A big-data approach to producing descriptive anthropometric references: a feasibility and validation study of paediatric growth charts

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Summary

Background Both national and WHO growth charts have been found to be poorly calibrated with the physical growth of children in many countries. We aimed to generate new national growth charts for French children in the context of huge datasets of physical growth measurements routinely collected by office-based health practitioners.

Methods We recruited 32 randomly sampled primary care paediatricians and ten volunteer general practitioners from across the French metropolitan territory who used the same electronic medical records software, from which we extracted all physical growth data for the paediatric patients, with anonymisation. We included measurements from all children born from Jan 1, 1990, and aged 1 month to 18 years by Feb 8, 2018, with birthweight greater than 2500 g, to which an automated process of data cleaning developed to detect and delete measurement or transcription errors was applied. Growth charts for weight and height were derived by using generalised additive models for location, scale, and shape with the Box-Cox power exponential distribution. We compared the new charts to WHO growth charts and existing French national growth charts, and validated our charts using growth data from recent national cross-sectional surveys.

Findings After data cleaning, we included 1 458 468 height and 1 690 340 weight measurements from 238 102 children. When compared with the existing French national and WHO growth charts, all height SD and weight percentile curves for the new growth charts were distinctly above those for the existing French national growth charts, as early as age 1 month, with an average difference of –0·75 SD for height and –0·50 SD for weight for both sexes. Comparison with national cross-sectional surveys showed satisfactory calibration, with generally good fit for children aged 5–6 years and 10–11 years in height and weight and small differences at age 14–15 years.

Interpretation We successfully produced calibrated paediatric growth charts by using a novel big-data approach applied to data routinely collected in clinical practice that could be used in many fields other than anthropometry.

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Introduction

Anthropometric charts are clinical tools for identifying normal and abnormal variations in various settings, such as clinical genetics, imaging, and growth monitoring. In early postnatal life, the main purpose of growth monitoring is to evaluate the adequacy of infant feeding in physiological or pathological situations.[1] Later, its main purpose is to contribute to the timely detection of serious health conditions to provide optimal care and reduce morbidity and mortality.[2] Growth monitoring requires the use of growth standards or references for comparing observed values in a child with expected values among their peers.

For decades, health-care practitioners worldwide have used national growth references mostly produced in countries with advanced economies. In 2006, WHO published international growth standards from birth to 5 years of age and growth references after age 5 years,[3,4] and recommended their use in all countries.[5] However, the WHO growth charts were found to be imperfectly calibrated with the growth of contemporary children in many countries, including France.[2] The growth of contemporary French children was shown to be closer to the WHO growth charts than the former French national growth charts, except for the first 6 months of life.[6] Some countries, such as the UK, decided to use the WHO growth charts for young children and national ones after age 4 years, which led to the production of growth charts with a sudden shift in curves at this age.[7,8] The consequences of such a choice on the performance

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See Online for appendix

Research in context

Evidence before this study

Anthropometric references, including human height and weight growth charts, have been produced for several decades by using data specifically collected for this purpose. The availability of massive routine datasets allows for new approaches to easily create calibrated anthropometric references or update them. No scientific literature review was done for this study.

Added value of this study

New descriptive growth charts were generated by applying an automatic process of data cleaning and modelling to height and weight measurements extracted from medical records of a representative sample of primary-care physicians across France. The final growth charts were based on 1 458 468 height and 1 690 340 weight measurements from 238 102 children. Comparison with national cross-sectional surveys showed satisfactory calibration.

Implications of all the available evidence

This new approach for generating growth charts could be applied in other countries and other medical domains, provided that related data are stored in medical-records databases from which they can be easily extracted.

of growth monitoring around this age has not been evaluated.

An alternative option would be to update former national growth charts to produce more accurate national growth charts that are perfectly calibrated to the population for which they will be used.[9–16] The collection of massive and representative anthropometric data needed to obtain adequate calibration at the national level is time consuming and costly using classical ad-hoc cross-sectional surveys.[9–16] The recent digital revolution has made available nearly unlimited auxological data routinely collected by healthcare professionals. For its appropriateness for use in creating new growth charts, such data must come from settings with a large national geographical basis and from facilities that care for children from birth to adulthood, who are mostly without chronic diseases that can affect growth. To be technically feasible, such facilities must use interoperable electronic medical records. In this context, we aimed to generate national growth charts by using a novel big-data approach.

Methods

Study design and participants

The two-step design of the study comprised the automatic extraction of data for individual paediatric patients from primary care physician files, followed by the analysis of the millions of height and weight measurements for these patients. The study protocol was approved by the ethics committee and the institutional review board of the French Institute of Medical Research and Health (Inserm IRB00003888, IOR0003254, FWA00005831), which provided a waiver of consent given the completely anonymous design of data collection. The study protocol was discussed and approved a priori by a scientific committee composed of mathematicians (J-CT, JM), biostatisticians (BK, JB, BH), epidemiologists (GB, JZ, M-AC, PS, MC, BF), data scientists (MLG, PS, BH, BF), primary care physicians (AW, NG, BC, JC, J-FS, MA, EJ), specialists in epidemiology of human growth (JB, BH), and physicians specialised in growth disorders (BC, CP, MB, SN'G, RR, MC). The protocol approval process was based on a three-step Delphi procedure that focused on inclusion criteria and thresholds to be used for the sample selection and automatic data-cleaning process.

The study population consisted of all children aged 1 month to 18 years who were born from Jan 1, 1990, had birthweight greater than 2500 g, and were weighed or measured at least once by participating primary care physicians who were paediatricians or general practitioners. Children with an excessive number of measurements after 6 months were excluded because the scientific committee considered that frequent medical visits after this age were likely to reflect an underlying condition that might affect growth. We determined thresholds for an excessive number of measurements from the distribution of the number of measurements between 6 and 12 months and every year until age 18 years by using the Tukey method (with $\pm 3 \times$IQR; appendix p 12).[17]

Participating physicians had to belong to one of two participating primary care medical societies, use the last version of the same commercial electronic medical records software (AxiSanté and its paediatric version Infansoft, produced by CompuGroup Medical, Nanterre, France), and provide written agreement for involvement in the study. The French Association for Ambulatory Paediatricians, the only national association of primary care paediatricians in France, unites about 1400 paediatricians nationwide. Among the 813 primary care paediatricians who used the required software, we anticipated a high participation rate, and a stratified random sampling was done by geographical area and size of urban area where the paediatricians practised (ie, four participants for each of the eight Research and National Development zones—two in large urban areas and two in small urban areas). The French Society of General Medicine, one of the largest national associations of general practitioners in France, unites more than 1200 general practitioners nationwide, of whom around 240 used the required software. A very low participation rate was expected, on the basis of previous experience, so all general practitioners were contacted and those who volunteered were included.

Data collection and cleaning process

Data were automatically and anonymously extracted from participating physicians' computers from Sept 27, 2017, to Feb 8, 2018, using a method compliant with the integrity, security, and confidentiality constraints required for health-care data in France.[18] Data extracted had been routinely entered into the electronic medical record by the practitioners during all consultations between Jan 1, 1990, and Feb 8, 2018, and included sex, year of birth, weight, height, and age at growth measurement (in days).

Data for each child underwent an automatic data-cleaning process to detect and delete measurement or transcription errors (appendix p 2). After removing duplicates, we calculated Z scores for weight and height based on the WHO growth charts and deleted values with absolute Z scores of at least 5 SD.[19] In case of two distinct values at the same age, the value with the Z score closest to proximate measurements was kept; an interpolated value between the previous and the next measurements was used if both were available or only the previous or the next measurement otherwise. Finally, to account for within-individual measurement consistency in the automatic data-cleaning process, we calculated Z score variations between two successive measurements. We described the distribution of these variations for height and weight and defined thresholds as absolute Z score variations (whatever the duration between the two measurements) less than the first percentile or greater than the 99th percentile of their distributions, corresponding to –0·5 SD and 1·0 SD changes for weight or –1·0 SD and 1·3 SD changes for height. We deleted measurements showing transient large Z score variations, characterised by important differences with both the previous and the next measurements. The scripts for the cleaning process, including the removal of duplicates, are available online.

Population and measurement selection criteria

We started the growth modelling from age 1 month (>30 days) because large weight variations and height measurement issues are frequent before this age. As a consequence of the national clinical practice guidelines,[20] many measurements were collected before age 2 years (>800 000 height and >880 000 weight measurements; appendix pp 3–4). We therefore randomly selected a smaller number of measurements per child to speed the computations and to reduce over-representation of those children weighed or measured more frequently, retaining no more than five measurements per child from age 1–6 months, no more than three measurements from ages 6–12 months, and no more than three measurements from ages 12–24 months.

Statistical analysis

We derived the height and weight growth charts as a function of age (in days) by using generalised additive models for location, scale, and shape (GAMLSS) with the Box-Cox power exponential (BCPE) distribution, using R version 3.4.2 and GAMLSS version 5.1.2.[21,22] This method allows a departure from the normal distribution by using the BCPE distribution, which relies on four parameters: median, variation, skewness, and kurtosis.[22] It also allows the overall distribution to vary by age with the time-dependent smoothing curves for these four parameters. We used cubic-penalised B-splines as smoothing functions for all parameters and determined the numbers of knots and equivalent degrees of freedom (EDF) separately for the median, variation, skewness, and kurtosis curves for weight and height charts for girls and boys.

Because of computational difficulties with the very large amount of data, we developed a strategy to obtain model convergence within a reasonable amount of time. The principle was to obtain the final model with a step-by-step process from the simplest model to the most complicated and final one, using the parameter estimations obtained at the previous step as the starting values for the model computation at the following step. At any step when models were compared, the best model was selected on the basis of the generalised Akaike information criterion.[21,22] The process summarised below was applied separately for weight and height and for girls and boys.

We hypothesised that the distribution of height was symmetrical at any age because all height growth charts published so far, including WHO growth charts, are symmetrical with the skewness parameter set to 1. We formally tested this hypothesis on a subsample of 115 304 children with more than 1 million height or weight measurements and found that allowing the skewness parameter to differ from 1 did not significantly improve the fit of the model for height in girls and boys. Consequently, the skewness parameter was set to 1 for the height modelling process. Another preliminary step consisted of determining the age-transformation power, λ, on a pre-determined model applied to a subsample. The λ obtained was fixed for the following steps.

A first model was computed on the complete sample with parameters for median, variation, skewness, and kurtosis curves fixed. The EDF for median or variation curves was set to 10 and for skewness (for weight modelling only) or kurtosis curves to 5. The number of knots was set to be equal to the EDF in all models but the last. Knots were spaced by equal time intervals. Then, parameters for the variation, skewness, and kurtosis curves were kept fixed, and using estimations of the first model as starting values, we ran a series of models in which the EDF of the median curve was allowed to vary until 20, to avoid overfitting with more than one knot per year of age, and we retained the best model. The EDF of the obtained median curve was fixed for the next step, in which we allowed the EDF of the variation curve to vary until 20, again retaining the best model. The same process was then applied to the skewness curve (for weight modelling only) and kurtosis curve. Once EDF values for all curves were obtained, we fixed the number of knots while allowing all the EDF values to vary, to

For the **cleaning process script** see https://github.com/paulinescherdel/EBGM-VI/blob/master/Cleaning.R

For the **script for removal of duplicates** see https://github.com/paulinescherdel/EBGM-VI/blob/master/Duplicates.R

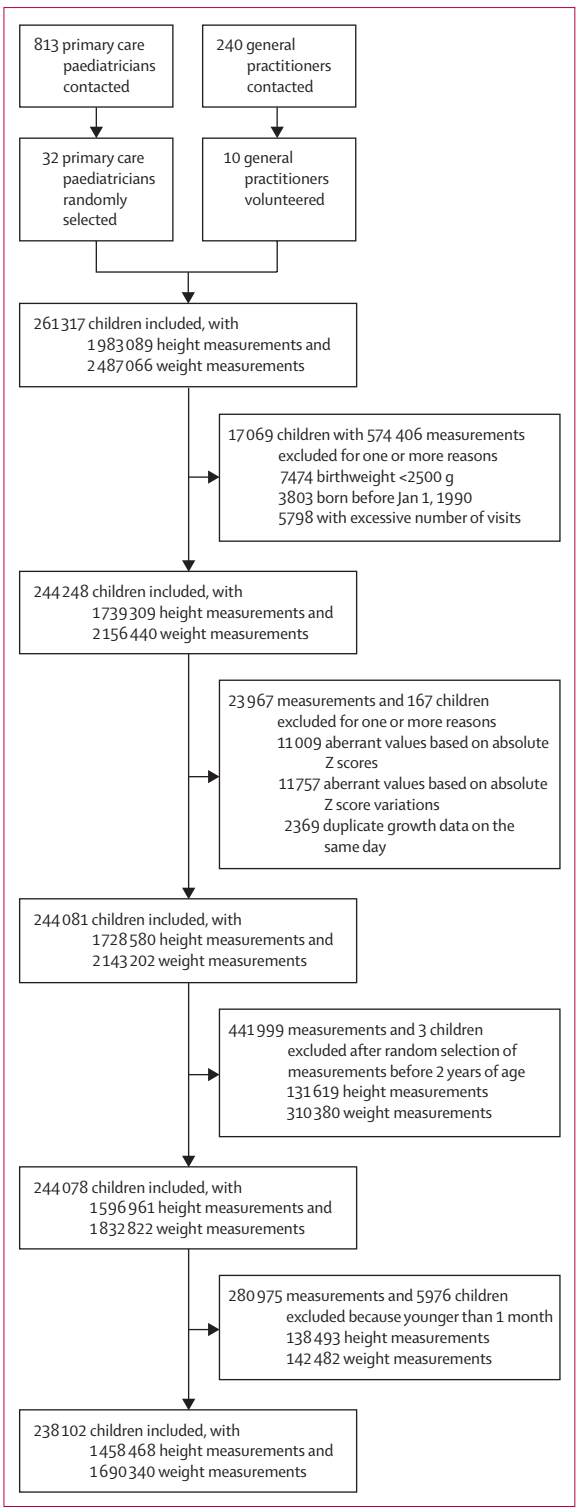

Figure 1: **Flow chart for selecting children and measurements**

For the **modelling scripts** see https://github.com/paulinescherdel/EBGM-VI/blob/master/Height%20modelling.R

obtain the best fit for the last model. The scripts for the modelling process are available online.

The internal fit of each final model was checked by visual inspection of the empirical SD or percentile curves and worm plots.[23] Empirical SD or percentile curves were calculated by grouping data by 3-month intervals, and worm plots were represented by 2-month intervals from 1 to 6 months, 3-month intervals from 6 to 12 months, 6-month intervals from 12 to 24 months, and 12-month intervals from 12 to 216 months.

We compared the new growth charts for height and weight to the WHO growth charts and existing French national growth charts published by Sempé et al[24] by using a graphical comparison of the third, 50th (median), and 97th percentiles for weight curves and –2 SD, 0 SD (median), and 2 SD for height curves. We also compared the median values from the WHO and existing French national growth charts to data from the new growth charts by converting the median values to Z scores on the basis of new growth charts.[25] The Z score evolution between ages 1 month and 18 years was represented graphically by age.

We analysed height and weight data obtained by three national cross-sectional representative school surveys done during three periods and for three distinct ages (5–6 years in nursery school from September, 2012, to July, 2013 [n=25 695]; 10–11 years in primary school from September, 2007, to July, 2008 [n=5800]; and 14–15 years in secondary school from September, 2008, to July, 2009 [n=4450]). These data are publicly available from the French Directorate for Research, Studies, Evaluation and Statistics.[26–28] The third, 50th, and 97th percentiles for weight and –2 SD, 0 SD, and 2 SD for height of children were graphically compared with data from the new growth charts. We provided the mean (SD) and median (IQR) for height and weight Z scores for girls and boys at the three survey periods. Then, we calculated the proportion of children according to different height and weight percentiles (under the first, fifth, and tenth percentiles and over the 50th, 90th, 95th, and 99th percentiles) from the new growth charts for girls and boys.

Role of the funding source

The funders had no role in the study design, data collection and analysis, preparation of the manuscript, and decision to publish. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We randomly selected 32 primary care paediatricians from the 16 French metropolitan geographical areas, and ten general practitioners throughout the French metropolitan territory volunteered to participate (figures 1, 2). From 261 317 children with at least one height or weight measurement present in the extracted data from these 42 primary care physicians, data for 238 102 children (102 874 [43·2%] were girls) were retained for analysis after the application of population selection criteria and the cleaning process. This process excluded more than 25 100 weight or height measurements, which resulted in

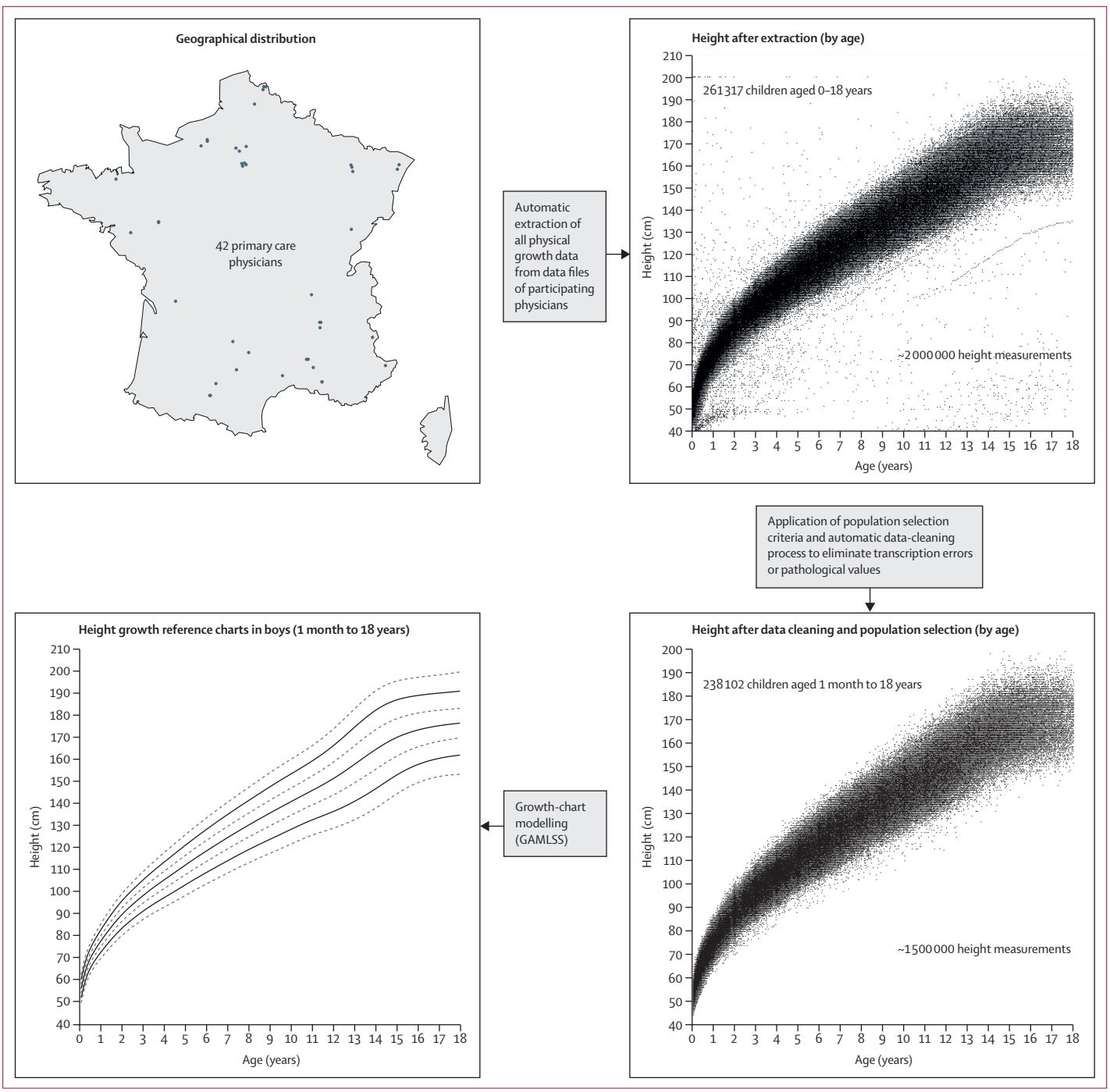

Figure 2: **Illustration of the big-data approach**
Figure illustrates the process for height growth reference charts; the procedure is the same for weight. GAMLSS=generalised additive models for location, scale, and shape.

the inclusion of 1458 468 height and 1690 340 weight measurements (figure 1). The median number of measurements per child was five (IQR 2–10) for height and five (1–11) for weight; 25% of children had one measurement for height or weight, 10% of children had two, and 65% of children had at least three.

Model specifications that provided the best fit for height and weight for girls and boys are detailed in the appendix (p 13), as well as the evolution of the SD curve (appendix p 5). When comparing empirical height SD and weight percentile curves with the modelled percentiles, very few differences were observed (figure 3).

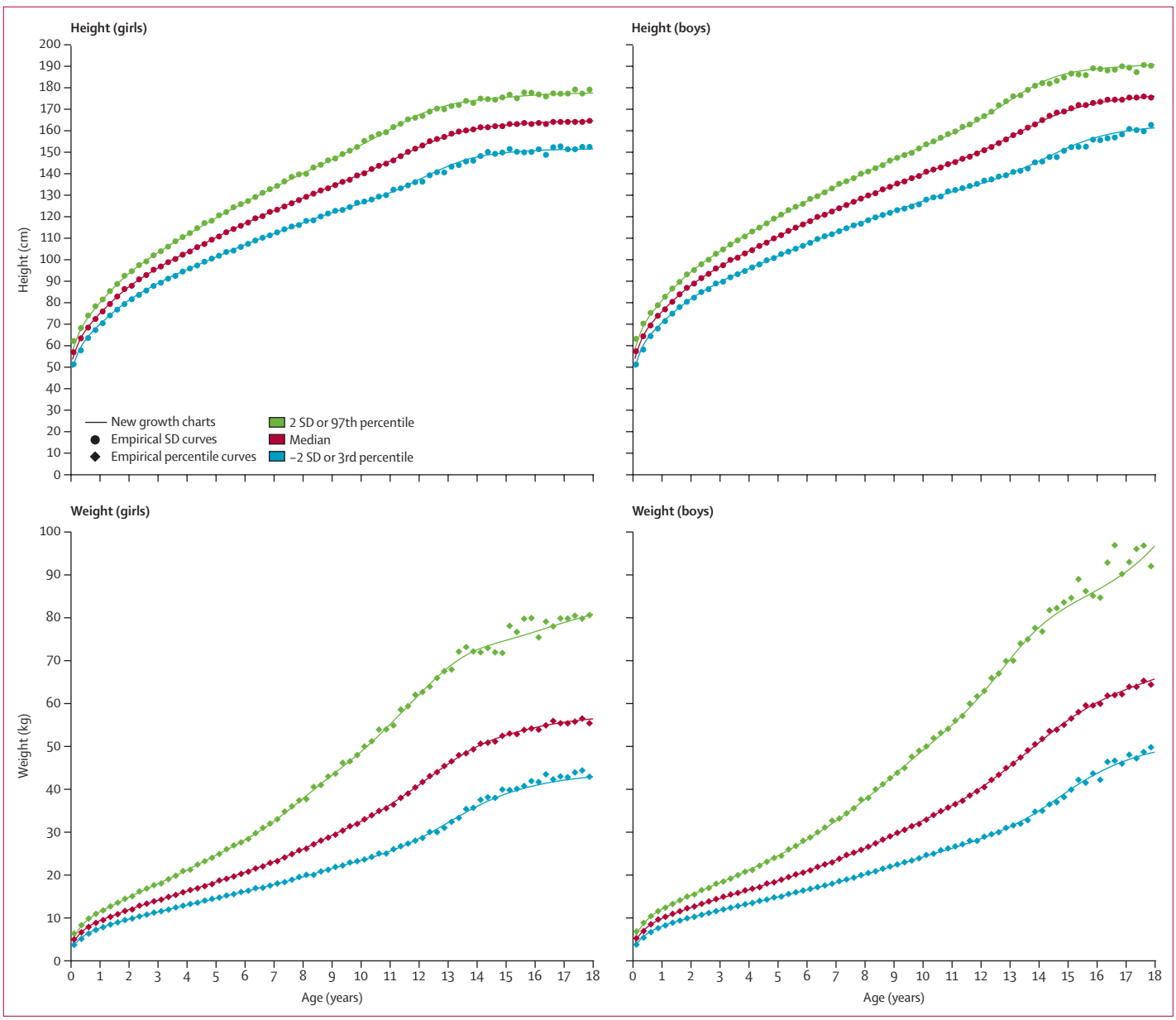

Figure 3: **Empirical height SD and weight percentile curves, for girls and boys**
Data are shown for ages 1 month to 18 years. The empirical SD curves for height or percentile curves for weight were calculated by grouping data by 3-month intervals.

Differences were only seen for extreme height SD or weight percentile curves and older ages, which showed more fluctuations in empirical assessments because of fewer measurements. Inspection of worm plots suggested good internal fit (appendix pp 6–9). When considering the empirical curves separately for primary care paediatricians and general practitioners, small differences were observed, and only for weight at the oldest ages (appendix pp 10–11).

When compared with the existing French national and WHO growth charts, all height SD and weight percentile curves for the new growth charts were distinctly above those for the existing French national growth charts, as early as age 1 month, for both girls and boys (figure 4), with an average difference of –0·75 SD for height and –0·50 SD for weight for both sexes (figure 5). The maximum height difference was –0·75 SD for boys (approximately at age 6 years) and –0·80 SD for girls (approximately at 2 years) whereas the maximum weight difference was –0·75 SD for boys and –0·75 SD for girls (both approximately at age 1 month; figure 5). The new growth charts were closer to the WHO growth charts but differed at some ages, as illustrated by a Z score evolution towards zero of the WHO median values based on the new growth charts (figure 5).

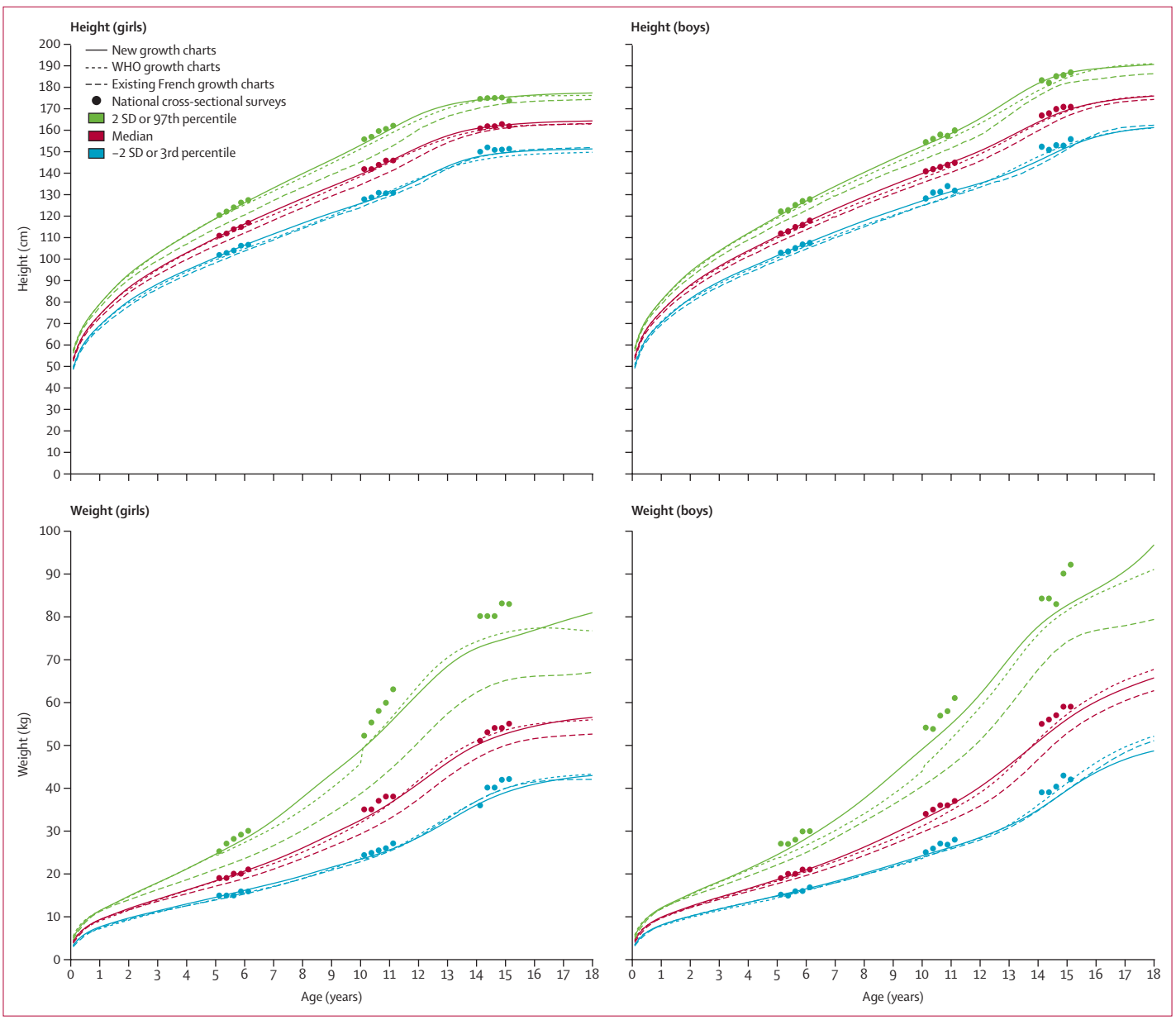

Figure 4: **New height and weight growth charts compared with existing growth charts and to auxological data from national cross-sectional representative surveys, for girls and boys**
Data are shown for ages 1 month to 18 years. Corresponding SDs for height or percentiles for weight from the national cross-sectional school surveys are shown for ages 5–6 years, 10–11 years, and 14–15 years.

When considering height and weight data from the national cross-sectional representative school surveys, the new growth charts fit very well with height SD curves for children aged 5–6 years and 10–11 years, with no difference observed between the new growth charts and curves from national school surveys (eg, the mean height Z score was –0·05 [SD 1·02] for girls aged 5–6 years and 0·02 [0·96] for boys aged 10–11 years; figure 4; appendix p 14). At age 14–15 years, the –2 SD and median height curves for the new growth charts were positioned slightly below the corresponding height SD curves for the national school surveys, most notably for boys (on average, 2·4 cm taller for boys and <0·1 cm taller for girls compared with median height curves for age 14–15 years; figure 4). The fit of the third and 50th percentile weight curves for the new growth charts again showed very good fit at age 5–6 years (eg, mean weight Z score for boys 0·06 [SD 1·07]) and were broadly correct at ages 10–11 years (eg, mean weight Z score for boys 0·16 [1·00]) and 14–15 years (eg, mean weight Z score for boys 0·26 [0·95]), with small differences being observed (on average, 3·1 kg more for boys and 1·7 kg more for girls

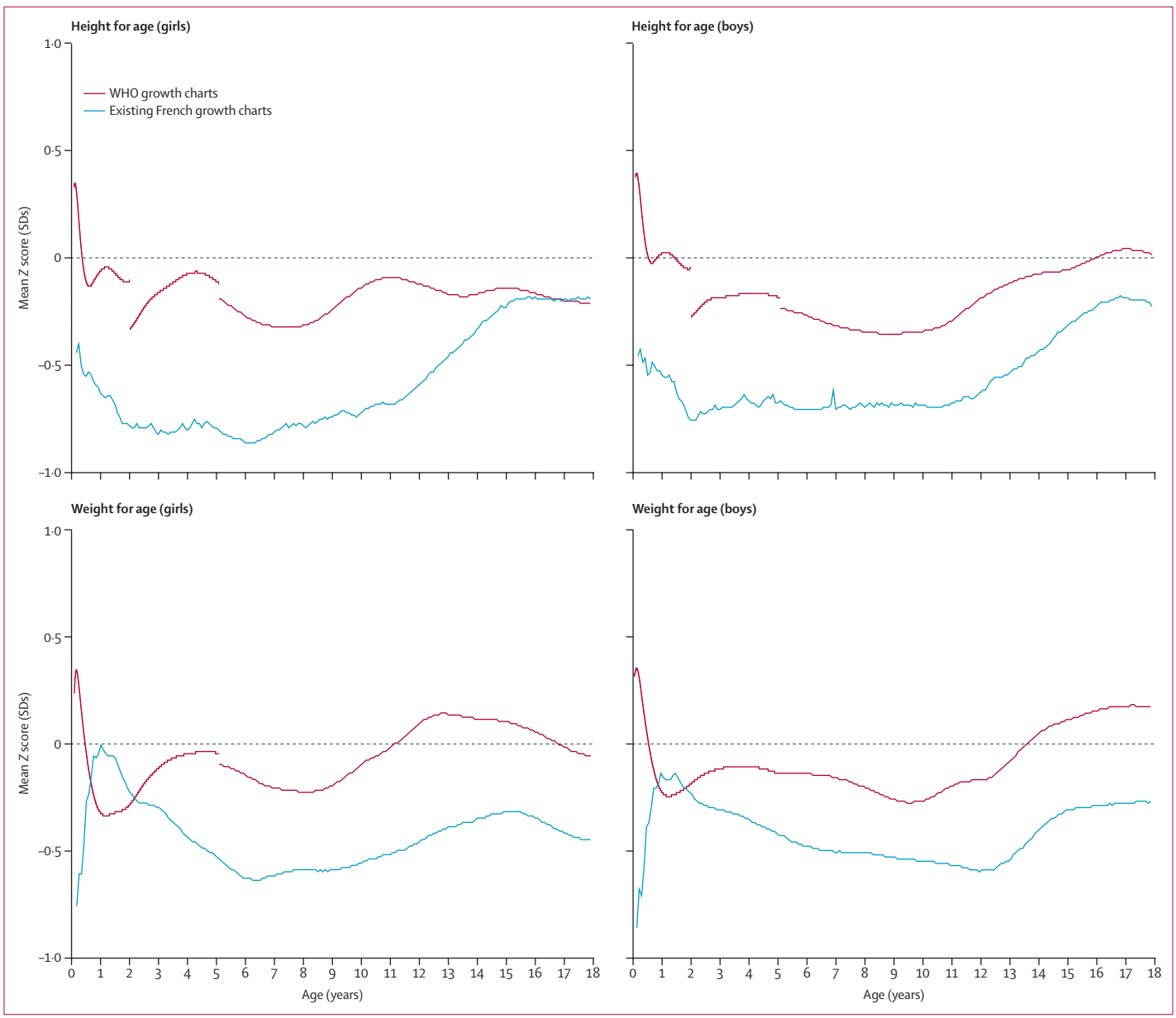

Figure 5: **Median height and weight values for existing growth charts based on the new growth charts, for girls and boys**

compared with the median weight curves for age 14–15 years; figure 4; appendix p 14). The 97th percentile weight curve was below the national school survey values at all considered ages for both boys and girls. For height, weight, and both sexes, the new growth charts generally matched the data from the national school surveys better than the existing French national growth charts and WHO growth charts. The proportions of children by different height and weight percentiles from the new growth charts for girls and boys are shown in the appendix (p 15). Globally, the observed distribution of children was close to the expected distribution for weight and height, for both sexes, except for weight at ages 10–11 years and 14–15 years. For example, only 5·5% of the 14–15-year-old boys had a weight under the tenth percentile.

Discussion

For the first time, to our knowledge, we used an automated approach to produce an updated version of the most used anthropometric charts: growth charts for children. This approach allowed for the quick collection and analysing of a huge amount of anthropometric data—more than 3 million measurements—for more than 230 000 children across France. By comparison, growth charts produced in the past two decades worldwide by means of ad-hoc

studies were based on measurements for a median of 17 000 children.[9–13,15,29,30] Our approach has become possible since the digital revolution and could be extended to other applications in anthropometry. It could offer a reduction in cost and time and potentially allows for the best possible calibration between anthropometric tools and the population to which they will be applied. Calibration is pivotal to optimise a tool's sensitivity and specificity.

However, such approaches are highly exposed to risk of bias and threats to generalisability, and their results need to be scrutinised carefully before any use. First, our process of selecting participating physicians might have introduced bias. Indeed, in France, primary care paediatricians care for only a small part of the paediatric population, from 80% of the population aged 1 year to 20% aged 2–12 years.[31] This part of the French paediatric population tends to be in a different health status than the rest of the population, notably in terms of parents' socioeconomic status.[31] To limit that potential bias, we also collected data from general practitioners, but the participation rate precluded any random selection. Only small differences were observed between paediatricians and general practitioners. Second, the selection process for a child's inclusion might also have introduced bias. Indeed, we were not able to check parameters other than birthweight. Thus, data for numerous children affected by moderate prematurity or intrauterine growth restriction or diseases that could affect growth might have been part of the analysed sample. We tried to limit their presence by excluding data for children with more measurements than expected, which we considered to be an indirect indicator of an ongoing pathological process. However, this strategy does not guarantee that our sample was free of sick children. Third, measurements or transcription errors were numerous, with more than 25 100 detected by the data-cleaning algorithm. Parameters used to exclude aberrant values based on extreme absolute Z scores or Z score variations during the automatic data-cleaning process depended on a wide professional consensus. However, this consensus relied on arbitrary rules and did not prevent selection of thresholds that were too narrow or broad. A last limitation is that we were not able to include a random effect in our models to take into consideration the dependency between observations because of computational limitations. However, we do not believe that this would have an impact on our results on the basis of previous research[32] and as confirmed by the very good fit of the new growth charts to the empirical data. Most previous initiatives have not used these methods, including the WHO growth charts.[3,4]

Given these concerns, external validation of our results was pivotal. The only recent physical growth data available at the national level in France were from three national cross-sectional representative school surveys. These national school surveys did not allow for modelling growth charts because they were limited to three short age periods. We found overall good calibration with the national school survey data for height at any age and weight at age 5–6 years. These results are reassuring regarding the potential effects of the discussed limitations of our study. However, more important discrepancies were observed for weight at ages 10–11 years and 14–15 years and to a lesser extent for height at age 14–15 years. Even if the school surveys are nationally representative, they are not exempt from methodological weaknesses. Indeed, contrary to routine practices in primary care, teenagers are not systematically examined in underwear during these surveys, leading to a potential overestimation of weight and height. However, the observed discrepancy might be related to a remaining selection bias, with disadvantaged families being less likely to be regularly followed up by participating primary care paediatricians than general practitioners. Thus, the well known negative social gradient in childhood body-mass index and overweight in high-income countries including France could explain differences that are stronger for weight than height.[33,34]

Should the new growth charts be used to monitor growth, with the alternative being the WHO growth charts? In a systematic review, we have shown that the WHO growth charts were imperfectly calibrated with the growth of contemporary children in many countries, including France.[2,35] This result naturally led us to suggest the need to generate French-specific growth charts. This choice is now supported by the results of the current study, because as compared with the existing French national growth charts and WHO growth charts, the new growth charts generally better matched data from the national cross-sectional representative school surveys. Of note, height differences between the new growth charts and existing French national or WHO growth charts were smaller when approaching adult ages. This result probably reflects a shift in the maturation tempo between cohorts born several decades apart.[6] The new growth charts we generated are descriptive charts and not prescriptive ones, contrary to those proposed by WHO. The choice of adopting growth charts that are prescriptive standards versus descriptive references has been widely debated and has to be considered in the overall context of growth monitoring. Indeed, the main objective of growth monitoring is to detect severe targeted conditions early. Previous studies have shown that the performance of algorithms proposed for growth monitoring can be strongly modified by the growth chart used (standards *vs* references), which highlights the need for calibration to improve performance.[35–37]

The need to update height growth charts is not debated, but the relevance of updating weight growth charts could be questioned in the context of the increasing prevalence of childhood overweight and obesity worldwide.[38–42] In France, the most recent assessment of the prevalence of French childhood overweight, as defined by the International Obesity Task Force threshold, was 12% for boys

and 14% for girls in 2015.[43] The new weight growth charts we describe reflect this distribution. For this reason, we did not generate body-mass index growth charts from our data. Instead, in line with current international recommendations, we encourage physicians to use the International Obesity Task Force body-mass index growth charts and thresholds and not the new weight growth charts.[44]

In this study, we have shown the feasibility of a new approach to produce any biometric chart using big data. Our approach offers novel perspectives for generating growth charts and could be applied in other countries and other medical domains, provided that related data are stored in medical-records databases from which they can be easily extracted.[45] However, extreme care should be taken regarding the potential risks of bias when extracting such large datasets. In this context, it is paramount to find ways to check for correct calibration.

Contributors

PS, BH, NG, AW, and MC conceived the study. MA, NG, J-FS, and AW provided data. AW and BF organised the data and were responsible for data extraction. BH, PS, MLG, DW, and JB did the statistical analysis. AW, NG, MA, MB, BC, JC, EJ, SN'G, CP, RR, J-FS, BK, JZ, JM, GB, J-CT, M-AC, JB, and MC provided clinical and statistical expertise. BH, PS, and MC drafted the manuscript. All authors approved the protocol and the final version of the manuscript.

Declaration of interests

BH, PS, AW, NG, BF, and MC are co-owners of the patent for the new national French AFPA/Inserm/CGM growth charts. All remaining authors declare no competing interests.

Data sharing

For the **data cleaning and modelling code** see https://github.com/paulinescherdel/EBGM-VI.git

R scripts for data cleaning and modelling are available online. Individual participant data cannot be shared because of an ongoing patent.

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