP measurements were taken on three separate occasions. The diagnosis of paediatric hypertension is not as straightforward as it is in adults, in whom the long-term impact on health of elevated BP is well documented.[2,30] It is recognised that the BP in children tends to increase up to adulthood and, in general, children whose BP values are in the right part of the distribution tend to keep the same position later in life,[1,2,31,32] possibly to a greater extent if co-existing with overweight or obesity.[33] However, the absolute risk of cardiovascular diseases associated with elevated BP in childhood remains to be evaluated.[34–36] Under these conditions, the normative BP values derived from the IDEFICS study population actually provide the cutoffs to identify those children who are at higher risk for paediatric hypertension and for whom further BP measurements should be scheduled or even a preventative, healthy lifestyle should be promoted.[1]

The present study is the first, to the best of our knowledge, to provide BP norms in a large multi-national European

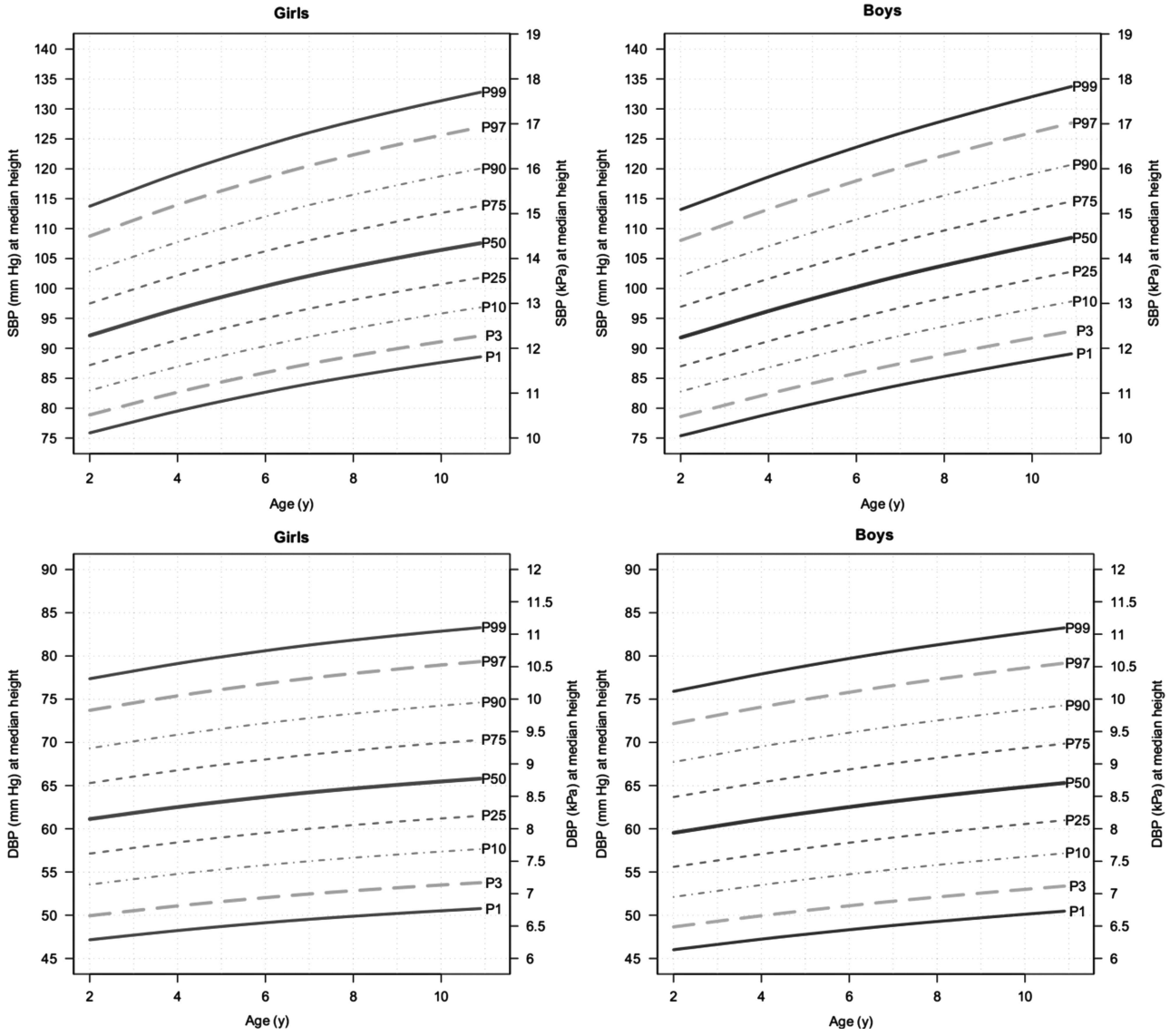

Figure 3. Systolic (top panels) and diastolic (bottom panels) blood pressure percentiles at median height by age in all children participating in the IDEFICS study. Results are shown separately for girls (left, $n = 8399$) and boys (right, $n = 8538$). DBP, diastolic blood pressure; SBP, systolic blood pressure.

paediatric population composed of non-overweight children, thus advancing current knowledge by (i) extending the national or local data recently published[6–11,23] in European population samples and (ii) updating the former European child BP norms.[37] Further strengths were the standardisation of the procedures across centres participating in the IDEFICS study[12–14] that strongly limited the possibility of technical biases and increased the reliability of collected data, and the adoption of updated statistical methods to calculate reference BP percentiles.

The comparison of the present data with other data from similar studies may be possibly limited by the different BP readings obtained from different automated devices, each one with its own calculation algorithm. In spite of this limitation, however, the use of automated devices is recommended in multi-centre studies because it avoids the occurrence of any possible observer bias. This characteristic of automated devices, in addition to the standardisation of the procedures in the IDEFICS study, confers robust reliability to collected data. One other possible limitation of the study is the age range of participants, which did not provide any information from early childhood to late adolescence. Nonetheless, in view of the paucity of available data, the absence of BP norms in adolescents appears to be less relevant. However, the collection of BP data in adolescents will be one of the objectives of our ongoing I.Family study (www.ifamilystudy.eu). Finally, the present analysis did not provide criteria for the diagnosis of paediatric hypertension: this aspect was discussed above but, regardless, it would have required a different study design.

The present study provides updated and timely information that may contribute to filling a gap in knowledge that may be prospectively useful in planning population strategies for disease prevention. Further, the results of the present analysis might also support clinical practice by providing reliable reference BP values in children and thus encouraging paediatricians to include blood pressure measurement as a routine procedure during physical examination.

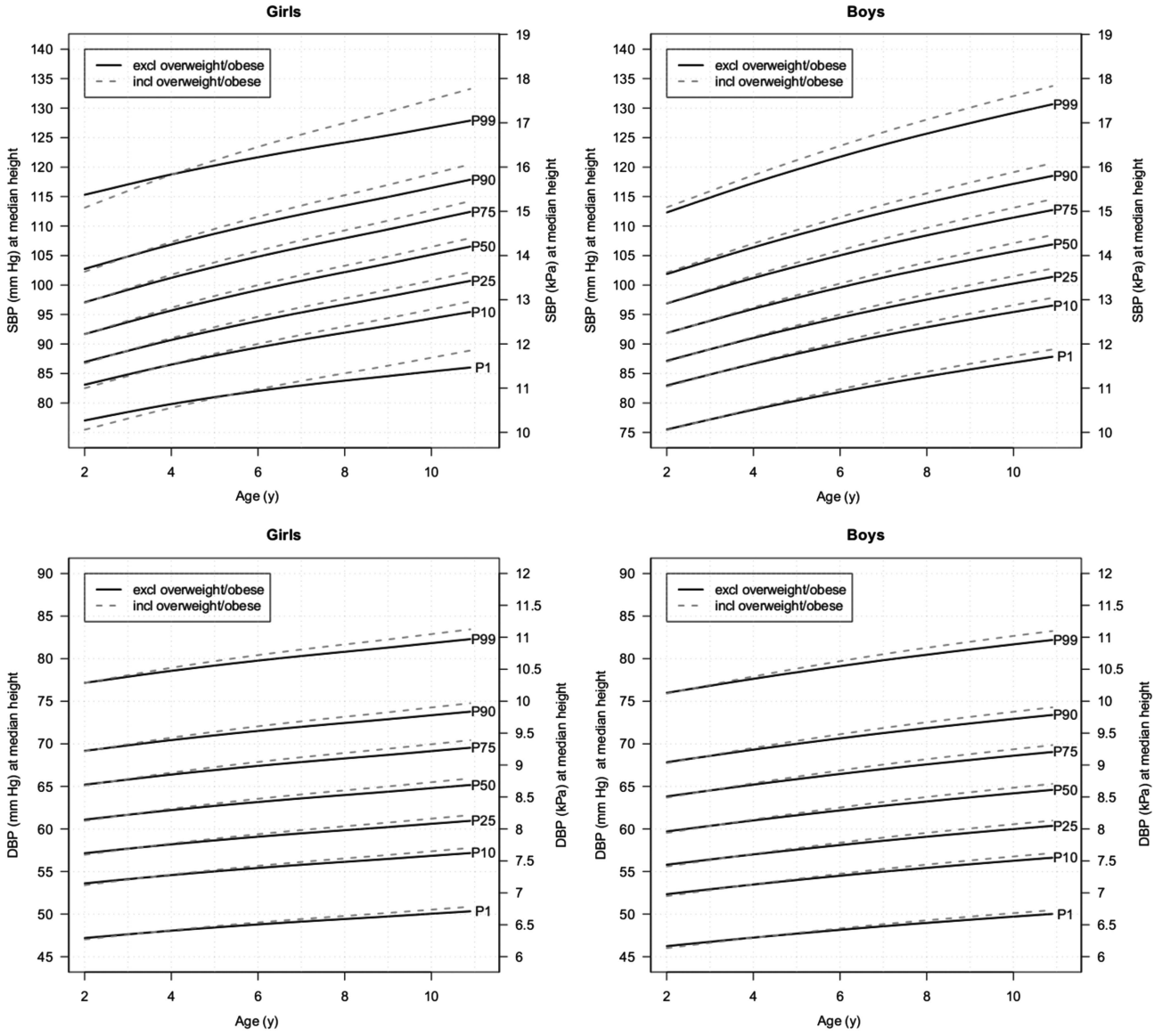

Figure 4. Comparison (sensitivity analysis) between systolic (top panels) and diastolic (bottom panels) blood pressure percentiles by age and median height in non-overweight children only (continuous line) and all participants (dotted line) in the IDEFICS study. Data are shown separately for girls (left) and boys (right). DBP, diastolic blood pressure; SBP, systolic blood pressure. Non-overweight children included thin and normal weight children according to Cole and Lobstein.[15]

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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DISCLAIMER

The information in this document reflects the authors' views and is provided as it is.

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